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EP Evaluator

QUALITY ASSURANCE... **SIMPLIFIED**

Release 11

DATA INNOVATIONS
Simple Ideas, Better Solutions

RHOADS
a brand of DATA INNOVATIONS

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Introduction

License Agreement

EP Evaluator software may be installed ("Trial version") and used for a 14-day trial period without the use of an unlock code on an unlimited number of computers. After the 14-day trial period (which begins with the initial launch and ends 14 days later), the EP Evaluator software will cease to function. However no data will be lost. In order to obtain an unlock code for EP Evaluator software to continue its use, the user must contact Data Innovations LLC to purchase a license.

The above is the first paragraph of the End User's License Agreement (EULA). The remainder of the agreement may be read when EE is initially launched.

Technical Support

One of our major goals in designing this program and writing this documentation is to be sufficiently clear and complete so that you will be able to find the answers to whatever questions you may have without calling us. However, if you do have questions, the EP Evaluator subscription includes the following resources:

1. Use of the software for 1 year.
2. Telephone support for the duration of the subscription.
3. Software updates (for the plan to which you subscribe) released during the subscription period.
4. Training Webcasts.

Software Licensing

Single PC License allows the user to install the software on one PC at a time. Only the user of that PC may access the data. In the event of failure of the PC on which the software was originally installed, or in the event that there is an administrative decision to move the software from one PC to another, the software can be installed on the new machine and DI will issue an new unlock code.

On-line Unlock Codes ("Web Activation Codes") may be purchased on a subscription basis. Up to three unlock codes may be issued. The first will be for one year from the date of issue. The second two will have the same expiration date as the first one regardless of when they are issued. This allows a user to install the program on multiple PC's but all subscriptions will have the same expiration date. However, if an additional unlock code beyond the initial three is needed for any reason, a new subscription will need to be purchased.

Network License provides for EP Evaluator, Release 11 (EE11) being installed on one server. Any PC which accesses that server may run EE11. The software will limit the number of users accessing the program at one time (concurrent users) to the number purchased. For example, if a facility has purchased a network license for 5 concurrent users, then many users can run the program but no more than 5 users can use the program at the same time. One major restriction is that only one user can access a given project at a time.

Duration of License: EE is available only on a subscription basis. Subscriptions are usually for a period of 1 year. Subscriptions for other periods are available upon request. If a new version is shipped during a user's subscription period, the user's software will be automatically upgraded to the new version. In addition, subscribers get unlimited free telephone support. This support does not include writing customers' documents or making decisions about the acceptability or interpretations of the results.

Acknowledgments

I am indebted to the following people for their terrific support for the development of EP Evaluator:

Dr. R. Neill Carey and **Dr. Carl Garber** for their continuing intellectual support to us and for their leadership in development of the role of allowable error in the statistical maintenance of control in the clinical laboratory.

Dr. Herbert Rose for his many good ideas on possible directions of EP Evaluator as well as his continuing support.

Marilyn K. Fleming, M.S., valued colleague and software developer extraordinaire, for her brilliant work in the process of designing and developing all EP Evaluator programs starting with EE4 as well as giving us significant intellectual guidance for this product. Her strong statistical background has been very helpful on many occasions.

Carol R. Lee for her help particularly with Hematology Method Comparison and Policy Definitions.

Elizabeth A. L. Rhoads, Ph.D., my wife for her patience and support during the long process of bringing EP Evaluator to fruition.

Gregory R. Vail and **David G. Potter** of Data Innovations, LLC for their vision in purchasing David G. Rhoads Associates, Inc. and providing a good home for EP Evaluator for many years to come.

Our many devoted users who have provided very useful feedback including many good ideas on what is really needed in software such as this.

My personal role in this project has been to guide (drive?) it to completion, to define the intellectual content and statistical modules, and to write and edit the user's manual.

David G. Rhoads, Ph.D., DABCC
Director, EP Evaluator
September 30, 2009

History of EP Evaluator, Rhoads and Data Innovations, LLC

The firm, David G. Rhoads Associates, Inc. (Rhoads) which initially developed EE was incorporated in 1983. It was always deeply involved in the science and technology of the clinical laboratory. This has evolved over the years to include quality assurance and lab management tools.

David G. Rhoads is the individual primarily responsible for the overall design of EE. He has had 9 years of experience as a hospital based clinical chemist. He has a Ph.D. in Biochemistry from Brandeis University, is Board Certified in Clinical Chemistry (DABCC) and has been a member of the AACC since 1975. He is very concerned with the quality of the work coming from clinical laboratories.

Data Innovations (DI) acquired Rhoads in July, 2009. DI was incorporated in 1989 by Gregory R. Vail and David G. Potter. Its primary product is middleware (MW). MW is a laboratory data management software application designed to increase efficiencies and improve workflow. MW supports pre-analytical, analytical, and post-analytical sample processing and non-analytical tasks such as equipment maintenance.

Data Innovations is the leading vendor of MW world-wide having installed over 6500 systems in over 60 counties. EP Evaluator® is the leading statistical quality assurance software package and is in use in well over 2000 labs in the United States and Canada.

Our customers and partners include large IVD vendors such as Roche Diagnostics, Abbott Laboratories, Sysmex-America and Beckman-Coulter; reference labs including Quest Diagnostics, ARUP and LabCorp plus many hospitals and medical centers, large and small throughout the world.

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Chapter

1

Getting Started

Physical Shipment Package Contents	Website Download Setup File Contents
CD-ROM[1] User's Manual in PDF form on CD-ROM	Executables in Setup File User's Manual may be obtained from Data Innovations.
Notes: 1. EE may also be downloaded from our website.	

The software as shipped is the same for all 5 desktop versions of EP Evaluator® Release 11. The actual version that the user sees and any limited dating, is controlled by the Unlock Code entered into EE when the program is initially launched. The same manual applies to all versions of EE11.

Available Versions				
Version	**Num Modules**	**Projects**	**Connectivity**	**Network Security and Audit Trail**
CLIA	10	–	–	–
COFRAC	10	–	–	–
Vendor	10	Y	Y	–
Standard	33	Y	–	–
Standard plus Data Capture	33	Y	Y	–
Professional	33	Y	Y	Y

As part of our Green Initiative, the manual is no longer automatically shipped with the software. It is available from two sources:

- CD-ROM. The PDF file for this manual is on the CD-ROM.
- On the Data Innovations website. Address: http://www.datainnovations.com/products/ep-evaluator

System Requirements

Hardware and software requirements for EE are listed in Appendix C, *Technical Notes for Network Administrators*.

Installation and Software Registration

Initiating the Installation Process from CD-ROM

- If your AutoRun facility is turned on for your CD-ROM drive, it will automatically install EE from the CD-ROM.
- If the program does not start up with the Auto Run feature, follow the instructions below:
  - Click on Start.
  - Click on Run. Type in the CD drive name such as "D:\" where D:\ is your CD drive.
  - Click on Browse.
  - Double click on the application with the name similar to SetupEE11– 0(36).EXE. (This name will change over time, but it will always have the form of SetupEE11-d(dd).exe where d represents a digit).
  - This will launch the installation process.
  - Follow the cues which then come up to prompt you through the rest of the installation process.

Installation Process

A series of prompts will be displayed which will lead through the installation process. These will be:

- A prompt notifying you that the installation process has started. You have the option of continuing or stopping at this point.
- A series of screens will be displayed which list the names of the files being automatically extracted.
- A screen is displayed which shows you the licensing agreement. You must accept this agreement before installation can continue past this screen. Select the "I agree" checkbox and click on OK to continue the installation process.
- A screen is displayed which displays the location in which EE is to be installed. If the specified location is not satisfactory, click on **Browse** to change to another location. Click on **OK** to continue.
- The installation process will now proceed to its conclusion. At its end, a small dialog box will announce this achievement. Click on **Finish** to conclude the process.

Windows 2008 Server/ XP/7

Read/write/delete access must be provided to the EE11 folder and its complete directory structure and to the user's application data folder! This includes being able to create and delete files even if the user does not have administrative privileges. These rights must be granted before EE can be launched and run. In many facilities, these rights are controlled by the IT department.

System Administrator rights are required to unlock (or web activate) the software. However, once the software is unlocked, a non-System Administrator may operate it.

System Administrator rights are also required to use EE in evaluation mode prior to unlocking it. If necessary, Data Innovations support can issue a short-dated unlock code to allow you to evaluate the software.

Initial Launch of EE

Every time you launch EE, before you have entered an unlock code, a screen similar to Figure 1.1. will be displayed. Various messages may be displayed just above the buttons. This example shows the number of days left in the trial period. You automatically will get a 14-day free trial period the first time you install the software on a PC. You must get an unlock code for use after that initial trial period.

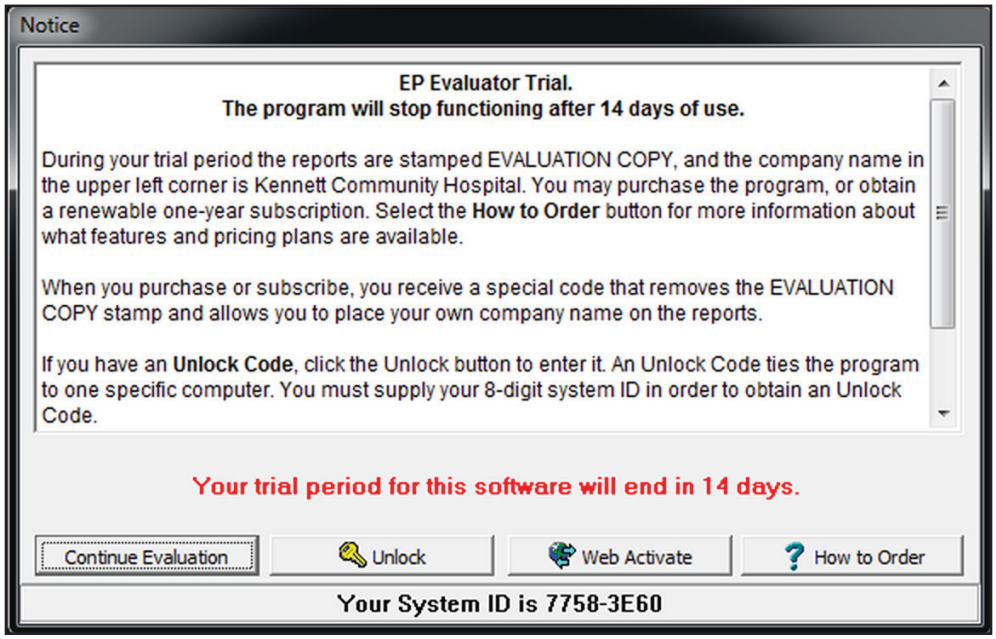
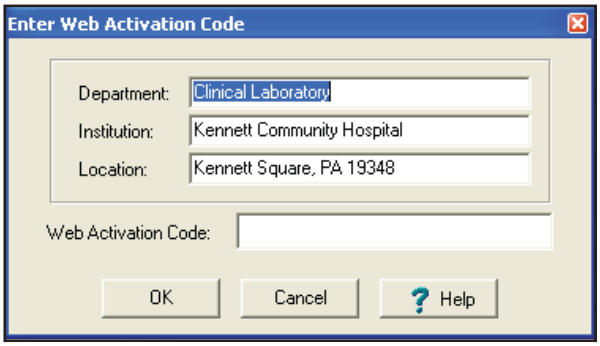


Figure 1.1. Trial Period Screen

There are two ways to unlock the software: 1) by **Web Activation**, or 2) by **Manual Activation** (obtaining an unlock code by phone or email, then typing it into the software.) These two methods are described below.

Web Activation

Web Activation allows you to unlock the software only once using the web activation code. The code is valid for the one year subscription period only. The activation code contains an expiration date which is typically one year from the date DI receives your purchase order for EP Evaluator. Please activate EP Evaluator as soon as you receive the activation code to ensure you benefit from the full subscription period. If you need to re-install the software on a different computer or server, contact Data Innovations support to obtain a new activation code. The provided code will be valid for the remaining term of your subscription.



Web activation is not available for all EE versions, and it is available for annual subscriptions only. To use web activation, you must have obtained a Web Activation Code (WAC) at the time of purchase.

Web Activation is extremely simple if EE is allowed direct access to the Internet. Click **Web Activate** on the Trial Period Screen. You will be asked for your Web Activation Code.

Enter your Department, Institution, and Location. The Department and Institution are printed on every page of every report. Once you enter them, you cannot change them without assistance from Data Innovations Support.

Enter your Web Activation Code, then click OK. EE will contact the Data Innovations Web Site, confirm your activation code, and unlock the software.

This simple form of web activation requires that EE be allowed access to the Internet. If your company prohibits access, you can still use your web activation code, though the process is a bit more difficult. Use your browser to go to http://www.datainnovations.com/products/ep-evaluator/web-activation and follow the instructions there. Note that you will need to provide both your WAC and your 8-digit System ID.

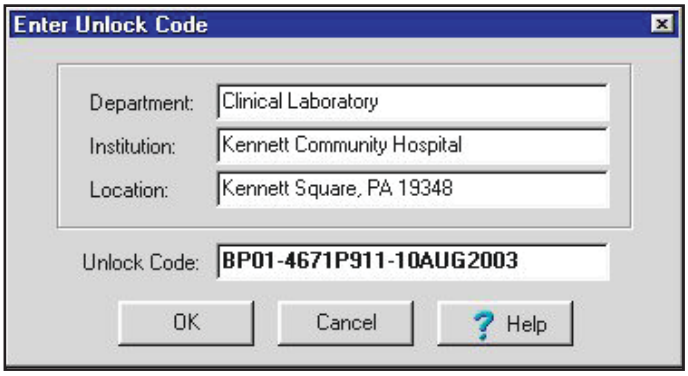
Manual Activation

You will have to provide Data Innovations with your PC-specific 8-digit System ID in order to get the Unlock Code. The 8-digit System ID can be found at the very bottom of the screen shown in Figure 1.1. In this example, it is F43A-004B.

Contact Data Innovations with your 8-digit System ID, your Support Number, your name, institution and address using the contact information provided in the Introduction of this manual.

Please provide a telephone number, fax number or email address so Data Innovations support can get back to you with your Unlock Code.

When you have your Unlock Code, click **Unlock** on the screen shown in Figure 1.1. The Registration Screen will be displayed.



First enter the registration information (Department, Institution and Location) for your institution. *The first two lines of this registration information will be displayed on every page of every report*. Then enter the Unlock Code you obtained from Data Innovations. Please make sure that you enter the correct registration information. It is difficult to change. If the registration must be changed, call Data Innovations and they can help you with that change.

Reinstallation or Updating Existing Software

Copies of EE can be legally re-installed on other machines providing the terms of the license are not violated. (See section on Software Licensing). Use the installation process described above. If the initial trial period or subscription period has expired, you will need to get a new Unlock Code from Data Innovations. EE can be updated repeatedly on the same machine. If your PC has been replaced, you will need to get a new Unlock Code.

Un-Installation

Un-installing Windows version of EP Evaluator (CLIA for Windows, Releases 4 through 10):

- Select **My Computer**. Select **Control Panel**. Select **Add/Remove Programs**.
- Click on the program name. This will delete executables and icons that were originally installed. Your data will NOT be deleted.
- To delete the remainder of EE, you can delete the whole EE folder using Windows Explorer. **NOTE: If any of the data in the database is important, make sure that you have a safe copy of it BEFORE you delete the folder.**

Un-installing Older DOS versions of EP Evaluator

To un-install older DOS versions of EP Evaluator (Releases 2 or 3), delete the EE folder (usually on the C drive) using Windows Explorer (or whatever it happens to be called on your system).

Bringing old data forward

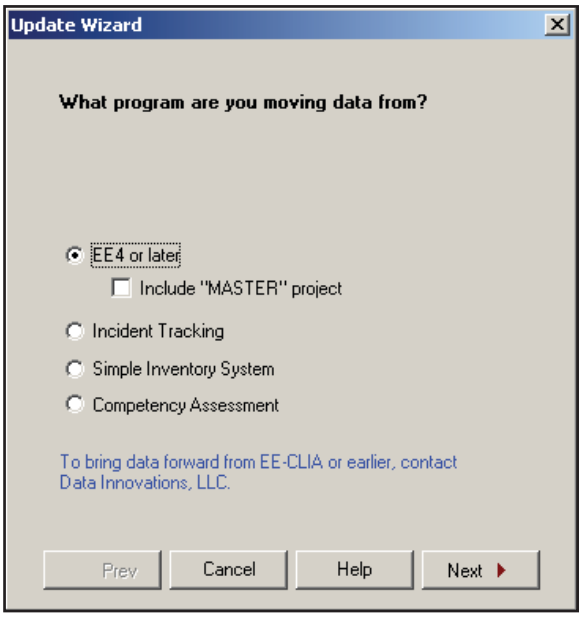
Many users will want to bring their data from previous versions of EP Evaluator forward to EE11. If the old data is on the same PC as the new one, the Update Wizard in EE will do this for you. **The update process will work for the following releases of EP Evaluator: EE Releases 4 through 10.** It will not work for EE-DOS (Releases 1-3) or EE-CLIA. See section entitled *Updating EECLIA or EE-DOS* on how to bring these data forward.

Important Note If you are updating from the Professional Version of EE5 through EE9 with User ID/Password login, a significant part of the upgrade process is manual. Also, your network administrator may need to be involved. See Chapter 40, *Professional Version: Security, User Groups and Audit Trails*, for more information.

Otherwise, the general principles of the updating process are:

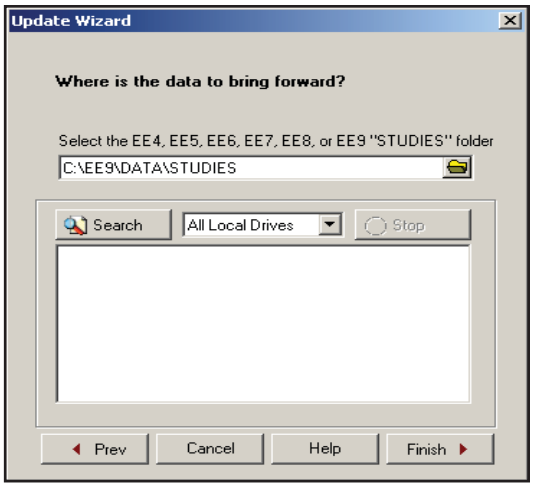
- Data as old as EE4 can be brought forward easily.
- No older data is deleted during the update process.

Do the following to access the Update Wizard.



- Launch EE. Enter the program until you get to the screen on which the title Statistical Modules is displayed.
- Click on the menu item **Utilities** on the second line near its right end. Click on **Update Wizard.**
- The Update Wizard displays a dialog box which asks you what program you want to bring your data forward from.
- Select one. You will need to select Incident Tracking, Inventory, or Competency Assessment if you want to bring those data forward. If you have data in a Master project, check that box.

Updating from EE4 through EE10



- Initially you will get a dialog box similar to the one at right. You may browse to the previous version(s) of EE, or you may have your PC search for it. Note that the search is for a “Studies” folder. The final folder in the path must be “studies” (i.e. C:\EE9\Studies). When you have identified the previous location, click on <Finish>.
- The Update Wizard will move all your old data forward. During this process, an Activity Screen will be displayed showing you what is happening.

Updating EECLIA or EEDOS

Create a ZIP file of your EE-DOS or EECLIA folder including all underlying folders. Contact Data Innovations to have them convert your data to the EE11 format. Data Innovations will convert your data to EE11 format at no charge.

After Running the Update Wizard (Releases 4 - 6 only)

For releases 4-6, the "Calibration Verification Only" option in the Linearity module verified only accuracy. In later releases, this option verifies both accuracy and reportable range. As a result of this change, reportable range and proximity limits are now required. Since these items won't be present in the data you brought forward, the experiments won't calculate.

One solution to this problem is to edit each calibration verification experiment, go to its Parameters Screen, and enter the missing items.

Bringing Data Forward From a Different PC

From EE4 through EE10 (Option 1)

- Back up your old data on EE4 and later. (**Utilities/File Manager/Backup**). This will create a ZIP file with the project name in the folder called **EEXX\ Backups** where x is the release number.
- Move those data to a folder accessible to your new copy of EE.
- In EE, select **Utilities/File Manager**. Locate the folder containing the backup files and restore them. At this point, EE will read the old data and restore it into EE.

From EE4 through EE10 (Option 2)

- Copy the whole EP Evaluator folder including the executables and the data to a target device with adequate capacity, often a memory stick.
- When you use the Update Wizard, point it at the appropriate folder on the target device and proceed as normal.

From EE-DOS or EECLIA

See brief section above on bringing EE-DOS data forward in the same machine.

Chapter

2

EE11 Overview

EP Evaluator® Release 11 (EE11) is a large, complex program. It includes many modules to evaluate clinical laboratory results as well as several to perform lab management tasks. Furthermore, it includes several tools to rapidly and accurately acquire data from a variety of sources, including spreadsheets and laboratory instruments.

This manual is divided into several groups of chapters:

- **Getting Started**. Chapter 1, *Getting Started*. Discussion of software installation, un-installation and bringing data forward from previous versions.
- **Getting Acquainted**. Chapters 2 and 3.
- **Statistical Modules**. Chapters 4-31. Details specific to each statistical module.
- **Lab Management Modules**. Chapters 32-35.
- **Rapid Results Entry**. Chapters 36 and 38 describe the techniques by which users may rapidly enter, transfer or capture data into EE. Sources of supplemental information on RRE are listed in Appendix B (Resources).
- **Policy Definitions.** Chapter 37 describes how to manage policies. Policies are things like test names, units, reference intervals, reportable ranges and the like. If these are present in advance, one can literally create a new experiment with a single mouse click, rather than entering data for many fields.
- **File Functions.** Chapter 39 describes tasks like project back-up and re-store, along with importing and exporting experiments.
- **Network Security Issues** are addressed in Chapter 40.
- **Translator.** Chapter 41 describes how to use the Translator program to create files to translate EE into another language.
- **Appendices** list some Performance Standards (Appendix A) and many Resources (Appendix B).

Modules

All the modules listed below are present in the Standard, Standard plus Data Capture and Professional versions. Ten modules, marked by ★ in the left margin, are present in the CLIA and Vendor versions. Modules marked by a ● in the left margin are present in the COFRAC version.

★ • **Linearity—Linearity and Calibration Verification**. Includes analysis of accuracy and reportable range. Also provides for integrating precision results with accuracy / linearity during method validation. (Chapter 4, *Linearity and Calibration Verification*).

★ • **Linearity—Simple Accuracy.** Implements a different type experiment which passes if all the results are within a range defined by the vendor. Does not explicitly assess linearity or use Performance Standards. (Chapter 5, *Simple Accuracy*)

• **Linearity—CLSI:EP6**. Implements CLSI's Linearity module. Does not assess accuracy or reportable range. (Chapter 6, *EP6 Linearity*)

● • **Linearity—Trueness.** Implements and extends the COFRAC calculations for Trueness and Accuracy. (Chapter 7, *Trueness*)

● ★ • **Precision—Simple**. Performs similar calculations to those done by a hand calculator. (Chapter 8, *Simple Precision*)

• **Precision—Complex**. ANOVA calculation of within-run, between-run, between-day and total precision. Includes CLSI:EP5. (Chapter 9, *Complex Precision*)

• **Method Comparison—CLSI:EP9**. Statistically rugged. Requires duplicate results for each specimen and a minimum of 40 specimens. For comparison of two methods only. One major use is for submission of method comparison results to regulatory bodies. (Chapter 10, *EP9 Method Comparison*)

● ★ • **Method Comparison—Alternate**. The type of method comparison done most commonly. Adequate for most purposes. Calculates linear regression statistics using both regular and Deming approaches. (Chapter 11, *Alternate (Quantitative) Method Comparison*).

★ • **Method Comparison—Qualitative**. Includes semi-quantitative method comparison. Statistical analysis includes two cases for qualitative method comparison which assume that the reference method is (a) absolutely and (b) relatively correct. (Chapter 12, *Qualitative and Semi-Quantitative Method Comparison*).

● • **Method Comparison—Multiple Instrument Comparison**. Compares multiple instruments without using linear regression. (Chapter 13, *Multiple Instrument Comparison*)

● ★ • **Method Comparison—Two Instrument Comparison**. A simple, straightforward procedure for comparing two instruments. Best MC approach when working with fewer specimens. Does not use linear regression when evaluating the data. (Chapter 14, *Two Instrument Comparison*)

- **Method Comparison— Glucose POC Instrument Evaluation**. This module is designed to compare results from a lab instrument with those from a POC glucose meter. (Chapter 15, *Glucose POC Instrument Evaluation*)

- **Method Comparison—Hematology**. This module is designed to compare results from two or more hematology methods, including a manual differential method and a variety of hematology instruments. (Chapter 16, *Hematology Studies*)

★ • **Sensitivity—Limits of Blank (LOB)**. Determines lowest concentration which is significantly different from zero. This module was previously called "Limits of Detection". (Chapter 17, *Sensitivity (Limits of Blank)*).

- **Sensitivity—Limits of Quantitation**. Determines lowest concentration which gives results which are "statistically reliable"; typically a CV no more than 20%. (Chapter 18, *Sensitivity (Limits of Quantitation)*)

● ★ • **Reference Interval—Verification**. Verifies that the proposed reference interval (typically from the manufacturer's package insert) is satisfactory for your patient population. (Chapter 19, *Verification of Reference Interval*)

● • **Reference Interval—Establishing Reference Intervals** establishes the normal range using both parametric and non-parametric approaches. The non-parametric approach implements CLSI C28-A2. (Chapter 20, *Establishing Reference Intervals*)

● • **Reference Interval—ROC Plots** provides for calculating cutoff values and comparing the diagnostic efficiencies for clinical laboratory tests. (Chapter 21, *ROC Curve Analysis*).

- **Coag—INR Geometric Mean and VRI**. Calculates the geometric mean for PT and then verifies the proposed reference interval. (Chapter 22, *Coag*)

- **Coag—PT/INR Method Comparison** compares results for both PT and INR between the existing system and the incoming one. (Chapter 22, *Coag*)

★ • **Coag—Manual INR Checker**. Compares the INR reported by the instrument with the INR calculated for each PT result. (Chapter 22, *Coag*)

- **Coag—Factor Sensitivity**. Provides a scientific basis for selection of a coagulation reagent which will adequately detect when the concentration of their respective coagulation factors are significantly diminished. (Chapter 23, *Factor Sensitivity*)

- **Other—CLSI EP10 Preliminary Evaluation of Methods**. This scheme for method validation calculates accuracy, precision, carryover, linearity and drift from an experiment in which 11 samples are assayed daily for 5 days. (Chapter 24, *CLSI EP10 Preliminary Evaluation of Methods*)

- **Other—Six Sigma Metrics**. Analyzes systematic and random error and frames the result in numbers of SD's which will fit in the error space available for random error. (Chapter 25, *Six Sigma Metrics*)

● ★ • **Other—Carryover**. Calculates specimen to specimen carryover. (Chapter 26, *Carryover*).

- **Other—Performance Standards**. Calculates Performance Standards (i.e. Allowable Total Error) using several different strategies. (Chapter 27, *Performance Standards*)
- **Other—Average of Normals**. Detects changes in the bias for the analytical process by monitoring patient results. (Chapter 28, *Average of Normals*)
- **Other—Interference.** Calculates the response of an analytical process to varying concentrations of an interfering material. (Chapter 29, *Interference*).
- **Other—Stability**. Calculates stability of a specimen or reagent. (Chapter 30, *Stability*)
- **Other—Histogram and Descriptive Stats**. Generalized Statistics module calculates many statistics related to means and SD. Graphs data as a histogram. (Chapter 31, *Histogram and Descriptive Statistics*)
- **Other—Cost per Test**. Calculates the cost to produce a result for a test in the clinical laboratory environment. (Chapter 32, *Cost per Test*)
- **Lab Management—Inventory Management**. This module manages physical inventory, plus receipt and dispensation of materials. Like Incident Tracking, it is an independent program which is accessible either from the Tool menu or from the Windows Desktop. (Chapter 33, *Simple Inventory System (SIS)*)
- **Lab Management—Incident Tracking**. A database for tracking and classifying laboratory incidents (errors). Technically, Incident Tracking is a completely separate program accessible either from within EE10 or from the Windows Desktop. You will find it in the Tools menu, rather than on the Statistical Module screen. (Chapter 34, *Incident Tracking*)
- **Lab Management—Competency Assessment**. Asks questions for competency Assessment. (Chapter 35, *Competency Assessment*)

User Interface - Key Concepts and Terms

EP Evaluator is divided into small (and sometimes not so small) pieces called **Statistical Modules**. Each statistical module performs a specific kind of calculation—like a Method Comparison or Calibration Verification.

Within a statistical module, you may analyze different sets of data. Each separate analysis is called an **Experiment**. Often an experiment is a calculation for one instrument and analyte. For example, verify the reference interval for Glucose on the Excimer 1000. Once you create an experiment, it is stored permanently in the EP Evaluator database until you delete it. This means you don't have to remember what file you put the data in. It also means that you can batch-print reports for many experiments with a single command.

Most of the statistical modules are organized around the same types of input screens. While the specific contents of the screens vary between modules, they perform similar functions across modules. The **Module Overview Screen** shows a list of the experiments in a module, together with the status and key statistics for each experiment. Results are entered into the **Experiment Detail** Screen which also shows graphs and tables similar to those on the printed report. Evaluation criteria and documentation fields (like analyst name and experiment date) are entered in the **Parameters Screen**.

Another fundamental concept is the **Project**. A Project is a folder that holds related work—perhaps all the analyses for a periodic inspection, or for initial validation of a new method. A project can contain experiments for several statistical modules including correlation studies, precision studies, and calibration verifications, all related to the same task. When the job is done, create a backup copy of the entire project and file it away for reference.

Thus a **Project** is a container that holds **Experiments** for one or more **Statistical Modules**. The first thing you do when starting EP Evaluator is to open the project that contains the experiments you want to work on. In a network environment, only one user at a time can have a specific project open.

CLIA Version Note

If you have the CLIA version, you can only use the two pre-installed projects (Default and Sample Data). You cannot create new ones.

Almost anything you do with EP Evaluator means *opening* or *creating* a project, *opening* a Statistical Module, and either *creating* a new experiment or opening an existing one. How this works, and how the various key screens fit together, is summarized in the **Tutorial**, and also in Chapter 3, *Common Operations*.

Moving Data Around

EP Evaluator offers an extensive set of **Rapid Results Entry (RRE)** features for getting experimental results into the program without typing them. Perhaps the most useful is the ability to **Copy** results from Microsoft Excel® and **Paste** them into EE.

If you have the Professional, Standard plus Data Capture, or Vendor version, results can be captured directly from the instrument, using an **Instrument Interface (IF) Program**. IF programs must be specially prepared for each instrument model. Contact Data Innovations for details.

Most experiments need two kinds of data: **experimental results** and **policies**. Experimental results are often available in Excel or in disk files. Policies, on the other hand, are descriptors of each test—such as test name, units, reportable range, reference intervals and the like. Very commonly, policies are entered manually into the parameter screen for each experiment, even if the results are obtained automatically.

Policies allow you to attach the parameters to the results as a part of the paste or capture process. This means you can paste Linearity results for many experiments, and get a complete set of evaluations within minutes instead of hours.

Rapid Results Entry is discussed in Chapter 36, *Introduction to Rapid Results Entry (RRE)*. There are also examples in the EE11\Resources folder. Policies are described in Chapter 37, *Policy Definition*.

Useful Tools

EE includes two lookup tables: a **Glossary** and a table of **Units Conversion Factors**. These tools, along with the two allowable error tables, reside in the Windows tray (at the lower right of the screen, where the clock is). Click on the open book icon to pop them up at any time.

Available resources are listed in Appendix B, *EP Evaluator Resources*. They include sources of training, performance standards, reference intervals, spreadsheet examples, example policies, file formats and various documents.

Security Features

The Professional version of EE provides security features to help users comply with CFR 21 Part 11. Access can be limited by requiring a user ID and password. Users can be assigned to independent groups. Data for these groups is physically separated, so only EE System Administrators have access to data outside their own group. An audit trail is available to record every change to an experimental result, including the operator who made the change, date of the change, and before-after values of the number. See Chapter 40, *Professional Version: Security, User Groups and Audit Trails* for details.

The Menu is the Road Map

Since almost every function in the program is initiated from the menu bar at the top of the screen, looking at the list of menu items provides a good summary of the program's features. There is a brief description of every menu item in Chapter 3, *Common Operations*.

Responsible Use of Statistics

EP Evaluator is a very powerful tool which can perform a wide variety of calculations on a wide variety of numbers. Properly used, the results of these calculations can be enlightening. Improperly used, they can lead to serious mistakes which may cause fatalities.

It is the responsibility of each user to ensure that their use of EP Evaluator is appropriate. Appropriateness has the following elements:

- Design of a suitable experiment, adequate to answer the issues in question.
- Collection and/or use of an adequate number of specimens suitable for the experiment.
- Proper analysis of the specimens in a timely fashion on all the instruments involved.
- Accurate entry of results into the appropriate statistical module.
- Correct interpretation of the results of the statistical evaluation.

Getting all these elements correct is not trivial. Please carefully plan your experiment before you start. You have a better chance of getting it right.

Significant Figures and Decimal Digits

One issue which scientists discuss extensively is how to express information, specifically numbers. The various types of numbers which appear here are concentrations (two types) and statistical. The rules that we have applied to these data are as follows:

- Entered concentrations are shown in the format in which they were entered.
- Calculated concentrations. Maximum decimal digits plus one. If the entered concentrations were all in the format of "x.x", then the calculated concentrations will be in the form "x.xx". If entered in the format "x.xx", then its output format will be "x.xxx".
- Statistics are presented in several formats. The values for slope are formatted with 3 decimal digits. Intercepts and standard deviations are treated the same as calculated concentrations. Unitless values (e.g., correlation coefficient) always have the same number of decimal digits.

A Rule of Thumb: When entering your data, keep in mind the quality of the result. In the clinical laboratory, only the rare test has a CV much better than 1%. Consequently, it is generally illogical to enter a result with more than 4 significant figures. For sodium, entry of a result of 141.11 implies that the instrument can realistically distinguish between values of 141.11 and 141.12. For most instruments, this cannot be done. Consequently, in this case, one should report a value of 141.1. Many instruments report results to a constant number of decimal digits. Appropriate roundoffs should be performed, especially for values at the upper end of the reportable range.

Report Interpretation Guides

Most of the statistical modules offer an optional report page which has suggestions to help with the interpretation of the statistical results. These interpretation guides are available because the person who is responsible for signing off on the report may not be familiar with the implications of the statistics. Consequently, they may need all the help they can get. This is an effort to give them at least a clue as to what some of the issues are.

Major Recent Changes in EP Evaluator

There have been a number of major changes after Release 8 was initially shipped in October, 2007. Some of these occurred during the later builds of EE8, others were introduced in EE9, EE10, or EE11.

Modules added in EE11

- Trueness

Modules added in EE10

- Factor Sensitivity

Modules added in EE9

- Simple Accuracy
- CLSI EP6
- Stability
- Histograms and Descriptive stats. This was previously present but usually hidden. Starting with EE9, it is available all the time.
- Competency Assessment

Rapid Results Entry

One major thrust in EE has been to facilitate the entry of results. Our object is to make it very easy to bring in results at one time for large numbers of experiments. In conjunction with this is the need to manage the associated data including multiple lot numbers and multiple linearity kits.

- Data Extraction from third-party applications using ODBC Connectivity. (EE11)
- Data Extraction from Data Innovations' Instrument Manager. (EE9)
- Use of lot numbers, sources and expiration dates. (EE8)
- Bulk entry of lot numbers, sources and expiration dates. (EE9)
- Easy handling of complex sets of results in which some are accepted and others rejected. (EE9)

Other changes

A number of other changes include:

- Can no longer bring data forward from EE releases prior to EE4.
- EE3 export format is no longer supported.

Chapter

3

Common Operations

Features common to all statistical modules in EP Evaluator® are discussed in this chapter. These include:

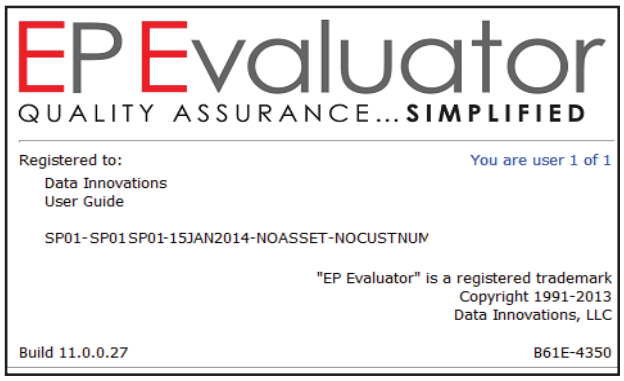
- Opening Screens (Splash Screen and Main Screen)
- Creating, selecting, editing, displaying and printing out an experiment in EE. This includes:
  - Module Overview Screen
  - Experiment Detail Screen
  - Parameter Screen
  - Print and Print Preview
- Using the nine menu items on the horizontal menu bar.
- Using the "Tool Bar" (the twelve icons on the third line down from the top left corner of every screen).
- Creating or opening a Project.
- Backing up and restoring a Project.
- Information on general user interface properties applying to the screens and the buttons.
- Using the Preferences Screen to define certain system-wide behaviors.
- Adding lot numbers to existing experiments.

First time users should take a few minutes when they first launch the program to familiarize themselves with the various functions they will need. The **Tutorial** is a good place to start. It is a PowerPoint-style presentation that introduces some of the key program concepts.

After viewing the Tutorial, click on the various menus and icons just to see what happens. This process is analogous to checking out the various stores, streets and other facilities when one moves to a new city. Normally example data will already be present in the program.

Opening Splash Screen

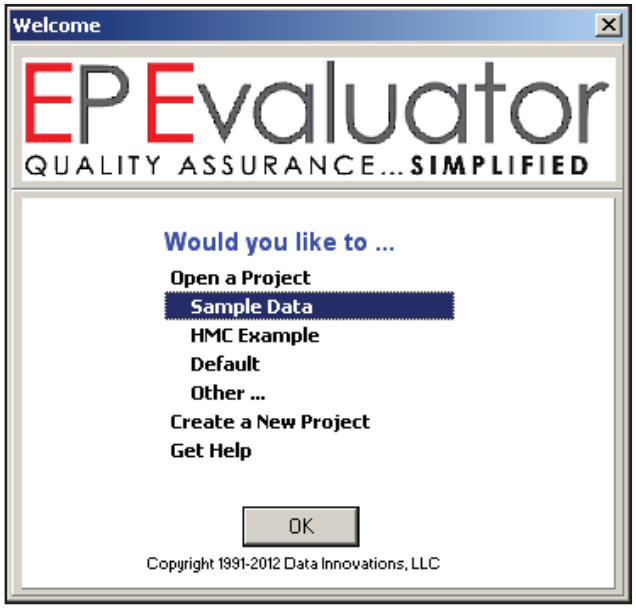
The opening splash screen displays the information listed below. It is displayed for 5 seconds or until the user hits a key, whichever comes first.



- Program name and icon
- Seat number (e.g., User 1 of 1)
- Registration information
- System ID (lower right)
- Build Number (lower left)
- Unlock Code (under the registration information)
- Copyright information

Welcome Screen

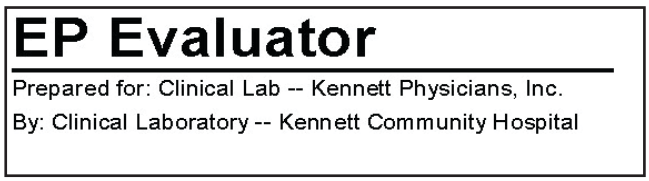
The Welcome Screen is one way to create or select a project. A project logically associates several experiments.



All versions start with two projects, Default and Sample Data. Users of the CLIA version will not be able to add any projects. All others will be able to create additional projects with no software limits on their number. The purpose of the Sample Data project is to provide complete functioning examples for each of the statistical modules. In most cases, these examples also appear in the Default Project.

There are two major advantages to using projects:

- All related experiments are logically placed together. Consequently you can print out all reports in a project for one statistical module with a few mouse clicks. For example, if you are validating a new instrument, you can put all those experiments in one project. At the end of the validation process, you can back-up that project and store that data in a safe place.
- Optional inclusion of the client's name (Clinical Lab, Kennett Physicians, Inc.) as shown at right. In the figure at right, the terms at the beginning of each line "Prepared for" and "By" are editable. See discussion **Report Headings for Client Reports** for details.



Statistical Module Screen

The Statistical Module screen (Figure 3.1) allows you to select a statistical module. Thirty one of the 34 modules are organized under the first seven buttons. Three of the four Lab Management modules (Incident Tracking, Inventory Management and Competency Assessment) can be found in the Tools menu. The final Lab Management module, **Cost Per Test**, is listed under the **Other** button.

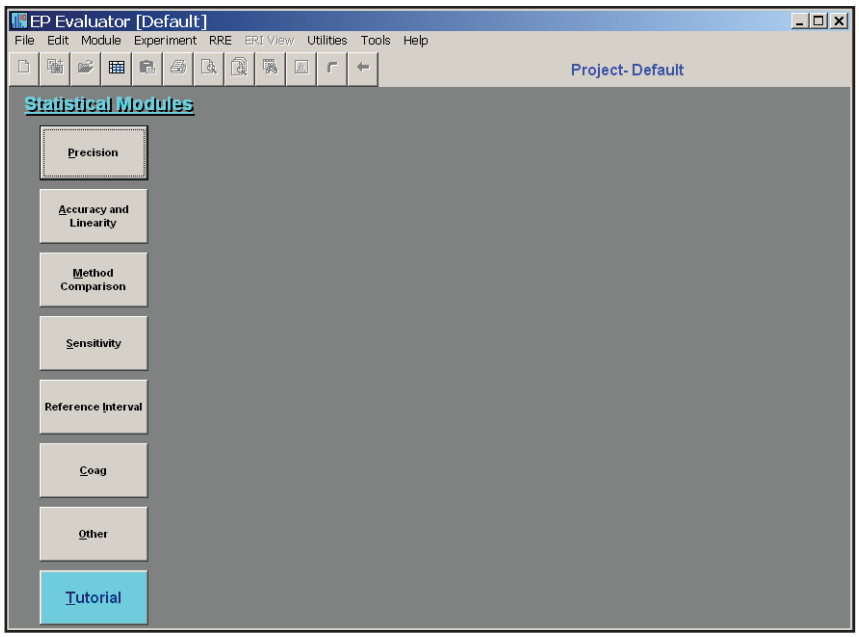


Figure 3.1 Statistical Module Screen

Below is a list of each module button and its associated statistical module:

- Precision button
  - Simple Precision
  - Complex Precision (includes CLSI:EP5)
- Accuracy and Linearity button
  - Linearity and Calibration Verification.
  - Simple Accuracy
  - CLSI:EP6 Linearity
  - Trueness
- Method Comparison button
  - Alternate (Quantitative)
  - CLSI:EP9
  - Qualitative and SemiQuant (includes CLSI:EP12)
  - 2-Instrument Comparison
  - Multiple Instrument Comparison
  - Glucose POC Instrument Evaluation
  - Hematology Studies
- Sensitivity button
  - Limit of Blank
  - Limit of Quantitation
- Reference Interval button
  - Verify Reference Interval
  - Establish Reference Interval/ROC
    These two modules have a common database and a slightly different user interface. Includes CLSI: C28 and CLSI:GP10.
- Coag button
  - INR - Geometric Mean and VRI
  - PT/INR - Method Comparison
  - Manual INR Check
  - Factor Sensitivity
- Other button
  - CLSI:EP10 Preliminary Evaluation
  - Carryover
  - Six Sigma Metrics
  - Performance Standards
  - Interference (CLSI:EP7)
  - Cost Per Test (Lab Management Module)
  - Average of Normals
  - Histogram and Descriptive Stats
  - Stability

- Tutorial button. This button starts the Tutorial to give you a brief overview of some key concepts and screens.

You may also access the menu items and the tool bar. Three of the four lab management modules are accessed from the Tools menu.

Module Overview Screen

The Module Overview Screen (Figure 3.2.) will be displayed upon accessing each statistical module. This screen allows you to create experiments, enter raw data, and calculate and print experimental results.

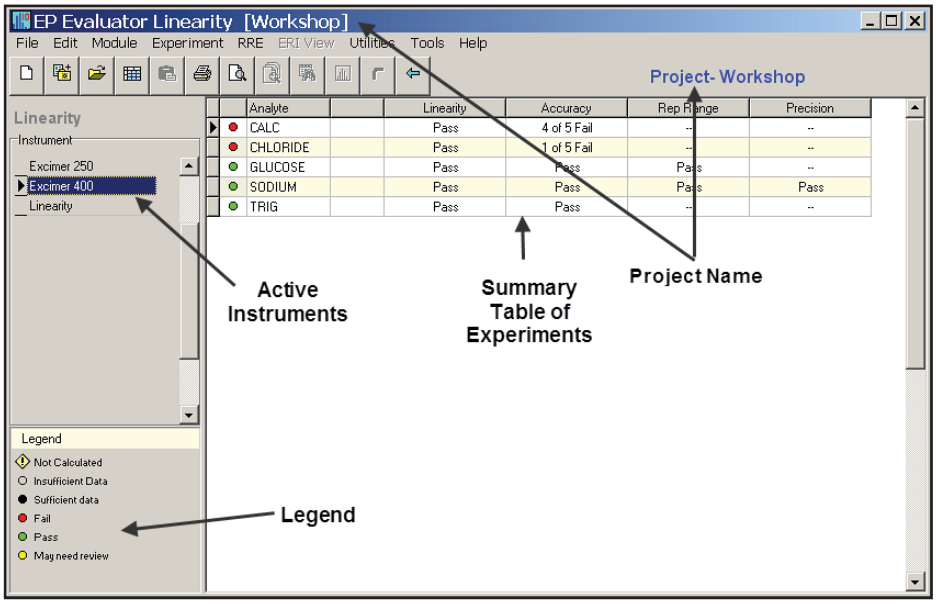


Figure 3.2 Module Overview Screen

Project name shows which project you are currently working on.

List of instruments (or methods) for which experiments in this module have been created. The highlighted one is currently selected.

Summary table of experiments for the selected instrument or method.

Legend of the symbols describing the status of the experiments.

Tool Bar

The tool bar is the row of twelve icons just below the menu. These icons are shortcuts to commonly used menu items. If you point at each icon for a few seconds, a small label (hint) will be displayed to show you what that icon does.

List of Instruments

The list of instruments in this project is shown on the left side of the screen (Figure 3.2). Click on an instrument to display its experiments in the Experiment Summary Table.

Experiment Summary Table

This table, which appears as part of the Module Overview Screen (Figure 3.2.), is a list of the experiments performed for the various analytes for an instrument. Double-click on a line to see the details of the experiment. Right-click on the line to get a pop-up menu which allows you to perform several different tasks on that experiment (Delete experiment, export the results and print the experiment).

The symbols beside the analyte name show the status of the experiment:

- **Exclamation point in yellow diamond.** Experiment has not been calculated, either because required parameters are missing or, if parameters are present, the calculation has not yet been done.
- **Green circle**. In a pass/fail module (like VRI), this experiment passes.
- **Red circle**. In a pass/fail module, this experiment fails.
- **Black circle**. There are enough results to perform the calculation, but Pass/Fail criteria have not been specified.
- **Open circle**. In a non-pass/fail module, more results are needed.
- **Yellow circle**. This experiment warrants review. For example, the program has detected outliers in a Method Comparison experiment or a subrange has been defined.

Key statistics for each experiment are also shown.

Menu Items

Details of the Menu Items follow for each:

File

New Project. Create a new experiment folder for a group of related experiments. This command is not available in the CLIA version of the software.

Open Project. Open an existing project.

Re-open Recent Project. Similar to Open, except you can select from a short list of the last few projects you used.

Project Inventory. Shows a list of what experiments are in the currently open project grouped by statistical module.

Merge Project. Merge Project allows you to copy all of the experiments from another project into the currently open project.

Import. Import data from another EE project that has been exported to the project \data\studies\IMP-EXP folder. Accessible from the Module Overview screen. See Chapter 39, *File Operations including Back-up and Import/Export* for details.

Export. Export (save) experiment data to a spreadsheet-readable CSV file format that can also be imported into another EE project. Accessible from the Module Overview Screen and from the Experiment Detail Screen. See Chapter 39, *File Operations including Back-up and Import/Export* for details.

Composite Report. Within a single project, combines reports created within multiple modules into one report.

Print and Print Preview. Generate printer images of reports. When invoked from the Module Overview Screen, these functions can preview and/or print all experiments in the statistical module. At the Experiment Detail Screen, these commands can preview and/or print only the one experiment that is open.

CR Print Preview. Generate printer images of reports for use in a Composite Report. When requested from the Module Overview Screen, this function can create a report for all experiments in the statistical module. From the Experiment Detail Screen, this option prints only the open experiment. This option is only enabled in modules selected for inclusion in the Composite Report.

Printer Setup. Select the printer to use.

Preferences. Define customized control settings that will apply to all new and existing experiments within a project.

Security. Commands to restrict access to the software and maintain an audit trail for 21 CFR Part 11 compliance. Available only in the Professional version. Security commands set up the software for User ID/Password login. See Chapter 40, *Professional Version: Security, User Groups and Audit Trails*.

Self Test. Performs basic validation of the software by running one case in each statistical module and comparing the resulting reports to known correct reports.

Exit. Exit the program.

Edit

Copy. When you are looking at a grid of experiment results on the screen, the Copy command will put the grid in the Windows clipboard, so it can be pasted into another experiment or application.

Paste. Creates or updates an experiment using data from the Windows clipboard.

Paste with Policies. Like Paste, except parameters from Policies are merged with experimental results, so experiments can be calculated with no further editing. (Not available in the CLIA version.)

Delete All Results. This command deletes all the results in an existing experiment, but does not delete the experiment.

Module

EE is organized into 30 statistical modules, and you work with one module at a time. You cannot do any useful work until you open a module. This menu is a second way to access the various statistical modules. The entries are identical to those on the Main Screen. Most of the commands in the Module menu provide an alternate way to access the various statistical modules without returning to the main Statistical Module screen. For example, the Linearity and Calibration Verification command opens the Linearity and Calibration Verification module. Other commands in the Module menu include:

Batch Edit Lot Numbers. For modules that report Calibrator, Control, or Reagent lot numbers, this function lets you assign lot numbers to existing experiments without having to edit each experiment individually.

Clear Overview Statistics. The Module Overview Screen shows a summary of key statistics for each of the module's experiments that have been successfully calculated. Clear Overview Statistics resets all of these statistics to a 'not calculated' state.

ReCalculate. Recalculates some or all experiments in the module with no need to open each one individually.

Summarize to History. Applies to the Linearity and Multiple Instrument Comparison modules, which maintain a history of previous results. Summarize to History moves the 'current' results to the history file and prepares a new, blank data entry grid. See Chapter 4, *Linearity and Calibration Verification* for details.

Experiment

Each statistical module contains a set of Experiments. Commands in the Experiment menu are used to manipulate the experiments. These commands include:

New. Create a new experiment.

New from Policies. This command also creates a new experiment, but with the analysis parameters already filled in. You pick the instrument and analyte names from a pick list. The program fills in the parameters based on your Policy definitions. (Not available in the CLIA version.)

Open. Open an existing experiment to show its detailed statistical analysis and graphs.

Delete. Delete one or more experiments.

Link X/Y Methods. This command applies only to the AMC, 2IC, QMC, EP9, and POC-Glucose method comparison modules. For these modules, experimental results are stored separately for each instrument. Before you can do a statistical analysis you must Link the results by selecting which available methods are the X and Y methods. When you create an experiment from the keyboard in the experiment detail screen, the program links it automatically. However, when experiments are imported or pasted from the clipboard, it does not show up in the module summary until you link it.

Custom Link. Normally, you can only link method comparison experiments when the analyte name is the same and instrument names are different. Cus-

tom lets you link other kinds of data, such comparing two different reagent lots for the same instrument

Delete Orphaned Specs. This command applies only to the AMC, 2IC, QMC, EP9, and POC-Glucose method comparison modules. It deletes orphan points from the experiment and from the applicable method database -- points with an X value but no Y value, or a Y value with no X value.

Rename Inst, Analyte, Etc. This command is like a find and replace for instrument, analyte, sample name, and units. This command allows you to fix a misspelled analyte or instrument name without deleting the whole experiment and retyping all of the results. The program enforces consistent capitalization of units. If you accidentally type MG/DL, it won't let you later use mg/dL, even on a new experiment. The Rename command lets you change these things for all experiments (within the same statistical module).

RRE (Rapid Results Entry)

Create Experiments. Use the Rapid Results Entry Wizard to create multiple experiments. This is the starting point for capturing results from an instrument interface or disk file. (You can also use "Keyboard Entry" to quickly type a panel of multiple results by specimen printout.)

ODBC Data Acquisition. Acquire data from a source application using ODBC. Additional requirements may apply to the source application; contact the source application vendor for information.

Define Policies. Define standard analysis parameters. These policies are applied automatically when you create new RRE experiments, when you create a single experiment with the **Experiment** / **New from Policies** command, or when you paste data in table or list format using **Edit** / **Paste with Policies**.

Lot Numbers. Define a pick list of Reagent, Calibrator, and Control lot numbers that can be used for multiple modules and easily selected into experiments.

Show Worksheet. Shows the RRE worksheet. When you create experiments with the RRE Wizard, its worksheet contents are retained until you change statistical modules. If you see a minor error, you can correct the worksheet and "Send" it again. Even after changing modules, saved worksheets plus the last three worksheets are available on disk. Use the worksheet's **File/Open** or **File/Reopen** command to retrieve them.

Summary of Last Capture. This function is a tool for troubleshooting instrument interfaces. It shows the test codes, instrument IDs, and flag settings from the last data capture or Paste with Policies, so the user can determine what is missing from Policy Definition.

AON Data Manager. Data is never typed into the Average of Normals (AON) module. Instead, it is read from files extracted from the LIS. The AON Data Manager is used to manipulate these files.

ERI View

Commands in this section apply only to the ERI/ROC module.

Sort by. Sort the data by spec ID, value, or attribute. You can also click on a column header to sort on that column.

Filter Specimens. Restrict the specimens to analyze. For example, analyze only men, only women, or only a specific age group

Show/Hide Columns. Choose a subset of variables to display in the data entry grid.

Restructure. Edit or Add fields to the ERI/ROC Data Definition Screen.

Explore. The main purpose of Explore is to identify and correct problems in your data. Shows a probability plot, plus either a histogram or dot plot. You can drag bounding lines to exclude unusually high or low values.

ERI Reports. Establish reference intervals for one or more analytes, or perform a Partitioning Analysis to test whether an attribute (such as gender or age) affects the analyte's distribution.

ROC Reports. Receiver Operating Curve Analysis. Analyze a single test, compare two tests, or batch print curves for any number of tests.

Recall Saved Case. Normally ERI/ROC reports are defined when they are created, and specific selections are not saved. Use the **Run** and **Save** command to save report settings such as selected analytes, partitions to evaluate, or report options. **Recall Saved Case** restores these saved settings.

Utilities

File Manager. Provides several options to manage and organize both current and archived projects. It includes backup, rename, copy, repair and restore functions.

Typing Help History Editor. Many of the screens in EP Evaluator® "remember" values you enter (e.g., Units), and you choose them from a list in the future. This command lets you delete or correct errors in the history.

Restore Installation Defaults. Remove the program memory of settings from previous program sessions (preferences, last values entered on forms, etc.)

Reload Standard Data. Inserts the original version of sample experiments into the active project.

Update Wizard. Brings data forward from older versions of EP Evaluator. This menu item is not available in the trial version of the software.

Tools

Incident Tracking. Launches the Incident Tracking lab management module.

Inventory (SIS). Launches the Inventory lab management module.

Competency Assessment (CAT). Launches the Competency Assessment lab management module.

Create Desktop Icon for ... Makes desktop icons for Incident Tracking, Inventory, and/or Competency Assessment so they can be started without running EP Evaluator.

Glossary, CLIA PT Limits, Biological Variation Data, Units Conversion Factors. These options display some useful reference tables. In addition to the Tools menu, these functions are also available from the **EE11 Reference Tools icon** in the Windows tray. This means you can look up CLIA PT Limits even when the menu command is not available -- like when you are entering input into a Parameters Screen.

My Tools / Configure My Tools. Allows you to configure other programs or files to start/open from the My Tools menu in EP Evaluator. For example, it may be useful to open the resource spreadsheets found in the EE Resources folder from within EE.

Help

Help Topics. Launches the Help program within EP Evaluator.

Check for Newer Version. If EE has permission for Internet access and if Internet access is available, the software contacts the Data Innovations website to ensure you have the latest build of your version of EP Evaluator. If you do not, you will be asked if you want to download and install the most recent version of EE.

Send a Bug Report or Comment. E-mail a bug report to the program developer, with ability to attach experiment data. The email facility requires Internet access, and EE must have permission to access the Internet. Alternatively, you can save the information to a disk file and mail it through normal channels.

About. Show program version and registered user

EULA. End-User License Agreement.

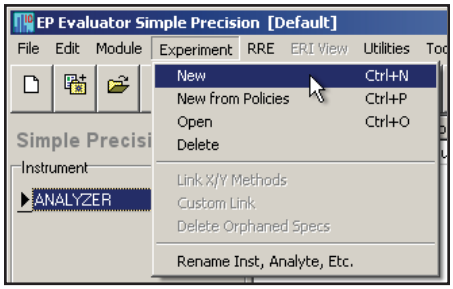
CLSI Notice. Describes how to obtain CLSI publications and explains that CLSI is not responsible for EP Evaluator implementation errors.

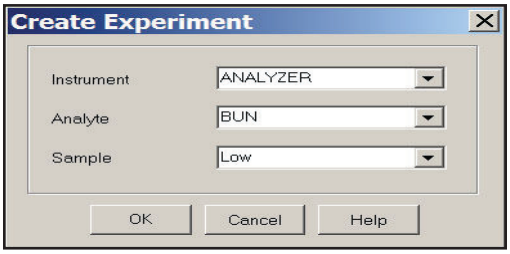
Renew Subscription. If you have a program subscription, brings up a screen where you can input an unlock code to renew it.

Creating a New Experiment

Steps to create a new experiment:

1. Select a statistical module from the Statistical Module Screen.
2. From the Module Overview Screen, click on the Experiment Menu.
3. Click on New (experiment).
4. Fill in the fields in the Create Experiment screen.
5. Click **OK**. At this point, you will go to the Parameters Screen (see Figure 3.3.) to set up the experiment.





Parameter Screen

The Parameter screen (Figure 3.3.) defines evaluation criteria (e.g., Allowable Error) and administrative details (Analyst, Date) for the experiment. Some of these parameters are required, and you can't enter results until you supply them. Required fields are highlighted in yellow. Once the parameters are complete, click **OK** to open the Experiment Detail Screen (Figure 3.4.) where you enter the experimental results.

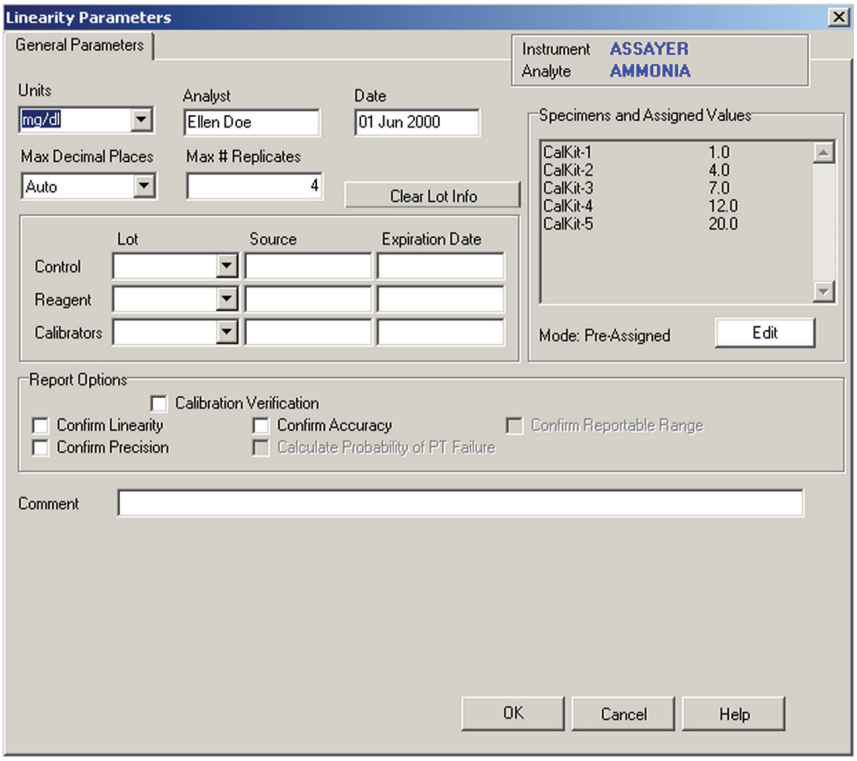


Figure 3.3 EP6 Linearity Parameter Screen

Experiment Detail Screen

This screen (Figure 3.4) provides total access to an individual experiment.

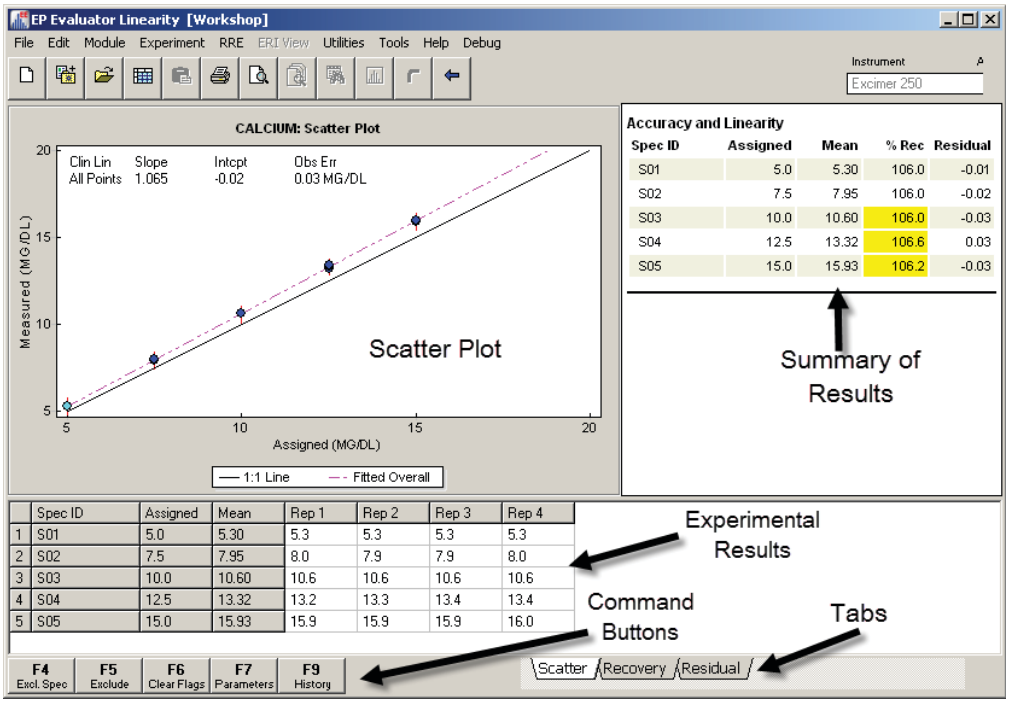


Figure 3.4 Experiment Detail Screen

The menu items and icons present on the Module Overview Screen are also present on the Experiment Detail Screen. Several other elements which often occur on the Experiment Detail Screens include:

Instrument and/or analyte name

This is a menu of the instruments and analytes applicable for that statistical module in the open Project. To view each experiment quickly, highlight an experiment and use the up/down arrows on the keyboard to page through them.

Statistical Table

A summary of the statistics and the results. This appears in various forms depending on which statistical module is used.

Control Buttons

The control buttons on many Experiment Detail Screens include:

F3: Add. Click to add results. (Not present in all modules.)

F4: **Delete**. Click to delete a specimen (and its result).

F5: Exclude toggles exclusion of results or specimens from the calculation process. When this key is pressed repeatedly, the exclusion is toggled on and off. In various screens, one may exclude either a single result, all results from a single specimen or other combinations depending on the position of the cursor when this button is pressed. Excluded items will still be present in the database but will not be used in the calculations.

F6: Clear flags. Click to clear outlier and exclusion flags from all results for this experiment.

F7: Parameters: Click on this button to access the Parameter Screen. The Parameter Screen allows you to enter/edit important elements with respect to your experiment. Items which are added in the Parameter Screens for various modules include: operator name, units, date on which experiment was done, allowable error parameters, and medical decision points to mention but a few. If you import data and are missing required data, you will be required to access the Parameter Screen to enter those items.

F8: ID Access: Click on this button to access the specimen ID field. (Not present in all the modules.)

F9:History: This function applies only to the Linearity and Multiple Instrument Comparison modules. These two modules maintain a history of previous results. The history button summarizes the current results to the History file, then clears the data entry grid for fresh input.

Results Grid and Specimen IDs

Results and specimen ID's are important components of the input data. Just click on the **F3: Add button** and start adding data into the grid.

In many modules, results are displayed in ASCII (alphanumeric) order by specimen ID. ASCII order is similar to alphabetical order but with some important differences. The following items are in ASCII order: 3A, 3Z, 8X, A01, A011, A012, A02, B05.

In some of the modules, the default sort order for Specimen IDs in the Experiment Detail screen is the order of entry. These modules include a **SpecID Sort** check box found on the bottom of the Experiment Detail screen. Checking this box sorts Specimen IDs in alphanumeric order.

One special feature is that when adding results, the program will propose the next specimen ID. The next specimen ID will be one greater than the previous one. Examples of this are: (S010 S011), (FIND FINE), and (S099 S100).

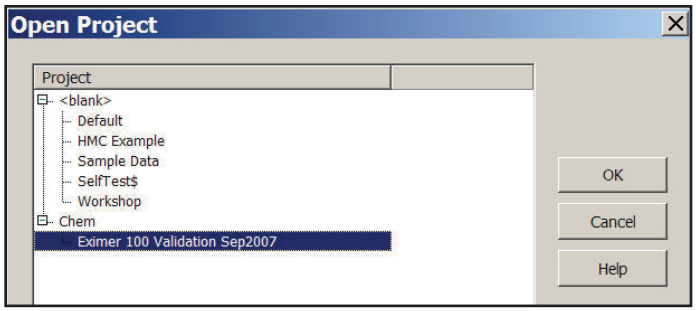
Using Projects

A Project is a group of related experiments—perhaps all of the calibration verifications and correlation studies you do for a semi-annual inspection, or the experiments for initial validation of a new method. Each Project has its own workspace, and its data can be backed up and restored without affecting other projects. You can define a client description so reports printed for the project show the client's institution in addition to your own. In a network environment, where different users at different computers run the same copy of EE, only one user at a time may work with a project.

CLIA Version Note If you have the CLIA version of EE, you cannot create a new project. You can only choose one of the pre-installed projects: Sample Data or Default. Default is intended for your data. Sample Data contains the examples provided to help you learn the program.

To open a project:

1. If you have an experiment open, close it.
2. Select **File/Open Project** from the program menu.
3. Highlight the project in the Open Project dialog, and click **OK**.
4. The active project name at the top of the screen will change to show the project you opened.
5. Projects are organized in a two-level outline. The top level is the "Prefix" you assign when creating the project (described below). Projects with no prefix assigned (like Default and Sample Data) appear under <blank>.

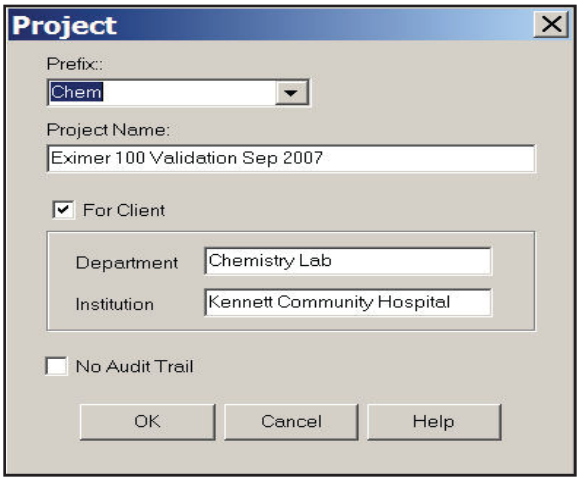


You can't open a prefix; you can only open a project at the second level. To "expand" a prefix to see what's under it, click the plus sign to the left of its name.

To create a new project:

- If you have an experiment open, close it. (You do not need to close the statistical module.)
- Select **File/New Project** from the program menu.

The program will show the project definition dialog illustrated below.



Prefix is the project's "parent". When you ask to open a project, the list of available projects is displayed in a two-level outline. This feature allows you to group related projects together so you can find them easily. For example, if several different departments are using EE, you might use the department name (such as Chem or Heme) for a Prefix.

You can leave the prefix blank, and the project will appear in the section labeled <blank>. When running the Professional version with security enabled, we suggest using your name or group as the prefix. If necessary, you can easily change it later.

Project name must be a legal name for a Windows folder. It may contain spaces, but it may not contain the following characters: asterisk, question mark, colon, or forward or backward slashes. It must start with a letter or number. We recommend that you include the instrument, task, month and year in the project name. That will make it easier to figure out what is in that project six months or a year later. An example is "Eximer 100 Validation Sep 2007".

For Client: Check this box if you want a client heading line on reports, and enter the client Department and Institution as you want them to appear on the reports.

No Audit Trail: This box appears only in the Professional version with security enabled, and only if you are an EE System Administrator. Uncheck it if you do not want to maintain Audit Trails for the project.

To merge projects

The **Merge Project** command allows you to copy experiments from another project into the currently open project. Only the currently opened project is altered by the merge process. Once you have performed Merge Project on a project, you cannot undo it. For this reason, back up the project you are merging into before proceeding with the merge.

If an experiment in the selected project already exists in the currently open project, it is skipped. The merge process does not overwrite the duplicate experiment, nor does it append result data to it.

To keep track of the experiments copied, perform a **Project Inventory** before you perform the Merge. You can copy the data into an Excel spreadsheet. Perform the **Merge Project**, then generate another **Project Inventory**. Paste this inventory into a different Excel spreadsheet to compare the project before and after the merge.

The incoming project data that you want to merge needs to be in the form of a Study folder, not a backup. If you only have access to a backup project, use **Utilities>File Manager** to restore the backup so that is appears in your active study menu. All of your active study folders normally reside in the folder **C:\EE11\DATA\STUDIES.**

1. Open the **Module Overview** screen.
2. Open a project.
3. Click **File>Merge Project**.
4. Click **Yes** to continue.
5. Browse to select a project to merge
6. Click **OK**.

If an experiment in the selected project already exists in the current project, that experiment is not copied. The Activity Log generates a list of duplicate experiments skipped by the Merge Project process.

To back up and restore projects:

When a project is backed up, an image of the project as of that moment is generated. This image is in the form of a ZIP file with the name **EEx backup of <projectName>~<date>~time.** Four types of EE backup files exist (See Table 3.1). Backup files can be copied, moved or deleted.

Table 3.1
Interchangeability of Backup File Types

Backup File Type	EE Release	
	Restore	Backup
EE4	All	EE4-5
EE6	EE6-11	EE6-8
EE9	EE9-EE11	EE9-EE11

We strongly encourage you to back-up your projects frequently especially when they are completed. Then you can move them from your computer to another location.

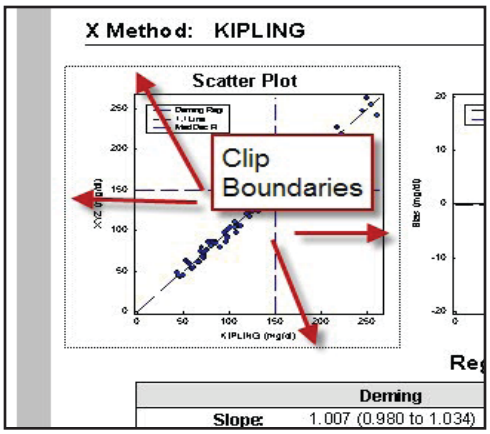
- **To Backup a Project:** From the Statistical Module screen, click on **Utilities**, then **File Manager**. Highlight a project in the upper box. Then click on **Back-up**. After the project is backed up, its backup will appear in the lower box.

- **To Restore a Project**: From the Statistical Module screen, click on **Utilities**, then **File Manager**. Highlight a backup file in the lower box. Then click on **Restore**. The name of the restored project will appear in the upper box.

- To **Copy a Project**: From the Statistical Module screen, click on **Utilities**, then **File Manager**. Highlight a project in the upper box. Then click on **Copy**. Enter a new name for your project and then click **OK**.

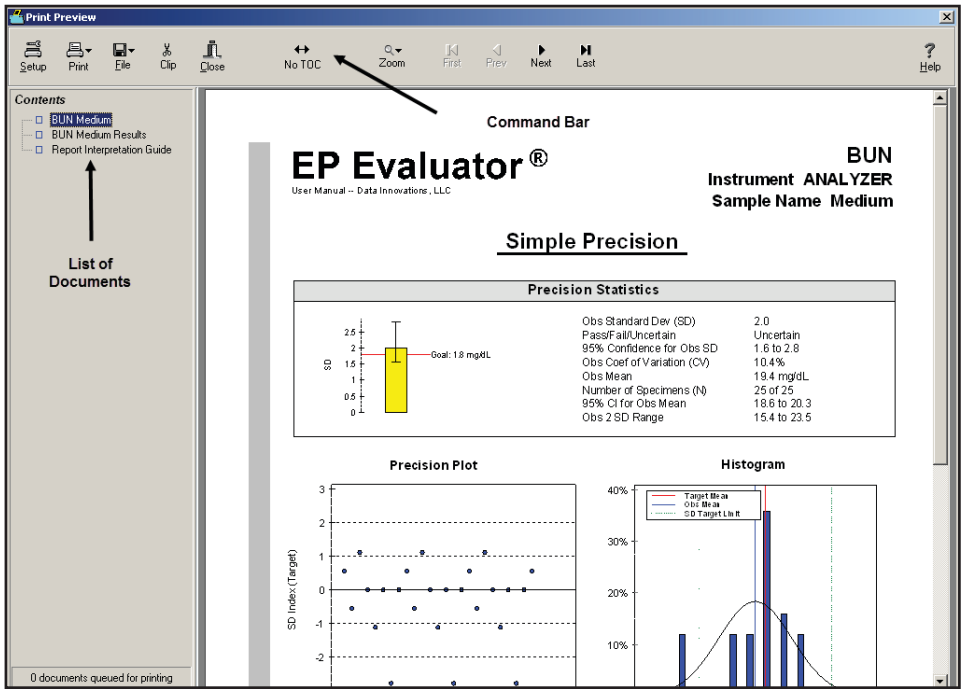
Printing and Previewing Reports

EP Evaluator provides a very powerful report generating tool. Not only can you output one or more reports to the printer or to other Windows printer devices, but you can also preview images of the reports on the screen and clip portions of images for inclusion in other documents.



Print Preview

This facility allows you to review the report on the screen before printing it. To access it, click on the Print Preview icon. At this point, EE will generate a report and display it in the Print Preview Screen.



There are several components to the Print Preview feature. They are the command bar across the top, table of contents (a list of pages presently viewable), and an image of one page of a report.

Command Bar

Tasks accessible through the Command Bar are:

Setup: Printer Setup dialog box to define the printer to which output will be directed.

Print: Displays a menu which allows you to print the current document, print queued documents, print all documents or clear the queue. For directions on how to queue a document, see section on List of Documents below.

File allows you to save the report in one of several available formats. Current Page, Queued Documents, and All Documents specify which document images are to be written to file. Configure defines the format in which the document images are written. See discussion below in **Clipping Part of a Page**.

Clip allows you to clip a portion of the image for inclusion in a Word document. See discussion below in **Clipping Part of a Page**.

Close returns control to the module overview screen of the module from which Print Preview was accessed.

No TOC toggles to close and open the Table of Contents window that appears to the left of the report window.

Zoom changes the magnification of the report from 50% to 200%, and Page view.

Several arrows near the top center of the screen navigate to display various pages of the report. Options in order are the **first page** of the report, the **previous page** of the report, the **next page** of the report and the **last page** of the report. These arrows are grayed out when it is inappropriate to access them.

List of Documents

The list of documents (one or more closely related pages) in the current report are shown in the left panel. Aspects include:

The little box next to a document name is used to queue the document for printing. If the little box is completely filled with blue, then all elements of that document are queued for printing. If the box is empty, no elements are queued for printing. If the box is half-filled, then some elements are queued for printing.

The little square filled with either a "+" or a "–" (not visible in this example) specifies that the document has several components. Click on the "+" to make the components visible. Click on the "–" to hide the components.

Report Page

A page is displayed at the current magnification. Scroll bars are available. Two other important controls are available by clicking on the right or left mouse buttons while pointing at the report page.

Left mouse button toggles the magnification between Page size and the current Zoom selection.

Right mouse button pops up a menu with two items: Print this document and Wide Screen View. Wide Screen View displays the page in the widest view possible.

Report File Format

Before you can save a file, you must select a file format. In fact, you select three formats: one for multi-page documents, one for single page documents, and one for page clips.

The first time you select a file function, the program will take you to the configuration screen automatically. It will then remember your selections, and not ask again. To change your configuration, select **File** at the top of the Print Preview screen, then select **Configure** from the pull down menu.

What is the best format?

- **Multi-page document**: If you want an archival copy of a report, either for your own records or to e-mail, the best format is PDF.
- **Single-page document**: The best choice for a full page is usually PDF, unless you want to use the document on a web page. For a web page, use either JPEG or PNG format.
- **Page clip**: If you want a figure to include in a paper for publication, use JPEG format. You can also copy it to the clipboard, then paste it directly into another document. Pasting the figure as metafile (rather than as a bitmap) gives better quality. However, it may not work with all word processors, and most magazines and journals do not accept the metafile format.

The tradeoff between size and quality

High resolution JPEG and PNG files can be very large. Unless you need publication-quality graphics, check Low-quality bitmaps to make smaller files. (This option does not affect the quality of PDF files.)

Saving a Report

Use the **File** and **Clip buttons** to save the report to disk so you can email it or include it in another document. You can save the whole report, selected pages, or part of a page (a clip).

To save a report:

1. Print preview the report
2. If you want to save only selected pages of the report, add those pages to the print queue.
3. Click **File** at the top of the Print Preview screen.
4. From the pull down menu, select either Current Page, Queued Documents, or All Documents.
5. The program will ask where to put the output. When you print to a single file, it asks for a file name. When you print to separate files, it asks for a folder name. It will create files called page1, page2, etc., in that folder. **Choose an empty folder; the program will over-write existing files without asking.**

Clipping part of a page

If you want to include a figure or table in a letter or memo:

1. Print preview the report, and display the page that contains the figure. Make sure the part of the page that you want to copy is completely visible.
2. Click Clip at the top of the Print Preview screen. The cursor changes to a cross to indicate that clip mode is active.
3. Move the mouse to the upper left corner of the rectangle you want to copy. Press and hold the left button while moving to the lower right corner. The program will draw a light gray rectangle around the selected area.
4. When you release the mouse button, the computer will beep to indicate that the image has been placed in the clipboard -- or, if you configured to save clips to file, it will prompt you for a file name. The cursor will change from a cross back to the normal magnifying glass.
5. When using the clipboard, start the program where you want to place the picture, and use the Paste function to place the picture in your document.

Creating a Composite Report

The **Composite Report** feature combines reports created in different modules into one all-inclusive PDF report. Each Composite Report (CR) consists of a title page and a table of contents, followed by a series of reports from various statistical modules. Only one CR can be defined per project.

Creating a Composite Report requires the following four steps:

1. Set up the Composite Report by adding title page text and by selecting the modules you want to include in the CR.
2. Open the appropriate modules.
3. Perform a **CR Print Preview** from within each module. CR Print Preview creates the module-specific PDF required for the CR.
4. Generate the Composite Report.

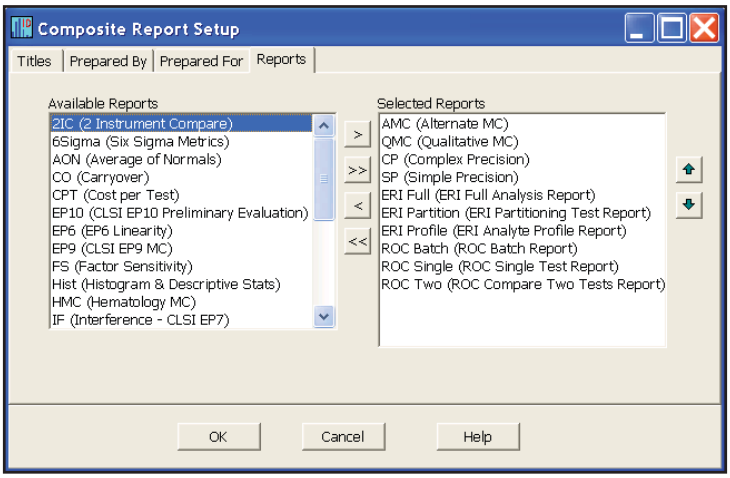
NOTE: Creating a CR for the Establishing Reference Intervals/ROC module requires a different workflow. See *Adding ERI or ROC Reports to a Composite Report* for more details.

Setup

To begin setting up your composite report, select **File**, **Composite Report**, then **Setup**. The **Composite Report Setup window** displays.

The **Composite Report Setup window** consists of four tabs. The first three tabs, **Titles**, **Prepared By**, and **Prepared For,** provide users the opportunity to customize some of the text populated onto the cover page of the report. Providing this information is optional.

Filling out the **Reports tab** is not optional. Until the module name is moved from the **Available Reports list** to the **Selected Reports list** on the Reports tab, you will not be able to create a module-specific PDF for that module.



To move modules between the two lists, select the module name and use the right or left arrow buttons. Using the double right arrow buttons moves all the modules

listed under Available Reports to the Selected Reports list, and vice versa. Double-clicking a module name also moves it between the two lists.

Use the up and down arrow buttons, to the right of the Selected Reports list, to define report order for the Composite Report.

CR Print Preview

The **CR Print Preview menu option** is enabled only in those modules listed in the **Selected Reports list** created in the **Composite Report**, **Setup** menu. CR Print Preview is accessible from the File menu and also from the **CR Print Preview button** on the toolbar.

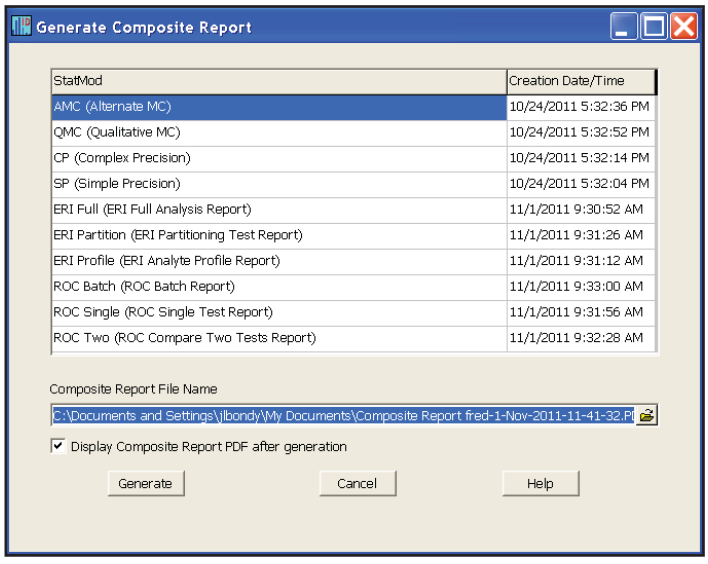
The CR Print Preview option creates and saves the module-specific PDF report in a folder that makes it available for inclusion in the overall Composite Report. Each time you run the CR Print Preview option, you are overwriting the existing module-specific PDF.

NOTE: Users with large amounts of data may notice a time delay as the module-specific PDF is generated.

NOTE: The CR Print Preview option is always disabled in the ERI/ROC module. To create a module-specific PDF for this module, see *Adding ERI or ROC Reports to a Composite Report* for instructions.

Generate

After viewing/creating the reports using CR Print Preview, use the **Composite Report**, **Generate** option to open the **Generate Composite Report** window. This window lists all modules included in the Composite Report. If a module-specific PDF already exists for a listed module, the **Creation Date/Time column** displays a timestamp. If there is no timestamp, the module-specific PDF for the listed module does not exist. You must either create the module-specific PDF or remove the module from the Selected Reports list in **Composite Report**, **Setup**.

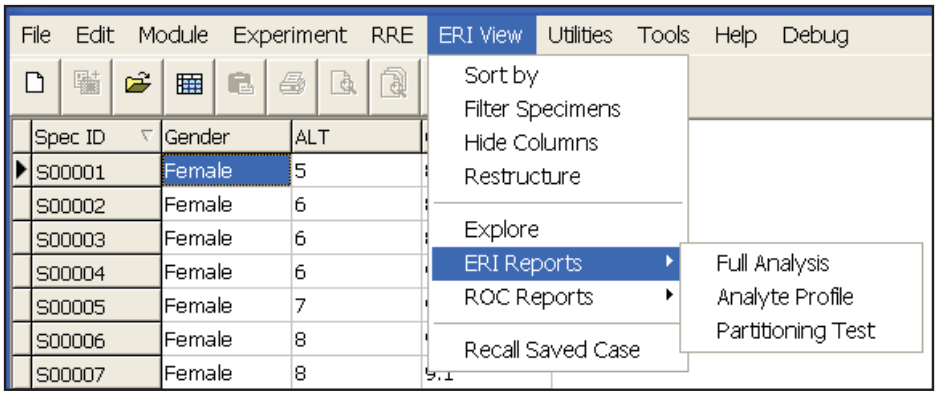


The Composite Report is saved to the folder location that you specify in the **Composite Report File Name field**. Use the folder icon at the end of the file name field to save the CR to another location. The default file name is the CR name plus the timestamp; this can be edited. Click **Generate** to create the Composite Report.

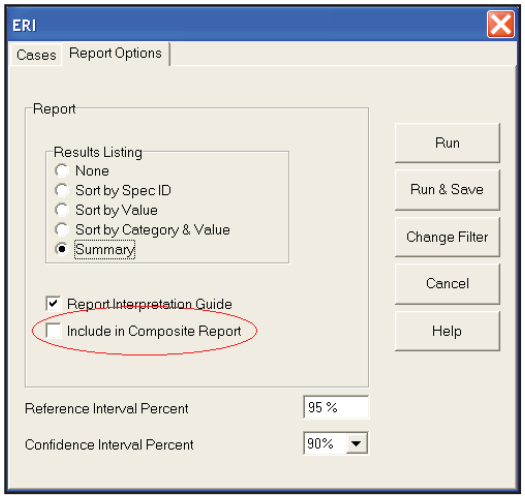
Adding ERI or ROC Reports to a Composite Report

Unlike any other module, the Establishing Reference Intervals/ROC module can generate six different reports: three ERI Reports and three ROC Reports. Each of these reports must be selected in the Composite Report Setup window separately, generated separately, and marked for inclusion in the CR using an option on the **Report Options tab**. Follow the instructions below to include ERI/ROC reports in the Composite Report:

1. Ensure the appropriate report is included in the **Composite Report Setup** window. In this example, we use the **ERI Full (ERI Full Analysis Report)**.
2. Open your study in the Establishing Reference Intervals/ROC statistical module and select the desired report from the ERI View menu.



3. Click the **Report Options** tab on ERI window and check the **Include in Composite Report box**.



4. Click the **Run button**. For all but two of the reports, this step generates a print preview of the PDF that will be included in the Composite Report. Close the Print Preview Screen to create the module-specific PDF. **If running the ROC Single Test or the ROC Compare Two Test, please continue to step 5.**
5. If running the Single Test or Compare Two Test Reports, a report is not immediately generated when you click the Run button. Instead, you will see a screen display with graphs of the data. Click the **Print Preview button** to create the PDF available for inclusion in the Composite Report.

Troubleshooting

- Any error message that refers to "DBISAM" indicates some sort of problem with the database. If the message refers to a "missing field", you can usually fix the problem by going to File Manager and doing a Quick Repair of the project.
- DBISAM error messages that say "Header corrupt" can't be fixed by a Quick Repair. This message indicates serious damage to the database, which may not be correctable. However, you can usually recover the data with a Full Repair from File Manager.
- Messages that use the word "access" (like Access denied, or unable to access) usually mean one of two things: 1) you don't have the necessary permissions to access EE data folders, or 2) some of your files have accidentally been write protected. Data Innovations support cannot fix permissions problems — your in-house IT staff must do it.
- EE keeps a log file of all unexpected error messages. If you use the menu command **Help / Send a Bug Report or Comment** to report problems, this information is automatically transmitted to Data Innovations.
- Use the **Save button** on the Preferences window to save your preference settings to a file. The Preferences.ini file is saved to C:\EE, where C:\ is the location EE is installed. Data Innovations Customer Support may request this file for troubleshooting purposes. Note that the file is automatically created and included in the package of files generated for a bug report.

Preferences

Several options are available for limited configuration of the reports and calculations. They are accessible under **File**, **Preferences** (Figure 3.5.). The choices made here often apply to a variety of statistical modules.

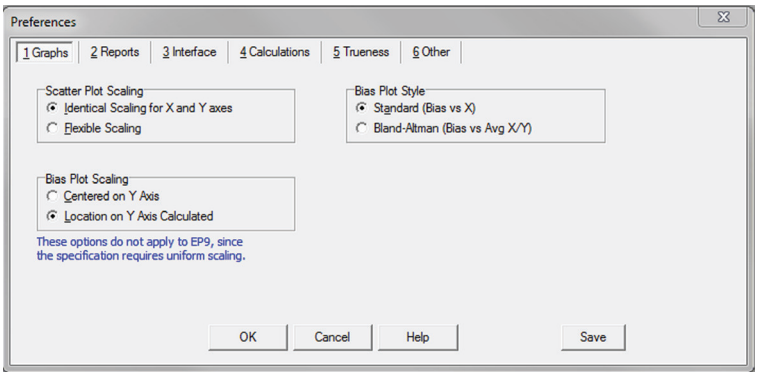


Figure 3.5 Preferences Screen

Use the **Save** button, found on every tab of the Preferences screen, to save Preferences settings to an INI file. For more information, see the section *Troubleshooting*.

Preferences Tab 1: Graphs

Scatter Plot Scaling (applies only to AMC) specifies whether or not the scatter plot will always have identical scaling for both the X and Y axes. An example where scaling is not identical would occur if the slope is 2. In this case, the X axis could be scaled from 0 to 100, the Y axis from 0 to 200.

Bias Plot Scaling (applies only to AMC) controls the centering of error plots -- residual, recovery, and precision plots. **Centered on Y Axis** means the zero line (or, for recovery, the 100% line) is exactly in the center of the Y axis. **Location on Y Axis Calculated** means excess white space is removed. For example, if the most negative residual is -500 and the most positive is +100, a centered plot would run from -500 to + 500, while a location calculated plot would run from -500 to + 100.

Bias Plot Style (applies to both AMC and EP9) provides for the selection of the source of data plotted on the X axis of the bias plots. The two options are:

- **Standard** approach (X axis data are the X results).
- **Bland-Altman** approach (X axis data is average of X and Y results).

Preferences Tab 2: Reports

Suppress Materials summary reports. When you report multiple experiments from a module that uses lot numbers (e.g., precision, linearity), normal behavior is to include a summary of materials sheet after the experiment summary sheet. Check this box if you don't want the materials summary.

Fixed-format Linearity Report. "Standard" linearity reports vary the report format depending on number of levels and number of replicates. Check this box to guarantee that the report always looks the same, as long as you are not verifying precision and don't have a history graph.

Approval lines on summary report. A column labeled "Accept" is placed on each summary report page so items can be initialed to indicate approval.

Suppress unmeasured linearity levels from report. Check this box to omit linearity levels that have no measured values. With this option, you can capture data for different linearity kits in the same capture without causing extra blank lines on the reports.

Always show printer selection dialog. Check this box if you want the program to prompt you to select a printer each time you print. This is useful if you frequently switch printers, and need to be reminded which one is active. You must use this option if you want to redirect printed reports to a disk file.

Report headings for client reports allows the user to change the labels displayed for the client and consultant. The default is "Prepared for: (client)" and "By (owner)". The size limit on the labels is 16 characters.

Check this box if blue lines don't print. Some of the graphs have blue lines. (i.e. AMC Scatter plots). These don't show up with some printers. If this is the case for your printer, check this box.

Omit Reference Intervals from HMC reports. When this box is checked, HMC reports do not show the MDP evaluation statistics. Note that reference intervals are not required in HMC policy definitions.

Suppress blank results in MC Results Listing. Do not include a specimen in the Method Comparison Results Listing if either the X or Y value is missing (blank). This option applies only to AMC, QMC, 2IC, and Glucose POC Instrument Evaluation.

HMC Flag Comparison Report by Default. Check this option to specify that any newly generated HMC studies start out with the Flag Comparison option checked. See Chapter 16, *Hematology Studies*, for more information about the Flag Comparison Report.

Enable Linearity Regression Summary Page. Check this option to create a Linearity Regression Summary report when printing or previewing a Linearity report for multiple experiments.

Preferences Tab 3: Interface

Ignore excess replicates when importing. Some statistical modules—notably Alternate and CLSI EP9 Method Comparison—require either unique Spec IDs or a specific number of replicates of each Spec ID. If this box is checked, EE will ignore extra replicates when it acquires results from a file or an instrument interface. If the box is not checked, the import will fail and you will have to fix your data before you can import it.

Don't interface flagged specimens. Normal operation for instrument interface and Paste with Policies is that results with non-benign flags are brought into EP Evaluator® as excluded results. If this box is checked, these results are not brought in at all.

Retain Linearity history when replacing. When you import a linearity experiment for the same instrument and analyte as an existing experiment, EE asks if you want to replace the existing experiment. Normally, when you answer Yes, any history for that experiment is destroyed. When the Retain Linearity History box is checked, the history is, instead, kept and attached to the new experiment.

Initialize interfaced /pasted HMC morphology parameters to 0. This option affects only morphology flags in the HMC module, when results are entered via **Edit/ Paste**, **Edit/Paste with Policies**, or instrument interface.

Separator for level in linearity spec IDs. When capturing data for linearity materials, the program normally expects specimen ID's of the form KK-nn, where KK is the kit instrument code and nn is the level number. Some instruments do not accept a dash in specimen IDs. Allowed characters are underscore, dash, or period. Also, it is possible to specify that no separator is used (so the spec id would be KKnn).

Keep newest (not oldest) rep when importing. AMC, 2IC, Glucose POC Instrument Evaluation and PT/INR Method Comparison modules accept only one replicate for each specimen ID. If the Ignore excess replicates option is checked, these modules normally accept the first replicate seen, and ignore the others. If you check this option, the program will keep the last replicate seen rather than the first.

Trim excess decimals when importing. Some instruments always report results to a large fixed number of decimal digits, often more than are appropriate. This option will trim the excess decimals to the number specified in Policies.

Preferences Tab 4: Calculations

Passing-Bablok Type (applies only to AMC) provides several choices with respect to the use of Passing-Bablok approach to calculating method comparison slopes.

- **None:** Passing-Bablok calculations are not used. (Default)
- **Regression:** Designed for predicting a value of Y from a value of X.
- **Method Comparison:** Designed for comparing two methods with approximately the same values.

AMC Graph/MDP. Changing the **AMC Passing-Bablok Type** option to Regression or Method Comparison displays the **AMC Graph/MDP** option, which allows users to configure the statistics used in the MDP and scatter plot regression line calculations.

Minimum R for estimating MDPs from. AMC uses either Deming Regression or Partitioned Biases to estimate Medical Decision Points, depending on the size of the Correlation Coefficient (R). If R is below the value chosen here, MDPs are estimated using the Partitioned Biases method. Otherwise, they are estimated using Deming Regression.

Simple Precision Verification. If **Pass/Fail** is selected and a goal for precision verification is specified, a small graph shows the 95% CI around the point estimate. A system will fail if the point estimate exceeds the precision goal. If **Pass/Fail/Uncertain** is selected, there are three possible outcomes: Pass when the upper 95% CI does not exceed the goal; Fail when the lower 95% CI exceeds the goal; Uncertain when the goal lies within the 95% CI.

Calculate QMC/ROC Conf Intervals on sensitivity, specificity and efficiency. CLSI recommends the Score method. See CLSI:EP12 for details.

Confidence Intervals for nonparametric reference intervals. This setting controls how confidence intervals are calculated for the nonparametric (CLSI:C28) method. The numbers published in CLSI:C28 differ from those in the IFCC specification. Select "CLSI Table" to match the CLSI document. Select "Formula" to use the exact formula, which generally matches the IFCC specs.

Show T Test for Alternate Method Comparison. AMC can, optionally, use a T test to determine whether the mean of Y-X is significantly different from zero. This test is inappropriate if the X and Y methods are not calibrated to slope=1.0 intercept=0.0, since it is a statistical test of whether X is numerically identical to Y. This option is off by default.

Allow limited amounts of missing MIC results. MIC can operate in one of two modes. In one mode, the program requires a result for each instrument for each specimen: if any instrument does not have a result for a specimen, the entire specimen is ignored when calculations are performed (as if it had been excluded). In the other mode, missing data is accepted and the existing data is processed under some conditions, as described in Chapter 13, *Multiple Instrument Comparison*. See the section in that chapter on Missing Data. This box is unchecked by default; check it if you wish to allow specimens which lack results for some instruments.

Allow 1-step difference in QMC with 5+ lvls. If this box is checked, semi-quantitative method comparison results will be considered identical if they are less than two levels apart. Applies only if the total number of levels is at least 5.

Preferences Tab 5: Trueness

Level Format: Define the default format used. Choose between Prefiix ("EQA-Low") and Suffix ("Low-EQA").

SD Reliability Threshold: Specify the number of specimens that will serve as a threshold between different statistical approaches. See Chapter 7, *Trueness*, for details on the specific statistical approach used at, above, and below the threshold value.

Default Analytical Goal Mode: Use the drop-down menu to specify the default Analytical Goal Mode for Trueness experiments.

Preferences Tab 6: Other

Decimal Places for INR modules is needed because EE does not have prior information about the number of decimal digits (nDD) for INR. In most modules EE gets this value from results that are entered. INR results are calculated, not entered.

Extra warning when deleting experiment controls how the **Experiment**, **Delete** menu works. When enabled, after you select the experiment for deletion and click OK, you are asked one final time whether you are certain that you wish to delete the experiments.

Self Test Mode normally should be left alone. Values are Normal, Slow and Manual Advance. The Mode should be changed if you get an error message when you run Self Test, which suggests that you should reduce the speed.

Max Decimal Places is used to specify the maximum number of decimal digits to be printed on the report. (It applies only to ERI/ROC and Hematology Method comparison). All digits are used for the calculations. Default is 4.

Check for Updates automatically. By checking this box, EE will automatically check the website for any revisions to the software and notify you on the Statistical Module screen if an update is available.

First Material Edited. Select the default material tab displayed when the Lot Numbers window is opened from the RRE menu.

Current system default language is: identifies the default language defined by the regional settings on the computer where EE is installed. This cannot be changed from within EP Evaluator.

Your preferred language is a dropdown field that displays any language files available for translating the EP Evaluator software. Language files are created using the Translator program shipped with EE. See the Chapter 41, *Translator*, for instructions on creating a translation file. Once a preferred language is selected, EE must be restarted for the new language to take effect.

Lot Numbers

Lot number (LN) is the term we will use to include the three material descriptors, (lot numbers, sources and expiration dates). The LN database includes “pick lists” for all three types. Once entered, LN can be used for experiments in all applicable modules within the particular project. Also Applies to CLIA version. There are three ways to enter lot numbers into the pick lists of an LN database.

- Module - Batch Edit Lot Numbers allows you to add new LNs manually into the LN database via the popup list.
- RRE - Lot numbers allows you to only add new LNs either manually or by cutting and pasting LN data from spreadsheets.
- Experiment Parameter screen - A check box allows you to enter a new lot number that will be retained in the LN database.

Once in the LN database, they can be easily added into many experiments. The two ways to do this are:

- Parameter Screen - LNs can be selected from a pick list of LNs in the database.
- Module - Batch Edit Lot Numbers let you associate LNs in the database with one or more experiments in the selected module at one time.

Chapter

4

Linearity and Calibration Verification

This module (loosely termed Linearity) provides a versatile and powerful facility to calculate all the parameters associated with specimens which have defined concentrations. These parameters include linearity, accuracy (recovery), calibration verification and, under appropriate circumstances, reportable range. Simple Precision calculations have also been included for method validation purposes. This module can also be used to calculate the Probability of Proficiency Testing Failure.

The powerful and innovative Clinical Linearity algorithm may be used to calculate whether one's data are linear within a specified allowable error. Refs: Castaneda-Mendez (1993), Rhoads and Castaneda-Mendez (1994).

Rhoads (2012) *Laboratory Statistics* manual has a chapter which discusses extensively the definition and derivation of the various terms, the Clinical Linearity algorithm, and interpretation of the reports.

Data Requirements

Each experiment may contain up to 11 specimens. Each specimen may have 1 to 20 replicates. Unless precision studies are being done, we recommend that 2 to 4 replicates be used. Precision requires a minimum of 10 replicates.

Experimental Design and Definitions

The experimental design varies somewhat depending on the objectives of the experiment. The primary choice is among the six report options shown on the Linearity Parameters Screen (Figure 4.1.). Determination of all items except Simple Linearity requires the entry of Allowable Error Criteria against which the performance of the method is evaluated. (See Rhoads (2012) *Laboratory Statistics* manual for discussion.)

Simple Linearity performs the simplest linearity experiment with a minimum of 3 specimens and 1 replicate for each specimen. Use of 5 to 6 specimens with 2 to 4 replicates for each specimen is customary. A linear regression line

is drawn through the points. No attempt is made to judge whether the data is linear or accurate by any objective criteria such as allowable error. This report uses the "eyeball" definition of linearity as described in the Rhoads (2012) *Laboratory Statistics* manual. The report will be labeled "Linearity."

Accuracy requires a minimum of 3 specimens with 1 replicate assayed for each. Use of 5 or 6 specimens distributed over the reportable range and 2 to 4 replicates for each specimen is customary. The concentrations of the specimens must be known in advance. A specimen passes the accuracy test if the observed mean is within the Allowable Systematic Error of its assigned value. In addition, each individual result must be within Allowable Total Error of its assigned value. The report title will include the word "Accuracy."

Clinical Linearity requires a minimum of 3 specimens. Use of 5 to 7 specimens covering the reportable range is customary. An experiment is linear if it passes the Clinical Linearity test, namely that the mean residual for each specimen does not exceed the Allowable Systematic Error at its assigned concentration. The report title will include the word "Linearity." If Confirm Linearity is selected, then Clinical Linearity will be done; otherwise linear regression analysis will be done.

Reportable Range is typically done in conjunction with an Accuracy experiment. The Reportable Range test is applied to two specimens, those with the lowest and highest concentrations in the series. Those two specimens should challenge the lower and upper limits of the Reportable Range. An experiment passes the test for Reportable Range if the first and last specimens are Accurate (see definition above) and meet Proximity Requirements. The Proximity Requirement is met if the assigned concentration of an appropriate specimen is sufficiently close (i.e. within proximity limits, a user-defined specification) to whichever limit of the reportable range is appropriate. The report title will include the word "Reportable Range."

Calibration Verification is the same experiment as a combination of Accuracy and Reportable Range. The only difference is that the title of the report is "Calibration Verification." Linear regression analysis is done on the data.

Precision is typically done in conjunction with an Accuracy experiment as part of the process of validating an instrument. Precision analysis requires a minimum of 10 replicates, but may have as many as 20 replicates. A specimen passes the precision test if its random error does not exceed the Allowable Random Error. Precision analysis is typically performed on two or three specimens. The report title will include the word "Precision."

Parameter Screen

After the experiment has been created (see Chapter 3, *Common Operations* for details), the essential elements of the experiment are entered in the Linearity Parameters Screens. These screens provide extensive control over the design of the experiment.

The first of two tabs (General Parameters – Figure 4.1.) which is always present, provides access to the primary parameters. The second of the two tabs (Proficiency Testing Parameters – Figure 4.2.) is visible only when the checkbox for Calculate Probability of Proficiency Test Failure is checked (in the Report Options section of the screen).

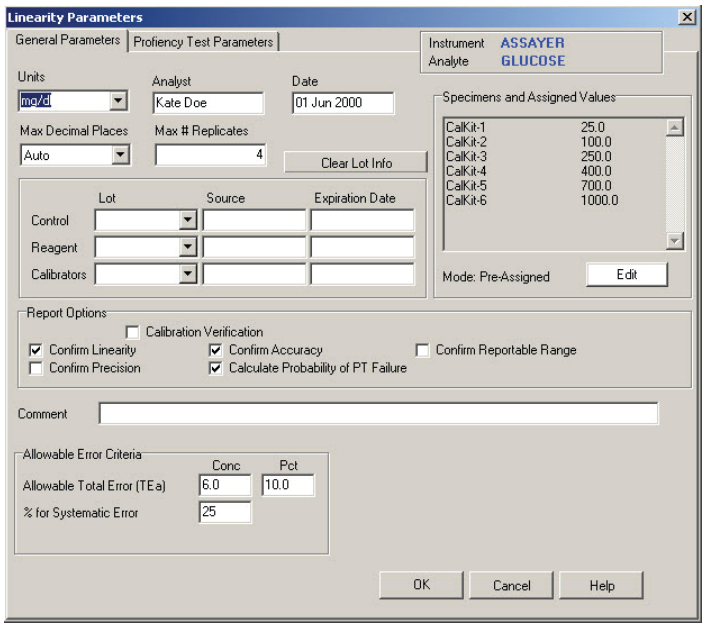


Figure 4.1 Linearity Parameter Screen - General Parameter Tab

General Parameters Tab

The fields accessible from this screen (Figure 4.1) are:

Units: The units in which analyte results are reported. **Required**.

Max decimal places: Maximum number of decimal places for reports. "Auto" means number of decimal places is determined from the data. Computed statistics (e.g., Mean) are usually printed with one more decimal place than the input results. This setting affects reports only; calculations are done on full-precision numbers.

Date: The date of the experiment. **Required**.

Analyst: The person responsible for performing the experiment. **Required**.

Lot Number: Lot identifier for reagents or linearity standard material. **Optional**.

Max Number of Replicates: This field defines the width of the grid, namely the maximum number of replicates expected for the specimen in the experiment with the largest number of replicates. The number of replicates must be between 1 and 20. If Confirm Precision is selected, then this value must be between 10 and 20. Otherwise the value is typically set in the range of 1 to 4. **Required**.

Comment may be used to describe why this analysis was performed (change in reagent lot number, instrument repair, and so on) or to record the other items of interest. Maximum field length: 50 characters. **Optional**.

Report Options

This section defines which of the following types of analysis are to be included in the report. If Calibration Verification is selected, then no other items can be selected. All the remaining elements may be included on a single report in various combinations as indicated below. These parameters can be defined on the Parameter screen (F7)

None selected: See Simple Linearity option above.

Calibration Verification: If this item is selected, then all the other options will disappear. If it is not selected, then they will be visible.

Confirm Linearity

Confirm Accuracy

Confirm Reportable Range: Requires Confirm Accuracy.

Confirm Precision

Calculate Probability of Proficiency Testing Failure: Requires that both Confirm Accuracy and Confirm Linearity be checked before it will become visible.

Allowable Error Criteria: Entries in this area are required whenever at least one of the Report Options is selected. They allow you to judge the performance of your instrument against objective criteria.

Allowable Total Error: One common definition of Allowable Total Error (TEa) are the Proficiency Testing Limits defined by CLIA '88. This may be expressed either as a concentration, a percent of concentration or both. If it is expressed as both, then the greater of the two at the specified concentration will be used. For example, the CLIA '88 limits for glucose are 6 mg/ dL or 10% whichever is more. At a glucose concentration of 40 mg/dL, the TEa limit is 6 mg/dL. At a glucose concentration of 120, the TEa limit is 12 mg/dL.

% for Systematic Error: (Synonym: Systematic Error Budget.) This is the fraction of the Allowable Total Error that is allocated for Systematic Error. This value should be in the range of 25% and 50%. It should not be less than 25% because of the expense involved in finding and fixing minor errors. It should not be greater than 50% because then insufficient space is left for random error.

% for Random Error: (Synonym: Random Error Budget). This defines the fraction of the Allowable Total Error which is allocated to 1 SD for the Confirm Precision option. We recommend that this value be in the range of 16% to 25%. Values much larger than 25% can increase the probability of failing proficiency testing to potentially dangerous levels. Keep in mind that the SD determined in this (usually one day) experiment will almost always be significantly smaller than an SD which is determined from results obtained over many days.

NOTE: For an evaluation of the potential impact your laboratory performance has on your ability to produce quality results, EE has two facilities which may prove helpful: (1) Probability of Proficiency Testing Failure – a component of this Linearity Module; (2) Six Sigma Metrics Module.

Reportable Range

This section defines the parameters used to determine whether a method passes Reportable Range. In order to pass the Reportable Range Test, the data must pass both the Accuracy Test and the Proximity Limits Test.

For the Proximity Limits Test, the assigned concentrations for the lowest and highest specimens must be suitably close to the lower and upper limits respectively of the Reportable Range. “Suitably close” is defined by the user. The CAP defines suitably close as 50% at the lower end and 10% at the upper end. However practical considerations may force different limits to be used. If you do use different criteria, you should document them in your procedure manual.

For example, suppose the reportable range for glucose is 10 to 600 mg/dL, that the allowable criteria for the lower limit is 20 mg/dL, and that the allowable criteria for the upper limit is 10%. In this case, if the assigned value of the specimen with the lowest concentration is 10 +/- 20 units (-10 to 30 units), it passes the proximity test. If it is outside those limits, (i.e. <10 or >30), then it fails the proximity test. Similarly, the acceptable proximity limits for the specimen with the highest concentration are 600 +/- 10% (540 to 660 units).

The fields in the **Reportable Range** box are:

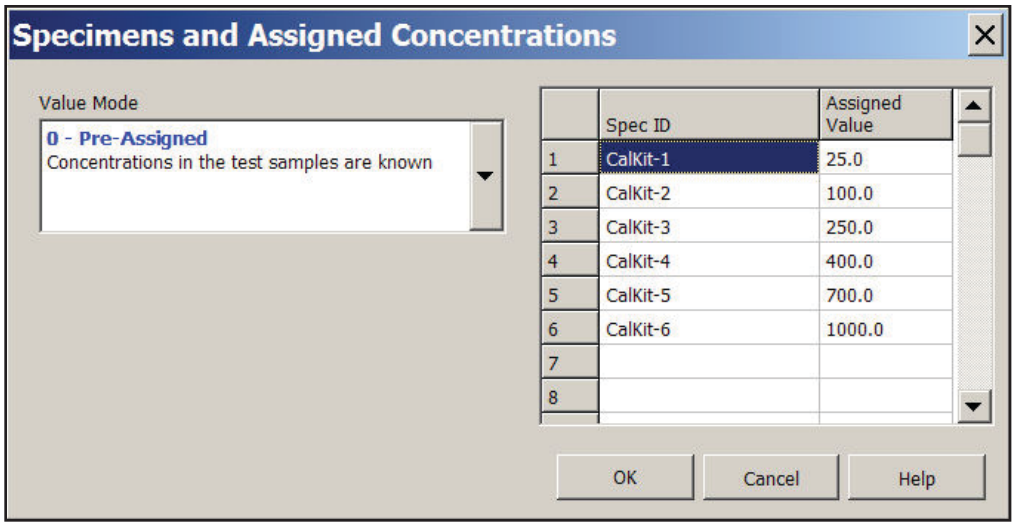
Lower and upper limits of the reportable range: In Figure 4.1., these limits are 25 and 950.

Proximity Limits: These define the maximum acceptable differences between one of the reportable range limits and its assigned concentration. This may be expressed as a concentration, a percent of concentration or both. The low end values tend to be expressed more often in concentration units, while the high end values often are expressed as a percent of concentration. Note that proximity limits are very different from allowable total error. One represents an amount of error, the other represents an acceptable difference between a assigned specimen concentration and its reportable range limit.

Specimens and Assigned Concentrations

This section defines the names and concentrations of the specimens. It also provides a value mode which specifies the way concentrations are defined.

Click **Edit** to access the screen into which these items are entered. There are two major sections to this screen:



Value Mode Section

This section provides for selection of one of the eleven Value Modes. It should be noted that without additional information, accuracy can only be determined with two of these value modes: Pre-Assigned and Pct-Assigned. The reason is that only in these two are the assigned concentrations based on an external source. In all the rest, the assigned concentrations are based on results measured on the instrument which are not necessarily accurate.

Pre-Assigned: Assigned values are entered by the user. This mode should be used when the concentrations in the test samples are known. Default.

Coded: Coded concentrations are defined in the Glossary. The advantages of this approach are that the exact concentrations do not have to be known and that the specimens occur at equal concentration intervals. If selected, then all the analyte concentrations will be automatically assigned integer values (i.e. 1 through 11).

Pct-Measured: Assigned concentrations are calculated as a percent of the mean measured value at 100% concentration. The user enters the percent concentrations and the measured results for all specimens. For example, if the mean of the measured results for the 100% specimen is 32, the 25%, 50%, 75% and 150% specimens will be assigned concentrations of 8, 16, 24 and 48 respectively.

Pct-Assigned: Assigned concentrations are calculated as a percent of the assigned value for the 100% specimen. If the 100% specimen has an assigned value of 80, the assigned values for the 25%, 50% and 75% specimens will be 20, 40 and 60. Percent concentrations are entered for all specimens. The only assigned concentration field into which the user can enter data is the 100% specimen.

Pct-Split: Assigned concentrations are based on the measured concentrations of the specimens with the lowest and highest percent concentrations. If the lowest and highest concentrations (and percents) for a set of specimens are 200 (20%) and 600 (100%), the 50% concentration will be 350. The assigned concentration fields are display only. The user can access only the percent fields.

Delta A/B: There are five items in this Series: Delta 1/5, Delta 2/3, Delta 3/4, Delta 1/3 and Delta 2/4. They are designed to work with specimens from a particular linearity specimen vendor (Maine Standards, Windham, ME). In the Assigned Concentration Table, indices are assigned for each specimen. Indices do not have to be a whole number. The A and B in Delta A/B refer to indices, not specimens. The recoveries of A and B are defined as 100%. The remaining recoveries are assigned in a linear relationship based on their own indices relative to A and B. See Table 4.1 for an example. Here, the second (index 1) and fourth (index 3) specimens define the concentrations of all the rest.

Table 4.1

Example based on Delta 1/3			
Index	**Assigned Conc**	**Measured Conc**	**% Recovery**
0.5	100	50	50
1	**200**	**200**	**100**
2	400	450	112.5
3	**600**	**600**	**100**
5	1000	900	90
Bolded rows define concentrations of remaining rows.			

Alternate Coded: The assigned values are defined by a straight line drawn through the points with the relative concentrations of the specimens based on the indices so that the slope is 1.0 and the intercept is 0.0.

The right section provides for entry of specimen IDs and the concentrations or percent concentration relationships. The right column in this section will be labeled “Concentration” or “Percent”, whichever is appropriate to the selected mode.

Probability of Proficiency Testing Tab

This module calculates the probabilities of failing PT from the random error obtained from the best fit line calculated for the current experiment, from a measure of random error (user's QC statistics) and from the PT Limits. The User's QC Statistics and the PT Limits are both entered in the screen shown in Figure 4.2.

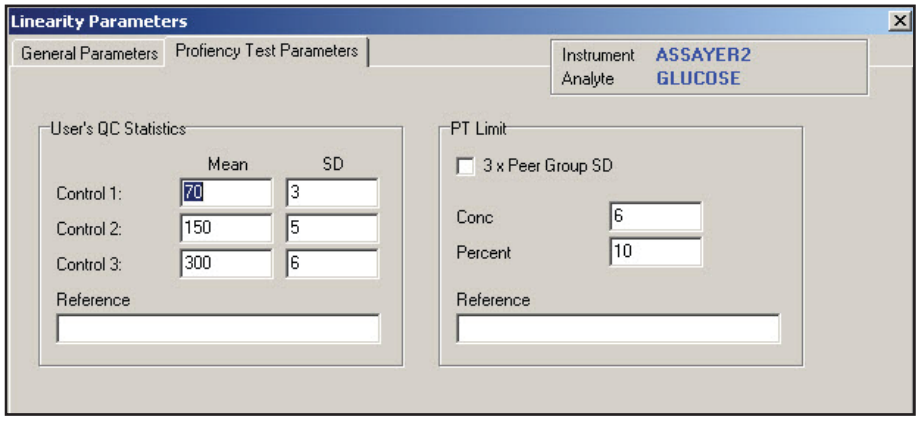


Figure 4.2 Linearity - Proficiency Test Parameters Screen Fragment

The random error is determined from the error profile entered in the section on the left side of the screen shown in Figure 4.2. The mean and SD for up to three QC materials can be entered. The error profile is calculated based on these values.

PT limits are entered in the right panel. Normally these numbers will be the same as the Allowable Total Error entered under the General Parameter tab. The default values are the Allowable Total Error values entered in the General Tab.

Experiment Detail Screen

The Experiment Detail Screen provides access to all details for linearity-type experiments. Fragments of this screen are shown at right.

Accuracy and Linearity

Spec ID	Assgn'd	Mean	% Rec.	Resid
CalKit-1	25.0	25.5	102.0	-0.9
CalKit-2	100.0	101.5	101.5	0.1
CalKit-3	250.0	249.5	99.8	-1.9
CalKit-4	400.0	407.8	101.9	6.5
CalKit-5	700.0	690.3	98.6	-10.9
CalKit-6	1000.0	938.0	93.8	-63.1

Assigned Concentrations are specified for each set of linearity specimens. They may be coded or un-coded. For a definition of coded specimens, see the Glossary.

Percent (the contents of the first column of the grid, but not shown in this figure) is another way to represent the assigned concentrations. Often in sets of linearity standards, concentrations are expressed as a percent.

Mean is the average of the experimental results.

Rep1, Rep2... are the experimental results. They are combined statistically with the Assigned Concentrations using linear regression or other techniques to calculate a slope and intercept.

Valid results must be present for at least 3 specimens. A valid result has an un-excluded specimen and is itself un-excluded.

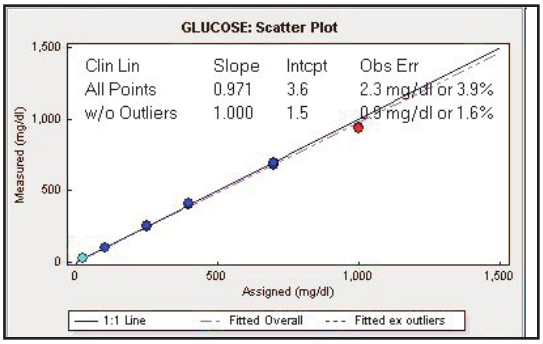
Entry of results is done by entering a number and then pressing <Enter>.

Control Buttons

History provides for storage and eventual display of historical data. Immediately after pressing this key, the program will ask "Summarize current data and prepare new empty record?" If Yes, the software calculates the means of the un-excluded data and stores them. It then clears the fields on that screen for the measured results. Results for up to two previous experiments can be stored. Stored results for any experiments prior to those are deleted.

The Experiment Detail Screen has up to five tabs, one for each of the five possible plots: Scatter Plot, Residual Plot, Recovery Plot, Precision Plot and History Plot. It also shows the slope and intercept. If Allowable Error parameters have been defined, then an error analysis is also displayed.

Scatter Plot

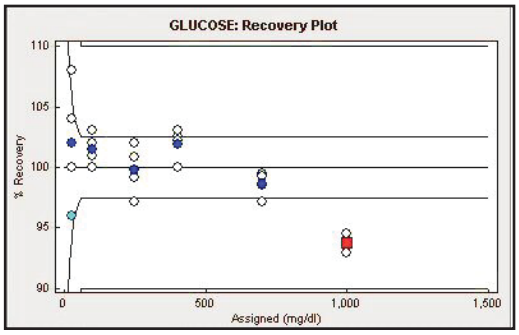


The Scatter Plot may appear in two different forms depending on whether or not Confirm Linearity (on the Parameters Screen) has been selected.

If Confirm Linearity has been entered, then the Clinical Linearity version is shown (in the form shown to the right). The lines shown indicate the best fit line through the data (not a regression line) with and without outliers. Another line shows the 1:1 relationship between the assigned and measured concentrations. The 1:1 line is not shown when the Defined Value Mode is "Coded." Error bars showing the allowable error for each specimen are centered on the mean of the results for each specimen. Outliers are shown as red dots in the screen plot.

If Confirm Linearity was not selected, calculations are done by linear regression statistics and the regression line is plotted. When the assigned concentrations are not coded, the 1:1 line is plotted.

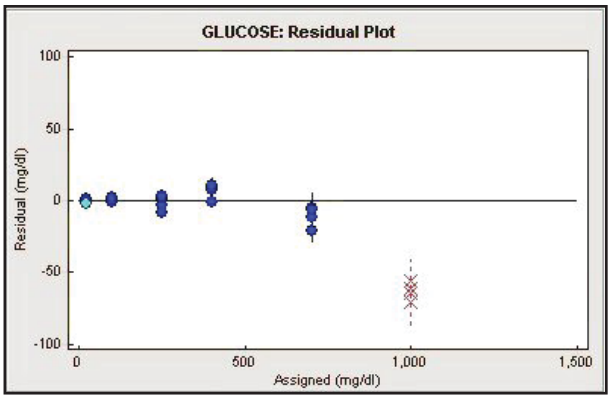
Recovery Plot



A Recovery Plot shows the percent each individual result (open circles) and each mean result (solid blue circles) is of the assigned value. Two error envelopes are shown, an outer one (line shown here near the bottom and top of the graph) for allowable total error and an inner

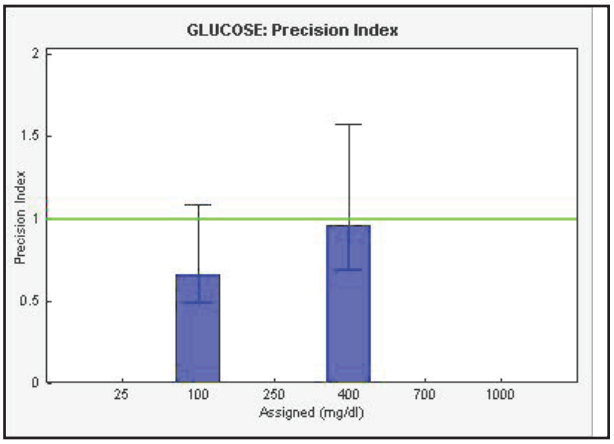
one (line near the middle) for allowable systematic error. (If only one error envelope is visible, the error budget is 100%). If the mean of a specimen's results lies outside the inner error envelope (see right-most point), then it is considered an outlier. Similarly, if an individual result lies outside the outer envelope, then that result is considered an outlier.

Clinical Linearity Residual Plot



A Residual Plot plots the residuals calculated using the Clinical Linearity algorithm. A residual is the difference between the Y value of an observed point and Y value for the line at that point's X value. The error bars indicate the allowable error for each point. Outliers are indicated in red on the screen. In this plot, the right-most set of points are outliers. Non-linear specimens may be easily recognized because their error bars do not intersect with the "0" line across the middle of the residual plot.

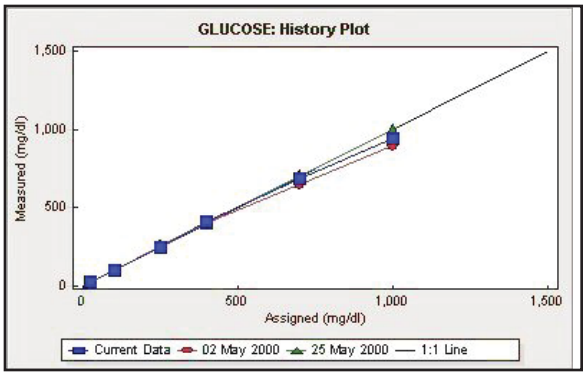
Precision Plot



The Precision Plot plots the Precision Index (PI). This innovative graph shows the random error as a fraction of the allowable random error. The line rising up above the bar at the top indicates the 95% Confidence Interval (CI) for the observed random error. Ideally, the top of the 95% CI point will have a value less than 1. If the actual (PI) is greater than 1, then the bar will be colored red.

One way to decrease the height of the 95% CI line is (if possible) to increase the number of replicates used to the maximum number of 20.

Historical Data Plot



This innovative graph summarizes up to 3 scatter plots on one graph. One plots the linearity results for the current data set. The other two show the data from up to two previous experiments. This allows the user to determine how linearity results have changed over a

period of time. The slopes and intercepts for these three sets of data are displayed to the right of the graph. The 1:1 line is plotted when the assigned concentrations are not coded. If the analytical system is stable, then all three lines will lie right on top of one another.

Linearity Reports

Due to the large number of combinations of report options, there are many different types of reports. In order to keep things relatively simple, the individual elements of the analysis can be presented in tables easily related to those in the report with some cosmetic differences. For a discussion of the Probability of Proficiency Testing Failure, see Rhoads (2012) Laboratory Statistics manual. The theory and the reports are discussed there in detail.

Figure 4.3 shows the components for Accuracy, Linearity, and Reportable Range. A similar table could also include a Precision component.

			Accuracy & Recovery				Rpt
	Assigned	N	Mean	% Rec.	Status	Linearity	Range
CalKit-1	25.0	4	25.5	102.0	Pass	Pass	Pass
CalKit-2	100.0	10	102.1	102.1	Pass	Pass	--
CalKit-3	250.0	4	249.5	99.8	Pass	Pass	--
CalKit-4	400.0	10	407.8	102.0	Pass	Pass	--
CalKit-5	700.0	4	690.3	98.6	Pass	Pass	--
CalKit-6	*1000.0*	*4*	*938.0*	*93.8*	*Fail*	*Fail*	*Fail*

See User's Specifications for Pass/Fail criteria

Figure 4.3. Linearity Report - Accuracy, Recovery, Linearity and Rpt Range Table

Assigned and **Pct** (Percent) are taken directly from the input data. In this case, **Pct** is not visible since the Defined Value Mode was Predefined and none of the three percent modes was used.

N is the number of replicates assayed for each specimen.

Mean is the average of all un-excluded measured values for a specimen.

% Rec (percent recovery) is the percent the mean value is of the assigned value. The ideal percent recovery is 100% (which represents perfect accuracy).

Status is calculated for all specimens when appropriate and is expressed as Pass/Fail. A specimen fails when the difference between the mean value and the assigned concentration exceeds the systematic allowable error.

Rpt Rng (Reportable Range) is only calculated on specimens with the lowest and highest concentrations in the list, when appropriate, and is expressed as Pass/Fail. A specimen passes if it is accurate AND the assigned concentration is within the Proximity Limits.

When generating a report for multiple analytes, EE creates a **Linearity Summary** report. To prompt EE to create an additional **Linearity Regression Summary** report, check the **Enable Linearity Regression Summary Page** option in the **File>Preferences>Reports** form.

Clinical Linearity Summary Table

An example of Clinical Linearity Summary Table is shown at right. In this case, the system is non-linear. The slope and intercept are calculated using the Clinical Linearity algorithm. In this case, they were calculated two times: once with all the points and once after the outliers were discarded. The criteria for linearity (Allowable Systematic Error) are listed below the table.

Linearity Summary

	Overall	*w/o Outliers*
Slope	0.971	1.000
Intercept	3.6	1.5
Obs. Err.	2.3 mg/dl or 3.9%	1.0 mg/dl or 1.6%
N	6	5

NON-LINEAR within Allowable Systematic Error of 1.50 mg/dl or 2.5%

Linear Regression Summary Table

An example of Linearity Regression Summary Table is shown at right. The slope and intercept are shown along with their standard deviations. The standard error of the estimate is also shown. This table is produced whenever Clinical Linearity is not selected.

Linearity Summary

	Reg. Regression
Slope	0.933 ± 0.024
Intercept	20.4 ± 13.8
SEE	17.0
N	5

User's Specifications Table

The User's Specifications table appears in all those reports which involve allowable error statistics. It displays the allowable error parameters input by the user.

User's Specifications

Allowable Total Error:	6.0 mg/dl or 10.0%
Systematic Error Budget:	25%
Allowable Systematic Error:	1.50 mg/dl or 2.5%
Reportable Range:	10 to 1000 mg/dl
RR-Low Range:	-10.0 to 30.0 mg/dl
RR-High Range:	800.0 to 1200.0 mg/dl

Supporting Statistics Table

The Supporting Statistics table appears in every report. It contains various non-numeric parameters (user, units, etc.) entered by the user.

Supporting Data

Analyst:	Kate Doe
Date:	01 Jun 2000
Value Mode:	Preassigned
Units:	mg/dl
Lot Number:	
Comment:	

Analytical Claim

A different Analytical Claim is generated for every report option. The one below (Figure 4.4.) was generated for an Accuracy report.

Analytical Claim

The Accuracy of Glucose was analyzed on Assayer over a measured range of 25.5 mg/dL to 938.0 mg/dL. This analysis assumes accurate defined values. Allowable systematic error (SEa) was 1.5 mg/dL or 2.5%. The maximum deviation for a mean recovery from 100% was 6.2% at a defined concentration of 1000.0 mg/dL. 5 of 6 mean recoveries were accurate within the SEa. 24 of 24 results were within the allowable total error of 6.0 mg/dL or 10.0%.

Figure 4.4 Linearity Report - Analytical Claim

Report Interpretation

For interpretation of the reports, consult the chapter in Rhoads (2012) *Laboratory Statistics* manual on Design and Interpretation of Linearity Experiments.

Precision, Accuracy, Rpt. Range and Linearity (Page 1)

EP Evaluator®

User's Manual -- Data Innovations

GLUCOSE

Instrument: ASSAYER2

Precision, Accuracy, Reportable Range, and Linearity

			Accuracy & Recovery			Precision					
	Assigned	N	Mean	% Rec.	Status	SD	95% CI	%CV	Status	Linearity	Rpt Range
CalKit-1	25.0	3	25.0	100.0	Pass	--	--	--	--	Pass	Pass
CalKit-2	100.0	10	102.0	102.0	Pass	2.2	3.9	2.12	Pass	Pass	--
CalKit-3	250.0	3	247.7	99.1	Pass	--	--	--	--	Pass	--
CalKit-4	400.0	3	406.3	101.6	Pass	--	--	--	--	Pass	--
CalKit-5	600	10	600.4	100.1	Pass	13.8	25.2	2.30	Pass	Pass	--
CalKit-6	*750*	*3*	*713.3*	*95.1*	*Fail*	--	--	--	--	*Fail*	*Fail*

See User's Specifications for Pass/Fail criteria

Linearity Summary

	Overall	*w/o Outliers*
Slope	0.978	1.001
Intercept	2.4	0.5
Obs. Err.	1.89 mg/dl or 3.1%	0.78 mg/dl or 1.3%
N	6	5

NON-LINEAR within Allowable Systematic Error of 1.5 mg/dl or 2.5%

Experimental Results

CalKit-1	24	26	25				
CalKit-2	101	102	100	103	105	103	102
	98	105	101				
CalKit-3	243	252	248				
CalKit-4	400	410	409				
CalKit-5	590	596	580	595	615	598	585
	610	620	615				
CalKit-6	700	740	700				

X: Excluded from calculations

User's Specifications

Allowable Total Error:	6 mg/dl or 10.0%
Systematic Error Budget:	25%
Random Error Budget:	25%
Allowable Systematic Error:	1.5 mg/dl or 2.5%
Allowable Random Error:	1.5 mg/dl or 2.5%
Reportable Range:	25 to 700 mg/dl
RR-Low Range:	22.5 to 27.5 mg/dl
RR-High Range:	630.0 to 770.0 mg/dl

Supporting Data

Analyst:	Kate Doe
Date:	01 Jun 2000
Value Mode:	Preassigned
Units:	mg/dl
Controls:	--
Reagent:	--
Calibrators:	--
Comment:	

Evaluation of Results

The Accuracy, Reportable Range, and Linearity of GLUCOSE were analyzed on ASSAYER2 over a measured range of 25.0 to 713.3 mg/dl. This analysis assumes accurate assigned values. Allowable systematic error (SEa) was 1.5 mg/dl or 2.5%. The accuracy test FAILED. The maximum deviation for a mean recovery from 100% was 4.9%. 5 of 6 mean recoveries were accurate within the SEa. 32 of 32 results were accurate within the allowable total error (TEa) of 6 mg/dl or 10.0%. The results are NON-LINEAR. The system FAILED reportable range tests. 1 of 2 specimens met accuracy requirements. Precision was analyzed at mean concentrations of 102.0 and 600.4 mg/dl. The precision test PASSED. The precision of 2 of 2 specimens was within the Allowable Random Error of 1.5 mg/dl or 2.5%.

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Signature Date

Precision, Accuracy, Rpt. Range and Linearity (Graphs)

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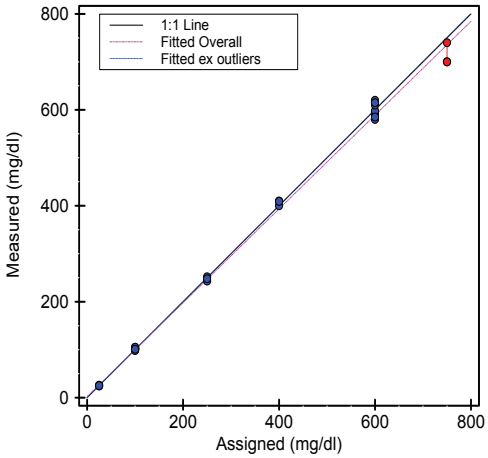
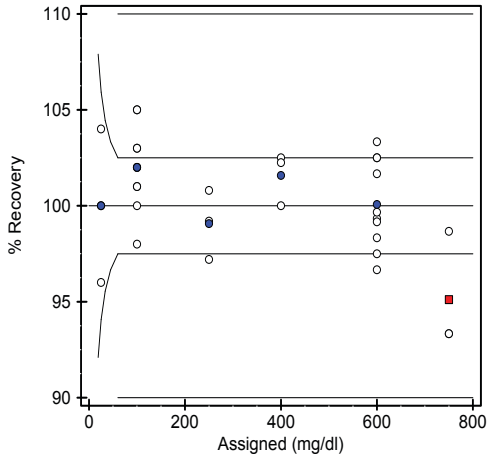
GLUCOSE
Instrument: ASSAYER2

Precision, Accuracy, Reportable Range, and Linearity

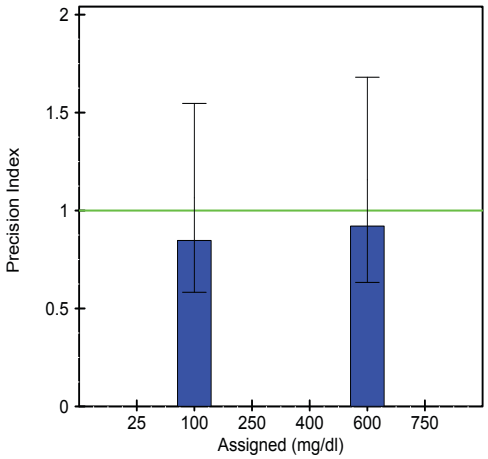
Scatter Plot



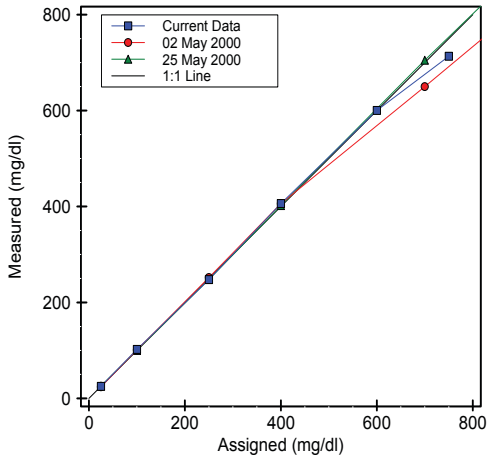
Percent Recovery



Precision Index



History Plot



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Calibration Verification (Statistics Page)

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GLUCOSE

Instrument: ASSAYER2

Calibration Verification

	Assigned	N	Mean	Percent Recovery	Status	
					Accuracy	Rpt Range
CalKit-1	25.0	3	25.0	100.0	Pass	Pass
CalKit-2	100.0	10	102.0	102.0	Pass	--
CalKit-3	250.0	3	247.7	99.1	Pass	--
CalKit-4	400.0	3	406.3	101.6	Pass	--
CalKit-5	600	10	600.4	100.1	Pass	--
CalKit-6	*750*	*3*	*713.3*	*95.1*	*Fail*	*Fail*

See User's Specifications for Pass/Fail criteria

Linearity Summary

	Reg. Regression
Slope	0.964 ± 0.021
Intercept	7.6 ± 9.3
SEE	13.5
N	6

Experimental Results

CalKit-1	24	26	25				
CalKit-2	101	102	100	103	105	103	102
	98	105	101				
CalKit-3	243	252	248				
CalKit-4	400	410	409				
CalKit-5	590	596	580	595	615	598	585
	610	620	615				
CalKit-6	700	740	700				

X: Excluded from calculations

User's Specifications

Allowable Total Error:	6 mg/dl or 10.0%
Systematic Error Budget:	25%
Allowable Systematic Error:	1.5 mg/dl or 2.5%
Reportable Range:	25 to 700 mg/dl
RR-Low Range:	22.5 to 27.5 mg/dl
RR-High Range:	630.0 to 770.0 mg/dl

Supporting Data

Analyst:	Kate Doe
Date:	01 Jun 2000
Value Mode:	Preassigned
Units:	mg/dl
Controls:	--
Reagent:	--
Calibrators:	--
Comment:	

Evaluation of Results

The Calibration Verification of GLUCOSE was analyzed on ASSAYER2 over a measured range of 25.0 to 713.3 mg/dl. Calibration Verification consists of verifying Accuracy and Reportable Range. This analysis assumes accurate assigned values. Allowable systematic error (SEa) was 1.5 mg/dl or 2.5%. The accuracy test FAILED. The maximum deviation for a mean recovery from 100% was 4.9%. 5 of 6 mean recoveries were accurate within the SEa. 32 of 32 results were accurate within the allowable total error (TEa) of 6 mg/dl or 10.0%. The system FAILED reportable range tests. 1 of 2 specimens met accuracy requirements.

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Probability of PT Failure Report

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GLUCOSE
Instrument: ASSAYER2

Probability of Failure in Proficiency Testing

	User's QC Statistics		PT Limits	
	Mean	SD		
Control 1:	70	3	Pct:	10
Control 2:	150	5	Units:	6
Control 3:	300	6		

Reference: Reference:

PT Analysis

	Concentration Units		Percent of PT Limits			Probability Result is Outside Limits	
	Assigned Conc'ns	PT Limits	Est. SD	Linear Bias	Recovery Bias	for Linearity	for Recovery
CalKit-1	25.0	6.0	31%	10%	0%	0.1%	0.05%
CalKit-2	100.0	10.0	38%	13%	20%	1%	1%
CalKit-3	250.0	25.0	23%	13%	9%	<0.01%	<0.01%
CalKit-4	400.0	40.0	17%	13%	16%	<0.01%	<0.01%
CalKit-5	600	60.0	13%	2%	1%	<0.01%	<0.01%
CalKit-6	750	75.0	12%	51%	49%	<0.01%	<0.01%

Linear bias based on Clinical Linearity

Failure Relationships

Probability Failure Outside Limits	Probability Failure Next Event	Probability Failure 1 of Next 2	Probability Failure 2 of Next 3
0.1%	0.001%	0.002%	0.0000%
0.2	0.005	0.01	0.0000
0.5	0.02	0.05	0.0000
1	0.1	0.2	0.0005
2	0.5	1	0.005
5	2	5	0.2
10	10	15	2
20	30	45	20
50	80	95	90

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Chapter

5

Simple Accuracy

This module provides the ability to calculate Accuracy and Reportable Range using a different model than that for the Linearity and Calibration Verification module. The fundamental difference is that in the latter one, the mean of multiple measurements is expected to be the target value of the linearity specimen. In this module, the mean of multiple measurements is expected to be anywhere in a vendor defined range of concentrations (target range). The reason for this is that the target range is established over multiple lot numbers and multiple instruments and the mean values are not identical. Failure occurs when even a single result is outside the target range.

This module may be used to assess accuracy and reportable range. By definition, calibration verification can also be assessed.

Data Requirements

Each experiment may contain between 2 and 11 specimens with up to five replicates for each specimen.

CLIA ‘88 Requirement

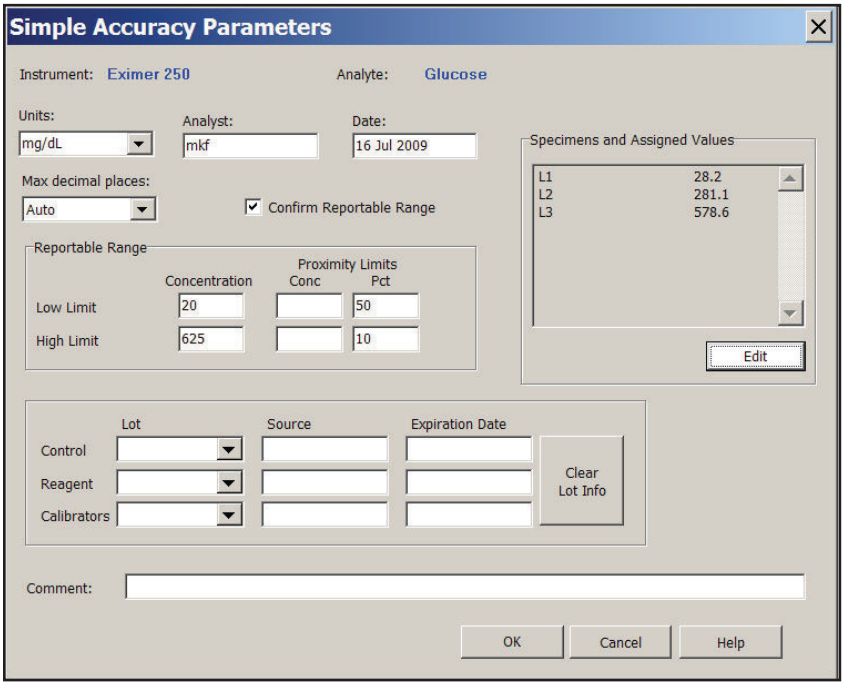
Although this module allows a minimum of two specimens, **the CLIA ‘88 regulations specify that at least three specimens be used for Calibration Verification**.

Experimental Design and Definitions

The experimental design is very simple. We recommend that each specimen be measured with 2 to 4 replicates. Then enter the results for calculation.

Parameter Screen

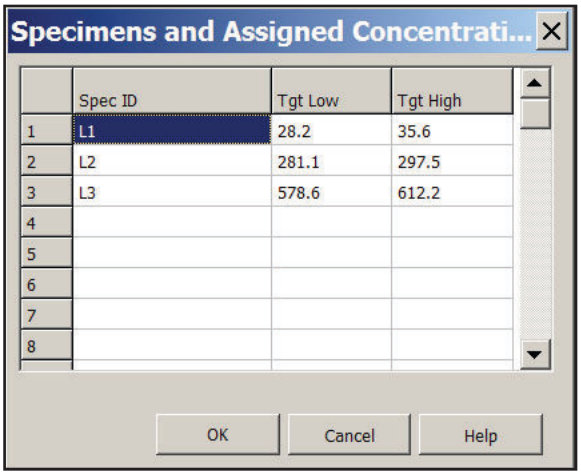
After the experiment has been created (see Chapter 3, *Common Operations* for details), the essential elements of the experiment are entered in the Simple Accuracy Parameters Screen.



The purpose of most of the fields is obvious.

To assess the Reportable Range, check the Reportable Range box. Enter the Reportable Range and the Proximity Limits. The same rules apply for defining these as with the Linearity and Accuracy module. **Optional**.

To **define specimens**, click on the Edit button in the Specimens and Assigned values section. The screen to the right will pop up. Enter the specID and the lower and upper values of the target range for each specimen. **Required**.



Comment may be used to describe why this analysis was performed (change in reagent lot number, instrument repair, and so on) or to record the other items of interest. Maximum field length: 50 characters. **Optional**.

Report Interpretation

Interpretation of the Simple Accuracy reports is relatively easy. There are only two elements on which judgment is passed: Accuracy and optionally, Reportable Range.

Statistical Analysis and Experimental Results

	Target Range	Target Midpoint	Measured Values		(1) Accuracy	(2) Rpt. Range
L1	28.2 to 35.6	31.9	32.7	32.6	Pass	Fail
L2	281.1 to 297.5	289.3	293.4	291.7	Pass	--
L3	578.6 to 612.2	595.4	603.8	602.5	Pass	Pass

(1) Accuracy passes if all measured values lie within the Target Range. 'x' indicates an excluded result.

Accuracy passes as long as all the results for each specimen lie within the target range. If any result is outside that range, then the experiment fails. We urge users of this module to be very conservative with respect to this interpretation. The vendor has performed an extensive analysis of these specimens across a broad range of instruments and reagent and calibrator lots and has determined that all results fall within the target range. If users find that results lie outside that range, the troubleshooting process should begin immediately.

Reportable Range passes if two criteria are met.

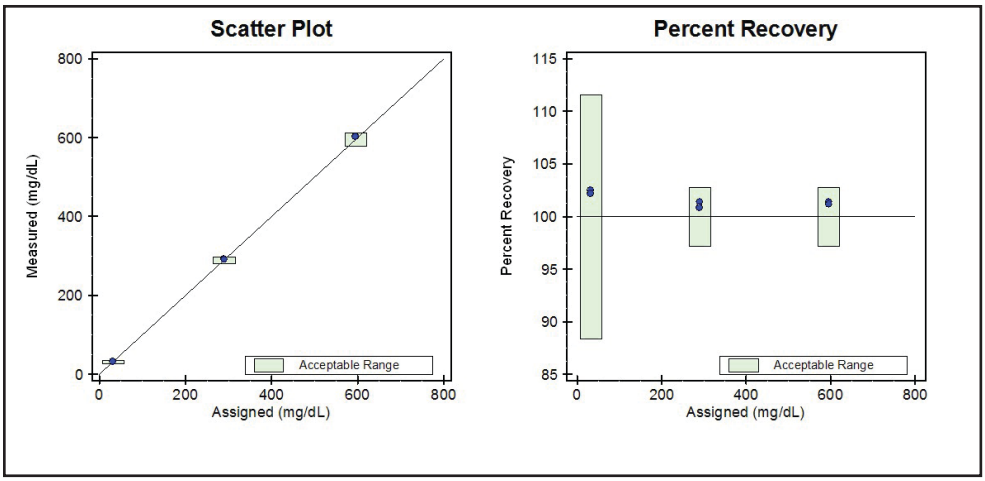
Reportable Range Criteria

Reportable Range:	20 to 625 mg/dL
Proximity Limits:	
Lower Limit	10.0 to 30.0 mg/dL
Upper Limit	562.5 to 687.5 mg/dL

- The lowest and highest specimens pass accuracy.
- The mean of the target range for the lowest and highest specimens are within proximity limits of the corresponding end of the reportable range.

Scatter and Recovery Plots

The acceptable ranges are shown in the figures by bars. If each of the results for each specimen is within the bar, the experiment passes.



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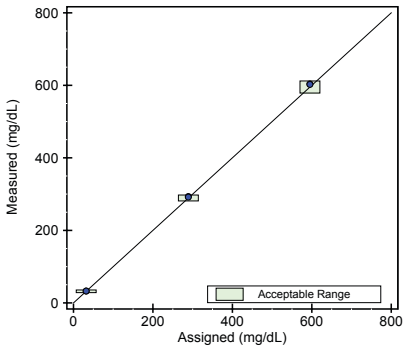
User's Manual -- Data Innovations

Glucose

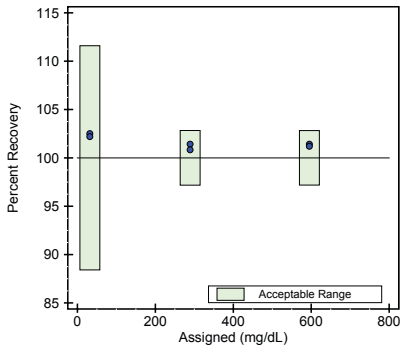
Instrument: Eximer 250

SIMPLE ACCURACY

Scatter Plot



Percent Recovery



Statistical Analysis and Experimental Results

	Target Range	Target Midpoint	Measured Values		(1) Accuracy	(2) Rpt. Range
L1	28.2 to 35.6	31.9	32.7	32.6	Pass	Fail
L2	281.1 to 297.5	289.3	293.4	291.7	Pass	--
L3	578.6 to 612.2	595.4	603.8	602.5	Pass	Pass

(1) Accuracy passes if all measured values lie within the Target Range. 'x' indicates an excluded result.

Supporting Data

Analyst:	mkf
Date:	16 Jul 2009
Units:	mg/dL
Reportable Range	20 to 625 mg/dL
Controls:	--
Reagent:	--
Calibrators:	--
Comment:	

Reportable Range Criteria

Reportable Range:	20 to 625 mg/dL
Proximity Limits:	
Lower Limit	10.0 to 30.0 mg/dL
Upper Limit	562.5 to 687.5 mg/dL

(2) Reportable range passes if the highest and lowest specimens meet accuracy criteria, and the midpoints of their Target Ranges are within Proximity Limits

Evaluation of Results

The Accuracy and Reportable Range of Glucose were analyzed on Eximer 250 over a range of 31.9 to 595.4 mg/dL. The accuracy test PASSED. All replicate measurements were within the target range for 3 of 3 specimens. Overall, 6 of 6 replicates were within their target ranges. The system FAILED reportable range tests. 1 of 2 specimens were within proximity limits.

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Signature Date

Chapter

6

EP6 Linearity

This module implements CLSI's EP6-A Linearity (CLSI:EP6) document. Since the definition of linearity is different than that in the Clinical Linearity (ClinLin) module (Chapter 4, *Linearity and Calibration Verification*), the determination of whether a set of data are linear or not should not always be expected to be the same by both methods. Reference: CLSI:EP6.

CLSI:EP6 has an advantage over ClinLin in that it is officially recognized by the FDA as being an acceptable definition of linearity.

ClinLin has an advantage over CLSI:EP6 in that the former's definition of linearity is easier to understand and that it is based solely on Performance Standards and does not include any additional complexity. Furthermore, it has been in frequent use in EE since 1995 with essentially no complaints over that period.

A brief summary of CLSI:EP6's process is:

- Prepare and assay specimens. The concentration relationships between the specimens must be known.
- Perform polynomial regression analysis using first, second and third order polynomials. Determine whether the second or third order fit is best.
- Determine the deviation for each point between the first order (linear) polynomial and the best of the other two polynomials. If any of those deviations exceeds the stated goal, then the system is not linear.

A great amount of detail in the CLSI:EP6 document has been omitted from this manual. We recommend the purchase of the CLSI:EP6 document from CLSI.

This module only assesses linearity. Unlike the other EE modules in the Linearity group, it does not assess accuracy, reportable range, nor does it verify calibration.

Experimental Design

The number of specimens and replicates recommended by CLSI:EP6 is:

- 9-11 levels, 2-4 replicates at each level to establish the linear range
- 7 - 9 levels, 2 - 3 replicates to validate a claim for an in-house or modified method.
- 5 - 7 levels, 2 replicates for laboratory confirmation of a manufacturer's range

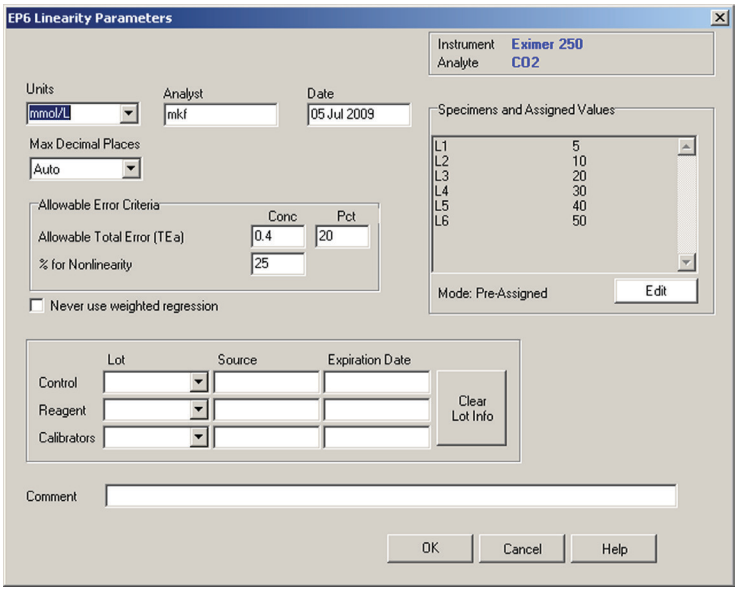
Assay the specimens in random order.

More (3 - 5) replicates may be needed, especially for those methods which exhibit large amounts of imprecision.

When the purpose is to establish a linear range, the specimens used in an initial experiment should cover a range 20 to 30% wider than the anticipated analytical range. This allows specimens at the end-points to be dropped in a subsequent experiment if the initial experiment detects nonlinearity.

Parameter Screen

After the experiment has been created (see Chapter 3, *Common Operations* for details), the essential elements of the experiment are entered in the Parameters Screens.



There are several major similarities between CLSI:EP6 and ClinLin. They include:

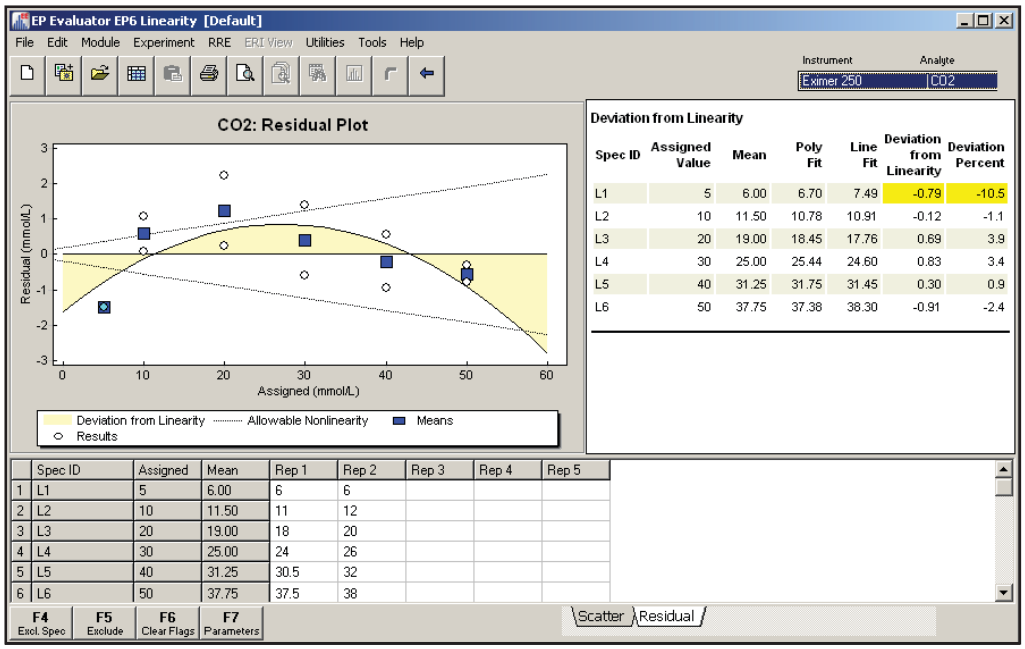
- Allowable Total Error is a required field.
- Specimens and their assigned values are described identically. See *Value Mode Section* in Chapter 4 for details.

Significant differences include:

- Entry of value for "% for Nonlinearity" is required in contrast to "% for Systematic Error" in ClinLin. We recommend a value between 10% and 25%. This is different from the 25 to 50% recommended for the Clinical Linearity module. The reason is that the Clinical Linearity bases its assessment on multiple types of systematic error. EP6 only assesses one type of systematic error, namely non-linearity. Consequently the percent allowed is smaller.
- A check box exists so the potential of using weighted regression can be turned off.
- No provisions are made for reportable range and/or random error.

Experiment Detail Screen

The Experiment Detail Screen (shown below) provides access to all details for linearity-type experiments and resembles the one in the Linearity module.



Linearity Reports

Linearity Claim

The Linearity Claim is shown below:

Data IS NOT linear within allowable nonlinearity of 0.1 mmol/L or 5%
Fit of polynomial to data is acceptable (p=0.356)
Power of test to detect nonlinearity is poor (ratio=1.5)

Statistical Analysis Table

The statistical analysis table displays the calculated results for each point. Among other things, it shows which point(s) are non-linear as well as certain statistics showing deviation from CLSI:EP6's defined linearity.

Statistical Analysis

Specimen	Assigned Value	Mean	Poly. Fit	Line Fit	Deviation from Linearity	Deviation Percent
L1	5	6.00	6.70	7.49	-0.79	-10.5o
L2	10	11.50	10.78	10.91	-0.12	-1.1
L3	20	19.00	18.45	17.76	0.69	3.9
L4	30	25.00	25.44	24.60	0.83	3.4
L5	40	31.25	31.75	31.45	0.30	0.9
L6	50	37.75	37.38	38.30	-0.91	-2.4

***: Absolute value > 99% x: Excluded o: Exceeds allowable nonlinearity

Evaluation Criteria

The criteria used to define linearity are displayed here.

Evaluation Criteria

Allowable Total Error (TEa)	0.4 mmol/L or 20.0%
% for Nonlinearity	25%
Allowable Nonlinearity	0.1 mmol/L or 5.0%
Use weighted regression?	If applicable

Supporting Data

Many types of data are shown in this screen. They include slope, intercept, units and value mode.

The slope and intercept are not very important in this context as the purpose of this module is to assess linearity, not accuracy. Furthermore, with many of the modes, the **true** concentrations of the specimens are not known. Only the concentrations relative to the other specimens in the series are known.

Supporting Data

Slope	0.685 (0.635 to 0.734)
Intercept	4.06 (2.56 to 5.56)
Analyst	mkf
Date	05 Jul 2009
Units	mmol/L
Value Mode	Pre-Assigned
Controls	--
Reagents	--
Calibrators	--

Experimental Results

A full listing of the results is displayed in this table. The sub-table at the bottom of this table refers to statistics calculated on the basis of the SD or the CV. Consult CLSI:EP6 for details.

Experimental Results

Specimen	Mean	SD	CV	Measured Concentrations	
L1	6.00	0.00	0.0	6	6
L2	11.50	0.71	6.1	11	12
L3	19.00	1.41	7.4	18	20
L4	25.00	1.41	5.7	24	26
L5	31.25	1.06	3.4	30.5	32
L6	37.75	0.35	0.9	37.5	38
Pooled		**0.98**	**4.8**		
Degrees of Freedom		6	6		
Bartlett's p		0.410	0.531		
Accept equality hypothesis?		Yes	Yes		

Polynomial Fit Analysis

The polynomial fit analysis shows the first, second and third order fits. The best of them is bolded. In this case, it is the second order fit which is best. Consult CLSI:EP6 for the criteria by which the best fitting curve is selected.

Polynomial Fit Analysis

Polynomial	Coefficients and their T statistics				Std Error of Estimate	"Best" Polynomial
	Constant	X	X^2	X^3		
Line	4.063 6.0	0.6847 30.9			1.223	
2nd Order	**2.447** **2.7**	**0.8675** **10.5**	**-0.003376** **2.3**		**1.028**	**Best**
3rd Order	0.1913 0.1 (*)	1.303 5.8	-0.02256 2.4	0.0002309 2.1 (*)	0.8825	

Analysis based on ordinary (unweighted) regression. Standard error expressed in concentration units (mmol/L)
(*) Statistically equivalent to zero

Report Interpretation

Interpretation of reports is quite different from the ClinLin module because of the difference in the purpose of the experiment and how the two types of linearity are defined. In ClinLin's case, linearity is defined by the ability to draw a straight line through a series of error bars. In CLSI:EP6's case, linearity is declared if the deviation between the two fitted values (linearity and best polynomial) does not exceed allowable non-linearity.

We invite you to experiment by fitting various sets of linearity data to both CLSI:EP6 and ClinLin. We are interested in your conclusions about which is best.

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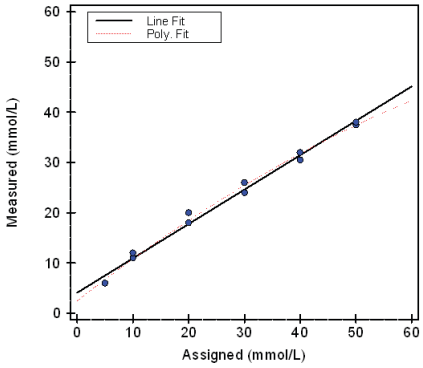
CO2

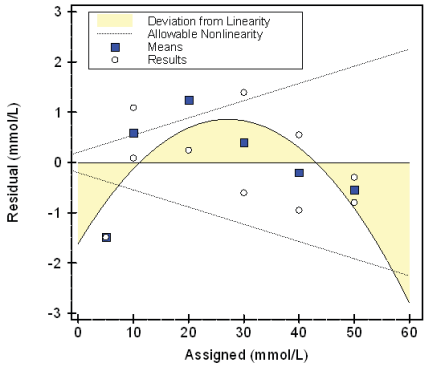
Instrument Eximer 250

CLSI EP6 Linearity

Scatter Plot



Residual Plot



Data IS NOT linear within allowable nonlinearity of 0.1 mmol/L or 5%

Fit of polynomial to data is acceptable (p=0.356)

Power of test to detect nonlinearity is poor (ratio=1.5)

Statistical Analysis

Specimen	Assigned Value	Mean	Poly. Fit	Line Fit	Deviation from Linearity	Deviation Percent
L1	5	6.00	6.70	7.49	-0.79	-10.5O
L2	10	11.50	10.78	10.91	-0.12	-1.1
L3	20	19.00	18.45	17.76	0.69	3.9
L4	30	25.00	25.44	24.60	0.83	3.4
L5	40	31.25	31.75	31.45	0.30	0.9
L6	50	37.75	37.38	38.30	-0.91	-2.4

***: Absolute value > 99% x: Excluded o: Exceeds allowable nonlinearity

Evaluation Criteria

Allowable Total Error (TEa)	0.4 mmol/L or 20.0%
% for Nonlinearity	25%
Allowable Nonlinearity	0.1 mmol/L or 5.0%
Use weighted regression?	If applicable

Supporting Data

Slope	0.685 (0.635 to 0.734)
Intercept	4.06 (2.56 to 5.56)
Analyst	mkf
Date	05 Jul 2009
Units	mmol/L
Value Mode	Pre-Assigned
Controls	--
Reagents	--
Calibrators	--
Comment	

Accepted by: _____ _____

Signature Date

EP Evaluator®

User Manual -- Data Innovations, LLC

CO2

Instrument Eximer 250

CLSI EP6 Linearity

Experimental Results

Specimen	Mean	SD	CV	Measured Concentrations	
L1	6.00	0.00	0.0	6	6
L2	11.50	0.71	6.1	11	12
L3	19.00	1.41	7.4	18	20
L4	25.00	1.41	5.7	24	26
L5	31.25	1.06	3.4	30.5	32
L6	37.75	0.35	0.9	37.5	38
Pooled		**0.98**	**4.8**		
Degrees of Freedom		6	6		
Bartlett's p		0.410	0.531		
Accept equality hypothesis?		Yes	Yes		

x: Excluded

Polynomial Fit Analysis

Polynomial	Coefficients and their T statistics				Std Error of Estimate	"Best" Polynomial
	Constant	X	X^2	X^3		
Line	4.063 6.0	0.6847 30.9			1.223	
2nd Order	**2.447** **2.7**	**0.8675** **10.5**	**-0.003376** **2.3**		**1.028**	**Best**
3rd Order	0.1913 0.1 (*)	1.303 5.8	-0.02256 2.4	0.0002309 2.1 (*)	0.8825	

Analysis based on ordinary (unweighted) regression. Standard error expressed in concentration units (mmol/L)
(*) Statistically equivalent to zero

Chapter

7 Trueness

The purpose of the EE Trueness Module is to provide a mechanism for clinical laboratories to assess the characteristics of Trueness, Accuracy, and Uncertainty for the methods used in their settings. This module is intended to satisfy the Trueness, Accuracy, and Uncertainty requirements for Comité Français d'Accréditation (COFRAC) certification in France. The source of the data for this module is monthly IQC summary data, EQC group data, or EQA group data.

Also known as proficiency testing, **External Quality Assurance (EQA)** programs, such as CAP or EQAS, provide a set of specimens to be analyzed by a laboratory as though they were patient specimens. The laboratory's single result for a measurand is submitted to the provider for accuracy assessment versus the defined target evaluation criteria. In the Trueness module, the laboratory's *single* result is compared to the selected group mean for the same specimen. The bias assessed in this manner is a measure of Accuracy. ISO/IEC Guide 99 defines **Accuracy** as the closeness of agreement between a measured quantity value and a true quantity value of a measurand.

Laboratories which participate in **External Quality Control** (EQC) programs use the specified lot numbers of control materials for their daily QC, and submit the summary results for the defined period (often monthly) to the provider for analysis. The group mean from multiple labs is the reference quantity, assumed to be the "true" result. The bias assessed in this manner is a measure of **Trueness**. Trueness is defined in ISO 3534-1 as "the closeness of agreement between the average value obtained from a large series of test results and an accepted reference value." In other words, EQC experiments compare the average of a lab's many test results to the reference value determined by the provider. The participating laboratory's values are compared to the selected group summary means for the same time period.

Uncertainty is evaluated for both EQA and EQC types of experiments. In the Trueness module, only the precision and bias components are used in the Uncertainty calculation. ISO/IEC Guide 99 defines Uncertainty as a "non-negative parameter characterizing the dispersion of the quantity values being attributed to a measurand, based on the information used". The magnitude of Uncertainty depends on contributions of the variables impacting either bias or imprecision involved in the scope of measurement, such as different days, different runs, different operators, method interferences, calibration error, etc.

Terms

Measurand: In the Trueness module, the term "measurand" is used instead of "analyte". The technical difference between the two terms is described in ISO 17511. The term analyte refers to a measurement of a given analytical component regardless of its environment, whereas measurand refers to an analytical component in a specific environment. For example, the analyte glucose in serum glucose, whole blood glucose, and urine glucose corresponds to three different measurands.

Method: In this module the term "method" is used rather than Instrument. The method describes the specific assay formulation or test for the measurand as applied to a specific platform. It includes the elements of sample type(s), reagents, software, and hardware. It could also denote a manually performed method.

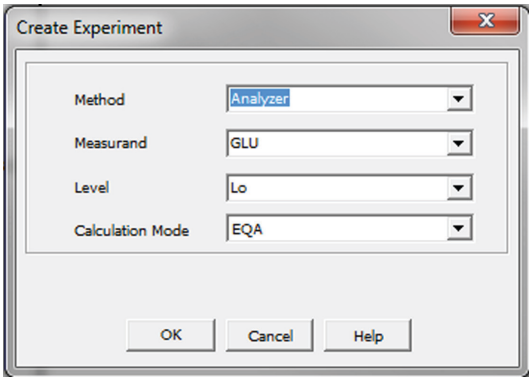
IQC: Internal Quality control result(s) for the laboratory daily QC. The IQC mean, SD, and CV% are input into the module parameter screen. Comparisons are improved if the lab IQC mean is near the level chosen for the experiment.

Setting Up a New Experiment

Here are three ways to create an experiment:

- Choose **New** from the **Experiment** menu
- Choose **New** from **Policies from the Experiment** menu
- Choose **Create Experiments** from the **Rapid Result Entry** menu

Access the **Create Experiment** window by selecting the **New** command on the **Experiment** menu. Use the **Create Experiment** window to define the key descriptors of a new experiment in the Trueness module:



Method: Select or enter the method.

Measurand: Select or enter the measurand.

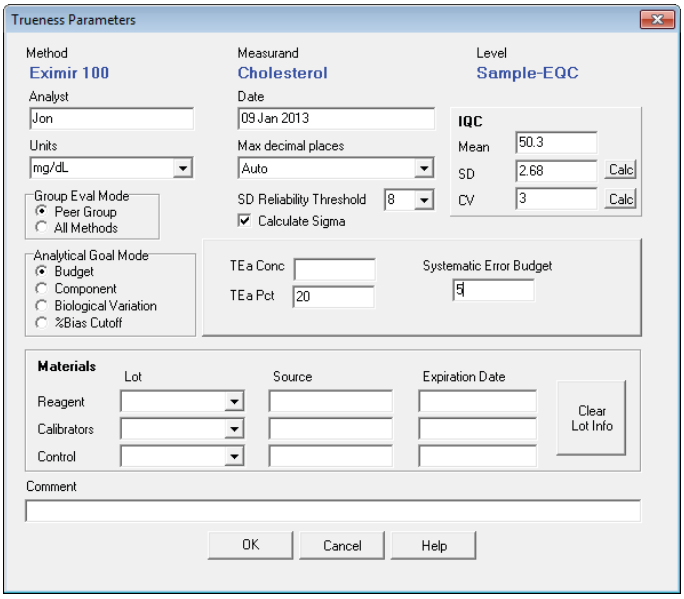
Level: Level describes the scope of the experiment. For example, in cases where all of the data for a Method and Measurand are used, the Level could be set to "All". In cases where only low result values are used, the level could be defined as "Low". Once the experiment is created, the level and calculation mode entered into this window are combined to form the experiment identifier.

Calculation Mode: Specify the Calculation Mode as either EQC (External Quality Control) or EQA (External Quality Assurance).

When creating an experiment using policies, you can define Level Cutoff values in Policies which can be used, in combination with RRE, to categorize incoming data by level. If no Cutoffs are specified in Policies, then all of the incoming data will be put in an experiment with Level of "All" (either "EQA-All" or "EQC-All", or "All-EQA" or "All-EQC", depending on the prefix/suffix value in Preferences, and the EQA/EQC option chosen during RRE). Example data can be found in the Resources folder in the EE installation directory. For more information on the Level Cutoff values see Chapter 37, *Policy Definition*.

Parameters

Define the parameters for each experiment from the Trueness Parameters window. Required fields will be highlighted in yellow. Note that the fields required depend on the selected Analytical Goal Mode.



IQC: Enter **Internal QC** values into the IQC panel.

IQC SD: Click the **Calc** button to calculate the IQC SD from the IQC Mean and CV.

IQC CV: Click the **Calc** button to calculate the IQC CV from the IQC Mean and SD.

SD Reliability Threshold (SDRT): Specify the number of specimens required to calculate reliable statistics using the mean of the biases.

- If the number of specimens falls below the threshold, Uncertainty is calculated using the maximum of the absolute value of the biases.
- If the number of specimens is greater than or equal to the SDRT, the absolute value of the mean of the biases is used in the Uncertainty calculation.

NOTE: The default SDRT is defined, and can be edited, on the **Trueness** tab of the **Preferences** window. Access the Preferences window from the **File** menu.

Calculate Sigma: This option is enabled only for EQC experiments when the Analytical Goal Mode is set to **Budget** in the Parameters screen. **TEa Conc** and/or **TEa Pct** values are required. Although the **Systematic Error Budget** field is required, this value is not used in the Sigma calculation. Additionally, you must enter Lab SD values in the Experiment Detail Screen.

Group Evaluation Mode: The Group Evaluation Mode allows you to select whether the Peer Group or All Methods group is used to evaluate if each specimen Passes or Fails.

Analytical Goal Mode (AG): Depending on the default analytical goal mode selected, different fields may be required on the Parameters screen. Synonyms for Analytical Goal are AG, TEa, allowable total error, and desirable analytical goal. While analytical goals can be shown in many forms and can be derived from several sources, this module can use four models for entry of AG to assess pass/fail criteria:

Budget: This is the traditional EE TEa model. A concentration and/or a percent are specified for TEa, and a budget specified for systematic error. The remainder is assumed to be the budget for random error. When both a concentration component and a percent are specified, there is a crossover point where the percent of that level is equivalent to the concentration component.

Component: Allowable bias is again specified as either concentration or percent or both, and often is available from the IVD manufacturer. If both the bias concentration and percent are entered, the report will include additional information about Uncertainty at or below a cutoff concentration.

Biological Variation (BV), a.k.a. Ricos: EP Evaluator uses the Ricos model to determine the AG goal. This model lets the user select a Factor to evaluate their method compared to a specified performance level as: minimal (3), desirable (2), and optimal (1). Values for many measurands can be obtained from the EE Tools menu, Biological Variation Table. These can be entered in the parameter screen as follows:

Inputs:	
CVi	Intra-individual biological variation
CVg	Inter-individual biological variation
Factor (F) for level of performance desired	Minimal (3), desirable (2), or optimal (1)
Z	Z = 1.65 for a 95% Confidence level and 2.33 for a 99% Confidence level

From these inputs, the AG goal is calculated as follows:

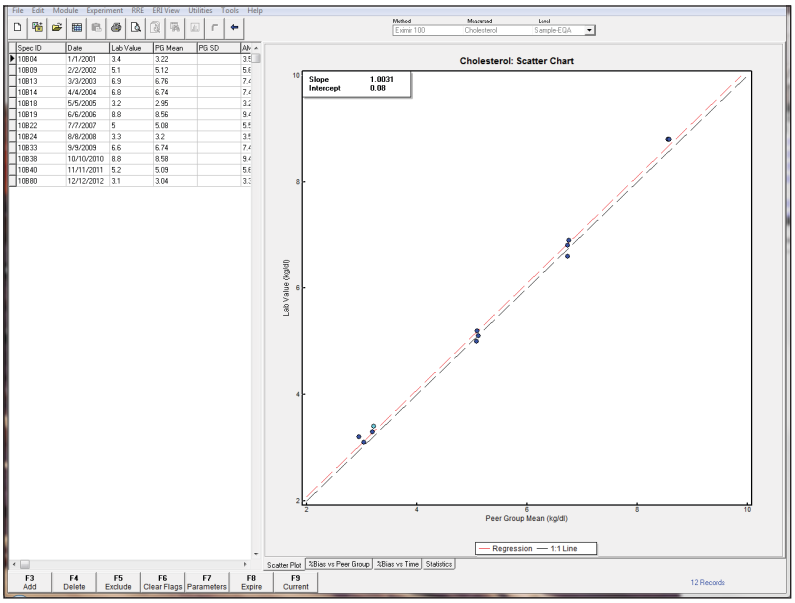
- CVa : (allowable analytical precision) CVa = F * 0.25 * CVi
- Ba: (allowable bias) Ba = F * 0.125 * sqrt(CVi^2 + CVg^2)
- Total Allowable Error : TEa = (Z * CVa) + Ba

The CVi and CVg biological variation values, the desired Level, and the Confidence Interval are required.

Percent Bias Cutoff: The %bias cutoff value is entered as a single value by the user.

Experiment Detail Screen

EQA Experiment Detail Screen



The experiment detail screen for an EQA experiment requires the entry of a specimen ID, date, lab value and either the peer group mean or all method mean. Enter the Peer Group SD and or the All Methods SD to estimate uncertainty for each specimen.

EQA experiments are limited to 50 specimens; the 51st specimen added to an EQA experiment prompts the automatic expiration of the oldest specimen. The dates are only present so that the specimens appear in chronological order in the Percent Bias Points graph.

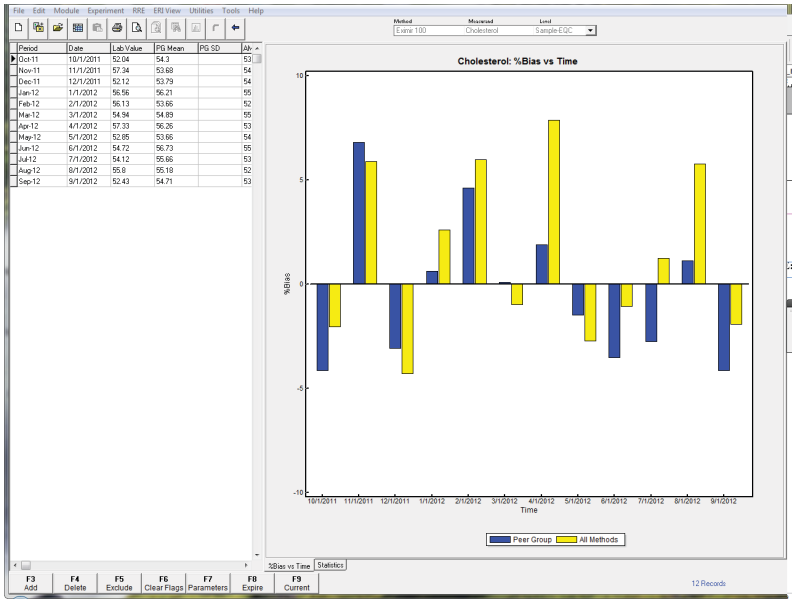
EQC Experiment Detail Screen

The experiment detail screen for an EQC experiment requires the entry of a time period, a date, a lab value, and either a peer group mean or an all method mean. If desired, users may enter both a peer group mean and all method mean, as both will be charted in the %Bias vs. Time plot. However, only the selected Group Evaluation Mode is used in Pass/Fail criteria.

In order to calculate Sigma, you must enter Lab SD value(s) in the Experiment Detail Screen. To calculate Uncertainty for each specimen, you must enter the Peer Group SD and/or the All Methods SD.

EQC experiments are limited to 12 specimens; the 13th specimen added to an experiment prompts the automatic expiration of the oldest specimen.

Functions Available from the Experiment Detail Screen



Add (F3): Add a row to the grid.

Delete (F4): Delete a row from the grid.

Exclude (F5): Select an included specimen and press **Exclude (F5)** to exclude it; the specimen will not be included in the calculation of statistics for the experiment. If the specimen is already excluded, **Exclude (F5)** will remove the Excluded flag from the specimen.

Clear Flags (F6): Clears the Excluded and Expired flags in the experiment.

Parameters (F7): Open the Parameters window to configure your Trueness Experiment.

Expire (F8): Select a specimen to toggle between Expire/Unexpired; once expired the specimen no longer appears in the Experiment Detail screen.

Current/All toggle: Toggle between showing all data and current data. **All** displays expired and unexpired specimens; **Current** display only unexpired specimens.

NOTE: To view all specimens in a Trueness experiment, including expired specimens, click the **Current/All (F9)** toggle button found at the bottom of the Experiment Detail Screen.

Trueness Calculation Modes

The Trueness module uses two calculation modes, which the user specifies upon the creation of a new experiment in the Trueness module.

NOTE: If a specimen mean for the selected comparator group is zero, this will make it impossible to compute the Percent Bias for that specimen, which in turn means the Trueness module can not evaluate Pass/Fail criteria for that specimen. In this scenario, the specimen (and the experiment) will Fail unless the specimen is excluded.

EQA Calculation Mode

External Quality Assurance (EQA) data is provided by organizations such as CAP or EQAS. These organizations provide a set of specimens to be analyzed by a laboratory as though they were patient specimens. In the Trueness module, the laboratory's single result is compared to the selected group mean for the same specimen. The bias assessed in this manner is a measure of Accuracy.

EQA Accuracy Report: The calculated bias for each EQA specimen is the difference between the lab value and the selected group mean. The calculated %bias is compared to the selected AG %bias cutoff to determine pass/fail for each specimen as well as for the overall experiment. In this mode, the IQC result is the lab's daily overall QC mean and SD at a particular level. The estimate of bias or uncertainty may be improved if the lab IQC value is near a key medical decision value, and/or separate experiments are created for different levels. The experiment evaluation is expressed as Pass/Fail versus the selected Analytical Goal (AG).

EQA Specific Calculations

AG is calculated assuming the presence of both systematic and random error components in the reported results. Therefore 100% of the TEa is used as the AG.

- **Budget model:**
  AG = TEa
- **Specimen component model:**
  AG = Bias component specification + (1.65 * (IQC SD))
- **Biological Variation model:**
  AG = TEa
- **%Bias cutoff:**
  AG = %Bias cutoff as entered by the user

EQA Graphs

1. **Scatter plot:** Shown for the EQA mode only, this plot shows each lab result vs. the selected group mean. A slope and intercept are calculated using ordinary least squares linear regression.
2. **Uncertainty plot:** Shown for the EQA mode only, and then only if at least one selected group SD is present; the Uncertainty calculated for each lab value is displayed vs. the corresponding group value. This is especially useful if multiple EQA levels have been entered.
3. **%Bias vs. Selected Group:** Shown for the EQA mode only, the observed %bias compared to the selected group is plotted vs. the selected group mean for each specimen. This is useful to visually compare the different levels
4. **%Bias vs. Time:** The observed %bias compared to the selected group mean is shown in the order of the date of observations. The EQA mode graph (unlike the EQC mode graph) only shows data for the selected group. Because this plot is chronological, it is useful for identifying bias trends over time.

EQC Calculation Mode

EQC data is usually extracted from reports provided by instrument or QC vendors. This data includes both lab means as well as peer group and all methods group means.

EQC Trueness Report: In this calculation mode, the lab value is the lab's Monthly Summary Mean for the level of EQC material being evaluated. The input IQC values are the laboratory Overall Mean and SD. The difference between the lab value and the selected group mean for the corresponding time period is the calculated bias for each EQC specimen. The calculated %bias is compared to the AG %bias cutoff to determine Pass/Fail for each specimen as well as for the overall experiment. The experiment evaluation is expressed as Pass/Fail versus the selected Analytical Goal.

EQC Specific Calculations

AG is calculated assuming the presence of systematic error only.

- **Budget model**:
  AG = TEa * Systematic error budget
- **Specimen component model**:
  AG = Bias component specification
- **Biological Variation model**:
  AG = Ba
- **%Bias cutoff**:
  AG = %Bias cutoff as entered by the user

EQC Graphs

1. **% Bias vs. Time:** The observed % bias compared to the selected group mean is shown in the order of the date of observations. If both Peer Group and All Method data is available, then both sets of data are plotted in the graph. However, the selected Group Evaluation Mode is used to specify the data used to determine Pass/Fail statistics. Because this plot is chronological, it is useful for identifying bias trends over time.

Pass/Fail Criteria for EQA or EQC:

- The experiment passes if there are at least 3 unexcluded specimens and all unexcluded specimens pass the bias test, as defined below:
  - **The bias test for Trueness (EQC mode)**: Each specimen passes if the bias from the selected group mean does not exceed the specified analytical goal (AG), Trueness is evaluated as Pass/Fail and is not revealed as a numerical value. If any result exceeds the AG, then the experiment fails.
  - **The bias test for Accuracy (EQA mode)**: Each specimen passes if the bias from the selected group mean does not exceed the analytical goal (AG) specified. Accuracy is only evaluated in a Pass/Fail manner: it is not revealed as a numerical value. If any result exceeds the AG, then the experiment fails.

Uncertainty

Uncertainty will be calculated for each specimen only if the SD from the selected group is entered. The overall Uncertainty at the IQC level is always calculated.

The relative Uncertainty is estimated at the crossover point in the following scenarios:

- If the AG goal is the budget model, and both a total allowable error concentration and a percent are entered
- If the AG goal is the Component mode, and a Bias Percent and Bias concentration are entered

The following example is for glucose with an IQC mean of 115, and a TEA of 6 mg/dL or 10%. The crossover value is 60:

> "At a value of 115 mg/dL, uncertainty is estimated to be 10 (absolute) or 8.3% (relative). At values less than or equal to 60 mg/dL, uncertainty is estimated to be 5 mg/dL. Calculated using mean of bias. The experiment Passes."

Uncertainty calculations follow the standard calculation as described in SH-GTA-14. Uncertainty is computed for 1 SD, and then multiplied by 2 to closely approximate the 95% confidence limit.

Uncertainty (U2) for individual specimens:

U2 = 2 * (sqrt(sd of selected group specimen)^2) + (ABS(bias of lab result to peer group)^2)

Overall Uncertainty:

U2 = 2 * sqrt (A^2 + B^2 + C^2) where

A = IQC SD

B = mean SD of the group bias across all specimens/periods.

When **N** <SDRT, B = 0.

C = D/sqrt(3)

If **N>= SDRT**, D =mean Bias of the group

If **N < SDRT**, D = max(absolute value of the Bias across all specimens/periods)

Sigma Calculation

The Sigma calculation is enabled by a checkbox in the Parameters screen, or if enabled in Trueness Policies\Modules and Options. Sigma will only be calculated when the calculation mode is EQC and the Analytical Goal Mode is set to Budget. The Lab SD is required for every period of EQC data. A single Sigma metric is calculated for the entire experiment, and uses mean values for all periods of EQC data.

Sigma is calculated using the following equation:

(AG TEa % minus the observed mean bias %) / the laboratory mean CV

The AG TEa % is derived from the budget TEa in the Parameters screen. If the applicable TEa for the selected group result is expressed as a concentration, the TEa % used in the Sigma calculation is TEa conc *100 /selected group mean. Sigma is calculated using 100% of the TEa, and is not affected by the SEa %. The Sigma metric does not have pass / fail criteria, however a Sigma metric greater than 6 is usually considered excellent performance. The larger the Sigma, the better the process:

- Sigma metric of 6.0 or greater - Excellence performance
- Sigma metric of 4.0 to 6.0 - Good performance
- Sigma metric of 3.0 to 4.0 - Fair performance
- Sigma metric of 2.0 to 3.0 - Marginal performance
- Sigma metric less than 2.0 - Poor performance

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User Guide -- Data Innovations

Cholesterol
Method Eximir 100
Level Sample-EQA

Trueness - EQA

At a value of 2.5 mmol/L, uncertainty is estimated to be 0.4 (absolute) or 12.5% (relative). Calculated using mean of bias.
The experiment Fails (Maximum %Bias was 8.5).

Statistical Summary

	Mean	*Bias*	*%Bias*	*Max %Bias*
Lab	5.52	--	--	--
Peer Group	5.42	0.09	1.7	8.5
All Methods	5.97	-0.45	-7.5	-10.9

N: 12

Supporting Data

Analyst	Jon
Expt Date	09 Jan 2013
Units	mmol/L
Reagent	--
Calibrator	--
SD Rel Thresh	8 (Calculated using mean of bias)
Comment	

User Specifications

Group Mode	Peer Group
AG Mode	%Bias Cutoff
%Bias Cutoff	3.5

IQC Stats

Mean	2.5
SD	0.076
CV	3

Trueness Data

		Peer Group				All Methods				%Bias	
SpecID	Lab	Result	SD	%Bias	Pass	Result	SD	%Bias	Pass	Cutoff	Uncert
10B04	3.4	3.22	--	5.6	No	3.54	--	-4.0	--	3.5	--
10B09	5.1	5.12	--	-0.4	Yes	5.63	--	-9.4	--	3.5	--
10B13	6.9	6.76	--	2.1	Yes	7.44	--	-7.3	--	3.5	--
10B14	6.8	6.74	--	0.9	Yes	7.41	--	-8.2	--	3.5	--
10B18	3.2	2.95	--	8.5	No	3.25	--	-1.5	--	3.5	--
10B19	8.8	8.56	--	2.8	Yes	9.42	--	-6.6	--	3.5	--
10B22	5	5.08	--	-1.6	Yes	5.59	--	-10.6	--	3.5	--
10B24	3.3	3.2	--	3.1	Yes	3.52	--	-6.3	--	3.5	--
10B33	6.6	6.74	--	-2.1	Yes	7.41	--	-10.9	--	3.5	--
10B38	8.8	8.58	--	2.6	Yes	9.44	--	-6.8	--	3.5	--
10B40	5.2	5.09	--	2.2	Yes	5.6	--	-7.1	--	3.5	--
10B80	3.1	3.04	--	2.0	Yes	3.34	--	-7.2	--	3.5	--

X: excluded from calculations

Accepted by: _____ _____
Signature Date

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Trueness Report - EQA

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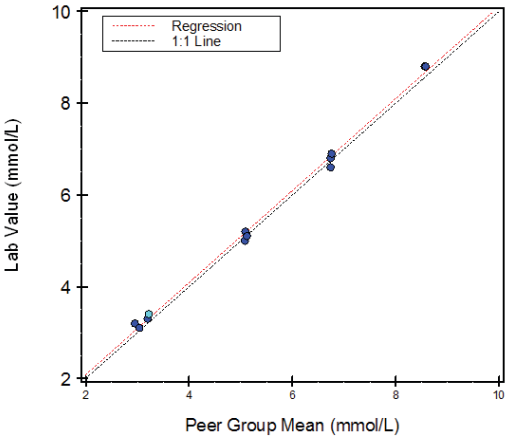
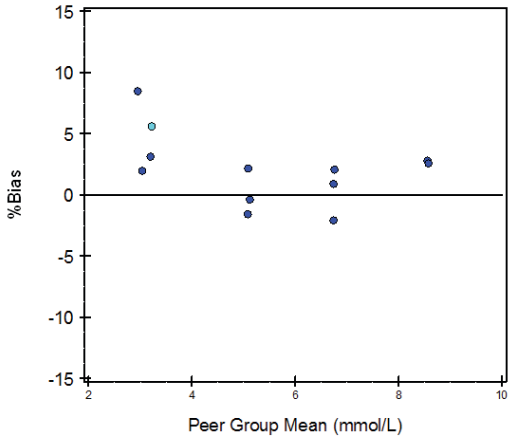
User Guide -- Data Innovations

Cholesterol
Method Eximir 100
Level Sample-EQA

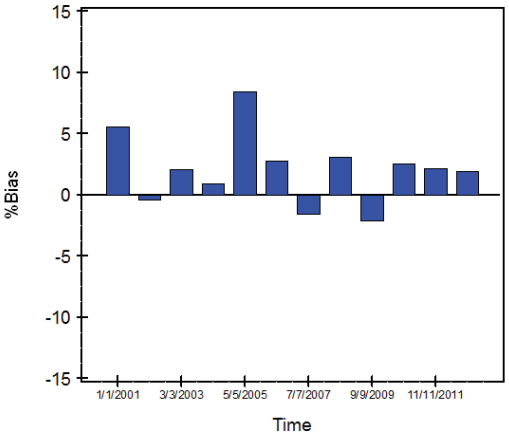
Scatter Plot



%Bias vs Peer Group



%Bias vs Time



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Trueness Report - EQC

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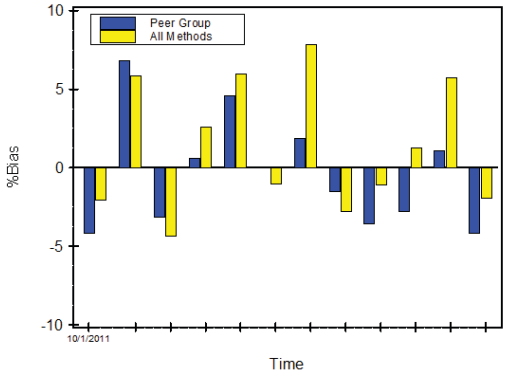
User Guide -- Data Innovations

Cholesterol
Method Eximir 100
Level Sample-EQC

Trueness - EQC

At a value of 50.3 mmol/L, uncertainty is estimated to be 6.7 (absolute) or 13.1% (relative). At values less than or equal to 100.0 mmol/L, uncertainty is estimated to be 13.2 mmol/L.
Calculated using mean of bias.
The experiment Passes.

%Bias vs Time



Supporting Data

Analyst	Jon
Expt Date	09 Jan 2013
Units	mmol/L
Reagent	--
Calibrator	--
Control	--
SD Rel Thresh	8 (Calculated using mean of bias)
Comment	

Statistical Summary

	Mean	*Bias*	*%Bias*	*Max %Bias*
Lab	54.70	--	--	--
Peer Group	54.89	-0.20	-0.4	6.8
All Methods	53.99	0.71	1.3	7.9

N: 12

User Specifications

Group Mode	Peer Group
AG Mode	Budget
Budget Conc	15
Budget Pct	15
Sys Error Budget	85

IQC Stats

Mean	50.3
SD	2.68
CV	3

Trueness Data

		Peer Group				All Methods				%Bias	
Period	**Lab**	**Result**	**SD**	**%Bias**	**Pass**	**Result**	**SD**	**%Bias**	**Pass**	**Cutoff**	**Uncert**
Oct-11	52.04	54.3	--	-4.2	Yes	53.14	--	-2.1	--	23.5	--
Nov-11	57.34	53.68	--	6.8	Yes	54.15	--	5.9	--	23.8	--
Dec-11	52.12	53.79	--	-3.1	Yes	54.48	--	-4.3	--	23.7	--
Jan-12	56.56	56.21	--	0.6	Yes	55.13	--	2.6	--	22.7	--
Feb-12	56.13	53.66	--	4.6	Yes	52.97	--	6.0	--	23.8	--
Mar-12	54.94	54.89	--	0.1	Yes	55.49	--	-1.0	--	23.2	--
Apr-12	57.33	56.26	--	1.9	Yes	53.15	--	7.9	--	22.7	--
May-12	52.85	53.66	--	-1.5	Yes	54.35	--	-2.8	--	23.8	--
Jun-12	54.72	56.73	--	-3.5	Yes	55.32	--	-1.1	--	22.5	--
Jul-12	54.12	55.66	--	-2.8	Yes	53.45	--	1.3	--	22.9	--
Aug-12	55.8	55.18	--	1.1	Yes	52.76	--	5.8	--	23.1	--
Sep-12	52.43	54.71	--	-4.2	Yes	53.47	--	-1.9	--	23.3	--

X: excluded from calculations

Accepted by: _____ _____
Signature Date

Trueness Report - EQC- Sigma Calculated

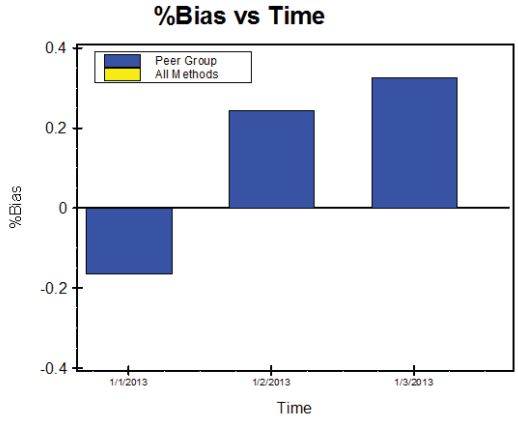
EP Evaluator®

Clinical Laboratory -- Kennett Community Hospital

Sodium
Method Eximir 100
Level Sigma-EQC

Trueness - EQC

At a value of 122.4 mmol/L, uncertainty is estimated to be 3 (absolute) or 1.7% (relative).
Calculated using maximum of bias.
Sigma: 3.9
The experiment Passes.



Supporting Data

Analyst	mkf
Expt Date	08 Jan 2014
Units	mmol/L
Reagent	--
Calibrator	--
Control	--
SD Rel Thresh	8 (Calculated using maximum of bias)
Comment	
Sigma	3.9

Statistical Summary

	Mean	*Bias*	*%Bias*	*Max %Bias*
Lab	122.7	--	--	--
Peer Group	122.6	0.2	0.1	0.3
All Methods	--	--	--	--

N: 3

User Specifications

Group Mode	Peer Group
AG Mode	Budget
Budget Conc	4
Budget Pct	
Sys Error Budget	50

IQC Stats

Mean	122.4
SD	0.995
CV	0.8

Trueness Data

	Lab		Peer Group				%Bias	
Period	**Result**	**SD**	**Result**	**SD**	**%Bias**	**Pass**	**Cutoff**	**Uncert**
Jan	122.2	0.962	122.4	--	-0.2	Yes	1.6	--
Feb	122.8	1.03	122.5	--	0.2	Yes	1.6	--
Mar	123.2	0.996	122.8	--	0.3	Yes	1.6	--
Means	122.7	1.0	122.6	--	0.1			

X: excluded from calculations

Accepted by: _____ _____
Signature Date

EP Evaluator 11.1.0.17
Default Printed: 19 Feb 2014 10:51:29 Page 1

Chapter

8

Simple Precision

The Simple Precision (SP) module calculates a mean, standard deviation (SD), coefficient of variation (CV), and a 95% confidence interval for the SD. This is the traditional precision calculation performed on a pocket calculator and is commonly used with sample populations.

Table 8.1
Differences between Simple and Complex Precision Modules

	Simple Precision	Complex Precision
Calculates within-run, between-run and between-day precision	No	Yes
Multiple-day experiment	Optional - All results are treated equally. Number of days doesn't matter	Required
Minimum Experiment Size	3 results. May be over one or more days	3 days or 8 runs, whichever is greater
Outlier Detection	None	Based on Preliminary Estimate of Precision

Data Requirements

A minimum of 3 results are required to display the graph on the screen and to generate a report. A good precision study should include 20-50 replicates. Mathematically, it is possible to calculate SD and CV from only 3 replicates, but it is not a very reliable estimate. There is no requirement nor provision for replicate results or multiple runs per day. The maximum number of results is 10,000.

NOTE: Delays can be expected if you try to calculate the results for an experiment with more than a few thousand results. If you attempt to manually enter large numbers of results (>500) there may be significant delays due to some computations being performed after each result is entered.

Key Statistics

Key Statistics for this module include:

Observed Mean: The mean of all unexcluded, numerical results entered into the SP experiment.

Target Mean: The mean that the user enters, hoping that it will match the observed mean.

Observed SD: The standard deviation of all unexcluded, numerical results entered into the SP experiment.

SD Goal: The maximum observed SD that the user will accept in order for the experiment to "pass". This SD is either entered by the user (for the Vendor Goal case) or is computed from the total allowable error (TEa case).

Observed CV: The CV of all of the results entered into the SP experiment.

Target CV: Derived from the SD Goal.

Pass/Fail: Configured from the Calculations Tab on the Preferences screen. If the Simple Precision Verification Mode is set to Pass/Fail, an experiment is flagged as Fail if the point estimate of precision, i.e., observed SD, exceeds the SD Goal; otherwise it is flagged as Pass. No judgement is made if the Precision Verification Goal is None.

Pass/Fail/Uncertain: Configured from the Calculations Tab on the Preferences screen. If the Simple Precision Verification Mode is set to Pass/Fail/Uncertain, the experiment will "Pass" when the upper 95% CI does not exceed the SD Goal; it will "Fail" when the lower 95% CI exceeds the SD Goal; and it will be "Uncertain" when the SD Goal lies within the 95% CI. No judgement is made if the Precision Verification Goal is None.

N: The number of results included in this calculation vs. the total number of results entered for this experiment.

Experiment Detail Screen

The Experimental Detail Screen (Figure 8.1) displays a wealth of detail about this experiment. In this example, the Simple Precision Verification Mode is set to Pass/Fail/Uncertain. Note the following:

Experimental Results are displayed on the left side. They are identified by an index which is strictly a counter.

Levey-Jennings chart is displayed to the right of the experimental results. SDI (standard deviation index) is plotted on the Y axis.

Key statistics (Observed Mean, Target Mean, Observed SD, etc.) are displayed near the bottom.

Pass/Fail or Pass/Fail/Uncertain is highlighted. Pass is highlighted in green, Fail in red, and Uncertain in yellow.

Precision Goal chart appears only when the Precision Verification Goal option on the Parameters screen is set to TEA Based or Vendor Based.

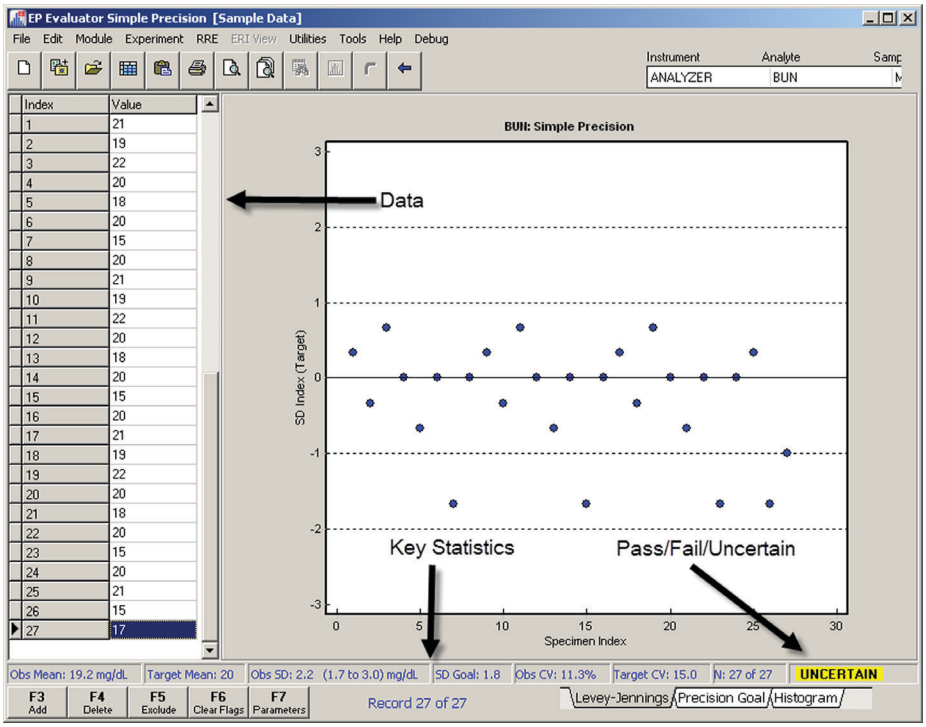


Figure 8.1 Simple Precision Experiment Detail Screen.

Levey-Jennings Chart: A scatter plot of Standard Deviation Index (SDI) on the Y-axis vs. specimen index on the X-axis. Specimen index reflects the order in which the results were typed into the program.

SDI = Result-observed (or target) Mean)/observed (or target) SD

Precision Goal: This chart appears only if the Verify Precision Goal option is set to TEA Based or Vendor Based. It shows the observed SD and its 95% confidence interval in relation to the user specified SD goal. The wide colored bar represents the SD. The fence marks above and below the top of the SD bar show the 95% confidence limits.

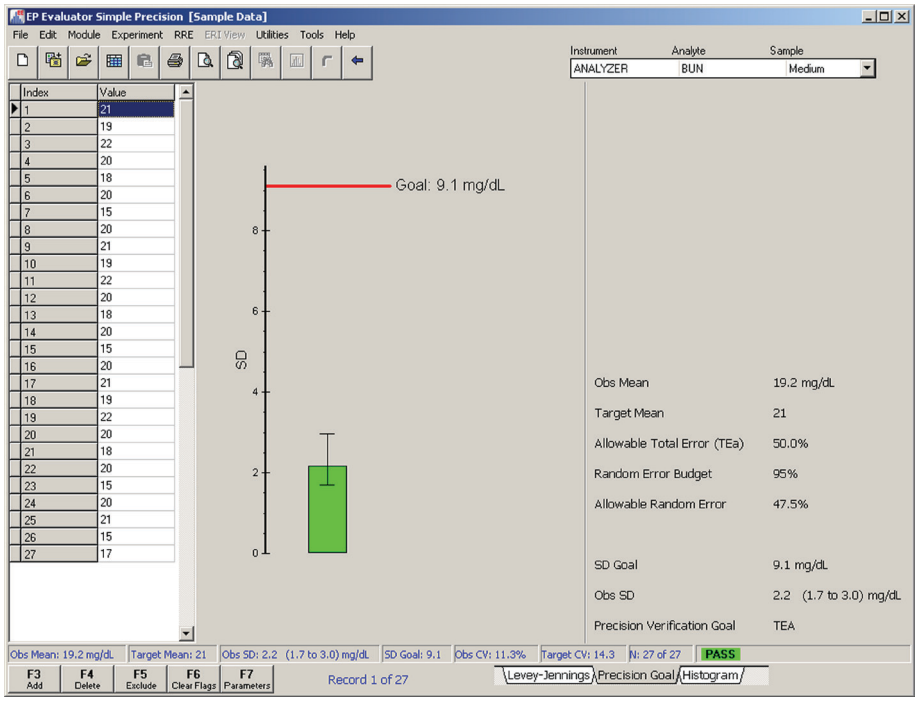


Figure 8.2 Precision Goal Chart

- If the Preference is for Pass/Fail: The experiment Passes if the horizontal line (SD Goal) is above the top of the colored bar (Observed SD), and Fails otherwise.
- If the Preference is for Pass/Fail/Uncertain: The experiment Passes if the horizontal line (SD Goal) is above the upper 95% confidence limit for the observed SD, is Uncertain if it is within the 95% confidence limits, and Fails if it is below the lower limit of the 95% confidence limits.
- The ideal situation is when the upper 95% confidence limit does not exceed the goal.

Parameters Screen

The Parameters screen (Figure 8.3) provides for entry of general parameter information to be used to configure a Simple Precision experiment.

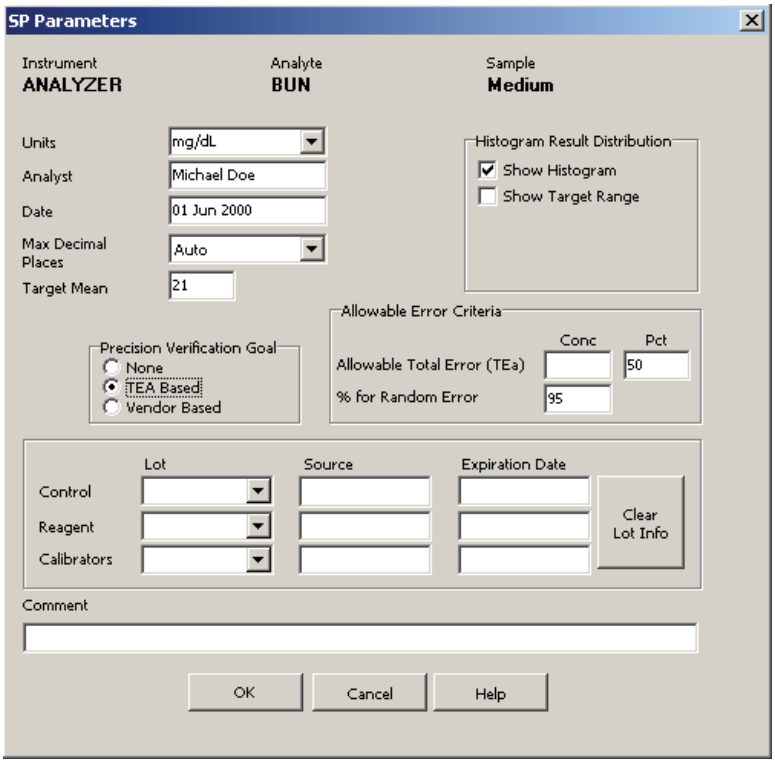


Figure 8.3 Simple Precision Parameters Screen.

Analyte, **Instrument** and **Concentration** are defined prior to entry. **Display only.**

Units refer to the units in which this analyte is reported. **Required**

Analyst is the person performing the experiment. The default value for Analyst is the user name most recently entered even if it was entered on a previous day. **Required**

Date is the day the experiment was performed. The default is today. **Required**.

Max decimal places is the maximum number of decimal places for reports. "Auto" means number of decimal places is determined from the data. Computed statistics (e.g., Mean) are usually printed with one more decimal place than the input results. This setting affects reports only; calculations are done on full-precision numbers.

Target Mean: If a Target Mean is provided, the Levey-Jennings graph computes SDI as:

(Result-Target Mean)/Target SD

Note that if a Target Mean is **not** provided, SDI is calculated as:

(Result-Observed Mean)/Observed SD

Precision Verification Goal:

- **None:** If the Precision Verification Goal is set to None, no judgement is made as to whether the experiment passes, fails, or cannot be determined.

- **TEA Based:** Select this radio button to show the Allowable Error Criteria fields.

  Allowable Total Error (TEa) may be entered in concentration units, as a percent, or both (indicates greater of concentration, percent). % **for Random Error** is percent of TEa allotted to random error.

- **Vendor Based**: Select this radio button to show the Vendor Precision Goal fields.

  Enter a Vendor Based **Within Run SD** and the program will evaluate the SD relative to your stated goal. You may also enter the **Conc at SD Goal** for documentation purposes. Manufacturers often publish these statistics in package inserts. They are typically computed from a more complex precision experiment that requires replicate measurements over several days. Total SD from this complex precision experiment is NOT comparable to EP Evaluator's Simple Precision SD.

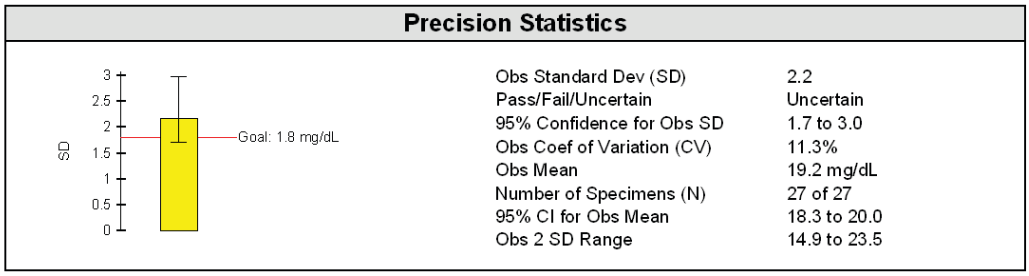
Histogram Result Distribution: Select the Show Histogram checkbox to specify that the program create a histogram displaying a frequency distribution of recovered results centered around the observed mean. Selecting this option shows the Show Target Range checkbox.

Show Target Range: Selecting this option shows the Target Range radio group. Entry of a target mean is required and the user is able to choose an SD target range (2SD, 2.5 SD, 3 SD, or 3.5 SD) to display around the target mean.

Comment provides for entry of up to 80 characters to document the experiment.

Report Interpretation

The components of the Simple Precision Report are the Precision Statistics Table, Precision Plot, Histogram, Supporting Data Table, User's Specifications, and Precision Data Table. A sample Simple Precision Report is shown at the end of this chapter.



Obs SD, Obs CV, Obs Mean, and Number of Specimens (N) have their usual meaning in the Precision Statistics Table. Briefly, the Observed Mean is the central tendency, namely the single value around which the results are distributed. Observed SD is a measurement of the distribution of the results around the mean. Observed CV is a measurement of the SD relative to the mean. Number of specimens used and number of total results are obvious.

95% Confidence for Obs SD is the range in which the SDs would be expected to fall in 95% of the cases of analysis of similar data.

95% CI for Obs Mean is the range in which the mean would be expected to fall in 95% of the cases of analysis of similar data.

Obs 2 SD Range is the total range of the mean +/-2 SDs. This is the range in which 95% of the results are expected to fall.

Simple Precision Report - Page 1

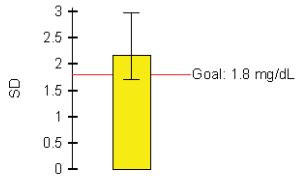
EP Evaluator®

User Manual -- Data Innovations, LLC

BUN
Instrument ANALYZER
Sample Name Medium

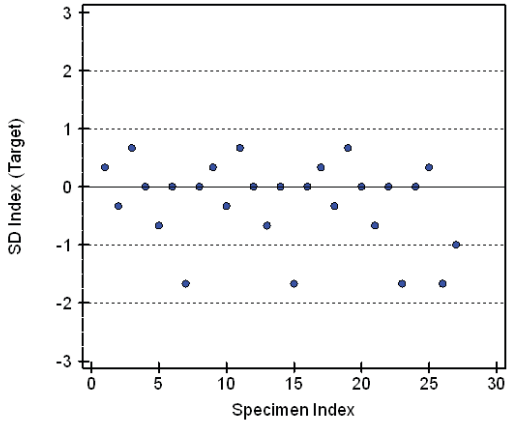
Simple Precision

Precision Statistics

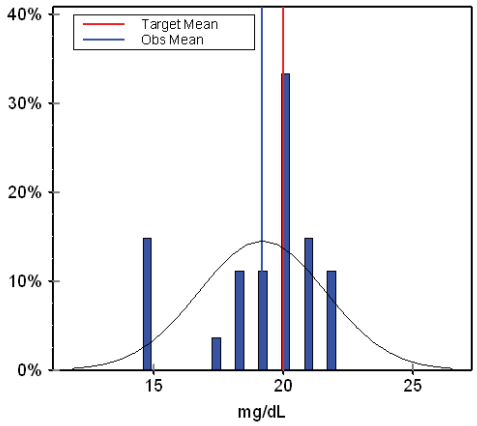


Obs Standard Dev (SD)	2.2
Pass/Fail/Uncertain	Uncertain
95% Confidence for Obs SD	1.7 to 3.0
Obs Coef of Variation (CV)	11.3%
Obs Mean	19.2 mg/dL
Number of Specimens (N)	27 of 27
95% CI for Obs Mean	18.3 to 20.0
Obs 2 SD Range	14.9 to 23.5

Precision Plot



Histogram



Supporting Data

Analyst	Michael Doe
Expt Date	01 Jun 2000
Units	mg/dL
Target Mean	20
Target Range	–
Target CV	15.0
Control Lot	–
Reag Lot	–
Cal Lot	–
Comment	

User's Specifications

Precision Verification Goal	TEA
Allowable Total Error	10.0%
Random Error Budget	95%
Allowable Random Error	9.5%

Accepted by: _____ _____

Signature Date

Sample Data Printed: 10 Jul 2012 16:53:27 Page 1

Chapter

9

Complex Precision

The Complex Precision Module includes a faithful implementation of the CLSI EP5-A Precision document (CLSI:EP5). This module is primarily used in four environments:

- The manufacturer wants a statistically rugged procedure, recognized in the industry, to determine precision for inclusion in official documents submitted to regulatory bodies.
- The user wants to determine whether an instrument meets the manufacturer's claim for precision using a statistically valid approach.
- The user wants to determine four types of precision: within-run, between-run, between-day, and total.
- The user wants to determine the precision component of CLSI:EP15.

Experimental Design

The fundamental design of this experiment is that a specimen is assayed repeatedly with multiple replicates per run, one or more runs per day, for a minimum of 20 days. The number of replicates per run and the number of runs per day must be constant throughout the experiment.

This experimental design allows calculation of within-run, between-run, between-day and total precision. After those elements are calculated, the program calculates whether the observed total precision is statistically less than the manufacturer's precision claims.

Reports will be labeled EP5 Precision if they meet EP5 guidelines; otherwise, they will be labeled Alternate Precision.

Data Requirements

The minimum data requirements for the module are left to the user's discretion. A minimum of 3 days or 6 runs (whichever is more) is recommended. Otherwise, the statistical significance of the between-day and between-run statistics is reduced, perhaps significantly. The maximum number of results is large (greater

than 500). The module will accept one to ten replicates per run, and one to ten runs per day. The number of replicates in each run and the number of runs in each day of the experiment must be the same (i.e. regular experiments). (This is done because accurate calculations are very difficult with non-regular experiments.)

The data requirements to establish precision specifications using CLSI:EP5 are two replicates per run, one or two runs per day, for a minimum of 20 days. CLSI:EP5 data requirements do not allow more than two replicates per run or more than two runs per day. Additionally, on the Outlier Rejection Criteria tab for the experimental parameters, the Source of Preliminary SD option must be set to **Calculated** with a multiplier of **5.5**.

Reports for experiments which meet CLSI:EP5 data requirements are labeled "EP5 Precision." Reports for experiments that do not meet those requirements are labeled "Alternate Precision." These designations may also appear on various screens in this module.

The data requirements to establish precision specifications using CLSI:EP15 are three replicates per run, one run per day, for a minimum of 5 days.

Experiments that do not meet CLSI:EP5 data requirements will generate reports with the watermark "PRELIMINARY" stamped on the report pages. An experiment is considered preliminary if the total number of runs is less than 6 AND the numbers of replicates per run, or runs per day, is 1. This watermark will also appear if the experiment was performed less than 3 days OR the total number of runs was less than 6.

Calculation Process

The calculation process as defined in the CLSI:EP5 document is:

Start New Experiment. Enter the instrument, analyte and sample name. Or click on an existing experiment.

Enter experimental parameters. This includes the number of replicates per run and the number of runs per day. If a method's precision is being verified, the manufacturer's claims are also included.

Click on the Outlier Rejection Criteria tab. Enter either a set of within-run results or a user defined SD. In either case, a number corresponding to the Outlier Rejection Criteria will be calculated.

Experimental Detail Screen. Enter experimental results.

Determine if outliers are present. They will be highlighted in yellow. A run will be declared to be an outlier run if the difference between two results in that run exceeds the Outlier Rejection Criteria.

Calculate statistics. To see the statistics, click on the Statistics tab. Only complete runs and complete days will be included in the calculations. A complete run has the designated numbers of replicates. A complete day has the designated number of unexcluded runs.

Experiment Detail Screen

As usual, the Experiment Detail Screen provides a display of real-time results and also provides for entry or editing of the results. There are two notable items on this screen:

Tabs

At the lower left of the Experiment Detail Screen are two tabs, one labeled "Plot" and the other labeled "Statistics." When the Plot tab has been selected, the Experiment Detail Screen is in Plot mode, and displays the Levey-Jennings graph. When the Statistics tab has been selected, the Experiment Detail Screen is in Statistics mode and shows a Summary Table of the statistical calculations. Interpretation of the contents of this table is discussed below.

Result Entry

The experimental results are entered in the table at the bottom of this screen. Note that the form of the data is multiple replicates within a run and multiple runs within a day. The numbers of replicates per run and runs per day must be the same across the whole experiment. If data is missing, then the partial data for the whole day must be discarded and replaced by complete data from another day.

Parameter Screen - General

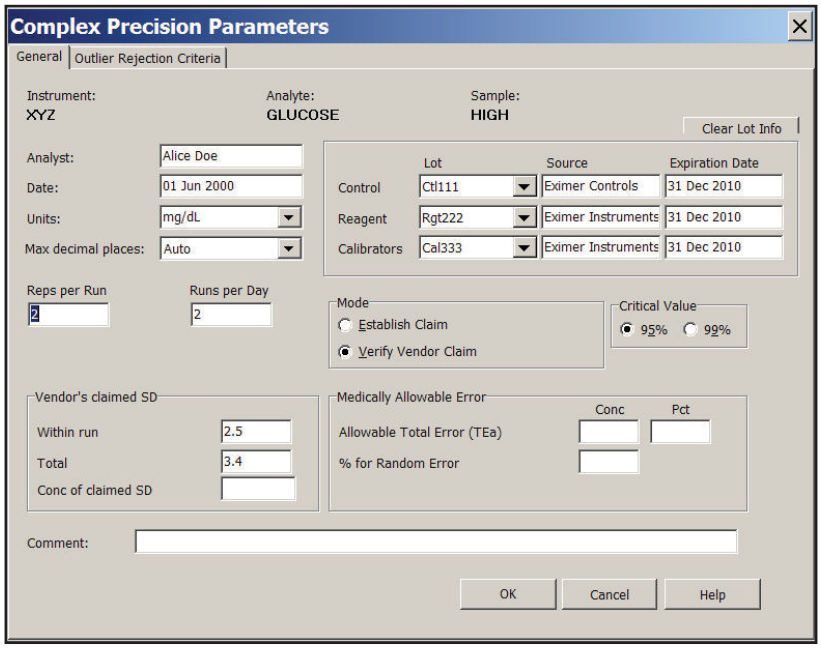


Figure 9.1. Complex Precision - Parameter Screen - General Tab

The contents of this screen (Figure 9.1.) define the shape and nature of the precision experiment. Many of the fields in this screen require data before the screen can be accepted. A required field which is missing data is highlighted in yellow.

Max decimal places is the maximum number of decimal places for reports. "Auto" means the number of decimal places is determined from the data. Computed statistics (e.g., Mean) are usually printed with one more decimal place than the input results. This setting affects reports only; calculations are done on full-precision numbers.

Reps per Run and Runs per Day define the dimensions of the experiment. All runs must have the specified number of replicates. All days must have the specified number of runs. Outlier and excluded runs do not count against the official total. **Required**.

Reagent and Calibrator Source and Lot number are needed because precision values do often change across lots. **Required**.

Mode defines the purpose of the experiment. Choices are establishing a claim and verifying a vendor's claim. If the latter case, the vendor's claimed SD's are required fields.

Critical Value: The user gets to specify whether the claims are to be tested to 95% or to 99% confidence. We recommend that you use whichever confidence level that the vendor used. It is easier to pass if you use 99%.

Vendor's Claimed SD: This box contains the vendor's claims for this test. It will be visible only when the mode is Verify Vendor Claim. The three fields contain the vendor's claims for within-run and total SD and the concentration of the analyte at which those claims were made.

Medically Allowable Error: In EE, Medically Required SD has been put in terms of Allowable Total Error and the fraction of that amount which is to be used for 1 SD.

Parameter Screen - Outlier Rejection Criteria

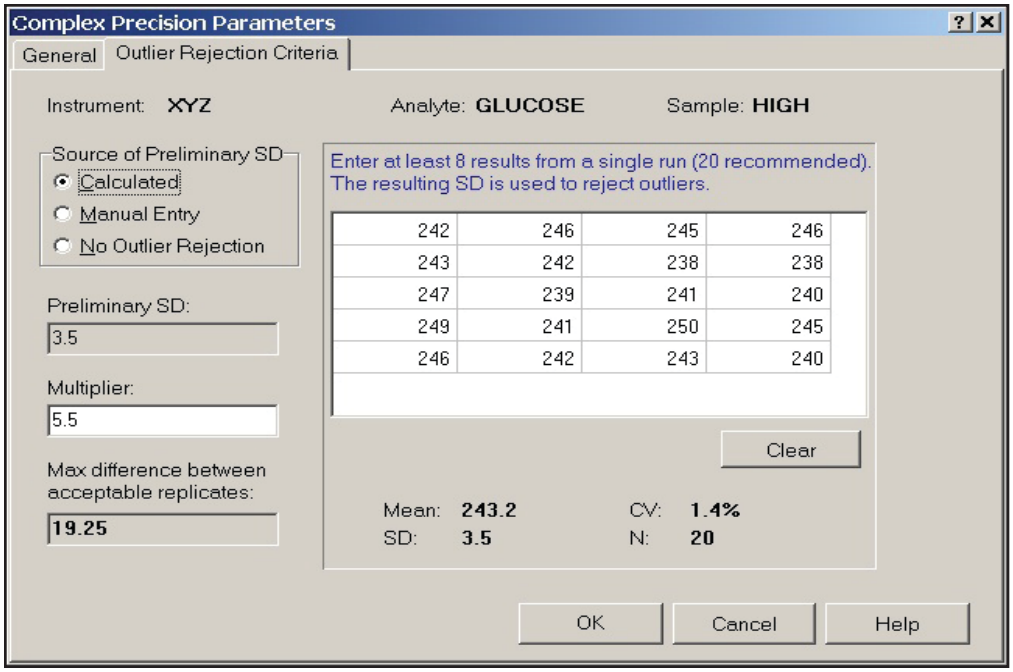


Figure 9.2. Complex Precision. Parameter Screen - Outlier Rejection Criteria

This screen (Figure 9.2.) defines the criteria used to declare runs as outliers. If two results in a run are different by an amount greater than the maximum difference between acceptable replicates, then that run has outliers and is NOT used in the calculation. Furthermore, all runs on that day are to be discarded and replaced by runs on another day.

The three approaches available for defining outliers are listed in the Source of Preliminary SD box: **Calculating the Preliminary SD, Manual definition of the Preliminary SD** and **No Outlier Rejection**. In the last case, no outliers will be found since no rejection criteria will have been entered. Experiments with no outlier criteria specified will be labeled “Alternate Precision.”

Preliminary SD is calculated from the Preliminary Precision data when appropriate. Otherwise it is entered by the user or ignored. **Required field** except when No Outlier Rejection is selected.

Multiplier is the factor by which the Preliminary SD is multiplied to give the maximum difference between acceptable replicates. Required field except when No Outlier Rejection is selected.

Preliminary Precision Data are used to establish the SD for outlier rejection. Up to 20 within-run precision values may be entered. **Optional field**.

Complex Precision Reports

Complete sample reports are shown at the end of this chapter. Various portions of the report are below.

Claim Evaluation Table

A report excerpt for Claim Evaluation is shown in Figure 9.3. **This is the most important section of the Complex Precision report**. This table is also shown when the Statistics Tab on the Experiment Detail Screen has been selected.

Claim Evaluation

User's Concentration: 244.3 **Claim Concentration: 273**

			Standard Deviation			
	df	User's % CV	User's	Claim	Verification Value (95%)	Pass/Fail
Within run	40	1.2	2.9	2.5	2.95	Pass
Between run		0.7	1.6			
Between day		0.5	1.3			
Total	67	1.5	3.6	3.4	3.88	Pass
Medical Req	67	1.5	3.6	6.1	7	Pass

The calculated value passes if it does not exceed the verification value.

Figure 9.3. Complex Precision Report - Claim Evaluation Table

df (Degrees of freedom) is calculated by the program. It is calculated using a complex algorithm from the numbers of runs and replicates. In the CLSI:EP5 example, an experiment with 80 replicates has 65 degrees of freedom.

User's Concentration is the grand mean value of the experimental results.

Claim Concentration is the concentration at which the vendor measured the claimed precision. This is included because precision often varies significantly with concentration and the concentration of one's specimen may be quite different from the one at which the claim was made.

User's % CV is calculated from the Standard Deviation (User's).

Standard Deviation (User's) is calculated from these results. The primary calculations are within-run and total SD's. Between-run and between-day SD's are derived from a complex calculation using the within-run and total SD's as well as other numbers.

Standard Deviation (Claim) is the SD claimed by the vendor and is entered by the user.

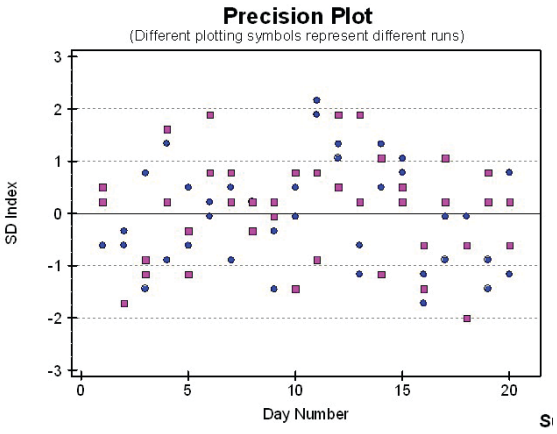
Medically Required SD is the maximum SD that is clinically acceptable. The value calculated by the program is in the User's column and is equal to the Total SD. The value entered by the user is in the Claimed column.

Verification Value is the maximum SD that is acceptable. In other words, any User's SD which is larger will fail. The value in parenthesis, 95% or 99%, specifies the critical value.

Pass/Fail value is a Pass if the User's SD does not exceed the Verification Value.

Precision Plot

The results in this graph are plotted in SD Index units. For definition of the SD Index, see entry in the Glossary. The different plotting symbols on each day represent different runs.



Outlier Rejection Criteria

The decision on which outliers are detected prior to rejection is based on the Max difference between duplicates. This value is the product of the SD and the Multiplier as shown in the Outlier Rejection Criteria Table. The SD may either be a user-entered value or a calculated value. When it is a calculated value, it is based on the SD obtained from an evaluation of the Preliminary Estimates of Precision.

Outlier Rejection Criteria

SD	3.5 (calculated)
Multiplier	5.5
Max difference between duplicates	19.25

Preliminary Estimate of Precision Table

This figure shows the data used to calculate the Preliminary Estimate of Precision. Also included are the resulting mean, SD and CV.

Preliminary estimate of precision

Mean	243.2	CV	1.4%	
SD	3.5	N	20	
Results:				
242	246	245	246	243
242	238	238	247	239
241	240	249	241	250
245	246	242	243	240

Supporting Data

The supporting data gives various essential details about the experiment. These are carried through directly from the user input. See the example at right.

Supporting Data

Analyst	Alice Doe
Analysis Date	12 May 2000 to 31 May 2000
Days (total/excl)	20 / 0
Runs per Day	2
Reps per Run	2
Critical Value	95%
Units	mg/dL
Verify Mode	Verify Vendor Claim
TEa	6.0 or mg/dL 10.0%
Rand. Err. Budget	25%
Allow Rand. Err.	1.5 or mg/dL 2.5%
Control	Eximer Controls Ctl111 exp 31 Dec 2010
Reagent	Eximer Instruments Rgt222 exp 31 Dec 2010
Calibrators	Eximer Instruments Cal333 exp 31 Dec 2010
Comment	

Upper 95% Tolerance Table

This table is required by CLSI:EP5. Its purpose is to allow the user to verify the manufacturer's claims by doing a smaller experiment than the standard EP5 experiment. This table is designed to be included in the manufacturer's documentation.

Upper 95% tolerance limit for 95% of user estimates

df for user's experiment	within run SD	total SD
10	3.9	4.8
20	3.6	4.5
30	3.5	4.3
40	3.4	4.2
50	3.4	4.2
60	3.4	4.1
70	3.3	4.1
80	3.3	4.1
90	3.3	4.0
100	3.2	4.0

This table provides data for a manufacturer to include in published material for users.

EP Evaluator®

User Manual -- Data Innovations, LLC

GLUCOSE
Instrument XYZ
Sample Name HIGH

EP5 Precision

Claim Evaluation

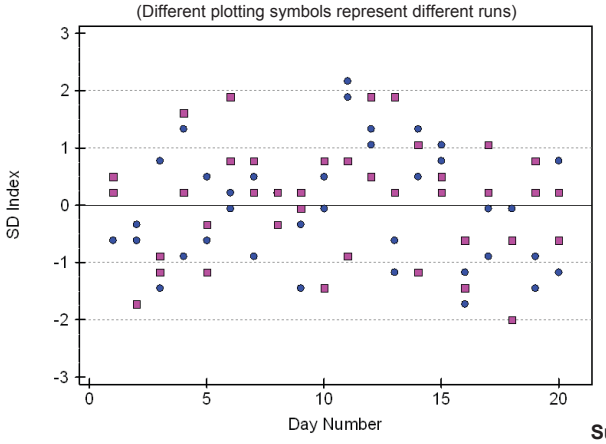
User's Concentration: 244.2 **Claim Concentration: --**

	df	User's % CV	Standard Deviation User's	Claim	Verification Value (95%)	Pass/Fail
Within Run	40	1.2	2.8	2.5	2.95	Pass
Between Run		0.7	1.8			
Between Day		0.6	1.4			
Total	65	1.5	3.6	3.4	3.88	Pass
Medical Reqd	65	1.5	3.6	--	--	--

The calculated value passes if it does not exceed the verification value.

Precision Plot

(Different plotting symbols represent different runs)



Outlier Rejection Criteria

SD	3.5 (calculated)
Multiplier	5.5
Max difference between duplicates	19.25

Preliminary estimate of precision

Mean	243.2	CV	1.4%
SD	3.5	N	20

Results

242	246	245	246	243
242	238	238	247	239
241	240	249	241	250
245	246	242	243	240

Upper 95% tolerance limit for 95% of user estimates

df for user's experiment	within run SD	total SD
10	3.8	4.9
20	3.5	4.5
30	3.4	4.3
40	3.3	4.2
50	3.3	4.2
60	3.2	4.1
70	3.2	4.1
80	3.2	4.1
90	3.1	4.0
100	3.1	4.0

This table provides data for a manufacturer to include in published materials for users.

Supporting Data

Analyst	Alice Doe
Analysis Date	12 May 2000 to 31 May 2000
Days (Tot/Excl)	20 / 0
Runs per Day	2
Reps per Run	2
Critical Value	95%
Units	mg/dL
Verify Mode	Verify Vendor Claim
TEa	--
Random Error Budget	--
Allow Rand. Err.	--
Control	--
Reagent	AA ABC 87011
Calibrators	BB DEF 4700
Comment	

Accepted by: _____ _____

Signature Date

Default Printed: 14 Aug 2012 15:08:55 Page 1

Complex Precision Report - (Page 2)

EP Evaluator®

User Manual -- Data Innovations, LLC

GLUCOSE
Instrument XYZ
Sample Name HIGH

EP5 Precision

Experimental Results

Date	Results		Date	Results		Date	Results	
12 May 2000	242	246	19 May 2000	245	245	26 May 2000	247	248
	245	246		243	245		245	246
13 May 2000	243	242	20 May 2000	243	239	27 May 2000	240	238
	238	238		244	245		239	242
14 May 2000	247	239	21 May 2000	244	246	28 May 2000	241	244
	241	240		247	239		245	248
15 May 2000	249	241	22 May 2000	252	251	29 May 2000	244	244
	250	245		247	241		237	242
16 May 2000	246	242	23 May 2000	249	248	30 May 2000	241	239
	243	240		251	246		247	245
17 May 2000	244	245	24 May 2000	242	240	31 May 2000	247	240
	251	247		251	245		245	242
18 May 2000	241	246	25 May 2000	246	249			
	245	247		248	240			

"X" indicates an excluded run, "O" indicates an outlier run, and "S" indicates a day that does not have a full complement of results. In all of these cases, the entire day is excluded from the calculations.

Chapter

10

CLSI EP9 Method Comparison

CLSI EP9 Method Comparison is a statistically rigorous and rugged protocol which requires significant effort to execute properly. It is excellent for preparing reports for regulatory agencies. It may also be used by a laboratory for rigorously evaluating methods.

CLSI EP9 (EP9) and Alternate Method Comparison (AMC) always compare two methods, a Comparative (X) method with a Test (Y) method. The X method should always be the Senior method. The definition of a Senior method is:

- When comparing two production methods, it is the existing method in the lab, not the method which is a candidate to be introduced into the lab. It may well be that the X method is not the "best" method. After all, that may be why it is being replaced.
- When comparing a reference or definitive method with a production method, it is the reference or definitive method.
- In all other cases, it is the method which will produce the best results.

EP9 Method Comparison is designed to compare two methods which produce results with similar units. It is not designed to compare items with disparate units (i.e. mg/dL vs. IU/L). Use AMC for those comparisons. For a list of similarities and differences between AMC and CLSI EP9, see Table 10.1.

Assumption

CLSI EP9 assumes that the two methods being compared will yield essentially identical results. If the underlying chemistries or standardization schemes for two methods are quite different, the result obtained for a specimen analyzed by one method may be many times higher (or lower) than that obtained by the other method. When analyte methodologies are expected to be dissimilar, the data should not be compared using CLSI EP9.

Comparison

Table 10.1

Comparison of CLSI EP9 and Alternate Method Comparison Modules		
	CLSI EP9	AMC
Replicates	2	1
Specimens used in calculation	39 to 1000+[1]	3 to 1000+[1]
Maximum number of excluded results or outliers in order to get a final report	<=1 within-method outlier and <=2.5% between-method outliers	<=5% outliers
1) While there is no upper software limitation the numbers of specimens, there is a practical limit on the number of specimens that can be entered from the keyboard because of the delays caused by real time calculations during the entry process. For small numbers of specimens (<200), the delays should be insignificant. The best way to enter large numbers of specimens is to import them.		

Key Statistics

The most important statistics are:

- 95% CI (confidence interval) of the Deming slope.
- 95% CI of the Deming intercept.
- 95% CI of the calculated Medical Decision Point.

Overall Process

Unlike many other protocols, CLSI EP9 places a significant responsibility on the user. These responsibilities are described in the CLSI:EP9 document, sections 1 through 7. Figures 1 and 2 in that document show the flowchart for the calculations process. The essential elements of the process are listed below.

- Select and assay, in duplicate by both methods, a suitable group of specimens.
- Define Medically Allowable Error. In EP Evaluator, this is referred to as Medically Allowable Error (TEa). The software will use Medically Allowable Error to determine:
  - The maximum allowable difference between methods for each specimen;
  - The maximum allowable difference between duplicate specimens for the same method;
  - The distance between the scatter plot bounds and the regression line, when the Scatter Plot Bounds are set to Total Allowable Error.
- Enter all four results. It is unacceptable to measure a specimen just once by any method and then enter that one result twice.
- Perform the calculations and review the results. The software will automatically perform validity checks on the differences between duplicates and the differences between specimens across methods. If the software finds problems, the Alert flag is set. This flag appears on the statistics bar near the bottom of the screen.

Your tasks:

- Visually check for linearity to see that the data is linear. If it is not linear, you may choose to select only a portion of the data to be included in the calculation using the Subrange feature. Keep in mind that you will need at least 39 specimens in the calculation in order to generate a final report.
- Check for "uniform scatter." A method passes the uniform scatter test if the ratio of the scatter at the high end to the scatter at the low end is between 0.33 and 3.0. For more details, see the section entitled *Controls*.

Specimen Selection and Analysis

According to CLSI:EP9 Guidelines:

- Select at least 40 specimens for analysis. Their results should cover a substantial portion of the reportable range. Furthermore the specimens should be selected so that certain percentages occur in various value ranges to ensure a good distribution of data. (See CLSI:EP9: Tables 1a and 1b.)
- The quality of the method comparison study, assuming properly assayed specimens, depends more on a good distribution of results than on any other single factor. Make an effort to get a significant number of specimens, with results throughout the reportable range. Usually, there is little added benefit from having a large number of specimens in the normal range.
- Assay the specimens in duplicate by both methods within a 2 hour period. This ensures the stability of the analyte. Assay no more than 8 specimens a day. This is specified so that the analytical process will incorporate day to day variation.

A limited number of specimens (<= 2.5%) may be excluded from the data set or declared outliers without affecting the process.

If enabled from the Experiment Detail Screen, the automated outlier identification process employs a statistical evaluation as well as a comparison to Medically Allowable Error. In general, an outlier is detected either when duplicate results for the same method are too different, or when one or both of a specimen's Y results compared to the mean of its X results are too different. In either case, the entire specimen would be declared an outlier, and removed from the final dataset. Ideally, you should re-assay both specimens in duplicate and attempt to determine the cause of the difference. The *Acceptability Limits* define the limits for the statistical evaluation, and *Medically Allowable Error* defines the limits for the Maximum Allowable Differences. For both types of outliers, if only one outlier is detected, it will be removed from the dataset, but will not cause an experiment failure. However, the experiment will fail if more than one within-method outlier is detected, and the maximum difference is outside Medically Allowable Error. The Experiment will also fail if more than 2.5% between-method outliers are detected and the maximum between-method difference is also outside Medically Allowable Error.

Experimental Parameters

The CLSI EP9 Experiment Parameter screen (Figure 10.1.) is displayed. This screen is also accessible from the Experiment Detail Screen.

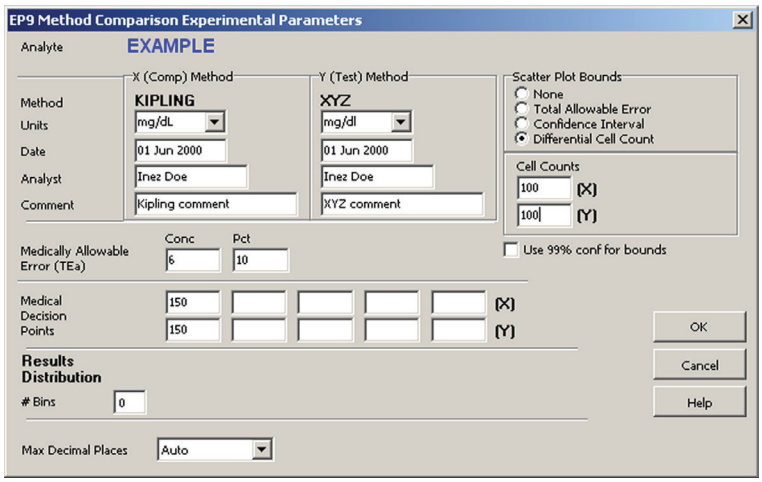


Figure 10.1. EP9 Method Comparison. Experiment Parameters Screen.

Parameters for both methods are entered and/or edited in this screen. The key items are:

Units: Analyte measurement units.

Date: Date when the experiment was run.

Analyst: Person responsible for doing the study.

Comment: Text describing the experiment.

Medically Allowable Error (TEa): The maximum allowable difference between the two methods. This error may be expressed in units of concentration, percent, or both. This information is used to compute the Scatter Plot Bounds, and in evaluating outliers.

Medical Decision Points: Analyte value that triggers a medical decision. You may enter up to five values, which are displayed as vertical dotted lines on the graph. The program computes a predicted Y value and confidence interval at each X decision point.

For many analytes, the medical decision points correspond to the lower and upper limits of the normal range. In other cases, there are more than two decision points.

Results Distribution (Analytical range, bins): Bins help you judge the range of the data. You may define up to 5 bins across the analytical range of your method. For example, if you defined 5 bins equally distributed in the range of 0 to 100, the first bin would be from 0 to 20, the second 21 to 40, and so on, up to 100. A suggested list of bin limits may be found in the CLSI:EP9 document.

The easiest way to request evenly spaced bins is to enter the number of bins, and the lower and upper limits of the analytical range. The program will then compute and display the upper limit points of the evenly spaced bins. You are free to change these suggested values.

Max decimal places: Maximum number of decimal places for reports. "Auto" means number of decimal places is determined from the data. Computed statistics (e.g., Mean) are usually printed with one more decimal place than the input results. This setting affects reports only; calculations are done on full-precision numbers.

Scatter plot bounds: The type of bounding lines drawn on the scatter plot to give a visual indication of goodness of fit. Choices are:

- **None**: No bounding lines.
- **Total Allowable Error**: The width of the error band is based on the specified Medically Allowable Error, not on the scatter in the data.
- **Confidence Interval**: Bounding lines represent a statistical 95% (or 99%) confidence interval for the regression line.
- **Differential Cell Count**: Bounding lines represent the expected error due to the process of counting cells. The calculation assumes the data are expressed in units of percent. The width of the error band depends on the number of cells counted for each method and on the confidence level.

Cell counts: If you select scatter plot bounds based on differential cell count, you must enter the total number of cells counted by each of the two methods. Typical numbers are 10,000 for a count by an instrument, and 100 or 200 for cells counted manually.

Use 99% conf for bounds: If confidence interval bounds are selected, and if this box is checked, scatter plot bounds are computed for a 99% confidence level. Otherwise, bounds are computed for a 95% confidence level.

Experiment Detail Screen

The CLSI EP9 Experiment Detail Screen provides rapid real-time access to all the information on an experiment.

Controls

The controls are all located on a pair of horizontal bars near the bottom of the Experiment Detail Screen. The Function buttons were described in Chapter 3. There are two specialized controls.

Subrange control: CLSI:EP9 recommends that you define a smaller range of results to be plotted if the full range is unsatisfactory in some way (i.e. non-linear). For an example of the screen during the process of selecting a sub-range, see Figure 10.2. Notice that the selected range ("43 to 254") is displayed to the right of the Subrange control button. The Define Subrange Box provides some directions for using the Subrange feature. To turn this feature on, simply press the Subrange button.

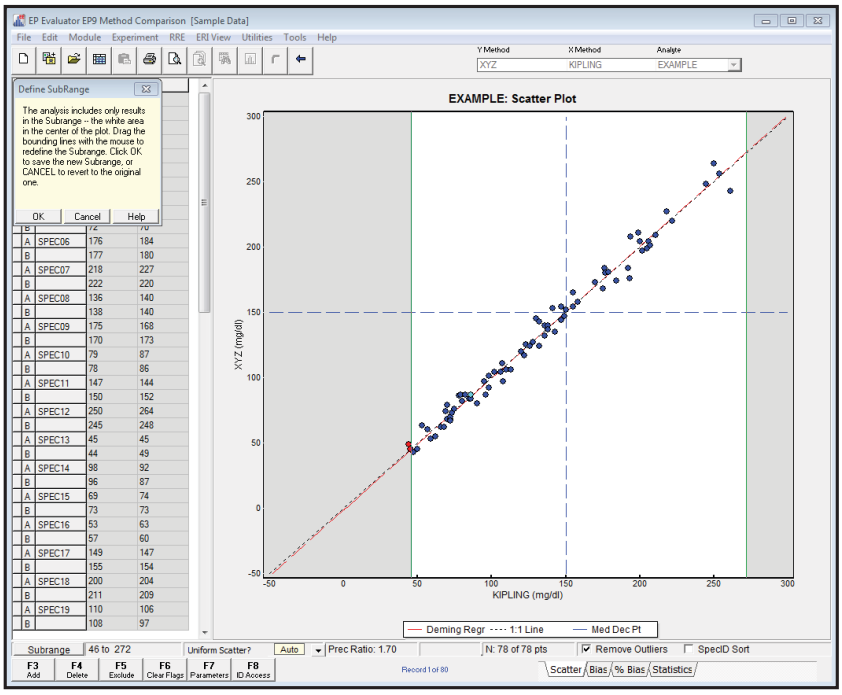


Figure 10.2. CLSI EP9 Method Comparison Experiment Detail Screen showing a Subrange.

Uniform Scatter?: CLSI:EP9 requires that the user evaluate Uniform Scatter. The software calculates and displays the Precision Ratio on the upper control bar as "Prec Ratio: x.xx." If the Precision Ratio is between 0.33 and 3, then the scatter is considered to be uniform. If the ratio is outside this range, (i.e. the scatter is not uniform), then the bias at the medical decision points is calculated using the Partitioned Bias approach. For more information on uniform scatter and the Precision Ratio, see the definition for **Visual check for "uniform scatter" (semi-automated)**.

Alerts. The panel on the Control bar between the "Prec Ratio" and the number of points will display "Alerts" in red if there is an issue with the data. Click on "Alerts" and a small screen pops up with a message describing the problem (e.g. "Too many within-method outliers").

Tabs. Control which display appears in the center of the screen. The options are described below:

Scatter: Displays a Scatter Plot of the data.

Bias: Displays a Bias Plot of the data.

% Bias: Displays a %Bias Plot of the data.

Statistics: Displays the statistics calculated, including the Slope, Intercept, Standard Error of the Estimate, and the Medical Decisions Point Analysis.

Remove Outliers. This checkbox controls whether outliers are removed. If you do not wish to remove outliers, uncheck the **Remove Outliers** checkbox.

SpecID Sort. By default, specimen IDs are listed in the order they are entered. To sort specimen IDs in alphanumeric order, check the **SpecID Sort** check box found on the Experiment Detail Screen. Uncheck this box to return specimen IDs to their default order.

CLSI EP9 Method Comparison Report

Immediately after the user requests that a report be generated, the small Report Option Screen pops up which allows the user to select whether graphs and/or results are to be included in the report.

The report is organized into three parts: the statistical summary on page 1, graphs on page 2 (optional), and a list of the results on pages 3 and following (optional). Portions of this report have been excerpted and are shown below.

Key Statistics

Assuming the preliminary data examination verifies the quantity and quality of the data, you may proceed to interpreting the results. The most important results on the page are in the two tables entitled Regression Analysis (Figure 10.3.) and Medical Decision Point Analysis (Figure 10.4.).

Experiment Description

	X Method	Y Method
ExptDate:	01 Jun 2000	01 Jun 2000
Rep SD:	3.1484	4.3373
Result Ranges:	44 to 261	43 to 264

Figure 10.3. CLSI EP9 Method Comparison Report - Regression Analysis Table

Slope, Intercept, and their Confidence Intervals: When two methods are statistically identical, the 95% confidence interval for the slope includes 1.00, and

the 95% confidence interval for the intercept includes 0.0. When the slope of 1.00 and/or the intercept of 0.0 are not included in the 95% CI, then the values are displayed in red.

> **Example:** If the 95% CI for the slope is 0.92 to 1.02, 1.00 is included in the interval. However, if the 95% CI is 0.82 to 0.92, 1.00 is not included in the interval.

If the experiment were repeated with different data, the slope and intercept would be a bit different. But in 95% of such experiments, those values are expected to fall within the confidence interval.

Standard Error of Estimate (SEE): Measures the dispersion of the x-y data (or random error) around the linear regression line. If both methods have similar random error across the full analytical range, SEE should be about 1.4 times the typical precision SD.

Medical Decision Point Analysis

Calculated by Deming Regression (R>=0.975)

X Method MDP	Y Method Pred. MDP	95% Conf. Limits Low	High
50	49.3	46.6	51.9
125	124.8	123.3	126.3
200	200.3	197.9	202.8

Figure 10.4 EP9 Method Comparison Report - MDP Analysis Table

Medical Decision Point Analysis: A Medical Decision Point is an analyte concentration at which medical decisions change. If the concentration is less than the MDP, one decision is made; if greater than the MDP, a different decision is made. For example, a Fasting Plasma Glucose above 126 mg/dL (7 mmol/L) indicates hyperglycemia which, if confirmed, establishes a diagnosis of diabetes. For obvious reasons, it is particularly important that the two methods agree at the MDPs.

When the two methods are statistically identical, the 95% Confidence Interval for each Y MDP includes the corresponding X MDP.

Preliminary Data Examination Table

This section of the report summarizes the checks to be performed on the data before the experiment is considered valid. Some of the checks require visual inspection, and cannot be automated. A line is provided where you can note whether the check passed or failed.

Preliminary Data Examination

Within-method outlier analysis	PASS	Acceptability Limits: Number of outliers:	X: 16 or 12.8%, Y: 20 or 15.7% 0 of 40 pairs
Between-method outlier analysis	PASS	Acceptability Limits: Number of outliers:	22 or 18.9% 0 of 40 pairs
Visual check for linear relationship	_____	Subrange bounds:	None
Test for adequate number of results	PASS	N = 40 pairs	
Test for adequate range of results	PASS	R = 0.9930	
Visual check for uniform scatter	_____	Computed precision ratio of 1.61 is within normal limits	

Outlier Determination (automated): For more information about within-method and between-method outlier detection, please see the section entitled *Specimen Selection and Analysis*.

Test for adequate number of results (automated): Start with at least 40 duplicate pairs. The test fails if there are fewer than 39 pairs available after outliers have been removed. This check must pass.

Test for adequate range of results (automated): If the correlation coefficient (R) is less than 0.975, the software considers the range of results inadequate. If possible, assay additional specimens to cover a wider range. While it is desirable for this check to pass, it is not absolutely necessary. If the check fails, confidence limits for the medical decision points are calculated using Partitioned Biases rather than by regression.

Visual check for linearity (manual): Does the data appear linear? If not, you may choose to select only a portion of the data to be included in the calculation using the subrange feature. (However, you need at least 39 specimens in the subrange.)

Visual check for "uniform scatter" (semi-automated): This check will allow you to decide whether to compute the medical decision points by Partitioned Biases instead of by Deming regression, provided the automated test for adequate range had passed. Examine the bias plot. Is the bias approximately constant across the range? The software divides the results into five groups sorted by X result value, then calculates the mean bias of the highest and lowest groups. The Precision Ratio is the mean bias of the highest group divided by the mean bias of the lowest group. There are three possible situations:

- Precision Ratio outside acceptable limits (less than 0.33 or greater than 3.0). In this case, scatter is clearly not uniform, and the software automatically fails the uniform scatter test. You cannot override this decision. Medical Decision Points are evaluated using Partitioned Bias.
- Precision Ratio within limits, but you conclude that scatter is not uniform. You can manually override the software's decision by selecting the "Scatter is NOT uniform" option from the **Uniform Scatter?** dropdown found on the Experiment Detail Screen. Medical Decision Points are evaluated using Partitioned Bias.
- Precision Ratio within limits, and you agree that scatter is uniform. MDPs are evaluated using Deming regression.

Experiment Description

Generally the items are self-explanatory. The only one which is not obvious is Rep SD, standing for Representative SD. These two values are the SDs calculated from the duplicate results for the X and Y methods respectively. These values are used as part of the Deming Regression.

Experiment Description

	X Method	Y Method
ExptDate:	01 Jun 2000	01 Jun 2000
Rep SD:	3.1484	4.3373
Result Ranges:	44 to 261	43 to 264
Units:	mg/dl	mg/dl
Comment:	Kipling comment	XYZ comment
Analyst:	Inez Doe	Inez Doe

Result Range Analysis

One of the CLSI:EP9 requirements is that the results be distributed over the most meaningful portion of the reportable range of the analyte. This table shows the percent of unexcluded specimens in each bin. Each set of 4 results (2 replicates each for the two methods) is assigned to a bin based on the value of the first X method result. This table only appears if bins were set up in the Parameter Screen.

Result Range Analysis

Range	Percent
<= 50	5%
51-125	45%
126-200	36%
> 200	14%

Graphs (Page 2)

Four graphs are plotted for CLSI EP9: two scatter plots and two bias plots (not shown). In the upper pair of graphs, all the individual points are plotted. In the lower pair, the mean of duplicate results is plotted.

The two Scatter Plots graph the results for the Test Method (Y Method) versus the results for the Comparative Method (X Method). The graph shows the 1:1 line, the best (regular) linear regression fit and the Medical Decision Level. All unexcluded points are plotted on the graph.

The two Bias Plots graph the differences (y_i - x_i) between pairs of results for the two methods. Note that you can change the graph to a Bland-Altman bias plot by changing an item as described in the section *Preferences*, in Chapter 3: *Common Operations*.

Results (Page 3 and following)

The tables of results are generally obvious.

Interpretation

For interpretation, see Rhoads (2012) *Lab Statistics - Fun and Easy*.

EP9 Method Comparison Report (Page 1)

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EXAMPLE

User Manual -- Data Innovations, LLC

CLSI EP9 Method Comparison

X Method KIPLING **Y Method XYZ**

Regression Analysis

	Deming	Regular
Slope	1.007 (0.980 to 1.034)	1.002 (0.975 to 1.029)
Intercept	-1.1 (-4.9 to 2.7)	-0.4 (-4.2 to 3.4)
Std Err Est	6.8	6.8

95% Confidence Intervals are shown in parentheses

Medical Decision Point Analysis

Calculated by Deming Regression (R>=0.975)

X Method MDP	Y Method Pred. MDP	95% Conf. Limits Low	High
150	150.0	148.3	151.6

Preliminary Data Examination

Within-method outlier analysis	PASS	Acceptability Limits:	X: 16 or 12.8%, Y: 20 or 15.7%
		Number of outliers:	0 of 40 pairs
Between-method outlier analysis	PASS	Acceptability Limits:	21 or 18.4%
		Number of outliers:	0 of 40 pairs
Visual check for linear relationship	_____	SubRange Bounds	None
Test for adequate number of results	PASS	N = 40 pairs	
Test for adequate range of results	PASS	R = 0.9930	
Visual check for uniform scatter	_____	Computed precision ratio of 1.61 is within normal limits	

User's Specifications

Medically Allowable Error	6.0 mg/dl or 10.0%	SubRange Bounds	None
Exclude Outliers	Yes	Scatter Plot Bounds	95% CI

Experiment Description

	X Method	Y Method
Date	01 Jun 2000	01 Jun 2000
Rep SD	3.1484	4.3373
Result Ranges	44 to 261	43 to 264
Units	mg/dl	mg/dl
Comment	Kipling comment	XYZ comment
Analyst	Inez Doe	Inez Doe

Accepted by: _____ _____

Signature Date

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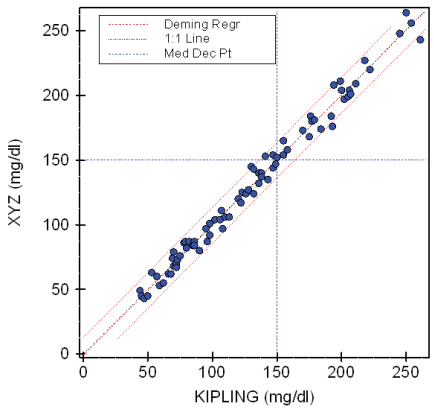
CLSI EP9 Method Comparison

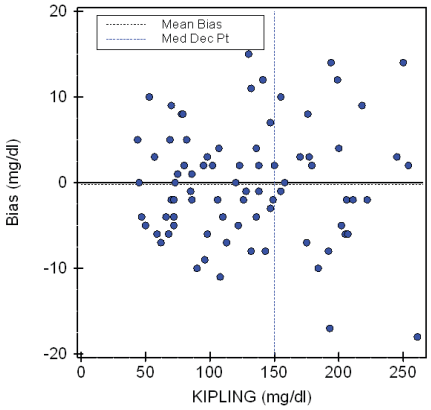
X Method KIPLING **Y Method XYZ**

Individual Results Plotted

Scatter Plot

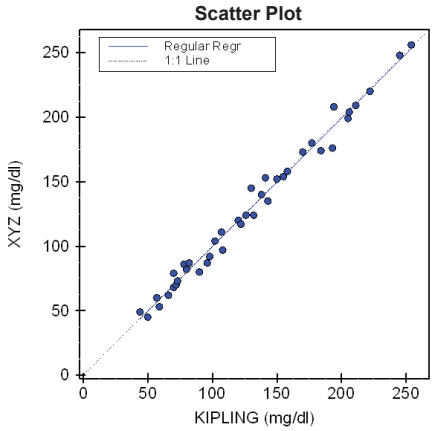


Bias Plot

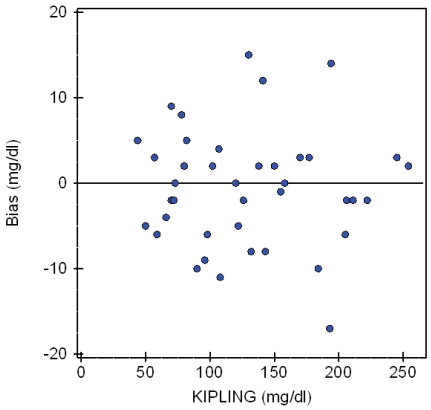


Means of Replicate Results Plotted

Scatter Plot



Bias Plot



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EXAMPLE

User Manual -- Data Innovations, LLC

CLSI EP9 Method Comparison

X Method KIPLING **Y Method XYZ**

Experimental Results

Spec ID	Y (Test) Result	Diff	X (Comp) Result	Diff	Bias (Y-X)	Calc'd Y	Residual
SPEC01	87		86		1	85.5	1.5
	82	5	80	6	2	79.5	2.5
SPEC02	165		155		10	155.0	10.0
	158	7	158	-3	0	158.0	0.0
SPEC03	197		202		-5	202.3	-5.3
	208	-11	194	8	14	194.3	13.7
SPEC04	43		47		-4	46.3	-3.3
	45	-2	50	-3	-5	49.3	-4.3
SPEC05	68		72		-4	71.4	-3.4
	70	-2	72	0	-2	71.4	-1.4
SPEC06	184		176		8	176.1	7.9
	180	4	177	-1	3	177.2	2.8
SPEC07	227		218		9	218.4	8.6
	220	7	222	-4	-2	222.5	-2.5
SPEC08	140		136		4	135.9	4.1
	140	0	138	-2	2	137.9	2.1
SPEC09	168		175		-7	175.1	-7.1
	173	-5	170	5	3	170.1	2.9
SPEC10	87		79		8	78.5	8.5
	86	1	78	1	8	77.5	8.5
SPEC11	144		147		-3	146.9	-2.9
	152	-8	150	-3	2	150.0	2.0
SPEC12	264		250		14	250.7	13.3
	248	16	245	5	3	245.6	2.4
SPEC13	45		45		0	44.2	0.8
	49	-4	44	1	5	43.2	5.8
SPEC14	92		98		-6	97.6	-5.6
	87	5	96	2	-9	95.6	-8.6
SPEC15	74		69		5	68.4	5.6
	73	1	73	-4	0	72.4	0.6
SPEC16	63		53		10	52.3	10.7
	60	3	57	-4	3	56.3	3.7
SPEC17	147		149		-2	149.0	-2.0
	154	-7	155	-6	-1	155.0	-1.0
SPEC18	204		200		4	200.3	3.7
	209	-5	211	-11	-2	211.4	-2.4
SPEC19	106		110		-4	109.7	-3.7
	97	9	108	2	-11	107.7	-10.7
SPEC20	125		123		2	122.8	2.2
	120	5	120	3	0	119.8	0.2
SPEC21	132		136		-4	135.9	-3.9
	124	8	132	4	-8	131.8	-7.8
SPEC22	101		98		3	97.6	3.4
	104	-3	102	-4	2	101.6	2.4
SPEC23	211		199		12	199.3	11.7
	204	7	206	-7	-2	206.4	-2.4
SPEC24	67		72		-5	71.4	-4.4
	68	-1	70	2	-2	69.4	-1.4
SPEC25	184		192		-8	192.3	-8.3
	176	8	193	-1	-17	193.3	-17.3
SPEC26	97		95		2	94.6	2.4
	92	5	98	-3	-6	97.6	-5.6
SPEC27	143		132		11	131.8	11.2
	145	-2	130	2	15	129.8	15.2
SPEC28	106		113		-7	112.7	-6.7
	117	-11	122	-9	-5	121.8	-4.8
SPEC29	84		86		-2	85.5	-1.5
	80	4	90	-4	-10	89.6	-9.6
SPEC30	201		207		-6	207.4	-6.4
	199	2	205	2	-6	205.3	-6.3
SPEC31	154		147		7	146.9	7.1
	153	1	141	6	12	140.9	12.1
SPEC32	76		75		1	74.4	1.6
	79	-3	70	5	9	69.4	9.6
SPEC33	55		62		-7	61.4	-6.4
	53	2	59	3	-6	58.3	-5.3
SPEC34	181		179		2	179.2	1.8
	174	7	184	-5	-10	184.2	-10.2
SPEC35	243		261		-18	261.7	-18.7
	256	-13	254	7	2	254.7	1.3
SPEC36	127		128		-1	127.8	-0.8
	124	3	126	2	-2	125.8	-1.8
SPEC37	84		85		-1	84.5	-0.5
	87	-3	82	3	5	81.5	5.5
SPEC38	62		68		-6	67.4	-5.4
	62	0	66	2	-4	65.4	-3.4
SPEC39	137		138		-1	137.9	-0.9
	135	2	143	-5	-8	142.9	-7.9
SPEC40	104		106		-2	105.7	-1.7
	111	-7	107	-1	4	106.7	4.3

Calculated values and residuals from Deming regression. Values marked with an "X" were excluded from the calculations. Outliers "O" were also excluded.

Chapter 11

Alternate (Quantitative) Method Comparison

The Alternate Method Comparison (AMC) module provides a flexible approach to Method Comparison. It is designed to be used for most routine method comparison analyses. By default, the analysis includes computation of both regular and Deming linear regression statistics. Additionally, it is possible to configure EE to compute and display Passing-Bablok regression statistics.

All relevant statistics are calculated, including the t Test, correlation coefficient, average bias, and the 95% confidence levels for slope, intercept and medical decision points. Three approaches are available for calculating the slope and intercept: Regular regression (often called ordinary least squares regression), Deming regression, and Passing-Bablok analysis.

Data Requirements

Results for several methods can be compared, one pair a time. Note that each pair of methods to be compared must be linked.

Replicate results are not required. A minimum of 3 specimens are required for analysis. The maximum exceeds 50,000. Note that Passing-Bablok regression is unavailable when there are more than 500 specimens.

This module does not accept replicate results for any one specimen. You can enter replicates only if you change the specimen IDs to make them appear distinct. Some statistical conclusions may be invalid if you use replicate specimens.

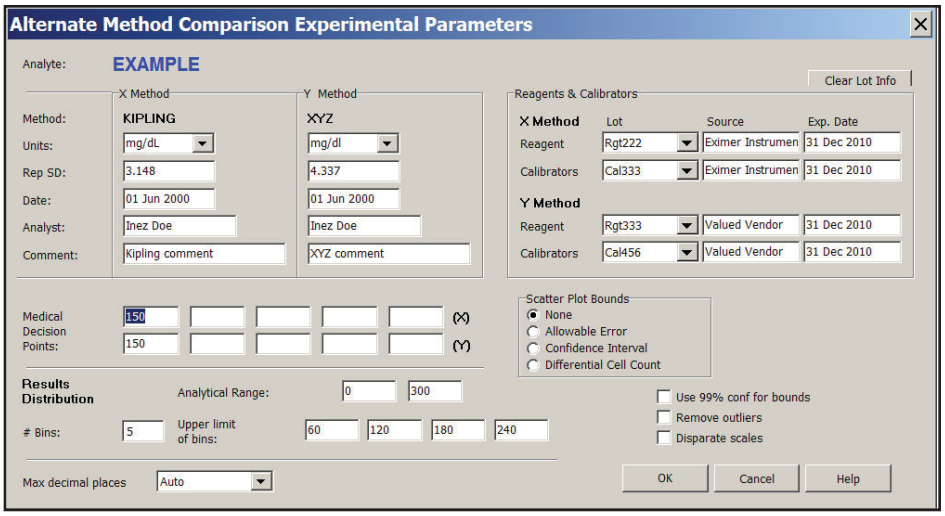
Experimental Design

The usual purpose of an AMC experiment is to determine whether two methods are statistically identical. For a discussion of this topic, see Rhoads (2012) *Lab Statistics* manual.

A good number of specimens ranges from 25 to 60. Range of results covered is much more important than the number of specimens. It is most important to use specimens which cover the full range of values to which the method applies. Often it is difficult to obtain specimens at the high or low end of the range. Statistical conclusions drawn from the method comparison experiment are valid only for the range studied. If the reportable range for a method is 20-600, but the range of results in the study is only 60-150, conclusions may not be valid over the full reportable range.

Parameters Screen

With the exception of the experimental results, the Parameters Screen provides for entry of all the data for an Alternate Method Comparison experiment.



Rep SD (Representative SD): Enter the relative error profile for the whole curve. This value is used in the calculations for Deming linear regression. A good approximation is to select the SD at a mid-range concentration. Choose a typical SD at similar concentrations for both methods. **Required**.

The calculation uses the ratio of the representative SDs. Small changes in the SD ratios usually have little effect on the statistics. The default representative SD of 1.0 is usually a good first approximation if both methods are similar. One notable exception occurs in hematology when comparing a manual cell count with an automated one. In this case, the representative SDs for the manual and automated methods should be 10 and 1 respectively. Another exception is when the two methods have different units. Then the representative SDs need to reflect the relative magnitude of those units.

Max decimal places is the maximum number of decimal places for reports. "Auto" means number of decimal places is determined from the data. Computed statistics (e.g., Mean) are usually printed with one more decimal place than the input results. This setting affects reports only; calculations are done on full-precision numbers.

Medical Decision Points

These are the values at which calculations of Average Bias and the ranges of the Y medical decision points (MDP's) (including uncertainty) are made. Often, the MDP's are the lower and upper limits of the reference (i.e. normal) interval. Up to five medical decision levels may be entered. **Optional**.

Scatter Plot Bounds

These describe the envelope lines to be drawn around the data on the scatter plot. Four choices are available from a menu. The default is **None**. **Optional**.

Allowable Error describes an error envelope defined by the user. It is defined in terms of concentration and/or percent of concentration (whichever is greater). The width of this envelope is independent of the scatter in the data. When this option is selected, the user must enter allowable error values. Typically these values are the allowable total error parameters.

Confidence Interval (95%) describes the envelope within which 95% of the results are expected to fall. The width of this envelope is dependent on the scatter in the results. The more scatter in the data, the wider it will be.

Differential Cell Count describes the error envelope (for the binomial distribution) expected due to the process of counting cells. It requires input of the number of cells counted by the two methods. The calculation assumes the data are expressed in units of percent. The width of this envelope is dependent solely on the numbers of cells counted for each method.

Results Distribution

This feature provides a mechanism to show the distribution of experimental results to an observer. Up to five (5) bins can be defined, which cover the analytical range. Results are counted into these bins based on the magnitude of the X result. Ideally, bins will be set up so there is a strong relationship to meaningful values in the current analyte. For glucose, as an example, bins can be set up to represent the hypoglycemic range, the normal range, the near hyperglycemic range and finally the high hyperglycemic range. Bins are only used administratively to show the numbers of results in each.

Number of Bins - This field accepts the numbers 0, 2, 3, 4, or 5. If nothing is entered, the default number, 0, is maintained. **Required**.

Analytical Range - When a value other than 0 is entered in the Number of Bins box, you can enter the analytical range. This defines the default bin limits for the individual compartments. **Optional**.

Upper Limits of Bins - Used to specify the maximum possible value of the data counted in a bin. With the exception of the first and last bins, the upper limit of each bin defines the lower limit of the next bin. The lower limit of the first bin is a very low number regardless of the lower limit of the analytical range. The upper limit of the last bin is a very high number. Medical decision points are often used for bin limits. **Optional**.

Other Items

Three other checkboxes are present to give the user options on how the data are calculated:

Use 99% Conf for bounds: Instead of using 95% confidence intervals for scatter plot bounds, 99% confidence intervals are used.

Remove Outliers: If this box is checked, the program automatically identifies and discards outliers.

Disparate Scales: Check this box if the units for the X and Y methods are different. For most applications, the X and Y methods are similar so that the slope and intercept are expected to be 1.0 and 0.0 respectively. However, in some cases this module is used for linear regression calculations of very disparate methods instead of the more specialized method comparison. The Reference Intervals for clotting time of an APTT reagent can be established by preparing and analyzing a series of APTT specimens containing varying amounts of heparin. The strategy for naming the experiment and filling in the parameters screen entry boxes is shown in the table below. Three changes in the calculation algorithm occur:

- The program will always use the linear regression approach to calculate MDP's regardless of the magnitude of R.
- The program doesn't calculate or report biases. Instead it reports the regression residual. In addition, the t Test is never performed.
- The scatter plot is drawn with flexible scaling (i.e. the range of the X axis is not forced to be identical with that of the Y axis).

Strategy to Determine Reference Interval of Clotting time (APTT) By Plotting APTT clotting time versus using Heparin Conc's		
What to enter in the New Experiment screen:		
Analyte	**Instrument Name**	
	X Method	**Y Method**
Method	Heparin	Clotting time
What to enter in the Parameters screen:		
Check box for Disparate Scales		
Rep SD	1	40
MDP's	Approx 0.3 and 0.7	n/a

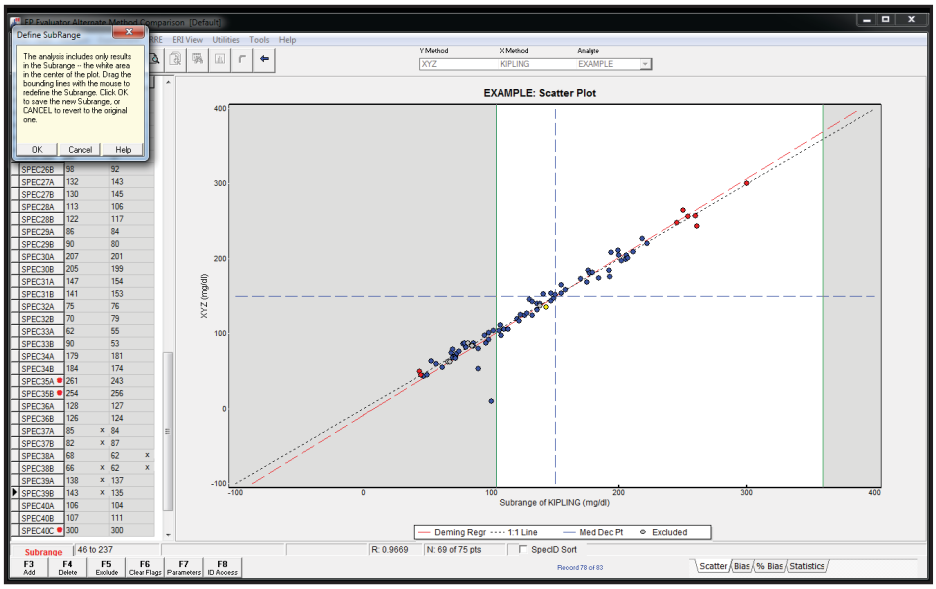
Experiment Detail Screen

This screen allows users to enter and edit experimental results. Users can change, exclude, or delete a result for a given specimen. An excluded result is not used in the calculations. The legend below the Scatter Plot displays the type of calculation used for the graph line.

By default, specimen IDs are listed in the Experiment Detail screen in the order they are entered. To sort specimen IDs in alphanumeric order on the Experiment Detail screen, select the **SpecID Sort** check box. Clear this box to return specimen IDs to the default order. This check box only applies to the Experiment Detail screen. The report always sorts specimen IDs in alphanumeric order.

Graphed Data Points

Points in the real-time graph are color- and shape-coded to show their use.



- Dark blue points are unexcluded results not currently being edited.
- Light blue points are unexcluded results being edited.
- Gray points are excluded results not currently being edited.
- Yellow points are excluded results being edited.
- Red points are outside the user-defined sub-range.
- Square points are outliers. Although they are yellow while being edited, they are otherwise white.

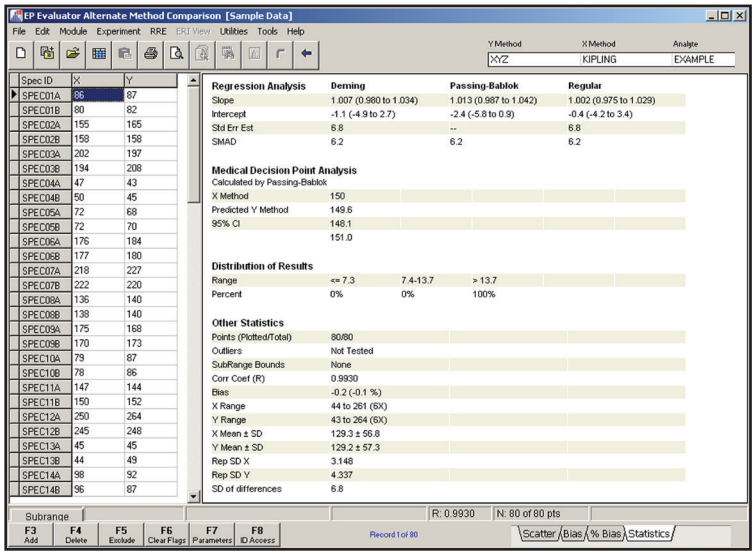
Subrange Controls

This feature allows the user to define a limited group of results to be included in the calculations based on the value of the X result. This is very useful when the data are non-linear or have large amounts of scatter at one or both ends, or when the data covers a very long range (over 100 fold). Note the following features.

The **Define Subrange** box provides the user the opportunity to save the current subrange. The **Subrange Limits** may be moved by the use of the mouse to define those points (contained in the white area) to be included in the calculation. The points in the gray area are colored red to show that they are excluded.

Calculation and Graphs

The AMC calculation process happens as results are added or edited manually. Calculations are displayed on the Statistics tab found on the Experiment Detail Screen:



Features of the calculation process include:

- By default, both Deming and regular regression statistics are calculated for every experiment. EE will also calculate and display Passing-Bablok regression statistics if the **AMC Passing-Bablok Type** option (found on the Calculations tab of the **Preferences screen**, accessible from the **File menu**) is set to Regression or Method Comparison.
- Changing the **AMC Passing-Bablok Type** option to Regression or Method Comparison displays the **AMC Graph/MDP** option, which allows users to configure the type of regression statistics used in the MDP and scatter plot regression line calculations.
- With respect to the calculation of the estimated Medical Decision Points for the Y method, see the section on Medical Decision Level Statistics.
- Outliers are detected automatically if the Remove Outliers checkbox in the Parameters Screen is checked. EP Evaluator uses a complex iterative algorithm to identify outliers. A point will be determined to be an outlier, if its distance from the regression line (residual) exceeds 10 times the Standard Error of Estimate (SEE). SEE is not computed from the full data set, but from the data set with outliers excluded.
- All non-outlier, unexcluded points in the defined subrange are included in the calculations of the regression statistics.
- Sometimes the slopes and intercepts will be red as compared with the expected black. This occurs when the 95% CI for the slope does not include 1.0 or the 95% CI for the intercept does not include zero.

- Bin analysis is used for administrative purposes only. For a discussion of this statistic, see section above on Experimental Parameters.
- Calculation of the t test can be turned off in **File**, **Preferences**.

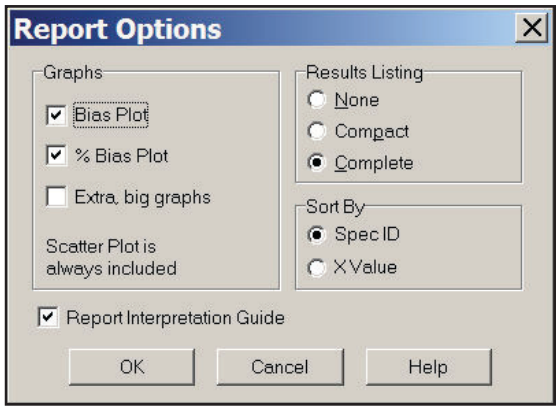
The user may select between several different graphing formats from the Graphs tab in **Preferences**, accessible from the **File** menu. The Scatter Plot Scaling option defines whether the X and Y axes on the scatter plot will have identical values (default is yes). The Bias Plot Scaling Option defines the placement of the zero bias line in the Bias plot. Either it will be calculated or placed in the middle of the Y axis. (Default is yes). The Bias Plot Style option controls whether the AMC analysis displays a Bias Plot or a Bland Altman Plot. (Default is Bias)

NOTE: When there are no more than a few hundred points, no delays are seen. However with a relatively slow computer and with large numbers (thousands) of points, there may be significant delays as each pair of points is added or edited. The way around these delays is to enter the points indirectly (either into a spreadsheet or into rapid results entry) and then import them into AMC.

Report Option Screen

This screen provides the user with a great deal of flexibility with respect to the reports. The elements on the reports under user control are:

The graphs and their size. You may choose whether the Bias Plot and Percent Bias Plot are to be included. (The scatter plot is always present.) You may also choose whether a second set of much larger graphs will be printed on another page. (Extra, big graphs).



The choices of results listings are: no results, a compact listing (listing includes X value, Y value and bias) and a complete listing (items in the compact listing plus the calculated Y value and the SEE factor).

Sort order for the results, either by specimen ID or by the magnitude of the X value.

Whether to include a Report Interpretation Guide. When printing multiple experiments, you will get only one copy of the guide.

The report is organized into several parts: tables describing the statistical results, graphs of results, and a list of results following the graphs. For a detailed discussion of the significance of these items, see Rhoads (2012) *Lab Statistics* manual.

Regression Analysis

The Regression Analysis Table is the most important table in this report.

Regression Analysis

	Deming	Passing-Bablok	Regular
Slope	1.007 (0.980 to 1.034)	1.012 (0.986 to 1.041)	1.002 (0.975 to 1.029)
Intercept	-1.1 (-4.9 to 2.7)	-2.3 (-5.7 to 1.0)	-0.4 (-4.2 to 3.4)
Std Err Est	6.8	--	6.8
SMAD	6.2	6.1	6.2

95% Confidence Intervals are shown in parentheses

Slope and its 95% confidence interval (CI) and Intercept and its 95% CI are calculated using all approaches.

Std Err Est is the standard error of the estimate, also expressed as SEE. It is calculated for the regular and Deming linear regression analyses.

SMAD (Scaled Median Absolute Deviation) is a value similar to Std Err Est in that it describes the scatter around best fit line, but developed with particular relevance to the Passing-Bablok approach as it is insensitive to outliers. The SMAD will only appear in the Regression Analysis table if Passing-Bablok statistics are calculated and displayed.

Medical Decision Level Statistics

The Medical Decision Point Analysis table is the second most important table in the report. However, it appears only when at least one Medical Decision Point (MDP) has been defined and when there are sufficient points to calculate reliable MDP's.

Medical Decision Point Analysis

Calculated by Passing-Bablok

X Method MDP	Y Method Pred. MDP	95% Conf. Limits Low	High
150	149.5	148.1	151.0

With respect to calculation of the estimated Medical Decision Points for the Y method, if R (correlation coefficient) is less than the user-selected value (0.975, 0.950 or 0.900), then the Partitioned Biases approach is used. A minimum of 12 sets of results are required for these statistics to be calculated. If the Partitioned Bias approach is used, these statistics will only be calculated if the MDP is within the range of results. The Partitioned Bias approach sorts the results into compartments. Then, it calculates the average bias and 95% CI from the results in each compartment. The number of compartments depends on the number of results. For 12 to 23 results, there will be 1 compartment; for 24 to 35 results, 2 compartments; and for 36 or more results, 3 compartments.

However, if R is greater than the user-selected value, MDPs for the Y method are calculated based on the settings configured by the user from the **Calculations** tab on the **File**, **Preferences** screen.

- If the AMC Passing-Bablok Type is set to **None**, MDPs are calculated using Deming.
- If the AMC Passing-Bablok Type is set to either **Regression** or **Method Comparison**, the **AMC Graph/MDP** option displays, allowing the user to specify if MDPs are calculated using Deming or Passing-Bablok.

Calculated by: The report displays whether the MDPs are calculated by Partitioned Bias, Deming, or Passing-Bablok.

X Method MDP is the medical decision point that the user inputs.

Y Method Pred. MDP is the MDP estimated statistically for the Y method.

95% Confidence Limits will fall within the ranges 95% of the time were the experiment to be conducted repeatedly on a similar population of specimens.

Supporting Statistics

The Supporting Statistics table contains the lesser statistical results. For a detailed discussion of the significance of these items, see Rhoads (2012) *Lab Statistics* manual.

Supporting Statistics

Corr Coef(R)	0.9930	Y Mean ± SD	129.2 ± 57.3	Points (Plotted/Total)	80/80
Bias	-0.2 (-0.1 %)	Std Dev Diffs	6.8	Outliers	Not Tested
X Mean ± SD	129.3 ± 56.8	SubRange Bounds	None	Scatter Plot Bounds	95% CI

Experiment Description

The Experiment Description table describes many of the non-statistical elements of the experiment. The remarkable item in this table is the Result Ranges which list the low and high result for each method.

Experiment Description

	X Method	Y Method
Expt Date:	01 Jun 2000	01 Jun 2000
Rep SD:	3.148	4.337
Result Ranges:	44 to 261	43 to 264
Units:	mg/dl	mg/dl
Reagent	Eximer Instruments Rgt222 exp 31 Dec 2010	Valued Vendor Rgt333 exp 31 Dec 2010
Calibrators	Eximer Instruments Cal333 exp 31 Dec 2010	Valued Vendor Cal456 exp 31 Dec 2010

Result Range Analysis

These data are printed only when there are at least 2 bins and the list of results has been requested. The bin data are based on the X Method.

Range defines the ranges of the bins. The purpose of this table is solely so the user can see the results distribution in each bin. A good distribution of results is essential to calculation of useful statistical values.

Result Range Analysis

Range	Percent
<= 60	9%
61-110	36%
111-175	30%
> 175	25%

Sample Reports

The two page sample report shown below is for one of the sample data sets included with EE as delivered. The report includes all major features (3 graphs, medical decision points, result range analysis) except the extra large graphs. Results are sorted by the magnitude of the X result.

Preliminary Marked on Reports

Occasionally, a large watermark “PRELIMINARY” will appear on the reports. The purpose of this is to encourage you to look more carefully at the report since one or more data points have been noted as unusual with respect to the rest of the data. Generally you can remove the watermark by excluding the point(s). The watermark is generated in the following cases:

- More than 5% of the data points are outliers.
- A distance between the highest (or lowest) point and the next point, exceeds 50% of the overall range of the data.

EP Evaluator®

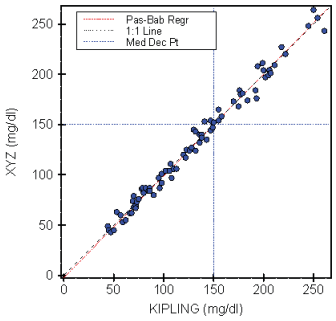
EXAMPLE

User Manual -- Data Innovations, LLC

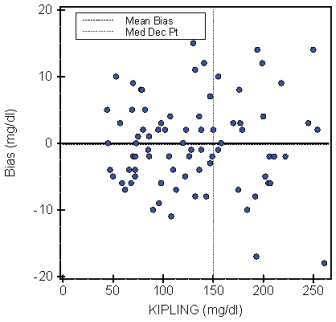
Alternate (Quantitative) Method Comparison

X Method KIPLING **Y Method XYZ**

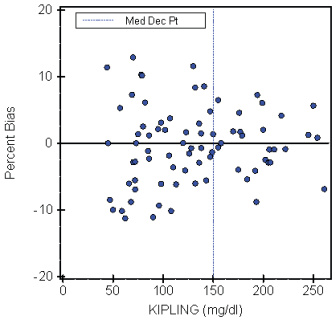
Scatter Plot



Bias



Percent Bias



Regression Analysis

	Deming	Passing-Bablok	Regular
Slope	1.007 (0.980 to 1.034)	1.013 (0.987 to 1.042)	1.002 (0.975 to 1.029)
Intercept	-1.1 (-4.9 to 2.7)	-2.4 (-5.8 to 0.9)	-0.4 (-4.2 to 3.4)
Std Err Est	6.8	--	6.8
SMAD	6.2	6.2	6.2

95% Confidence Intervals are shown in parentheses

Medical Decision Point Analysis

Calculated by Passing-Bablok

X Method MDP	Y Method Pred. MDP	95% Conf. Limits Low	High
150	149.6	148.1	151.0

Supporting Statistics

Corr Coef (R)	0.9930	Y Mean ± SD	129.2 ± 57.3	Points (Plotted/Total)	80/80
Bias	-0.2 (-0.1 %)	Std Dev Diffs	6.8	Outliers	Not Tested
X Mean ± SD	129.3 ± 56.8	SubRange Bounds	None	Scatter Plot Bounds	None

Experiment Description

	X Method	Y Method
Expt Date	01 Jun 2000	01 Jun 2000
Rep SD	3.148	4.337
Result Ranges	44 to 261	43 to 264
Units	mg/dl	mg/dl
Reagent	--	--
Calibrators	--	--
Analyst	Inez Doe	Inez Doe
Comment	Kipling comment	XYZ comment

Accepted by: _____ _____

Signature Date

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EXAMPLE

User Manual -- Data Innovations, LLC

Alternate (Quantitative) Method Comparison

X Method KIPLING **Y Method XYZ**

Experimental Results

Specimen	X	Y	Bias	Specimen	X	Y	Bias	Specimen	X	Y	Bias
SPEC01A	86	87	1	SPEC14B	96	87	-9	SPEC28A	113	106	-7
SPEC01B	80	82	2	SPEC15A	69	74	5	SPEC28B	122	117	-5
SPEC02A	155	165	10	SPEC15B	73	73	0	SPEC29A	86	84	-2
SPEC02B	158	158	0	SPEC16A	53	63	10	SPEC29B	90	80	-10
SPEC03A	202	197	-5	SPEC16B	57	60	3	SPEC30A	207	201	-6
SPEC03B	194	208	14	SPEC17A	149	147	-2	SPEC30B	205	199	-6
SPEC04A	47	43	-4	SPEC17B	155	154	-1	SPEC31A	147	154	7
SPEC04B	50	45	-5	SPEC18A	200	204	4	SPEC31B	141	153	12
SPEC05A	72	68	-4	SPEC18B	211	209	-2	SPEC32A	75	76	1
SPEC05B	72	70	-2	SPEC19A	110	106	-4	SPEC32B	70	79	9
SPEC06A	176	184	8	SPEC19B	108	97	-11	SPEC33A	62	55	-7
SPEC06B	177	180	3	SPEC20A	123	125	2	SPEC33B	59	53	-6
SPEC07A	218	227	9	SPEC20B	120	120	0	SPEC34A	179	181	2
SPEC07B	222	220	-2	SPEC21A	136	132	-4	SPEC34B	184	174	-10
SPEC08A	136	140	4	SPEC21B	132	124	-8	SPEC35A	261	243	-18
SPEC08B	138	140	2	SPEC22A	98	101	3	SPEC35B	254	256	2
SPEC09A	175	168	-7	SPEC22B	102	104	2	SPEC36A	128	127	-1
SPEC09B	170	173	3	SPEC23A	199	211	12	SPEC36B	126	124	-2
SPEC10A	79	87	8	SPEC23B	206	204	-2	SPEC37A	85	84	-1
SPEC10B	78	86	8	SPEC24A	72	67	-5	SPEC37B	82	87	5
SPEC11A	147	144	-3	SPEC24B	70	68	-2	SPEC38A	68	62	-6
SPEC11B	150	152	2	SPEC25A	192	184	-8	SPEC38B	66	62	-4
SPEC12A	250	264	14	SPEC25B	193	176	-17	SPEC39A	138	137	-1
SPEC12B	245	248	3	SPEC26A	95	97	2	SPEC39B	143	135	-8
SPEC13A	45	45	0	SPEC26B	98	92	-6	SPEC40A	106	104	-2
SPEC13B	44	49	5	SPEC27A	132	143	11	SPEC40B	107	111	4
SPEC14A	98	92	-6	SPEC27B	130	145	15				

Values with an "X" were excluded from the calculations.

Chapter

12

Qualitative and Semi-Quantitative Method Comparison

This module provides for entry and comparison of results for both qualitative and semi-quantitative methods. The qualitative analysis implements the CLSI EP12-A (CLSI:EP12) document. Three different types of method comparison calculations may be done on the results using this module:

- **Qualitative with Gold Standard**
- **Qualitative without Gold Standard**
- **Semi-quantitative**

Gold Standard calculations assume that the reference method is absolutely correct. It applies only to qualitative evaluations. It calculates items such as specificity and sensitivity.

Non-Gold Standard calculations make no assumptions about whether either method is correct or not. They can be applied to either qualitative or semi-quantitative evaluations to calculate the degree of agreement and the direction of disagreement if any.

Experiment Examples

Method Comparison Approach: Specimens can be selected to represent a wide variety of patient conditions without regard for their frequency in the population. The selected specimens are known as a reference panel. This approach determines the ability of a method to detect a certain condition.

Qualitative with Gold Standard Example: A study by prospective users of automated hematology instruments to determine the ability of an instrument to detect pathological conditions. The specimens are selected from an oncology clinic to represent a broad sampling of hematological disease. Positives are defined as being any one of a certain list of pathological cells. The gold standard reference method is manual cell count differential.

Qualitative without Gold Standard Example: A study by prospective users comparing the performance of two instruments for several drugs of abuse (DAU) analytes. The specimens are selected from the specimens routinely analyzed by the lab.

Semi-quantitative Example: A study comparing two assays for urinary protein, one a semi-quantitative dipstick method, the other a quantitative method. The results for the quantitative method are divided into groups corresponding to the various semi-quantitative categories. This approach can be used to compare semi-quantitative POC tests with quantitative tests from the main laboratory.

Clinical Utility Approach (Qualitative with Gold Standard): Specimens are obtained from unselected patients representing a specific population. Typically, specimens are obtained from several hundred (or more) consecutive patients presenting to a clinic for a specified reason. The reference method may be either a definitive laboratory method or some other definitive clinical test. This module is designed to assess the ability of a qualitative method to detect the condition in a population. Reference: Galen and Gambino (1975).

NOTE: If you want to determine the **Clinical Utility of Quantitative Methods**, please use the ROC Curve module (see Chapter 21, *ROC Curve Analysis*). It provides a much better statistical analysis than QMC for these types of experiments.

Data Requirements

A minimum of 20 specimens is required for a comparison. In reality, 50 specimens or more of each class as defined by the reference method are needed in order to obtain good statistics.

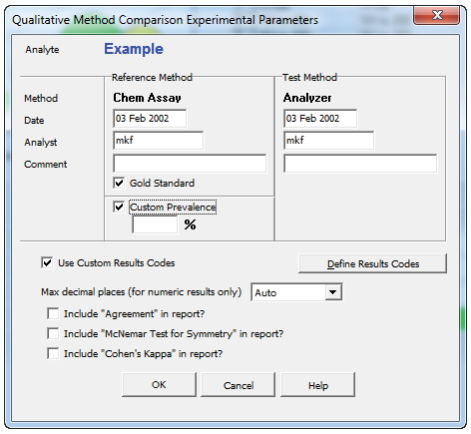
No effective upper limit on the number of specimens is defined in the program. Since calculations are done at run-time, when the number of specimens is several thousand, the calculations will become so slow that manual entry of results will not be acceptable. The way around this is to import results for large experiments from a file.

Results for many methods can be compared—two methods at a time. To perform a comparison, a pair of methods must be linked. One method may be linked to several other methods simultaneously.

Incoming results may be either qualitative, semi-quantitative, or quantitative. Quantitative results are transformed to the other two varieties by defining limits. In other words, a result of 0 to 0.4 might be “negative”, 0.5 to 1.9 “trace”, 2.0 to 10.0 “1+” and so on.

Qualitative results by default have values of P (positive) or N (negative). Other values can be assigned. Semi-quantitative results must have values assigned prior to their input into the system.

Parameters Screen



The basic parameters entered in this screen for each method are listed below. Define the existing or reference method as the X method and the other one(s) as the Y method.
Two fields apply only to qualitative studies.

Gold Standard: Select if the reference method is a gold standard.

Custom Prevalence: Select if you want to specify a prevalence of positive and negative specimens different from that encountered in the study population. This is the percent of positive individuals in a defined population. It only applies to Gold Standard situations and is used to calculate only the Predictive Value of a Positive or Negative.

Custom Results Code: Primarily applies to semi-quantitative studies. It allows the user to define names for the different categories such as “Negative”, “Trace”, “1+” and so on. If selected, a new button **Define Results Codes** appears which provides access to the **Define Results Coding** screen.

Max decimal places is applicable only when numeric results are used. It is the maximum number of decimal places for reports.

To include the following statistics on both the Experiment Detail screen and in the report, check the applicable check boxes on the Parameters screen.

Agreement refers to the percent of total cases in which the two methods give the same result.

McNemar Test for Symmetry is a test for bias—whether one method is consistently larger than the other. If the number of cases where X>Y is equal (within random error) to the number of cases where X<Y, the method is unbiased and the symmetry test passes. If most of the differences between X and Y occur when X>Y (or when X<Y), the symmetry test fails.

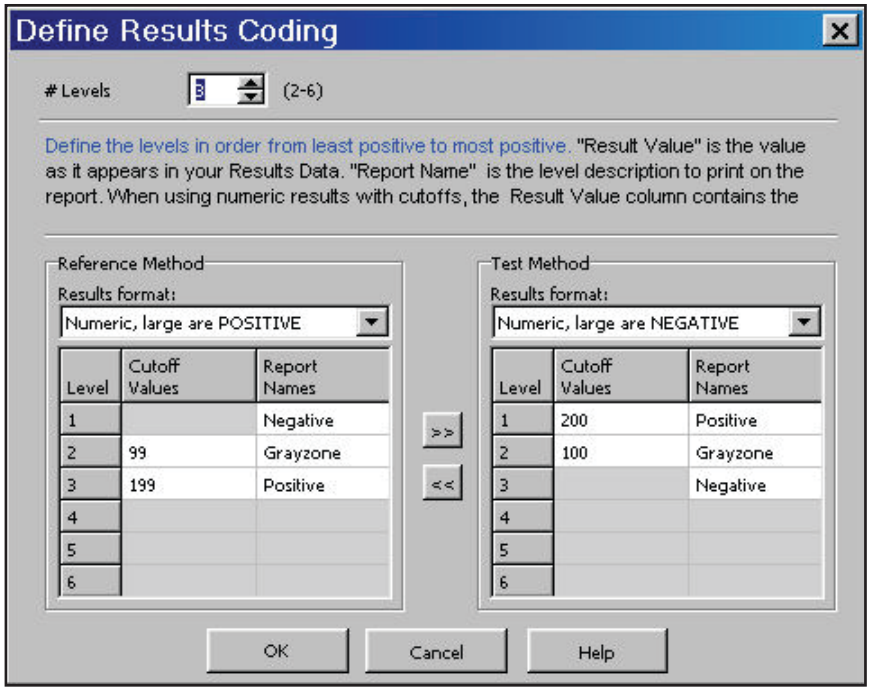
Cohen’s Kappa is similar to Agreement, but adjusted for the probability that the two methods agree by chance. Kappa ranges between -100% and 100%. A value of 0% indicates random agreement. A value of 100% indicates perfect agreement. It is desirable for this value to be well above 75%.

Define Results Coding

This dialog screen is used to define the names and cutoff values, if any, for the variables used in qualitative and semi-quantitative experiments. If data are to be captured from another source, the names of the results must be defined before the results are captured. Otherwise EE will not know what to do with them.

The fields in this screen are:

- Number of levels (2 to 6). Qualitative is always 2; the rest are semi-quantitative.
- Under the Define Results Coding screen, a drop-down menu appears which provides 3 categories:
  1. **Alphanumeric** for cases in which the results are already qualitative or semi-quantitative. Alphanumeric level designations appear in a drop-down list when results are entered in the Experiment Detail Screen.



  2. **Numeric, large are POSITIVE** for cases in which the positive quantitative results are greater than the cutoff.
  3. **Numeric, large are NEGATIVE** for cases in which the positive quantitative results are less than the cutoff.

- A column for each method to specify cutoff values for the numeric methods. The location and cutoff values for semi-quantitative methods is potentially confusing. See discussion below on assignment of cutoff values.
- A column for each method to provide names for each level which will appear in a table on the report.

Note also the two double arrows in the center of the screen. These provide for rapid transfer of the cutoff values and report names from one side to the other.

Assignment of Cutoff Values: Numeric, Large are Positive

The key elements to remember for this case are:

- The content of the cutoff value column for the first level is blank.
- The content of the cutoff value for the each succeeding level is the highest value of the next lower level.
  For example, suppose there are three levels. Negative (range 0-99), Gray zone (range 100-199), and Positive (range 200-1000). The values entered next to Negative will be blank, next to Gray zone will be 99, and next to Positive will be 199.

Assignment of Cutoff Values: Numeric, Large are Negative

The key elements to remember for this case are:

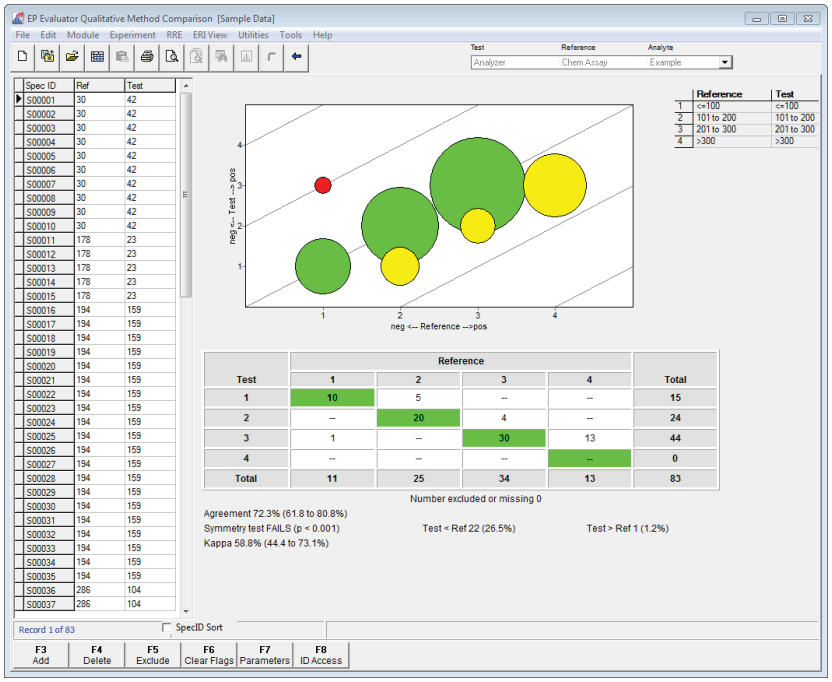
- The content of the cutoff value column for the last level is blank.
- The content of the cutoff value for the each succeeding level (going down) is the highest value of the next higher level.

  For example, suppose there are three levels. Negative (range 200-1000), Gray zone (range 100-199), and Positive (range 0-99). The values entered next to Negative will be 199, next to Gray zone will be 99, and next to Positive will be blank.

Experiment Detail Screen

This screen works like most of the other module detail screens. There is a grid on the left where you enter results, and buttons at the bottom for common operations.

The X axis represents the reference method, and the Y axis is the test method. The 1, 2, 3, 4, axis labels are the test levels. The actual names of the levels are usually too long to fit conveniently on the graph, but are described in the legend to the right of the graph.



By default, specimen IDs are listed in the Experiment Detail screen in the order they are entered. To sort specimen IDs in alphanumeric order on the Experiment Detail screen, select the **SpecID Sort** check box. Clear this box to return specimen IDs to the default order. This check box only applies to the Experiment Detail screen. The report always sorts specimen IDs in alphanumeric order.

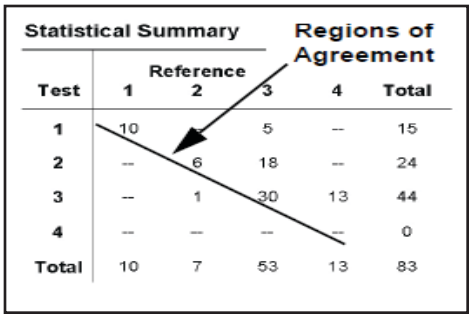
Interpreting Results

The major elements involved in interpreting results are:

- Statistical Summary (Truth Table)
- Bubble Chart
- Statistical Analysis

Statistical Summary (Truth Table)

The Statistical Summary is one of the most important elements in this report as it counts the specimens in each region. In a qualitative comparison, there are four regions. In semi-quantitative comparisons, there are more.



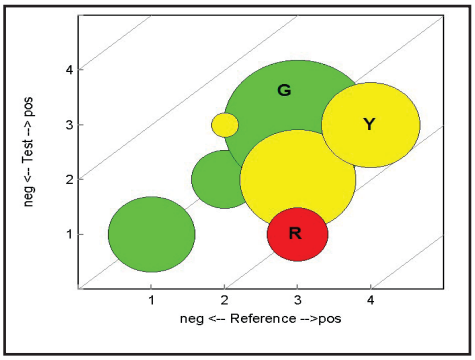
The regions of agreement are on the diagonal running from the top left corner to the bottom right corner. All the other regions represent disagreements, some more serious than others, namely which is worse, false positives or false negatives. Two environments in which disagreement is particularly important are:

Qualitative False Negatives are undesirable in situations (such as hematology white cell differentials) in which failure to detect disease can be disastrous.

Qualitative False Positives are undesirable in situations (such as drugs of abuse testing) in which a serious consequences can result from positive results.

Bubble Chart

This chart provides a colorful summary of the results. Note that the size of the bubbles (area) reflects the relative number of items in that category.



- Green bubbles (agreement) are on the central diagonal.
- Yellow bubbles (1 level of disagreement) are immediately adjacent to the central diagonal. (Semi-quantitative only)
- Red bubbles (Qualitative: all disagreement; Semi-Quantitative: >1 level of disagreement) are further away from the central diagonal.

Statistics Tables

These statistical measures evaluate the probability that a test will detect a positive condition in specimens presented to it. There are two different types of tables, one for Qualitative comparisons with Gold Standards, and one for everything else.

Qualitative - Gold Standard: These terms are defined in the Glossary. Please note that 95% confidence intervals are calculated for several statistics.

Statistical Analysis
(Comparison of Test Method to a Gold Standard)

Agreement	94.1% (87.8 to 97.3%)
Sensitivity	93.4% (84.3 to 97.4%)
Specificity	95.1% (83.9 to 98.7%)

95% confidence intervals calculated by the "Score" method.

Positive Agreement	93.4%
Negative Agreement	95.1%
Prevalence	59.8%
Predictive Value Positive	96.6%
Predictive Value Negative	90.7%

Prevalence estimated from experimental results.

Everything else: Several of the terms in this table are unfamiliar to most clinical laboratorians. They are:

- **McNemar Test for Symmetry**
- **Cohen's Kappa**

Statistical Analysis
(Comparison of two Laboratory Methods)

Agreement	94.6% (92.3 to 96.2%)
Positive Agreement	95.3%
Negative Agreement	93.7%

95% confidence interval calculated by the "Score" method.

McNemar Test for Symmetry:

Test < Reference	14 (2.6%)
Test > Reference	15 (2.8%)

Symmetry test PASSES p = 0.853 (ChiSq=0.034, 1 df)
A value of p<0.05 suggests that one method is consistently "larger".

Cohen's Kappa	89.0% (85.1 to 92.9%)

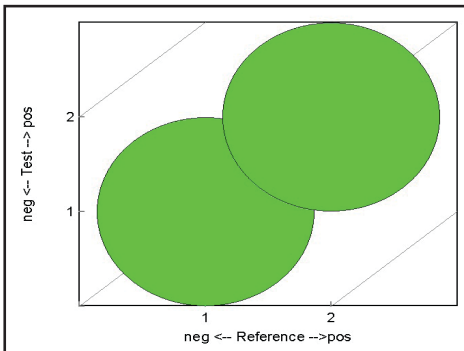
Kappa is the portion of agreement above what is expected by chance.
The rule of thumb is that Kappa > 75% indicates "high" agreement.
We would like to see VERY high agreement (close to 100%).

Case Studies

A few case studies are useful to show results from various types of studies.

A Perfect Case

In this case there is total agreement. No points are off the diagonal. The test for symmetry PASSES. Cohen's Kappa test scores at 100%.



Statistical Analysis
(Comparison of two Laboratory Methods)

Agreement	100.0% (96.3 to 100.0%)
Positive Agreement	100.0%
Negative Agreement	100.0%

95% confidence intervals calculated by the "Score" method.

McNemar Test for Symmetry:

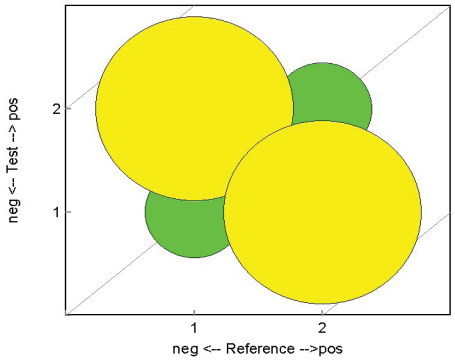
Test < Reference	0 (0.0%)
Test > Reference	0 (0.0%)
Symmetry test PASSES	

Cohen's Kappa	100.0% (100.0 to 100.0%)

Kappa is the proportion of agreement above what's expected by chance. Rule of thumb is Kappa>75% indicates "high" agreement. We would like to see VERY high (close to 100%) agreement.

An Awful Case

In this case there is substantial disagreement. Of the 100 points, there are only 10 with positive agreement and 10 with negative agreement. McNemar's Test for Symmetry PASSES, but Cohen's Kappa yields a score of -60%.



Statistical Analysis
(Comparison of two Laboratory Methods)

Agreement	20.0% (13.3 to 28.9%)
Positive Agreement	20.0%
Negative Agreement	20.0%

95% confidence intervals calculated by the "Score" method.

McNemar Test for Symmetry:

Test < Reference	40 (40.0%)
Test > Reference	40 (40.0%)
Symmetry test PASSES	p > 0.999 (ChiSq=0.000, 1 df)

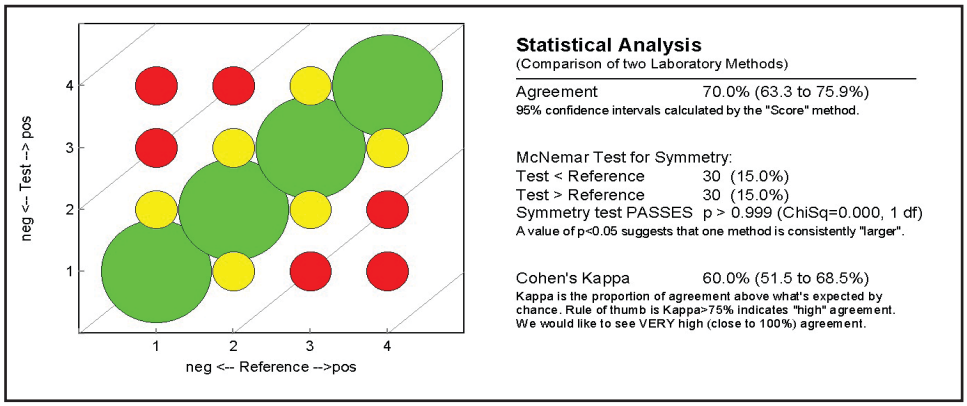
A value of p<0.05 suggests that one method is consistently "larger".

Cohen's Kappa	-60.0% (-75.7 to -44.3%)

Kappa is the proportion of agreement above what's expected by chance. Rule of thumb is Kappa>75% indicates "high" agreement. We would like to see VERY high (close to 100%) agreement.

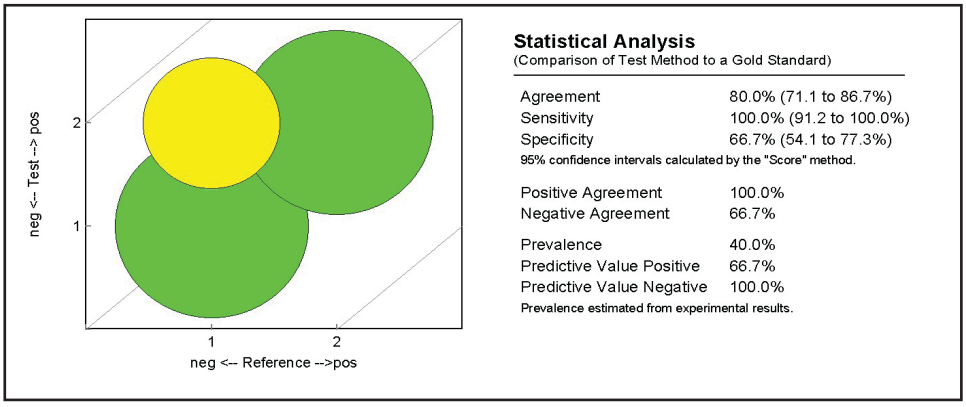
Even Distribution

In this semi-quantitative case with 4 states, 70% of the results are in agreement; 5% of the results are in each of disagreement regions. McNemar's Test for Symmetry PASS-ES. Cohen's Kappa yields a score of 60%.



Hematology - Fairly Good Case

This case would be considered to be fairly good in a hematology environment.



The experiment: white cell differential results from a hematology instrument are being compared with the results of a manual cell differential. The manual differential is a gold standard.

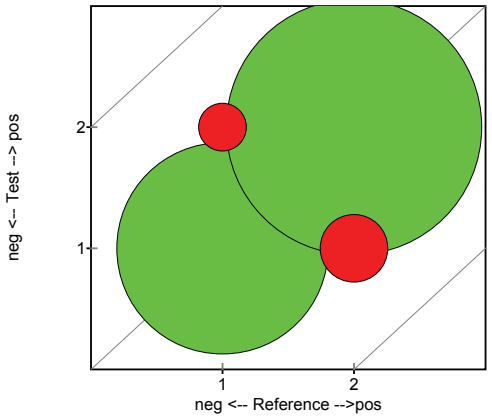
This is considered a reasonably good test because there were NO false negatives. In other words, the instrument detected all the cases which were morphologically positive. No cases in which the patient had the disease were missed. This is a major positive.

The instrument does leave something to be desired in that it detected a substantial number of false positives (20% of total cases, 40% of negative cases).

Qualitative Method Comparison Report - (Gold Standard)

Qualitative Method Comparison

Ref. Method: H. pylori **Test Method: NCCLSEx1a**



Statistical Analysis
(Comparison of Test Method to a Gold Standard)

Agreement	94.1% (87.8 to 97.3%)
Sensitivity	93.4% (84.3 to 97.4%)
Specificity	95.1% (83.9 to 98.7%)

95% confidence intervals calculated by the "Score" method.

Positive Agreement	93.4%
Negative Agreement	95.1%
Prevalence	59.8%
Predictive Value Positive	96.6%
Predictive Value Negative	90.7%

Prevalence estimated from experimental results.

Statistical Summary

	Negative Reference	Positive Reference	Total
Negative Test	39	4	43
Positive Test	2	57	59
Total	41	61	102

Number excluded or missing: 0

Legend:

	Reference	Test
1	Negative (N)	Negative (N)
2	Positive (P)	Positive (P)

Experiment Description

	Reference Method	Test Method
Analyst:	mkf	mkf
Date:	08 Dec 2001	08 Dec 2001
Comment:		

Accepted by: _____ _____
Signature Date

Qualitative Method Comparison Report - (Other)

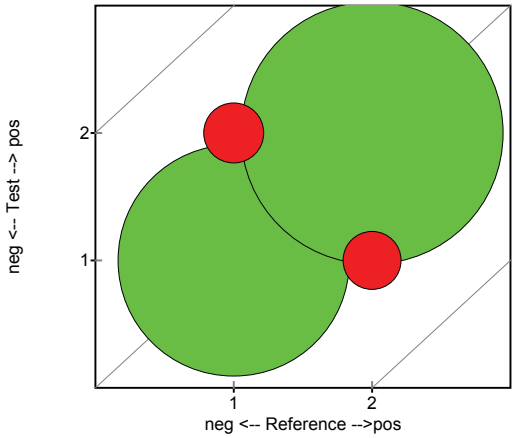
EP Evaluator®

ELISA

User's Manual -- Data Innovations

Qualitative Method Comparison

Ref. Method: Immunochromatic **Test Method: NCCLSEx2**



Statistical Analysis

(Comparison of two Laboratory Methods)

Agreement	94.6% (92.3 to 96.2%)
Positive Agreement	95.3%
Negative Agreement	93.7%

95% confidence intervals calculated by the "Score" method.

McNemar Test for Symmetry:

Test < Reference	14 (2.6%)
Test > Reference	15 (2.8%)
Symmetry test PASSES	p = 0.853 (ChiSq=0.034, 1 df)

A value of p<0.05 suggests that one method is consistently "larger".

Cohen's Kappa	89.0% (85.1 to 92.9%)

Kappa is the proportion of agreement above what's expected by chance. Rule of thumb is Kappa>75% indicates "high" agreement. We would like to see VERY high (close to 100%) agreement.

Statistical Summary

	Negative Reference	Positive Reference	Total
Negative Test	222	14	236
Positive Test	15	285	300
Total	237	299	536

Number excluded or missing: 0

Legend:

	Reference	Test
1	Negative (N)	Negative (N)
2	Positive (P)	Positive (P)

Experiment Description

	Reference Method	Test Method
Analyst:	mkf	mkf
Date:	07 Dec 2001	07 Dec 2001
Comment:		

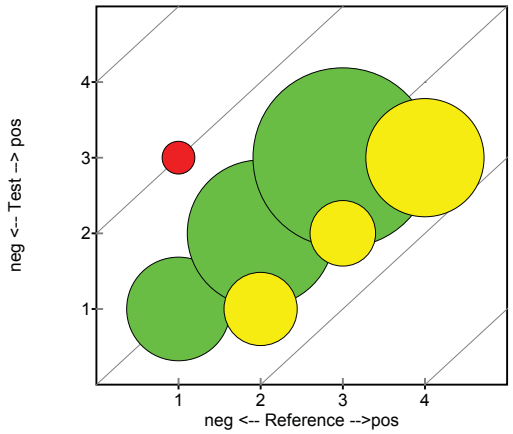
Accepted by: _____ _____

Signature Date

Semi-Qualitative Method Comparison Report

Semi-Quantitative Method Comparison

Ref. Method: Chem Assay **Test Method: Analyzer**



Statistical Analysis
(Comparison of two Laboratory Methods)

Agreement 72.3% (61.8 to 80.8%)
95% confidence intervals calculated by the "Score" method.

McNemar Test for Symmetry:
Test < Reference 22 (26.5%)
Test > Reference 1 (1.2%)
Symmetry test FAILS p < 0.001 (ChiSq=19.174, 1 df)
A value of p<0.05 suggests that one method is consistently "larger".

Cohen's Kappa 58.8% (44.4 to 73.1%)
Kappa is the proportion of agreement above what's expected by chance. Rule of thumb is Kappa>75% indicates "high" agreement. We would like to see VERY high (close to 100%) agreement.

Statistical Summary

Test	Reference 1	2	3	4	Total
1	10	5	--	--	15
2	--	20	4	--	24
3	1	--	30	13	44
4	--	--	--	--	0
Total	11	25	34	13	83

Number excluded or missing: 0

Legend:

	Reference	Test
1	Very Negative (<=100)	Very Negative (<=100)
2	Negative (101 to 200)	Negative (101 to 200)
3	Positive (201 to 300)	Positive (201 to 300)
4	Very Positive (>300)	Very Positive (>300)

Experiment Description

	Reference Method	Test Method
Analyst:	mkf	mkf
Date:	03 Feb 2002	03 Feb 2002
Comment:		

Accepted by: _____ _____
Signature Date

Qualitative Method Comparison Report - (Results)

Qualitative Method Comparison

Ref. Method: H. pylori **Test Method: NCCLSEx1a**

Experimental Results

Spec ID	Ref	Test	Spec ID		Ref	Test	Spec ID	Ref	Test
S00001	N	N	S00035		N	N	S00069	P	P
S00002	N	N	S00036		N	N	S00070	P	P
S00003	N	N	S00037		N	N	S00071	P	P
S00004	N	N	S00038		N	N	S00072	P	P
S00005	N	N	S00039		N	N	S00073	P	P
S00006	N	N	*S00040*	*FN*	*P*	*N*	S00074	P	P
S00007	N	N	*S00041*	*FN*	*P*	*N*	S00075	P	P
S00008	N	N	*S00042*	*FN*	*P*	*N*	S00076	P	P
S00009	N	N	*S00043*	*FN*	*P*	*N*	S00077	P	P
S00010	N	N	*S00044*	*FP*	*N*	*P*	S00078	P	P
S00011	N	N	*S00045*	*FP*	*N*	*P*	S00079	P	P
S00012	N	N	S00046		P	P	S00080	P	P
S00013	N	N	S00047		P	P	S00081	P	P
S00014	N	N	S00048		P	P	S00082	P	P
S00015	N	N	S00049		P	P	S00083	P	P
S00016	N	N	S00050		P	P	S00084	P	P
S00017	N	N	S00051		P	P	S00085	P	P
S00018	N	N	S00052		P	P	S00086	P	P
S00019	N	N	S00053		P	P	S00087	P	P
S00020	N	N	S00054		P	P	S00088	P	P
S00021	N	N	S00055		P	P	S00089	P	P
S00022	N	N	S00056		P	P	S00090	P	P
S00023	N	N	S00057		P	P	S00091	P	P
S00024	N	N	S00058		P	P	S00092	P	P
S00025	N	N	S00059		P	P	S00093	P	P
S00026	N	N	S00060		P	P	S00094	P	P
S00027	N	N	S00061		P	P	S00095	P	P
S00028	N	N	S00062		P	P	S00096	P	P
S00029	N	N	S00063		P	P	S00097	P	P
S00030	N	N	S00064		P	P	S00098	P	P
S00031	N	N	S00065		P	P	S00099	P	P
S00032	N	N	S00066		P	P	S00100	P	P
S00033	N	N	S00067		P	P	S00101	P	P
S00034	N	N	S00068		P	P	S00102	P	P

X:Excluded FP:False Positive FN:False Negative

Chapter

13

Multiple Instrument Comparison

This Multiple Instrument Comparison (MIC) module provides for comparison of multiple harmonized quantitative instruments. This operation is performed for several reasons:

- It gives labs confidence that they are getting similar results from their various instruments;
- It is required by CLIA ‘88 (Section 493.1281; Comparison of test results). CLIA requires that labs compare their instruments at least once every six months. Some labs may want to check them more often.

MIC is designed to compare multiple instruments which are currently being used for production in a health care facility. These instruments are assumed to be harmonized, i.e. they are expected to produce identical quantitative results within an expected range of error.

MIC is not designed to compare a prospective instrument with an existing instrument, also known as a crossover experiment. That type of experiment should be done using Alternate Method Comparison or CLSI EP9 Method Comparison.

Definitions

Target value is the result for a given specimen and analyte which is considered to be the best estimate of the true value. Target values are calculated two different ways:

- No target instruments are specified. In this case, target values are calculated from the median results of all the instruments. All instruments are evaluated and graphed.
- Target instrument(s) are specified. Target values are calculated from the median result(s) of only the target instruments. In this case, only non-target instruments are evaluated and graphed. This case is useful when evaluating POC devices.

Target instrument is an instrument which produces results used to establish the target values for each specimen.

Evaluated instrument (also called a non-target instrument) is an instrument for which statistics are calculated; there must be at least two of these in an experiment.

Coverage ratio is the percent overlap between the range of target values used in the experiment and the reportable range of the method. The higher the better. At minimum, the specimens should cover the range of results normally encountered by a lab. For example, it is generally not satisfactory to test only specimens in the normal range if a significant portion of the specimens which the laboratory normally encounters are much higher than the normal range.

Allowable error is a user-defined maximum acceptable difference between a result and the corresponding target value. The instrument will pass as long as none of the differences between any of its results and the corresponding target values exceed the allowable error. Statistically, one cannot justify setting the allowable error to be greater than the Total Allowable Error for the method. For the CLIA analytes in the United States, allowable error may be set at the proficiency testing limits.

Missing Data

Missing data is dealt with in two ways:

- If any data is missing, then that specimen is totally ignored and no calculations are done on it at all. This is recommended when the number of instruments is small (5 or less).
- If any data is missing, then the calculations are done on the remaining data under the conditions specified below.

This MIC missing data mode is controlled by going to the Files menu, Preferences form, and clicking on the Calculations tab. Near the bottom, you will find a check box labeled “Allow limited amounts of missing MIC results”. The default is to require all data to be present (un-checked); however, if you check this box, a limited amount of specimens with missing results are eligible for calculations.

In the “checked” mode, the following rules apply:

Calculations are only performed on a specimen for a given instrument if both a result and a target value exist.

Case 1: Target Instruments are specified:
If the number of Target Instruments is less than 3, then target values for a specimen are only calculated if all results for the Target Instruments are present.
If the number of Target Instruments exceeds 3, then target values for a specimen are calculated so long as no more than one result for the Target Instruments is missing.
Case 2: Target Instruments are not specified:
If the number of Instruments is less than 3, then target values for a specimen are only calculated if all results are present.

If the number of Instruments exceeds 3, then target values for a specimen are calculated so long as results exist for more than 50% of the instruments.

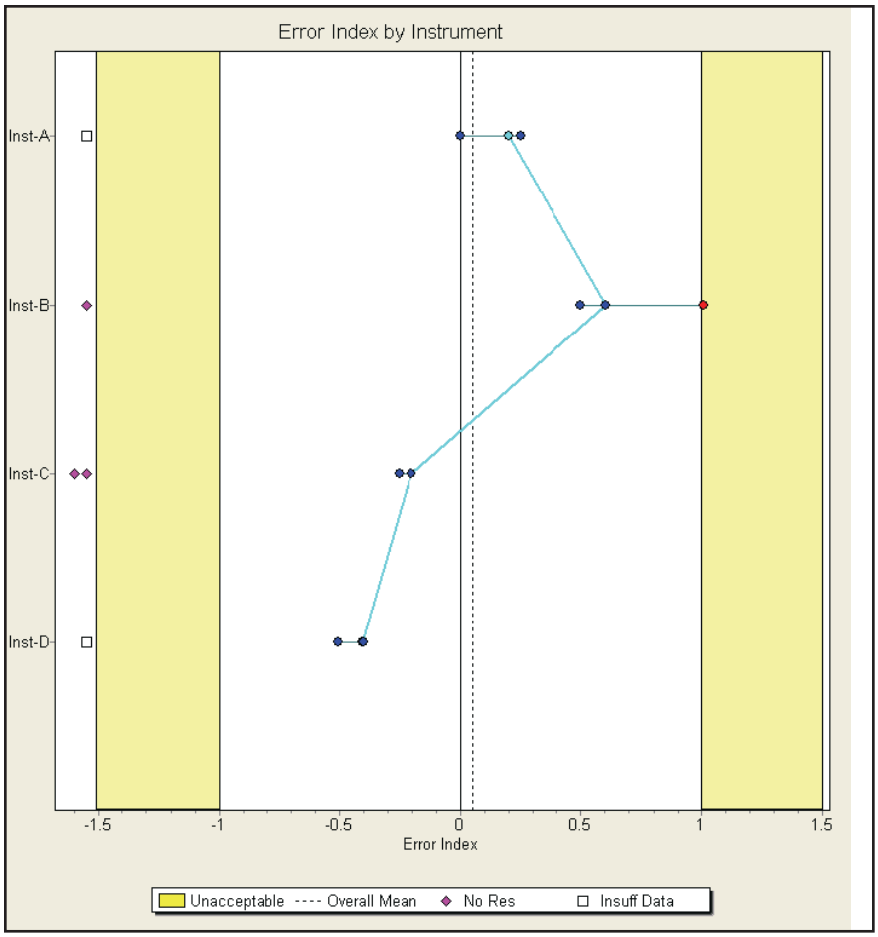
Missing results are highlighted in purple, and a new button is provided (labeled "Missing") which allows you to move to the next missing result quickly and easily.

Record 1 of 4

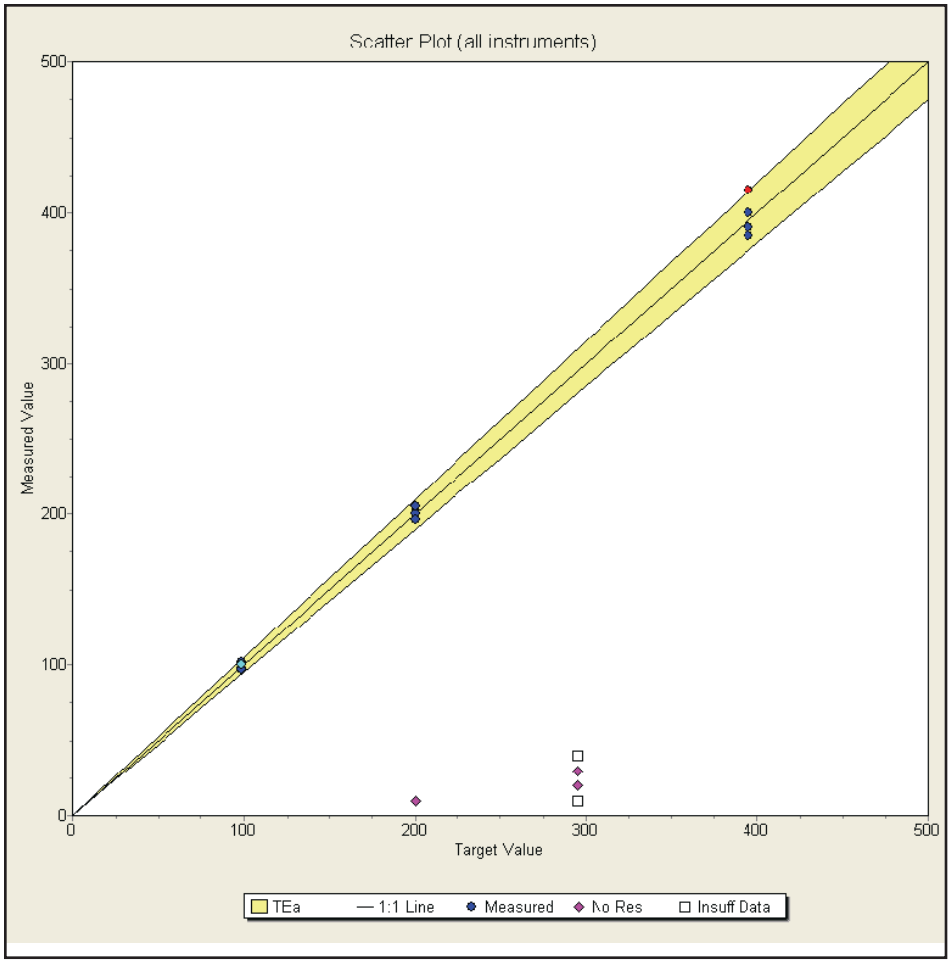
SpecID	Inst-A	Inst-B	Inst-C	Inst-D
S00001	100	102	98	97
S00002	200	205		196
S00003	300			290
S00004	400	415	390	385

Missing results are graphed as follows:

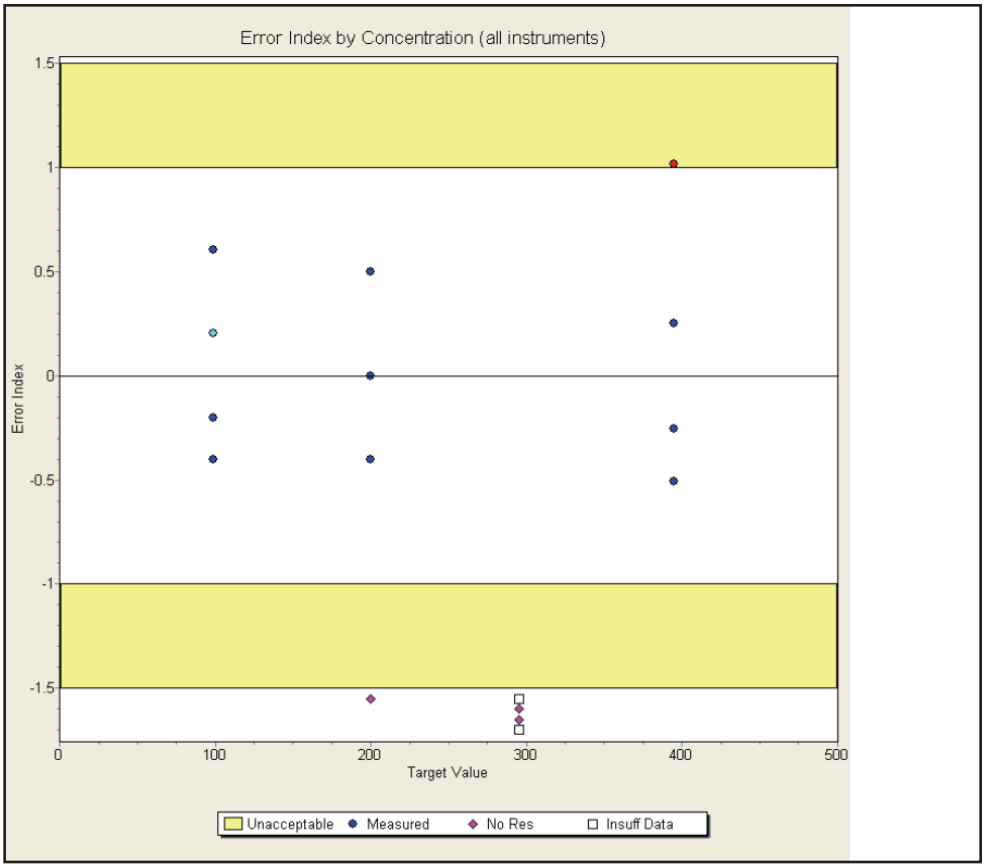
- **Error Index by Instrument**: a purple diamond is placed along the left side of the graph for each missing result, next to the name of the appropriate instrument. An empty square is placed along the left side of the graph for any result which is present for a specimen for which a target value could not be calculated. The following graph embodies the data as shown above:



- **Scatter Plot**: a purple diamond is placed at the bottom of the graph for each missing result, with an X value equal to that of the specimen's target value. An empty square is placed at the bottom of the graph for any result which is present for a specimen for which a target value could not be calculated.



- **Error by Concentration:** a purple diamond is placed at the bottom of the graph for each missing result, with an X value equal to that of the specimen's target value. An empty square is placed at the bottom of the graph for any result which is present for a specimen for which a target value could not be calculated.



Experimental Design

The MIC experiment is designed to analyze the results of several specimens for a series of analyzers which are assayed concurrently.

- The analyzers to which this experiment is applied are assumed to be harmonized, (i.e. when given a specimen for analysis, the results are expected to be the same within a user-specified allowable error).
- The user specifies the instruments to be included in the experiment. Maximum number of instruments in one experiment is 30.
- The user selects the specimens so that the results cover the range commonly encountered in patient testing. These may be patient specimens or manufactured specimens (calibrators, QC specimens, linearity standards). Additional criteria for selection of specimens are:
  - The concentration of the analytes must be stable over the few hours during which the experiment is conducted.
  - There must be no matrix effects across the instruments being tested. See the Glossary for a definition of matrix effects.

  - There must be sufficient volume for each specimen so that it can be assayed by all the instruments. If several bottles of a manufacturer's material for a given specimen are required to have sufficient volume for an experiment, mix the contents of all the bottles together before the experiment to eliminate the possibility of dilution error.
- The user analyzes the specimens on all the instruments. This must occur in a time period such that the concentration of the analytes does not change significantly. Normally this should be no more than 2 to 3 hours. The shorter this time period, the less opportunity there will be for error from this source.
- After the analyses are complete, the results are entered into EE for statistical analysis.

The module is designed to accommodate a maximum of one experiment a day for a given set of instruments. It stores the 3 most recent experiments. If results for 3 experiments are stored, addition of data for another experiment bumps the oldest one off the end.

Specimen Selection Issues

Generally two types of specimens will be used in an MIC experiment.

- **Patient specimens.** The advantage of these specimens is that they have no matrix effects. The disadvantages are two-fold: volume and magnitude of result. One may need to combine several specimens in order to get sufficient volume. Often it is not easy to obtain specimens which have relatively high and low results.

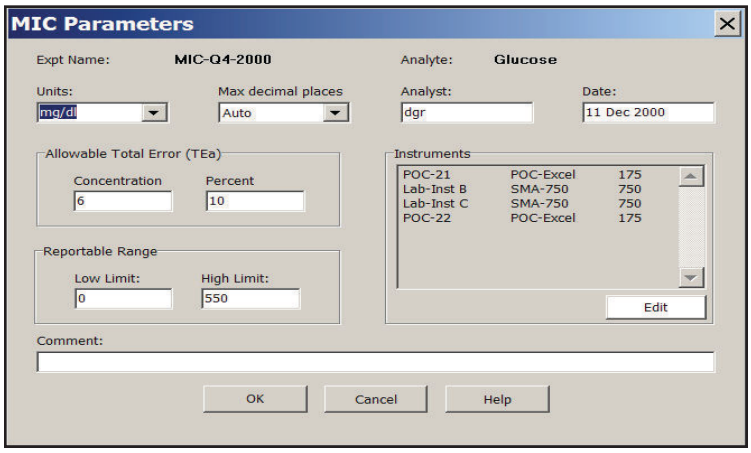
- **Linearity or calibration specimens**: The advantages of these specimens are that they are easily obtainable in sufficient quantity and the expected concentrations are known in advance. The disadvantage of these specimens is the matrix effects which may appear when they are tested across multiple analytical platforms.

Data Requirements

Table 13.1

MIC Data Requirements			
	Minimum	**Maximum**	**Recommended**
Number of analytes	1	No software limits	n/a
Number of instruments	3	30 total, including target	n/a
Number of specimens	3	No software limits	5-10

Parameter Screen

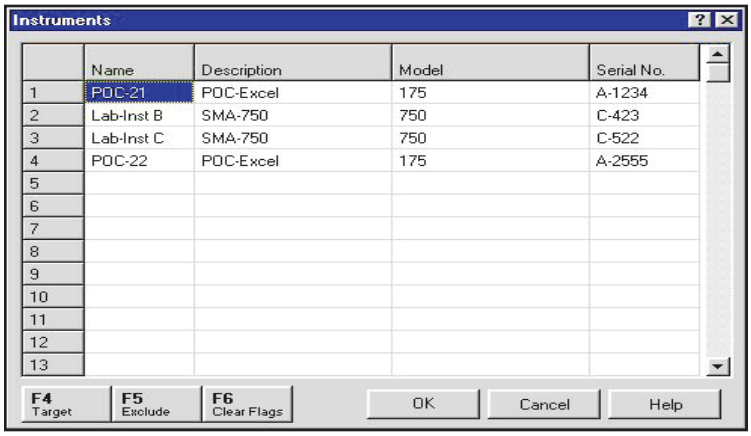


The Parameter Screen provides for entry of the elements which define the criteria by which the experiment is judged. These elements are in addition to elements such as units, analyst and others:

Allowable Total Error (either concentration or percent of concentration.) Required.

Reportable Range. If specified, the reportable range is used in calculation of the Coverage Ratio.

Instruments lists the instruments included in the experiment. If you click on Edit, you will be able to enter 4 items of information on each instrument: Name, Description, Model, and Serial Number. Instrument names must be unique. The <F4:Target> button allows you to connect an entry to a target instrument. If you change an instrument name, all its data will be lost. **Required**.



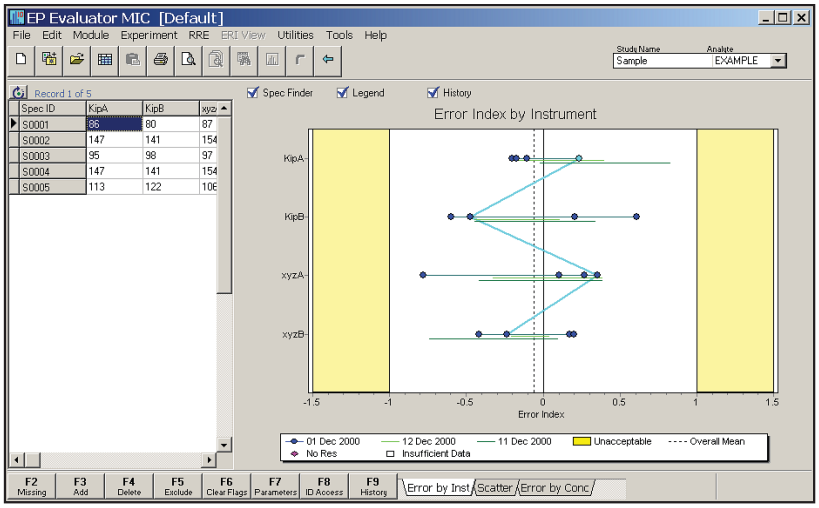


Figure 13.1. MIC Experiment Detail Screen

Experiment Detail Screen

The Experiment Detail screen (Figure 13.1.) has several unique elements:

Results Entry Grid

Always visible on left side of screen.

Displays

Available plots: Error by Instrument, Scatter Plot, and Error by Concentration. No data from target instruments are plotted.

Error by Instrument: MIC operates in two modes, one of which requires that every result be present for every specimen and the other of which is more relaxed. See the preceding section on Missing Data for details about how the modes operate.

The plot shows the "Error Index" (ratio of observed error to TEa) for each instrument. An error index greater than 1.0 or less than -1.0 is unacceptable; it means observed error exceeds TEa.

The MIC module's "Error index chart" displays an overall "error index" mean as a vertical dotted line labeled "Overall mean". This line is computed by averaging the error indices for all results used in the calculations; it does not include results that have been excluded or "failed" data points with an error index > 1.0.

There may be up to three lines on the plot for each instrument, depending on how much **history** is available. The line with circles on it is the current period. Each circle represents a specimen. If the plot is too cluttered to read easily, uncheck the History box above the plot to hide the history lines. Another way to reduce clutter is to uncheck the Legend box to hide the **legend**.

Check the **Spec Finder** box to draw a line connecting measurements for a single specimen. When you click a point on the graph or highlight a cell in the results grid, the spec finder line shifts to show results for that specimen.

Scatter Plot and **Error by Concentration** are discussed in the Interpretation section below.

Controls

The usual controls are available at the bottom of this screen. The **F9: History** button is unique to Multiple Instrument Comparison. It summarizes current results to history, then prepares the system for the next experiment.

Interpretation

Interpretation of these experiments is not complicated. Keep in mind the source of the target values. It may be either all your instruments, or a select set of instruments. (The select set would be used for POC instruments.) A discrepant result on an instrument occurs when that result is more than 1.0 times allowable error (TEa) away from the target value.

There are two cases:

- **No target instrument explicitly defined.** In this case, The target value for each specimen is the median of the instrument results for that specimen, measured over all the instruments. Discrepant results are those for which at least one result was more than the TEa from the target value. This is similar to the procedure used in Proficiency Test programs, where the target value for a PT specimen is set at the participant average. As is the case with PT, it is desirable to have a large number of "participants" (instruments) to establish a good target when no definitive reference method is available.
- Two evaluated instruments can differ from each other by more than TEa and still be considered acceptable. This is because each instrument may deviate from the target value by as much as TEa. If the result for instrument Y is 0.99 x TEa higher than the true value, and the result for instrument X is 0.99 x TEa lower than the true value, neither instrument's error exceeds TEa even though the difference between them is 1.98 x TEa. If you consider the experiment unacceptable if the difference between two instruments exceeds TEa, or if you want to compare one instrument to another specific instrument, consider using the 2IC module (Chapter 14, *Two Instrument Comparison*) instead of MIC.

- **Some are target instruments.** Target values are the medians of the results for each specimen as measured on the target instruments (i.e. those selected as targets). In this case, target instruments are not evaluated. Their values are used to evaluate the non-target instruments.

When you work to determine the cause(s) of discrepant results, remember that such problems can occur because of problems in either the target instrument(s) or in the tested instruments or both. Just because the probability is higher that an instrument produces better results, does not automatically eliminate that instrument from consideration as a problem source.

Key Statistics

- **Within Allowable Error**: All results must be within allowable error limits of the target median for that specimen for the experiment to pass.
- **Range of Target Values**: The lowest and highest target value in the experiment.
- **Coverage Ratio:** This is the percent of the reportable range covered by the target values. It is computed only if the user chooses to enter reportable range on the Parameters Screen. The ideal value is 100%. However coverage is not used to determine whether the experiment passes or fails.

Multiple Instrument Comparison Report

This report has three major components:

- Main page (shown in the report as page 1)
- Scatter and Error Index plots by concentration (report page 2)
- Results listing (report page 3).

Main Page Components

The focal point of the Main Page is the Error Index by instrument plot. This is the same plot as the one shown in Figure 13.1., except that the Spec Finder isn't visible. The Legend always appears on the printed report. Also, history is always shown if available.

All within Allowable Error? Fail	Range of Target Values: 78.0 to 153.0	Coverage Ratio: 75%

Key statistics are shown just below the plot. The experiment passes if each specimen for each instrument is within TEa of the target; otherwise it fails. The Coverage Ratio is shown for information, but it is not used to determine whether the experiment passes or fails.

Results are judged according to the data presented in the User Specifications Table.

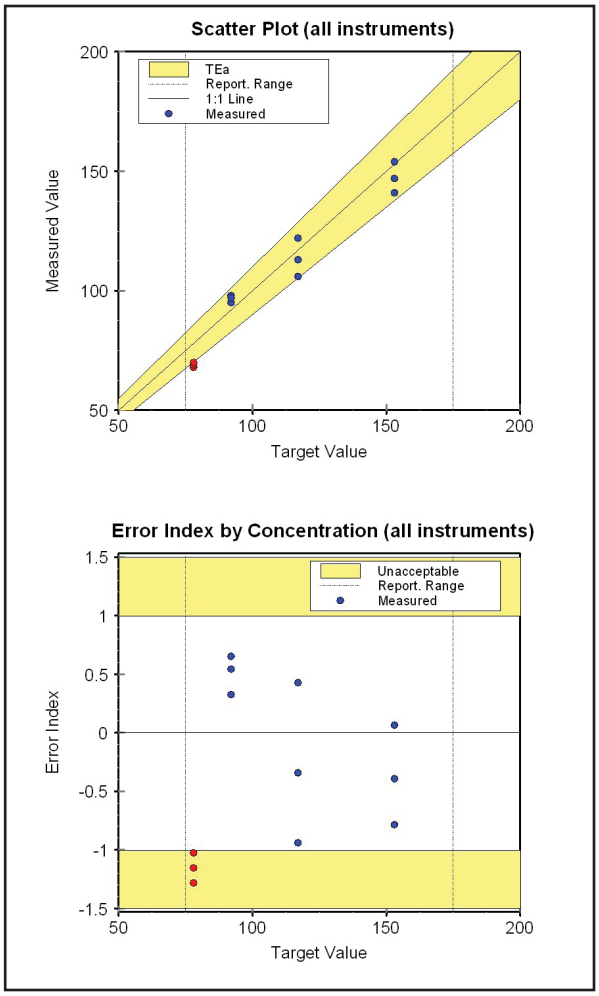
User's Specifications

Allowable Total Error:	10%
Reportable Range	75 to 175 mg/dL
Target values is average for 4 comparative instrument(s)	

The third table on the Main Report Page is the Supporting Data Table (not shown here). It contains general information about the experiment such as date, user and comment.

Scatter and Error Index Plots

One weakness of the plot on the main page is that, while it shows discrepant instruments, it gives no sense of either what range of values the experiment covered or which specific concentrations caused the discrepancy. The Scatter and Error Index Plots by Concentration (target value) provide this extra information. All the instruments are shown together, in a format similar to that of an ordinary comparison of two instruments. Target value is plotted on the X axis, and measured value on the Y axis. Note that there is no regression line on the scatter plot. The center line is the 1:1 (Y=X) line.



The plots illustrated here show clearly that the experiment covers a substantial part of the reportable range. Also:

- The problem is specific to the low concentration; other specimens are acceptable, and
- The problem is common to all instruments.

In the ideal case, all the plot points would fall within the central band on both plots.

Results Report Page

This page contains the individual results of the experiment.

Instr.	Spec.	Result	Target	Obs. Error	Allow Error	Error Index
KipA						
Third Floor, KIPLING S/N 1111-11						
	S0001	86	84.0	2.0	±8.4	0.24
	S0003	95	96.0	-1.0	±9.6	-0.10
	S0005	113	115.0	-2.0	±11.5	-0.17
	S0004	147	150.0	-3.0	±15.0	-0.20
	S0002	147	150.0	-3.0	±15.0	-0.20

For each result, the report lists the result, the target value, the difference (observed error), allowable total error (TEa) calculated for that target value and the error index (the ratio of the observed error divided by the TEa). When generating the report, the Results Sort Order option allows you to specify a Results Sort Order.

Multiple Instrument Comparison Report (page 1)

EP Evaluator®
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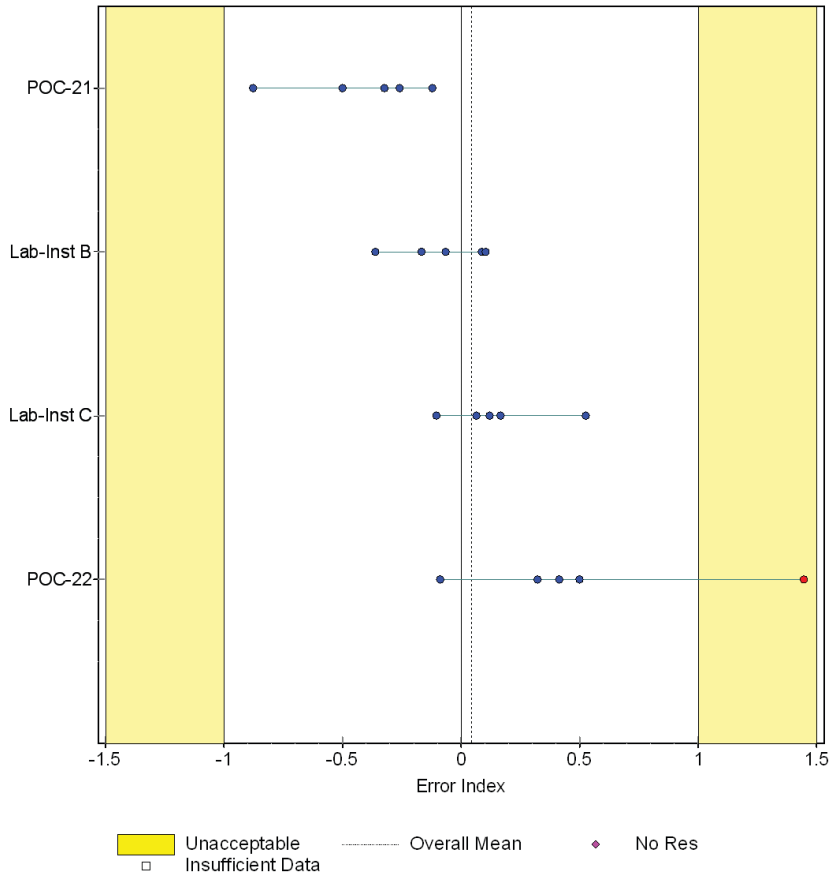
Glucose
Experiment MIC-Q4-2000

Multiple Instrument Comparison

Error Index by Instrument



All within Allowable Error? No Range of Target Values 51.0 to 193.0 Coverage Ratio 26%

User's Specifications

Allowable Total Error	6 mg/dl or 10%
Reportable Range	0 to 550 mg/dl

Target value is median for 4 comparative instrument(s).

Supporting Data

Analyst	dgr
Units	mg/dl
Number of Specimens	5 of 5
Expt Date	11 Dec 2000
Comment	

Accepted by: _____ _____
Signature Date

EP Evaluator 10.1.x.x
Sample Data Printed: 13 Jul 2012 16:48:02 Page 1

Multiple Instrument Comparison Report (page 2)

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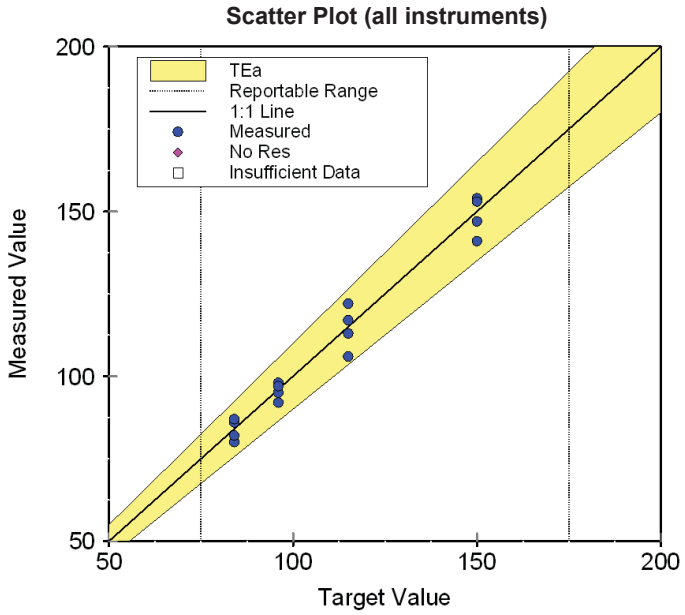
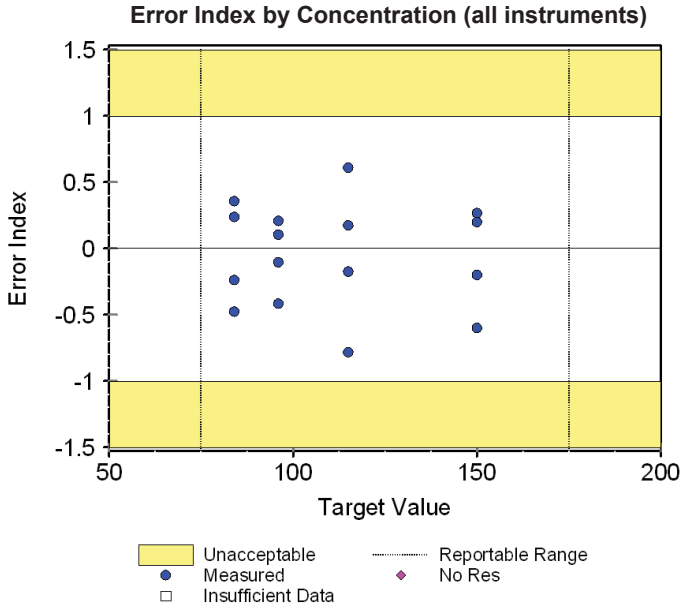
EXAMPLE
Experiment Sample

Multiple Instrument Comparison





Sample Data Printed: 13 Jul 2012 16:50:25

Multiple Instrument Comparison Report (page 3)

EP Evaluator®
User Manual -- Data Innovations, LLC

EXAMPLE
Experiment Sample

Multiple Instrument Comparison

Results Listing

Spec.	Result	Target	Obs. Error	Allow Error	Error Index
KipA					
Third Floor, KIPLING S/N 1111-11					
S0002	147	150.0	-3.0	±15.0	-0.20
S0004	147	150.0	-3.0	±15.0	-0.20
S0005	113	115.0	-2.0	±11.5	-0.17
S0003	95	96.0	-1.0	±9.6	-0.10
S0001	86	84.0	2.0	±8.4	0.24
KipB					
Fifth Floor, KIPLING S/N 2222-22					
S0002	141	150.0	-9.0	±15.0	-0.60
S0004	141	150.0	-9.0	±15.0	-0.60
S0005	122	115.0	7.0	±11.5	0.61
S0003	98	96.0	2.0	±9.6	0.21
S0001	80	84.0	-4.0	±8.4	-0.48

Spec.	Result	Target	Obs. Error	Allow Error	Error Index
xyzA					
Third Floor, XYZ S/N 3333-33					
S0002	154	150.0	4.0	±15.0	0.27
S0004	154	150.0	4.0	±15.0	0.27
S0005	106	115.0	-9.0	±11.5	-0.78
S0003	97	96.0	1.0	±9.6	0.10
S0001	87	84.0	3.0	±8.4	0.36
xyzB					
Fifth Floor, XYZ S/N 4444-44					
S0002	153	150.0	3.0	±15.0	0.20
S0004	153	150.0	3.0	±15.0	0.20
S0005	117	115.0	2.0	±11.5	0.17
S0003	92	96.0	-4.0	±9.6	-0.42
S0001	82	84.0	-2.0	±8.4	-0.24

F: value exceeds allowable error; X: specimen excluded from the analysis; T: target instrument.

Chapter

14

Two Instrument Comparison

The Two Instrument Comparison (2IC) module provides for comparison of the results from two quantitative instruments. The X method results are assumed to be truth. This plot is unique in that the location of the points are tested against a user-specified allowable error. If any result is outside that allowable error, then failure exists. Linear regression statistics are informational only, and are not used to determine whether the experiment passes or fails. This module is closely related to Multiple Instrument Comparison.

There are several experiments which may be analyzed using this approach.

- This is a good way to compare two harmonized instruments, i.e. a pair of instruments that are in production. These two instruments are assumed to be producing results which are supposed to be statistically identical. Performance of this experiment will meet the CLIA requirement for labs to compare instruments performing the same test on a semi-annual basis (Section 493.1281(a)).
- It provides a device to compare Point of Care (POC) instruments with the lab instruments, especially Glucose.
- It provides a device to compare analytes which have been assayed using amplification procedures. In this case, the scales should be logarithmic because the ranges of the data is so large.

One special feature of this module is that the Import/Export data formats are compatible with two other method comparison modules, Glucose POC Instrument Evaluation and Alternate Method Comparison. This allows data to be easily moved between these three modules (see Chapter 39, *File Operations including Backup and Import/Export*).

Definitions

Allowable error is a user-defined maximum acceptable difference between the X and Y results. The experiment passes as long as none of the differences exceeds allowable error. Statistically, one cannot justify setting the allowable error to be greater than the Total Allowable Error for the method. For the CLIA analytes in the United States, allowable error may be set at the proficiency testing limits (See Appendix A, Published Performance Standards).

Coverage ratio is the percent overlap between the range of X values and the reportable range of the method. The higher the better. At minimum, the specimens should cover the range of results normally encountered by a lab. For example, it is generally not satisfactory to test only specimens in the normal range if a significant portion of the specimens which the laboratory normally encounters are much higher than the normal range.

Error index is the ratio of $(Y_i - X_i)$ / Allowable Error (evaluated at X.) The error index is calculated for each X-Y pair. An index greater than 1.00 or less than -1.00 is unacceptable—it means the difference between the methods exceeds TEa. The experiment fails under the following conditions:

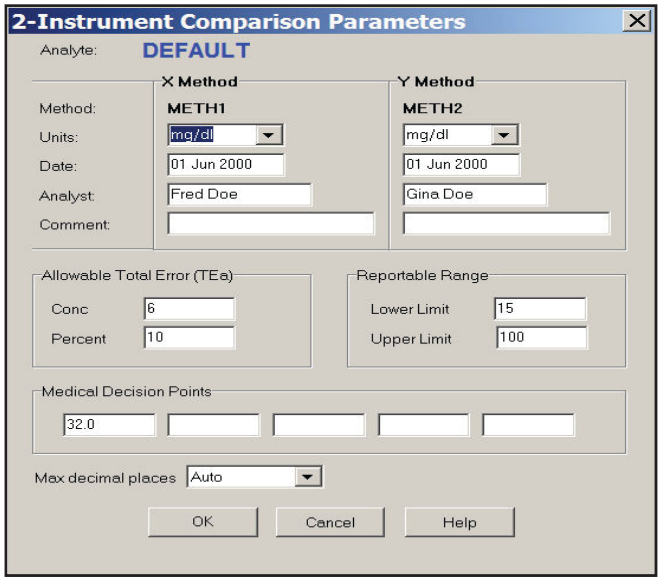
- for fewer than 20 specimens, at least one specimen is outside the error index
- for 20 or more specimens, more than 5% of the specimens are outside the error index

Experimental Design and Data Requirements

The experiment design is identical to that for Multiple Instrument Comparison (Chapter 13, Multiple Instrument Comparison). The recommended number of specimens is 5-10, with a minimum of 5. A larger number (40–50) is appropriate for analytes assayed using an amplification procedure. There is no software-imposed maximum.

Parameter Screen

The Parameters screen provides for entry of the elements which define the criteria by which the experiment is judged. These elements are in addition to elements such as units, analyst, and others:



Allowable Total Error (either concentration or percent of concentration.) Required.

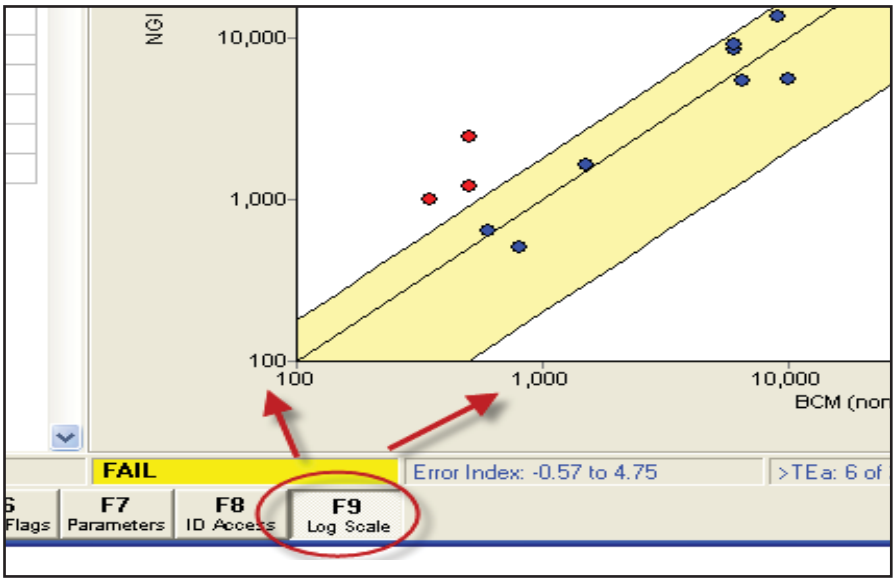
Reportable Range. If specified, the reportable range is used in calculation of the Coverage Ratio.

Medical Decision Points. Values where medical decisions change. These values are marked on the chart, but no calculations are based on them.

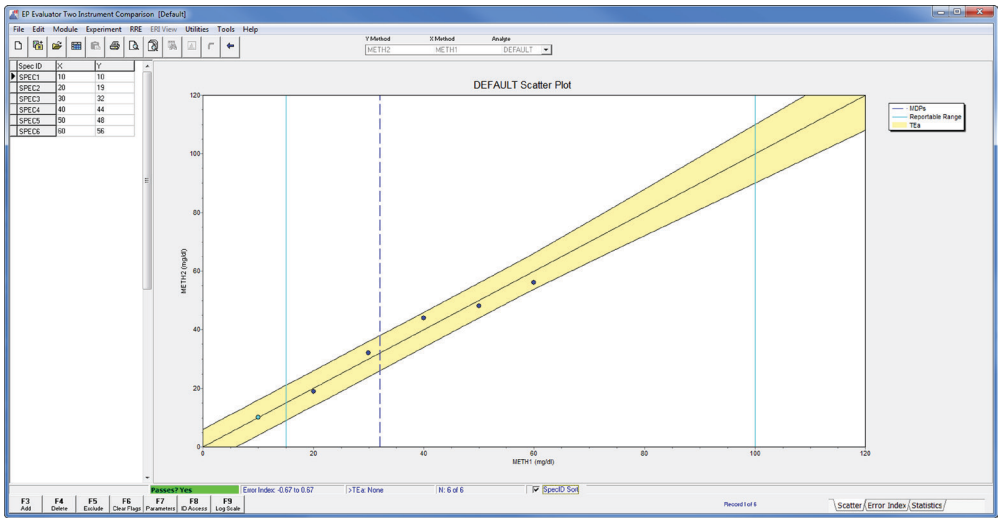
Max decimal places. Maximum number of decimal places for reports. Auto means number of decimal places is determined from the data. Computed statistics (e.g., Mean) are usually printed with one more decimal place than the input results. This setting affects reports only; calculations are done on full-precision numbers.

Experiment Detail Screen Log Scale Button

The Log Scale button is a toggle. When depressed, the plot is on a log scale; when not depressed, the plot is on a linear scale.



Experiment Detail Screen SpecID Sort



By default, specimen IDs are listed in the Experiment Detail screen in the order they are entered. To sort specimen IDs in alphanumeric order on the Experiment Detail screen, select the SpecID Sort check box. Clear this box to return specimen IDs to the default order. This check box only applies to the Experiment Detail screen. The report always sorts specimen IDs in alphanumeric order.

Interpretation

Plots

The plots are illustrated in Figure 14.1. The X instrument is plotted on the X axis, and the Y instrument on the Y axis. The central band on the charts is the acceptable region, where Y_i-X_i does not exceed allowable error. Note that the center line on the plot is NOT a regression line. It is the 1:1 line (Y=X).

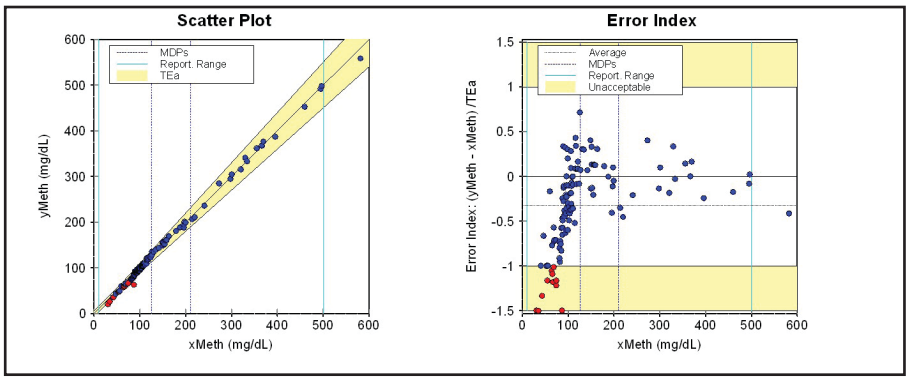


Figure 14.1. 2IC Plots when X is a Gold Standard

Evaluation Criteria

The Evaluation Criteria table shows user criteria for a specimen passing or failing.

An experiment fails under the following conditions:

- Less than 20 specimens are included and any specimen fails.
- 20 or more specimens are included and more than 5% of the specimens fail.

Evaluation Criteria:	
Allowable Total Error	6 mg/dl or 10%
Reportable Range	15 to 100 mg/dl

Key Statistics

Average Error Index: The error index for a specimen is (Y_i-Target$_i$)/Allowable Error$_i$. In 2IC, the target value is defined by the result for the X specimen.

Error Index Range: The lowest and highest error index in the experiment.

Coverage Ratio: This is the percent of the reportable range covered by the target values. It is computed if the user chooses to enter reportable range on the Parameters screen. The ideal value is 100%. Coverage is not used to determine whether the experiment passes or fails.

Key Statistics:	
Average Error Index	-0.03
Error Index Range	-0.67 to 0.67
Coverage Ratio	53%

Deming Regression Statistics

This table is included because you may be asked for the correlation coefficient, slope, or intercept during an inspection. These statistics are not used to determine whether the experiment passes or fails.

Deming Regression Statistics:
Y = Slope * X + Intercept

Correlation Coeff (R)	0.9987
Slope	1.005 (0.996 to 1.014)
Intercept	-3.4 (-4.9 to -1.8)
Std. Err of Estimate	5.2
N	123 of 123

When the graph is plotted on logarithmic scale, the regression is calculated on the logarithms of X and Y. The Standard Error of Estimate is in log units, not concentration units.

Deming Regression Statistics:
ln(Y) = Slope * ln(X) + Intercept

Correlation Coeff (R)	0.9830
Slope	1.018 (0.933 to 1.103)
Intercept	0.184 (-0.6935 to 1.061)
Std. Err of Estimate	0.524
N	23 of 23

Two Instrument Comparison Report (linear scale)

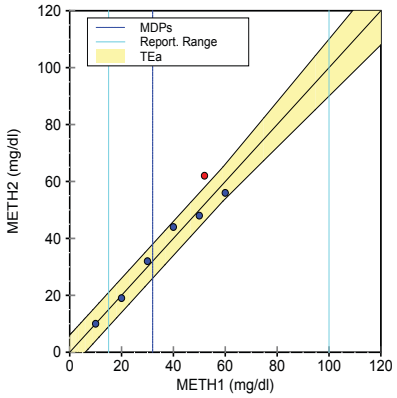
EP Evaluator® DEFAULT

User's Manual -- Data Innovations

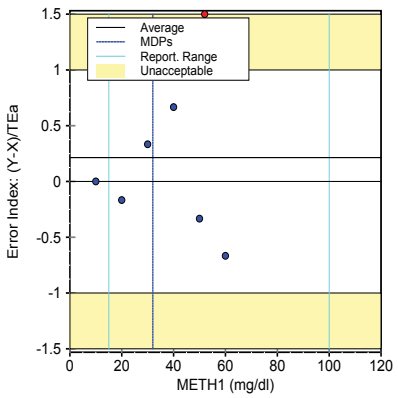
Two Instrument Comparison

X Method: METH1 **Y Method: METH2**

Scatter Plot



Error Index



Evaluation of Results

DEFAULT was analyzed by methods METH1 and METH2 to determine whether the methods are equivalent within Allowable Total Error of 6 mg/dl or 10%. 7 specimens were compared over a range of 10 to 60 mg/dl. The test FAILED. The difference between the two methods was within allowable error for 6 of 7 specimens (85.7%). The average Error Index (Y-X)/TEa was 0.21, with a range of -0.67 to 1.67. The largest Error Index occured at a concentration of 52 mg/dl.

Key Statistics:	
Average Error Index	0.21
Error Index Range	-0.67 to 1.67
Coverage Ratio	53%
Evaluation Criteria:	
Allowable Total Error	6 mg/dl or 10%
Reportable Range	15 to 100 mg/dl

Deming Regression Statistics:	
Y = Slope * X + Intercept	
Correlation Coeff (R)	0.9705
Slope	1.054 (0.760 to 1.348)
Intercept	-0.7 (-12.8 to 11.3)
Std. Err of Estimate	5.1
N	7 of 7

Experiment Description

	X Method	Y Method
Expt Date:	01 Jun 2000	01 Jun 2000
Result Ranges:	10 to 60	10 to 62
Mean ± SD:	37.4 ± 18.2	38.7 ± 19.2
Units:	mg/dl	mg/dl
Analyst:	Fred Doe	Gina Doe
Comment:		

Accepted by: _____ _____

Signature Date

Two Instrument Comparison Report (log scale)

EP Evaluator®

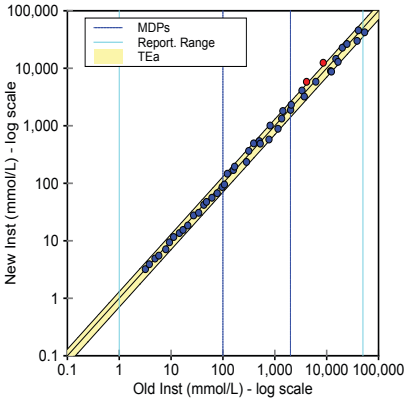
Log Scale

User's Manual -- Data Innovations

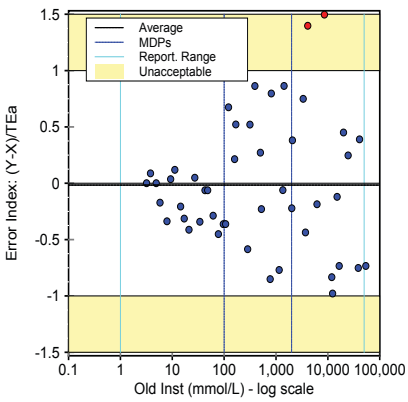
Two Instrument Comparison

X Method: Old Inst **Y Method: New Inst**

Scatter Plot



Error Index



Evaluation of Results

Log Scale was analyzed by methods Old Inst and New Inst to determine whether the methods are equivalent within Allowable Total Error of 30%. 47 specimens were compared over a range of 3.2 to 54057.1 mmol/L. The test PASSED. The difference between the two methods was within allowable error for 45 of 47 specimens (95.7%). The average Error Index (Y-X)/TEa was -0.02, with a range of -0.98 to 1.50. The largest Error Index occured at a concentration of 8604.2 mmol/L.

Key Statistics:	
Average Error Index	-0.02
Error Index Range	-0.98 to 1.50
Coverage Ratio	100%
Evaluation Criteria:	
Allowable Total Error	30%
Reportable Range	1 to 50000 mmol/L

Deming Regression Statistics:	
ln(Y) = Slope * ln(X) + Intercept	
Correlation Coeff (R)	0.9983
Slope	1.000 (0.983 to 1.018)
Intercept	-0.02163 (-0.1379 to 0.09463)
Std. Err of Estimate	0.1703
N	47 of 47

Experiment Description

	X Method	Y Method
Expt Date:	21 Sep 2009	21 Sep 2009
Result Ranges:	3.2 to 54057.1	3.2 to 45586.8
Mean ± SD:	5800.46 ± 11859.82	5453.26 ± 10802.61
Units:	mmol/L	mmol/L
Analyst:	Inez Doe	Inez Doe
Comment:		

Accepted by: _____ _____

Signature Date

Two Instrument Comparison (resulting listing)

EP Evaluator® **DEFAULT**

User's Manual -- Data Innovations

Two Instrument Comparison

X Method: METH1 **Y Method: METH2**

Experimental Results

Specimen	X	Y	Error Index	Specimen	X	Y	Error Index	Specimen	X	Y	Error Index
SPEC1	10	10	0.00	SPEC4	40	44	0.67	*SPEC7*	*52*	*62*	*1.67*
SPEC2	20	19	-0.17	SPEC5	50	48	-0.33				
SPEC3	30	32	0.33	SPEC6	60	56	-0.67				

Values with an "X" were excluded from the calculations.

Chapter

15

Glucose POC Instrument Evaluation

Glucose is the single most popular analyte which is assayed in Point of Care (POC) locations. It comprises well over 50% of the total market. A major complicating feature of POC Glucose is that it is **the one test** which is treated differently from a regulatory point of view in the POC version than it is the laboratory situation. POC Glucose has received a waiver with respect to meeting CLIA PT limits.

Generally, when assayed using laboratory instruments, glucose has a CV of approximately 2 to 4%. When assayed using POC instruments, the corresponding CV is 10% or more. This difference between the two types of methods is the driving reason for this statistical module because if the differences are excessive, the life of the patient is put at substantial risk.

In this module, results from the laboratory instrument are assumed to be accurate. The point of course, is to evaluate the performance of the POC Glucose devices. In this module, the scatter plot is divided into 5 different regions corresponding to varying degrees of agreement as shown below:

Glucose POC regions		
Region	**Name**	**Color**
A	**Good Agreement**	**Green**
B	**Acceptable Agreement**	**Blue**
C	**Fair Agreement**	**Yellow**
D	**Poor Agreement**	**Orange**
E	**Potentially Lethal**	**Red**

The point of this evaluation is to compare POC glucose results with those from laboratory instruments in a very specific format. Consequently, the X and Y axes are both fixed in magnitude. Results are expressed either as mg/dL or as mMol/L, no other choices.

Experimental Design and Data Requirements

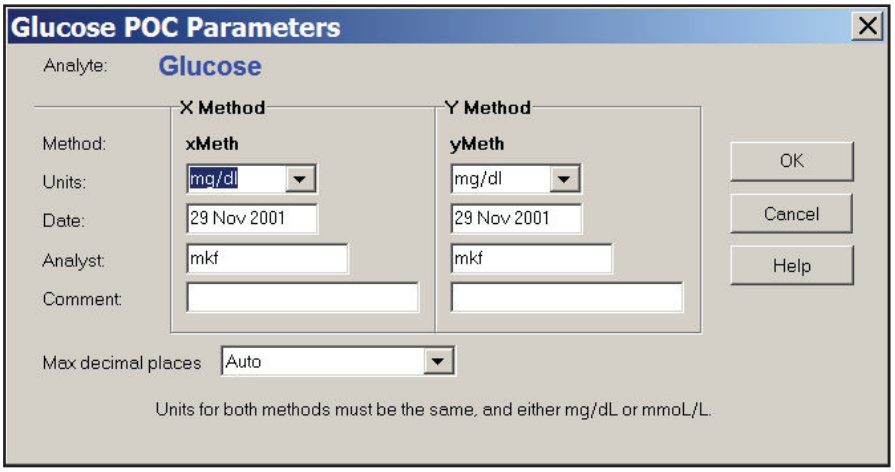
A minimum of 20 specimens is required.

The experiment should be performed as follows:

- Gather specimens from 50 to 100 patients who are in various stages of glucose control varying from excellent to poor. Two specimens need to be obtained within a few minutes of one another, one for analysis on the POC device and one tube of blood for analysis in the laboratory.
- Assay the two specimens in their respective devices.
- Enter the results into EP Evaluator, perform calculations and print the report.

Parameter Screen

This screen is as simple as can be. Only general information is entered.

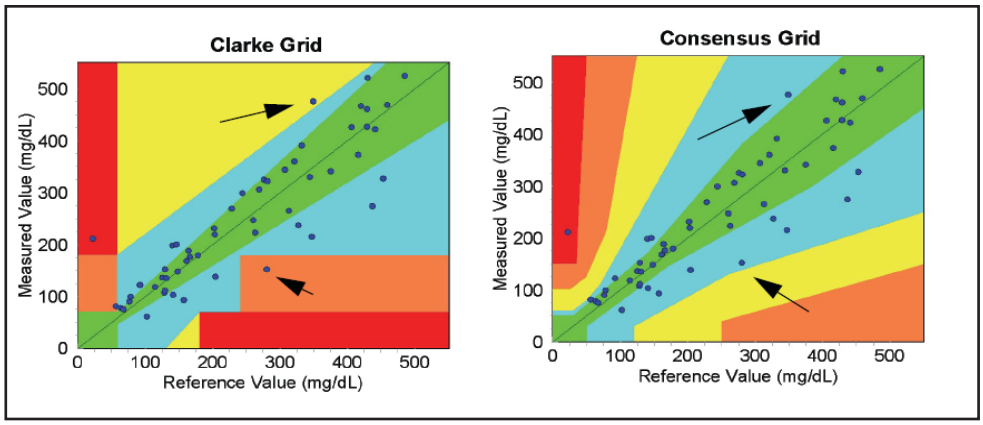


Max decimal places is the maximum number of decimal places for reports. "Auto" means number of decimal places is determined from the data. Computed statistics (e.g., Mean) are usually printed with one more decimal place than the input results. This setting affects reports only; calculations are done on full-precision numbers.

Interpretation of Results

The key feature of the reports is where the points lie with respect to the various regions on the grids. Ideally all the results will be in region A. It is a major danger signal if any results are in regions D or E.

On examination of the diagrams, one notices that two results (see arrows) are in the regions C and D in the Clarke diagram. However, those two points are in (the more acceptable) region B in the Consensus diagram. The reason is that the locations of the regions of the Consensus diagram were more carefully designed than those in the Clarke diagram.



The Clarke Diagram was developed to be easily programmable on a spreadsheet. The Consensus Diagram was developed later in response to the problems that are evident with the Clarke Diagram. Both diagrams are presented in EE. However, we recommend that you base your decisions on the results with the Consensus Diagram.

Two tables of statistics, one for each diagram, are presented to summarize the results. Only one of the pair of these tables is shown here.

Region	Count	Percent	Cum Percent
A	60	100%	100%
B	0	0%	100%
C	0	0%	100%
D	0	0%	100%
E	0	0%	100%
Excluded	0		
Out/Bnds	0		
Total	60		

A third table summarizes the statistical relationships of the two sets of data. For this table the differences between pairs of points are calculated for all included specimens and are expressed as a percent of the laboratory instrument (X) value (differences).

Statistical Analysis

Mean % Error:	33.5%
95th Percentile:	44.9%
N	54 of 61

Mean %Error is the mean of the differences.

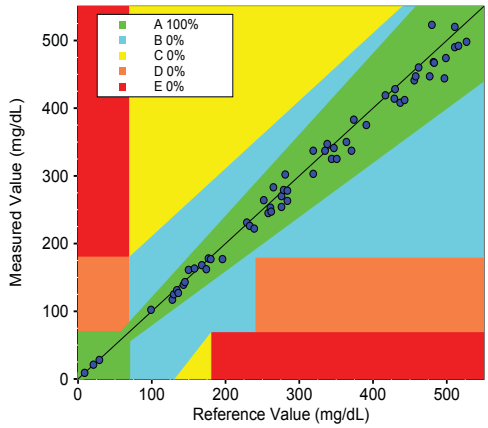
95% Percentile: 95% of all the differences are less than or equal to the displayed number.

Glucose POC (Statistics Page)

Glucose POC Instrument Evaluation

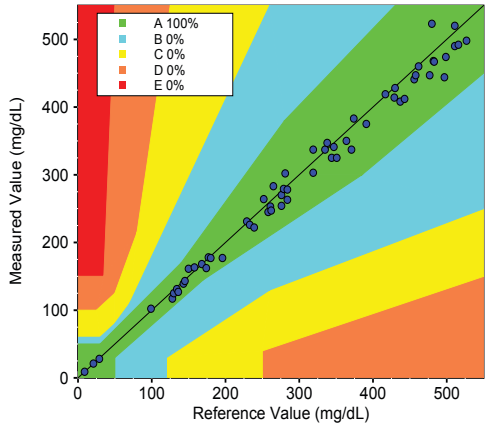
X Method: xMeth **Y Method: yMeth**

Clarke Grid



Region	Count	Percent	Cum Percent
A	60	100%	100%
B	0	0%	100%
C	0	0%	100%
D	0	0%	100%
E	0	0%	100%
Excluded	0		
Out/Bnds	0		
Total	60		

Consensus Grid



Region	Count	Percent	Cum Percent
A	60	100%	100%
B	0	0%	100%
C	0	0%	100%
D	0	0%	100%
E	0	0%	100%
Excluded	0		
Out/Bnds	0		
Total	60		

Statistical Analysis

Mean % Error:	4.2%
95th Percentile:	9.2%
N	60 of 60

Experiment Description

	X Method	Y Method
Date:	29 Nov 2001	29 Nov 2001
Analyst:	mkf	mkf
Units:	mg/dL	mg/dL
Comment:		

Accepted by: _____ _____
Signature Date

Glucose POC (Results Page)

Glucose POC Instrument Evaluation

X Method: xMeth **Y Method: yMeth**

Experimental Results

Spec ID	Results X	Y	Bias	% Bias	Region Clark	Cons	Spec ID	Results X	Y	Bias	% Bias	Region Clark	Cons
S00012	9	9	0	0.0	A	A	S00018	284	278	-6	-2.1	A	A
S00052	21	21	0	0.0	A	A	S00003	319	337	18	5.6	A	A
S00041	29	28	-1	-3.4	A	A	S00009	319	303	-16	-5.0	A	A
S00029	99	102	3	3.0	A	A	S00060	335	337	2	0.6	A	A
S00022	128	117	-11	-8.6	A	A	S00050	338	347	9	2.7	A	A
S00006	130	125	-5	-3.8	A	A	S00040	344	325	-19	-5.5	A	A
S00020	134	131	-3	-2.2	A	A	S00057	347	341	-6	-1.7	A	A
S00023	136	127	-9	-6.6	A	A	S00025	351	325	-26	-7.4	A	A
S00021	143	139	-4	-2.8	A	A	S00037	364	350	-14	-3.8	A	A
S00044	145	143	-2	-1.4	A	A	S00034	371	337	-34	-9.2	A	A
S00017	150	161	11	7.3	A	A	S00055	374	383	9	2.4	A	A
S00053	158	163	5	3.2	A	A	S00013	391	375	-16	-4.1	A	A
S00014	168	168	0	0.0	A	A	S00015	417	419	2	0.5	A	A
S00036	174	162	-12	-6.9	A	A	S00049	429	414	-15	-3.5	A	A
S00010	177	178	1	0.6	A	A	S00032	430	428	-2	-0.5	A	A
S00051	180	177	-3	-1.7	A	A	S00005	437	408	-29	-6.6	A	A
S00045	196	177	-19	-9.7	A	A	S00001	443	412	-31	-7.0	A	A
S00058	229	231	2	0.9	A	A	S00046	456	441	-15	-3.3	A	A
S00038	233	226	-7	-3.0	A	A	S00030	458	447	-11	-2.4	A	A
S00039	239	222	-17	-7.1	A	A	S00026	462	460	-2	-0.4	A	A
S00047	252	264	12	4.8	A	A	S00028	477	447	-30	-6.3	A	A
S00059	258	245	-13	-5.0	A	A	S00027	480	523	43	9.0	A	A
S00035	261	253	-8	-3.1	A	A	S00024	482	468	-14	-2.9	A	A
S00031	262	247	-15	-5.7	A	A	S00056	483	467	-16	-3.3	A	A
S00048	265	283	18	6.8	A	A	S00033	497	444	-53	-10.7	A	A
S00011	276	270	-6	-2.2	A	A	S00043	499	474	-25	-5.0	A	A
S00054	276	254	-22	-8.0	A	A	S00008	511	490	-21	-4.1	A	A
S00007	279	279	0	0.0	A	A	S00019	511	520	9	1.8	A	A
S00016	281	302	21	7.5	A	A	S00004	516	492	-24	-4.7	A	A
S00002	284	263	-21	-7.4	A	A	S00042	527	498	-29	-5.5	A	A

X = excluded O = out of range

Chapter

16

Hematology Studies

Hematology Studies approaches Method Comparison in a rather different way than the traditional quantitative approaches for other EP Evaluator Method Comparison Modules. The traditional approach basically treats the list of specimen test results as a series of independent analytes. Hematology Method Comparison is able to evaluate the diagnostic morphology of each specimen as defined by the interdependence of its reported parameters. Here are two examples of this interdependence:

- The Manual White Cell Differential procedure counts 100 white cells for each specimen, thus each differential always adds up to 100%. To make an accurate assessment, both relative percentages and absolute values must be considered. For example a relative value of 70% neutrophils may seem within normal limits. However, if the total WBC is 20,000, the absolute value (70% x 20,000) would be an abnormally high count of 14,000. Positive Morphology applies to the entire specimen based on assessing multiple parameters. It is determined by assessing whether any combination of one or more parameters is outside defined cutoff values.
- Several parameters such as MXD%, MCH, MCV or Lymph% are calculated from other measured parameters.

Additionally, the HMC statistical module differs from the other statistical modules in several other major respects:

- The list of parameters is similar across a wide variety of instruments. The differences are for only a handful of cell types and a few instrument specific parameters.
- A “Gold Standard” exists and is widely accepted, namely the Manual Differential.
- One major object of the evaluation process is to identify specimens which are morphologically positive by each method (sensitivity analysis) and to compare the totals in a Truth Table. Ideally the automated methods evaluated will be in total agreement with the Manual Differential. Failing that, the first priority is to eliminate false negatives and the second priority is to minimize false positives.
- More than any other, this module is designed to manage multiple parameters in a single experiment.

One of the major driving forces in Hematology is to decrease the amount of tech time required to generate a report. One labor intensive task is manually reading cell differentials to confirm the positives identified by the automated instrument. Ideally, the only specimens that should be read manually are those suspected of being morphologically positive (i.e. contain cells which indicate the presence of a leukemia or other blood cell disorder). As the automated analytical process becomes more reliable, fewer slides will need to be manually confirmed, resulting in savings on labor costs.

A significant amount of preparative work **MUST BE DONE** in EE before the Hematology Studies Module experiment is created. This module requires Policy Definitions in order to function. While it is possible to adjust many Policy Definitions after a Study has been created, they should be defined before performing the experiment.

Example Policies: In the EE11\Resources and in the EE11\DATA\Backups folders, the "Example Policies" project is included as a backup file. "Example Policies" includes policy data for many current automated analyzers with parameters and some characteristics. It does not include experimental data. (Open the HMC Example Project to see a project that includes experimental data.) While "Example Policies" illustrates what is needed and is close to what the projects should eventually resemble, you must edit it and verify that it fits your specific situation. *This file has been provided to save you a great deal of work understanding and setting up this module.*

Data Requirements and Experiment Design

Results are required for at least two methods for the parameters of interest for a sufficient number of specimens. There are two major cases:

Manual Cell Differential results are included and you wish to verify the sensitivity of your test method: Results from 75 to 150 specimens are needed with 50% to 75% of these specimens being morphologically positive by the Gold Standard method. The specimens should be obtained from patients with a wide variety of hematological disorders so you can test whether the instruments can detect the various pathologies present in your patient population. This Experiment design forms the basis for the Clinical Utility study. Results are required for each parameter on each specimen.

Manual Cell Differential Results are not included and your goal is to verify the statistical equivalency of the test methods: Two assumptions are made: a) the detection of specimens with positive morphologies is not important; and b) only regression analysis of the specific parameters is important. Results from 35 to 50 specimens are tested by each of the instruments. In this case, it is desirable to select specimens so that a wide range of results are present for each parameter.

Very Important: Remember that zero is a valid result. Often in the recording of a manual differential on a form, a blank means that no cells of that type were found. In entering your results into EP Evaluator do not leave a cell blank unless the parameter really was not measured. Fields that are blank are considered to have no data reported. Entering a zero means it was measured and had a value of zero.

Specimens with blank cells will not be included in the parameter regression reports unless you checked the box: “Do not require a result for all methods” in the HMC Study setup wizard. This has major implications with respect to the calculations of positive morphologies. The clinical utility chart may not be accurate if you check this box. Regression statistics may also be affected because the set of results used for the calculations will not be exactly the same, as some results may be missing for one method but present for another.

Checking the “Initialize interfaced/pasted morphology parameters to 0)” check box, accessible from the Interface tab on the File, Preferences window, will automatically replace a blank with zero (0). This will apply when importing data from an instrument, an instrument file, or copying and pasting from a spreadsheet.

Projects, Studies and Experiments in HMC

A Project may contain any number of Studies. However, these studies must use a common set of parameter names. Within a single project, you can't call a parameter "PLT" in one study and "Platelets" in another.

The current Project holds its own working copy of Policies plus a collection of studies and/or experiments. The HMC Module overview screen shows a table of all studies started in HMC. Clicking on a study opens it to show the data workbook created for each Study.

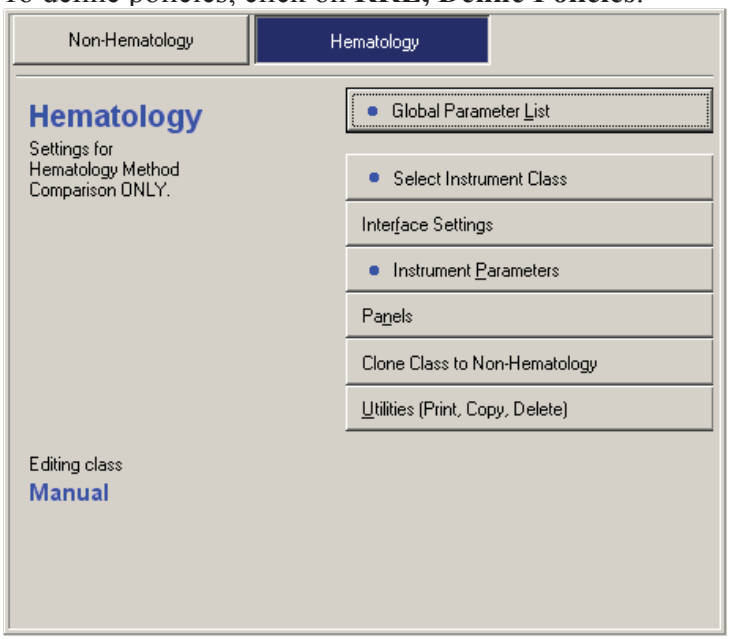
A Study contains the complete set of analyses of all the methods and parameters being compared. EE evaluates the results obtained for each method and generates the appropriate comparisons based on your specific policy definitions within the project. For every parameter and every pair of instruments in the study, there is one comparison.

Once the policy definitions are set up and a study initiated, any minor adjustments to the study made by the operator in the study setup screen are LIMITED to that study. They are not copied back into the RRE policy definitions. In addition, unlike the rest of EE policy definitions, the changes you make in policies do NOT affect any other studies.

Setting up Policy Definitions

A unique feature of this statistical module is that the user is required to set up a minimum set of policy definitions before any data is entered. This includes definition of the parameters (i.e. analytes), at least 1 instrument class (i.e. automated instruments or Manual Diff), method descriptors (units, reference interval, Positive Morphology cutoffs and the like) and Panels (parameters to be displayed together in a specified order).

To define policies, click on **RRE, Define Policies**.



Options are:

Global Parameters List: Click on this item to define the list of parameters for all instrument classes and methods. In order to select a parameter for an instrument class method, it must be present in this list.

Select Instrument Class: Click on this item to switch between instrument classes.

Interface Settings: Click on this item to change serial interface properties for the currently selected Instrument Class.

Instrument Parameters: Click on this item to change instrument parameters and their associated characteristics for the currently selected Instrument Class.

Panels: Click here to add or change panel definitions for the currently selected Instrument Class.

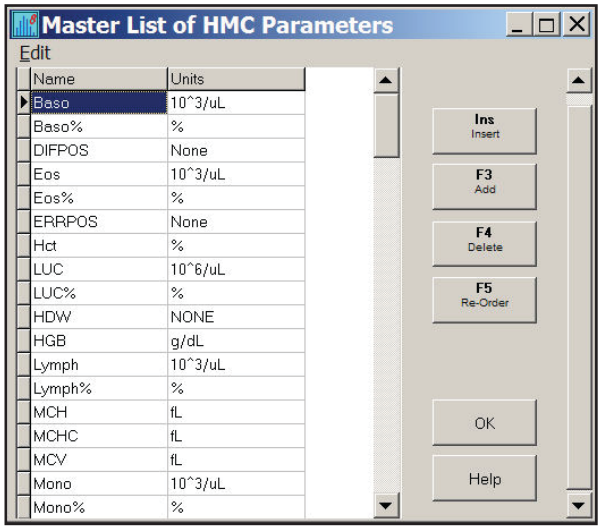
Clone Class to Non-Hematology: Click on this item to copy the parameters for the current Instrument Class or for all Instrument Classes. New Instrument Class(es) will be created (or revised/updated) in the non-Hematology section of Policies.

Utilities: Click here to print, copy or delete policies.

Global Parameter List

The purpose of this list is to define the overall list of parameters (analytes) to be referenced by all experiments created using this policy definition. Under the Instrument Parameter (properties) Screen, selection of parameters for each instrument is made from this list. You may add or delete parameters and insert new ones in the middle of the current list. Button F5 (re-order) displays a screen that lets you rearrange the order of the parameters.

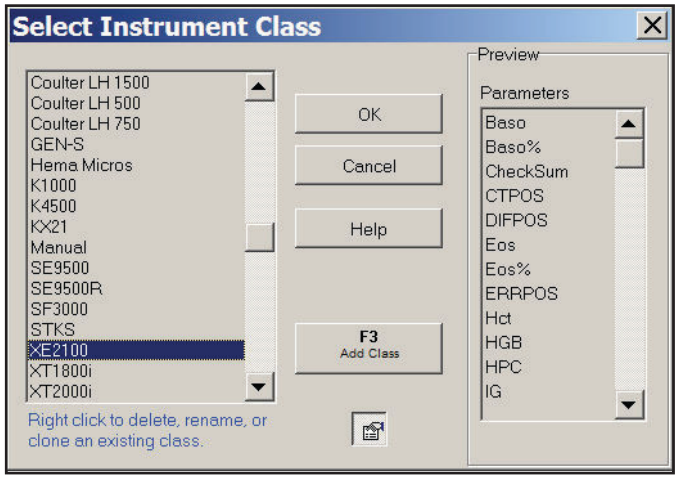
The Global Parameter List defines the order of parameters in the reports. A study will always respect the parameter order defined at the time of its creation. Any parameter order changes made in policies will not retroactively apply to existing studies, but will apply to all studies created going forward.



Select Instrument Class

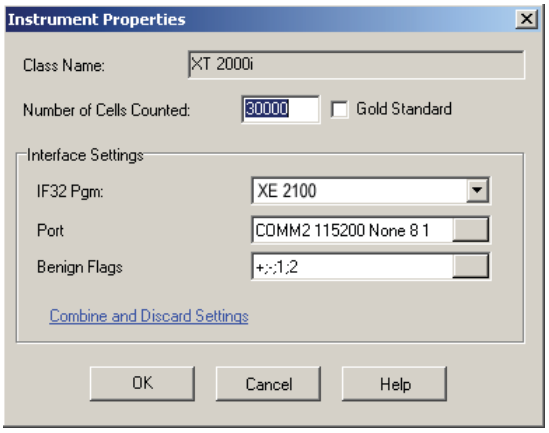
A menu of available instruments is displayed. You will be able to make changes in the parameters of the one you select. Note that you can add a new instrument class from this screen by clicking the F3 button.

To rename, delete, or clone an existing class, highlight an instrument name and then right-click. This is the only way you can do these tasks.



Interface Settings

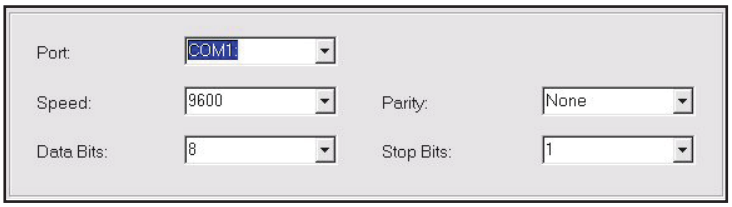
In the top portion of the screen the number of cells counted is defined (required field). There you may designate the method as a “Gold Standard” method. While your policies can have more than one class as a “Gold Standard”, a given study can have only one “Gold Standard” instrument or method.



The lower portion of the screen applies only to instruments that are interfaced to EP Evaluator. IF32 Pgm provides for selection of the interfacing program (driver). Access the Interface Port settings, where you can change the “comm port” and baud rate, by clicking on the square box at the right end of the “Port” field. To change the benign flags, click on the square box at the right end of the “Benign Flags” field.

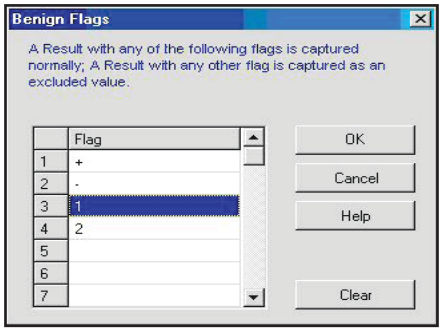
Interface Port Settings

Use this screen to define your serial port parameters such as comm port, baud rate, data, stop bits and parity. To import data from an instrument generated file using the appropriate driver, chose “File” from the dropdown. Note that this information is stored at a project level, not a study level. Consequently, if for any reason these parameters need to be changed, they can only be changed here in the program.



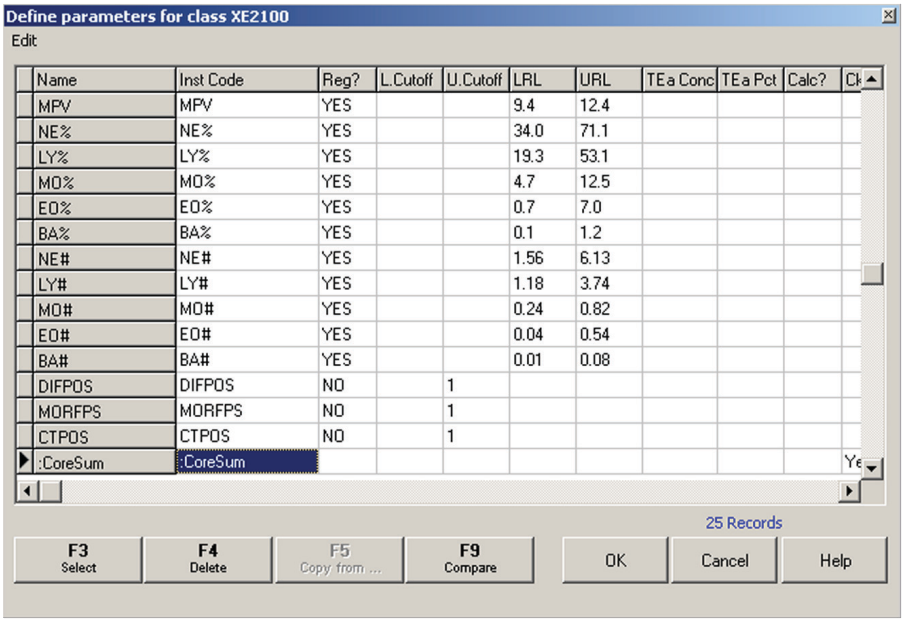
Benign Flags

These flags refer to specimen-specific conditions rather than compromised instrument performance. For example, when many instruments detect a short sample, or some analytical problem, they will report the result with a flag indicating that a problem was detected in the analytical process. Some instruments suppress a result with such a flag. In contrast, a benign flag is one in which no analytical problems were detected. It might indicate that a result is above or below the reference interval or is a critical value. Use this form to define result flags that you consider to be benign; all others are assumed to be an analytical process flag and will be excluded from the calculations. In this screen, enter one flag per line. A flag may have one or more characters.



Instrument Parameters

Correct descriptors for each parameter are an important component of an experiment because they define how the parameters are to be used.



- **InstCode**: The name of the parameter as sent by the instrument to the LIS. Some instruments may use a numeric code (e.g. "24") or text codes to identify a test. The EP Evaluator default is the same as the parameter name.
- **Reg?**: Is regression analysis to be done on this parameter? For example, regression analysis is usually done on Hct. It is not usually done on flags such as "CTPOS." YES requests a regression analysis for this parameter. Type "Y" or "y" into the cell and the program will fill in YES. Type N into the cell , or leave it blank, and the program will not perform a regression analysis. Reasons you might not want a regression:
  - The parameter is used only to establish positive morphology for a Clinical Utility study (e.g. NRBC%).
  - It is an intermediate value such as a CheckSum parameter.
- **L.Cutoff and U.Cutoff**: Specimens with results less than or equal to L.Cutoff or greater than or equal to U.Cutoff will be flagged as being morphologically positive. Leave the cutoff values blank for a parameter that is not used to determine morphology (blank, not zero).

NOTE: If you set **Reg?** to NO and don't define a Positive Morphology Cutoff Range, the parameter will be not be shown in the study reports (even though data may be entered in the workbook).

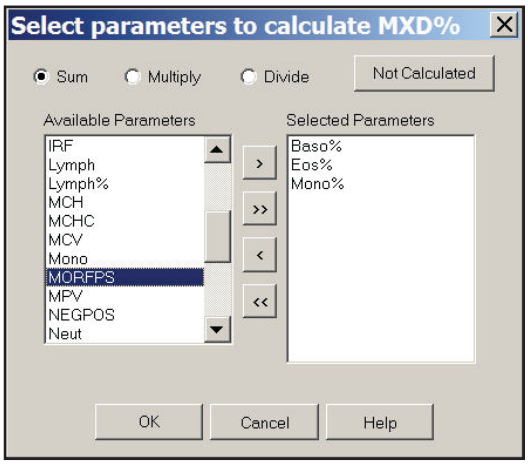
- **LRL and URL**: These values define the lower and upper limits of the reference range respectively. These values are optional and are used only when **Reg?** is set to YES. If present, the regression analysis will report predicted MDP values and confidence intervals at the reference limits.
- **TEa Conc** and **TEa Pct:** These optional values are used only in regression analysis to construct a scatter plot boundary envelope defined by the allowable error around the regression line on the scatter plot. If one of the methods is

designated "Gold Standard," the boundary envelope uses a binomial function as described in CLSI:H47.

- **Calc?** A calculated parameter is a clinically meaningful result that is not measured directly by the method.
  Example: MXD% = MO% + EO% + BA%.

  To activate this feature, click on the field in the **Calc?** column.

  On the popup "Select parameters to calculate" screen, select BA%, EO%, and MO%. Click **OK** to close the popup. The Calc cell should now display "sum", indicating that MXD% is a computed sum.



  MXD% can now be used for either regression analysis or in the Clinical Utility Study, just as if it had been measured directly. You are able to add, multiply, or divide parameters. Click "not calculated" to undo a previously entered calculation.

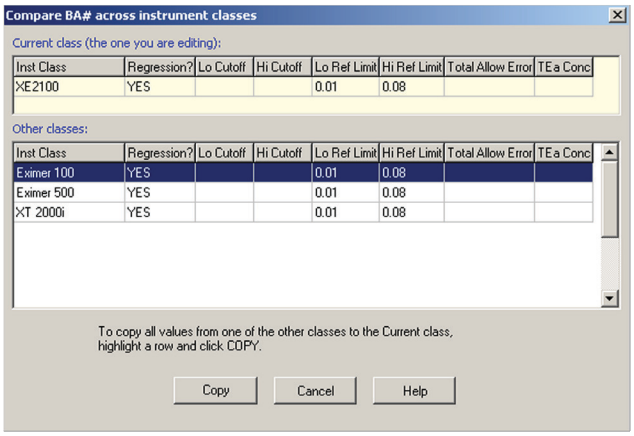
NOTE: Some instruments will report their own calculated parameters. In setting up our instrument selections, calculated parameters reported by those instruments are treated as though they were actually measured by the instrument. Do not check Calc for them.

- **CkSum?**: A user-defined Checksum parameter is not a clinically meaningful result, but a specific form of data validation, i.e., to ensure that the differential cell results have been entered correctly. Checksum is intended to apply to a subset of parameter results for a specimen that should total 100%. A specimen with a sum outside the range 99 to 101, or with a blank result for any of the Checksum parameters, will be red-flagged on the experimental data entry screen to warn you of a possible data error. It can be used for any method.

Buttons

There are several useful buttons at the bottom of the Instrument Parameters Screen (not shown).

- **F3 Select:** Click this button to display a form containing the global list of parameters. Check the ones to be used for this class. Each class can have up to 250 parameters.
- **F4 Delete**: Use this button to delete parameters from the list for this class.
- **F9 Compare**: Select a parameter and then click on this button. This will compare the descriptors for this parameter across all classes that use it. This is useful when cloning new classes from an existing class. Make the necessary changes in the "Define Parameters" screen to customize the new classes. Then use the F9 compare button to compare and copy reference intervals from one class to another, if applicable.



Panels

You can define Panels for each class as a subset of its selected list of parameters that can be displayed in a user-defined order. Specification of their order allows you to enter the results in the same order that they appear on the report. For more details on how to create and edit panels, see *Panels* Chapter 37, *Policy Definition*.

Clone Class to Non-Hematology

In addition to running Hematology Method Comparison on your Hematology data, you may want to evaluate some non-Hematology statistics. In order to facilitate this, you can click on the Clone Class to Non-Hematology button. You will be asked whether you wish to copy the parameters for the current class, or for all classes. New Instrument Class(es) will be created (or revised/updated) in the non-Hematology section of Policies.

The Instrument Class names defined in Policies are shared between the non-Hematology and Hematology groups. Due to this, you cannot have a non-Hematology Instrument Class of "Advia 250" as well as a Hematology Instrument Class of "Advia 250". Thus, when Hematology parameters are copied from a Hematology Instrument Class, the non-Hematology Instrument Class is appended with "~H". For example, the Hematology Instrument Class "Advia 250" becomes "Advia 250~H" when copied to the non-Hematology Instrument Class. The "~H" is supposed to remind you that 1) this Instrument Class is not for Hematology, and 2) that it was in fact derived from a similar Instrument Class in Hematology.

The policy data for non-Hematology can be extensive (depending on which statistical modules you intend to use), so this feature can only get you started defining your non-Hematology policies

Utilities (Print, Copy, Delete)

This feature allows you to move your policy definitions between various projects. The key element of this transfer process is that the Master Project is special. It has the sole role of being the program-wide custodian of all policies. For a complete review of managing policy data, see Chapter 37, *Policy Definition*.

Performing an Experiment

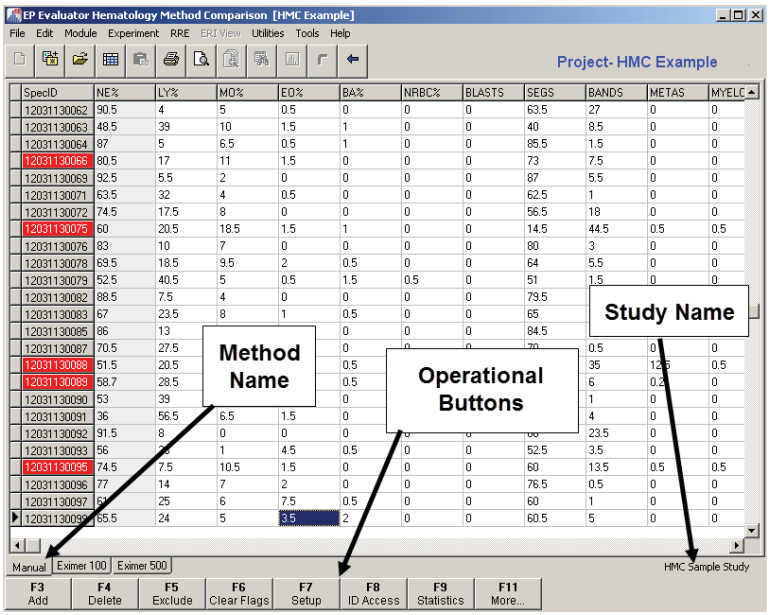
Once policy definitions are complete, setting up a new experiment and entering data into Hematology Studies becomes quite simple. New studies can only be generated via the New Studies Wizard which can be launched in several ways.

- Click on **Experiment / New from policies**. Or
- Click on the **New Experiment from policies** icon in the icon bar.
- With data for an instrument in the clipboard, click on **Edit / Paste**.
- Click on the “F3 Add” button (lower left corner) in the Module Overview Screen.

Creating an Experiment from Policies

The **HMC Study Setup Wizard** will guide you through the process of creating the study and defining the instruments. You may optionally select a panel for each method. The Wizard will also ask whether a specimen needs to have results for all instruments before it will be included in the regression analysis. The advantage of this requirement is that your regression statistics will be comparable across all instruments. Otherwise the statistics will not be comparable since a different set of specimens could be used for each pair of compared instruments.

After completion of the Wizard screens, an empty Experiment Detail Screen will be displayed. Each Study has one Data Workbook where experimental results are entered for that study. It is a tabbed workbook, with one tab page for each method of the Study. It is similar to the one shown except that it contains no data. Several options for data entry are described later in this chapter.



Note the tabs in the lower left corner. These provide access to data for each of the methods.

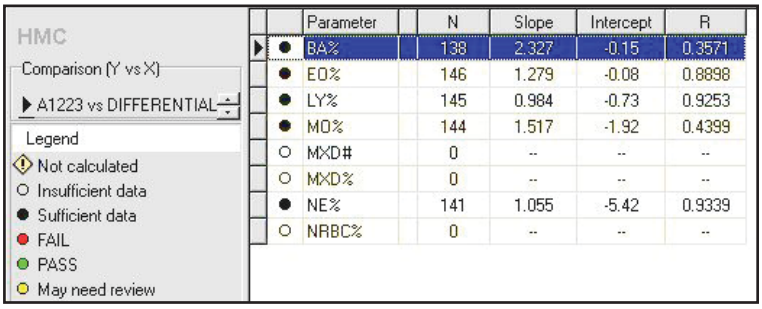
On occasion, some result fields have a light gray color. That gray color indicates that data may not be entered directly into that field. The reason is that the result in that field is calculated from other fields.

Buttons

At the bottom of the screen, buttons provide access to a number of very important functions. Several of them allow you to quickly figure out why your results are not what you may have expected. Keep in mind that a "short" HMC report may be 75 pages.

- **F3 Add** – Add a specimen. Alternatively, you can scroll to the bottom of the grid, then cursor down to add a line.
- **F4 Delete** – Permanently deletes the highlighted specimen (only from the method on the tab page you are editing).
- **F5 Exclude** – Toggles exclusion of the highlighted specimen. Excluding a specimen removes it from the calculations, although it is still in the file. It can be restored by selecting **Exclude** a second time. Excluded specimens are shown on the Data Sheet with an X next to the specimen ID. Reports have two forms of data listing: the Method Comparison Data Listing for a specific pair of methods and the CBC/Diff Data Listing that lists results for all methods in the study. Excluded results do not appear in the Method Comparison Data Listing. They do appear (suitably flagged) in the CBC/Diff Data Listing.
- **F6 Clear Flags** – Clears all exclusion flags (only for the method on the tab page you are editing).
- **F7 Setup** – Provides a way to change the basic structure of the study. For example, you might want to remove a parameter from the analysis or change its Morphology Cutoff Range. This is described in more detail in the "HMC Setup" discussion in the next section.

- **F8 ID Access** – Toggles whether you can type in the Spec ID column. When ID Access is enabled, the background color of the column changes from gray to white: if it is white, you can edit it, but if it is gray, you cannot. The gray column remains visible when you scroll to the right side of the grid while the white form will not.
- **F9 Stats** – Lets you review statistics and graphs for the individual experiments in a format similar to that used in the Alternate Method Comparison module. You cannot edit the data in this mode, but you can quickly identify and review experiments that have problems like low R or slope far from 1.00.

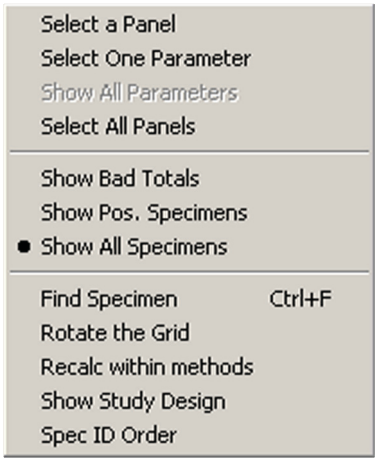


F9 Stats displays a list of key regression statistics for all parameters across all instrument combinations. A fragment of the screen is shown. It allows you to review the basic statistics prior to printing the report.

- **F11 More**. Last but not least, this button provides access to many functions which greatly ease management of these studies.

F11 - More

Click this button to activate the More menu. Within this menu, there are several functions arranged in three (3) groups:

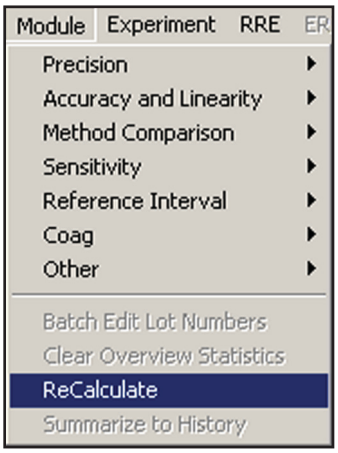


1. **Define the parameters** for which results are to be displayed. The default is to show all parameters in an undefined order. Often users expect to see the parameters in a specific order. Your selection will apply only to the current method.
   - **Select a Panel** provides for changing the panel used to select and order the parameters displayed on the grid. Selected Panels will "stick" between uses of your HMC Study.
   - **Select One Parameter** will display the results for a single parameter.
   - **Show All Parameters** displays results for all parameters.
   - **Select All Panels** allows users to select a Panel for every Method in your Study, all at once. Selected Panels will "stick" between uses of your HMC Study.
2. **Define the specimens** to be displayed.
   - **Show Bad Totals** selects the red-flagged specimens for display (i.e. those for which the ChkSum total is not in the range of 99 to 101).

- **Show Pos. Specimens** selects the specimens that are not red-flagged (i.e. those for which the ChkSum total is in the range of 99 to 101).
- **Show All Specimens** does what it says.

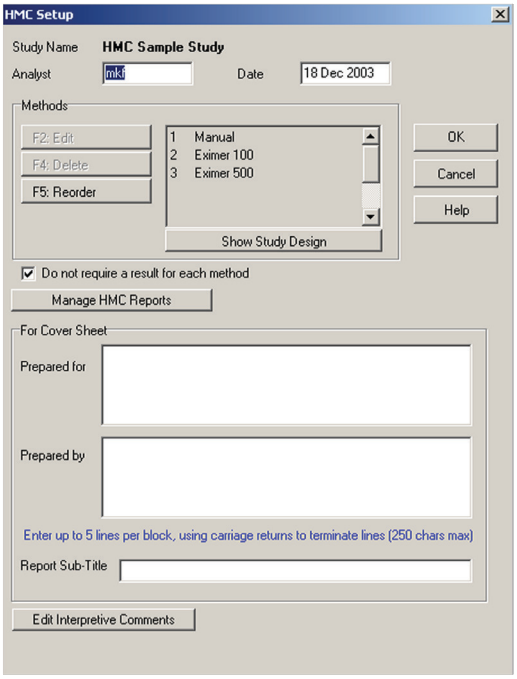
3. **Several Miscellaneous Functions:**
   - **Find Specimen:** Highlights the first specimen which matches the entered specimen ID.
   - **Rotate the Grid**: Normally each row displays the results of a single specimen with results for each parameter listed in columns. If the Grid is Rotated, then each row contains the results for a single parameter, and results for each specimen are listed in the columns.
   - **Recalc within methods**: This option recalculates all of the sums and morphologies for each specimen in each method. It **does not** perform any method comparison computations.
   - **Show Study Design**: See description in the specific section below.
   - **SpecID Order**: Re-orders the specimens so they will be in ASCII order. This is useful when the specimen reports are not ordered prior to entering results into the system.

NOTE: To recompute all of the reports, including the method comparisons, go to the Module menu and select **ReCalculate.**



HMC Setup Screen

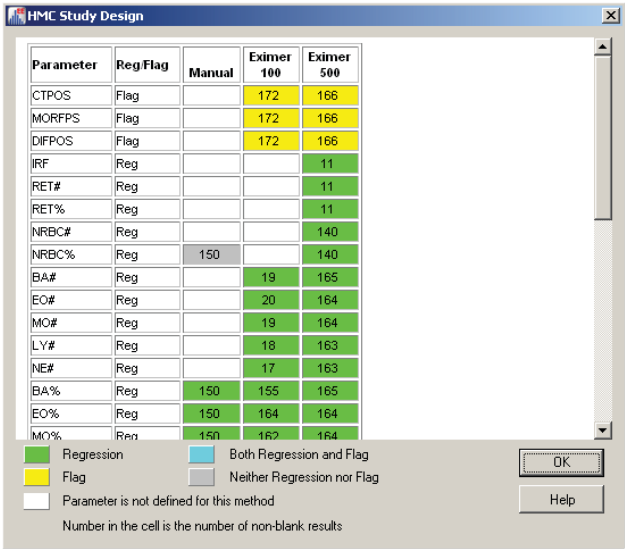
The HMC Setup screen provides access to the design of the experiment after its creation. Access it from F7 Setup in the Experiment Detail Screen.



- **F2: Edit**: One of the buttons on the left provides access to the parameters after the study has been created. In order for F2 to appear, highlight one of the methods in the center box. With this facility, new parameters can be selected for individual instruments, and policy data can be edited for existing instruments and parameters.
- **F4: Delete**: Deletes a highlighted instrument.
- **F5: Reorder**: Displays a box allowing you to change the order in which the instruments are listed.
- **Show Study Design**: Click on the button below the center box to open the Study Design screen as described below.
- **Do not require a result for each method:** Uncheck this box to exclude specimens that do not have a result for all methods.
- **Manage HMC Reports:** Clicking this button displays a form that allows users to control the presence of many of the HMC report components. Check the checkbox for a listed component to include that component in the report. Uncheck the checkbox for a listed component to exclude that component from the report.
- **For Cover Sheet:** Enter a Report Sub-Title, Prepared for and Prepared by text.
- **Edit Interpretive Comments**: Click this button to open an editor which allows you to enter and edit interpretive comments. When information is entered here, and saved, the Interpretive Comments Report will be the last report included in the Hematology Studies report.

Show Study Design

This screen shows the "design" of the results. It will help you understand why certain reports are present or absent. It shows how many results are present for each parameter and instrument, and how those results are used. The second column specifies whether that parameter is being used for regression, as a flagged parameter, or both. The numbers in the boxes indicate the numbers of results available for each parameter and method. The significance of the colors is listed in the legend:



- **Blue**: Used for both flags (morphology analysis) and regression analysis.
- **Green**: Used for regression analysis only.
- **Yellow**: Used for morphology analysis only.
- **Gray**: Neither Regression nor Flag.
- **White**: Parameter is not defined for the method.

Data Entry

After generating a new experiment, you are in the Experiment Detail Screen Workbook.

Four approaches can be used for data entry:

1. Direct entry into the Experiment Detail screen Workbook Method Tabs.
2. Direct entry into the secondary RRE Worksheet.
3. Capture of data from an instrument. (Standard+Data Capture and Professional versions only).
4. Data capture from Instrument Manager as described in Chapter 38, *Rapid Results Entry with Policies*.

   Data entry for the first three approaches are discussed below.

Experiment Detail Screen Approach

Two types of data entry are possible with this approach.

- Entry of data from the keyboard. This is relatively simple. The major issues are making sure that data gets entered in the correct fields relative to specimen ID and parameter. It is very useful to define a panel with all the tests on the report from which you will be working.
- Entry of data using the **Edit, Paste** function via the clipboard. The workbooks created in this way are ideal for copying and pasting from an Excel

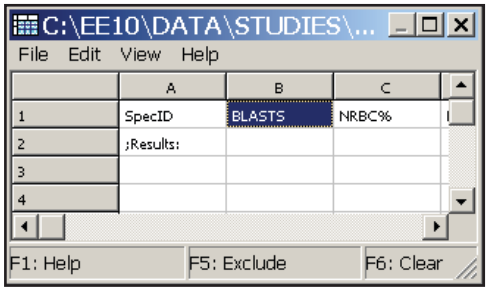
spreadsheet. The system is smart enough to recognize the headers on the Excel sheets and will collate the results into the correct columns no matter what order they are in.

1. In EP Evaluator, select the method tab you want to paste data into.
2. Switch to your Excel spreadsheet tab for that same method and select your data, including SpecIDs and the headers. (You can select the whole sheet by clicking on the empty gray box at the top left of the data grid and selecting copy.) In your Excel spreadsheet, the order of the parameters or the sequence of the specimens does not matter.
3. Switch back to EE and select that instrument/method tab in the workbook.
4. Click on **Edit, Paste**. The data is automatically collated and pasted into the correct columns.
5. Repeat for other instruments/ methods.

RRE Worksheet Approach

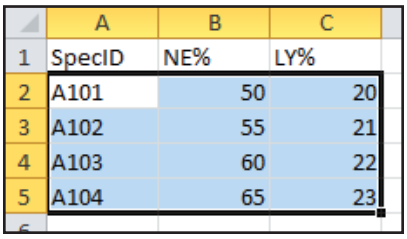
Like the Experiment Detail Screen approach, there are two available types of data entry: one by typing data into the worksheet from the keyboard and the other by pasting clipboard data into the worksheet from a spreadsheet. In both cases, the worksheet must be created before data can be pasted in. This procedure takes more steps but is the best way to enter data from instrument printouts, because the EP Evaluator RRE worksheet is formatted in the defined panel order for the selected instrument.

1. Starting in the EE Experiment Detail Screen workbook, select the method tab you want paste data into.
2. Click **RRE, Create Experiments** to launch the RRE Wizard and generate an intermediate RRE worksheet that is formatted with headers in the selected panel order.
3. Select **Keyboard Entry** then press **Next**. (This screen also gives you an opportunity to modify policies if necessary.)
4. Select an instrument or create a new instrument name in the class of the current workbook tab. Once you enter a new instrument name and serial number, it will be in the **RRE, Create Experiment** dropdown list but will not transfer to policies. Entry of instrument model, serial number, and MIC Code is optional.
5. Select a Panel. The panel is important because you can define which parameters are to be used, and the order in which they are listed in the worksheet.



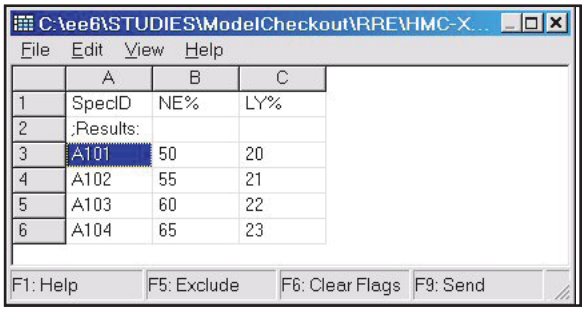
NOTE: The panel selected in the RRE Wizard does not alter the panels specified in the HMC Study Setup Wizard; instead, the panel selected in the RRE Wizard serves to simplify the data entry process by filtering the parameters displayed in the RRE worksheet.

6. Specify whether you are going to use Specimen IDs. It is strongly recommended that they be used in this module because of the complexity of the experiment.
7. Click **Next.**
8. Click **Finish** to create the template.
9. Switch to Excel and copy your results with specIDs for that instrument. Do not copy headers. Data must be in the same panel order.



	A	B	C
1	SpecID	NE%	LY%
2	A101	50	20
3	A102	55	21
4	A103	60	22
5	A104	65	23

10. Switch back to the EP Evaluator RRE Worksheet. Place the cursor at cell A3 and hit <Ctrl-V> to paste the data into the worksheet. The results are shown.



	A	B	C
1	SpecID	NE%	LY%
2	;Results:		
3	A101	50	20
4	A102	55	21
5	A103	60	22
6	A104	65	23

11. Click on **F9/Send** to move the data into the program. The data is collated and pasted automatically into the correct columns in the HMC Experiment Detail Screen. A popup box will appear asking you to confirm the method tab name you are sending the data to.
12. Repeat for other methods/instruments as needed. For each worksheet, the file path and filename for the data worksheet appear at the top. **The file is not automatically saved**. If you want to reuse the data in the worksheet, you must save it manually using **File**, **Save**. If you have not manually saved the worksheet when attempting to close the screen, a popup box will appear prompting you to save.

Data Capture from Instruments

Data is available from instruments in multiple forms depending on the instrument. In some cases, the data is available as a file which can be read into a spreadsheet. If this is the case, then the data capture option is not necessary. In other cases, the data can be captured either directly from the instrument's generated file or via the instrument's serial port. This requires that a special program be written to communicate with the instrument, or its file, and then to communicate that data to EP Evaluator so it will appear in the Worksheet. This feature for Hematology Studies is only available in the Standard+Data Capture and Professional versions of EP Evaluator.

To capture data from an instrument across a serial port, perform the following steps:

1. If you have not already defined the serial communications parameters, click on **RRE / Define Policies**.
2. Select your instrument class. Select Instrument Settings. Adjust those settings so they match those on the instrument.
3. Click on **RRE / Create Experiments**.

4. Select **Instrument Interface**.
5. Select your instrument.
6. After you click on **Next**, the PC waits for data from the instrument.
7. At the instrument, transmit the data. The data can be transmitted in one or more batches. The major restriction is that the data capture program will time-out after 30 seconds have elapsed after the previous batch of data is captured.
8. If you want to use the captured data, allow the program to time-out. If you hit <Escape>, you force a termination of the data capture process. Consequently, the captured data will be discarded.
9. After the time-out has occurred, the program will ask you to select a Panel. Then the captured results will be displayed in a worksheet. You can move the data into the statistical module by hitting <F9>.

Interpretation

There are two major components to interpretation of a Hematology Study: 1) Regression Analysis and 2) Sensitivity or Truth Table Analysis. For interpretation of the Regression Analysis portion, please refer to Rhoads (2012) *Lab Statistics* manual.

It is important that there is a good range of results for each of the parameters. It is more important to have a good range of results spread than a large number of specimens. It is more likely is that a large percentage of results will fall in the normal range, with a few specimens reaching a broader range of results.

The Sensitivity Analysis is both simpler and more complex. It is simpler because there are fewer numbers to analyze. It is more complex because the underlying data is complicated due to the large number of parameters and Morphology Positive Cutoff values.

The ideal Sensitivity Table will have only True Positive and True Negative results. There will be over 100 specimens which will represent a good variety of normal and pathological cell types.

Reports

Sample pages from a Hematology Study report are shown at the end of this chapter. In a recent case, the printout of a comparison of a reasonably complete set of parameters for four methods totaled well over 100 pages. Consequently, it probably will be useful to preview your results before printing them. To preview your results, click on the Print Preview icon. A list of the 12 report sections includes:

1. Cover page for the entire report.
2. Positive Morphology Cutoffs.
3. Method Comparison Summary Report – Key Regression Statistics – All Parameters for each pair of methods compared.
4. Morphology discrepancy page – for each pair of methods.
5. If requested, Flag Comparison.
6. Morphology discrepancy page – for each pair of methods.
7. Method Comparison Report of individual parameters – with plots for each pair of methods.
8. Method Comparison Data Listing – Method bias for parameters used in regression analysis – each method pair.
9. Data Listing for Differential Count Parameters by specimen for all methods.
10. Data Listing for complete CBC – by specimen for all methods.
11. If requested, HMC Interpretive Comments.
12. If requested, the Report Interpretation Guide.

Acknowledgements:

We would like to acknowledge the following instrument manufacturers and their present or former personnel for their significant contributions to the development of this module:
Beckman Coulter, Inc. : Cindy Kessler, Cindy Friedman, Alvera Stevens
Roche Diagnostics: Joe Fall
Sysmex America, Inc.: Barb Butler, Janis Anthony, Janice Cory, Sam McClelland, Debbie Low, Jill Fabrisiak

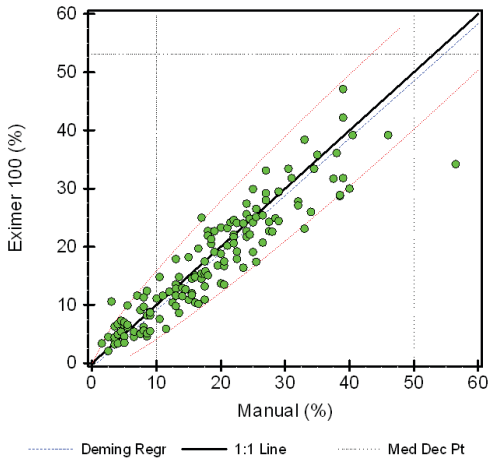
EP Evaluator®

LY%
User Manual -- Data Innovations, LLC

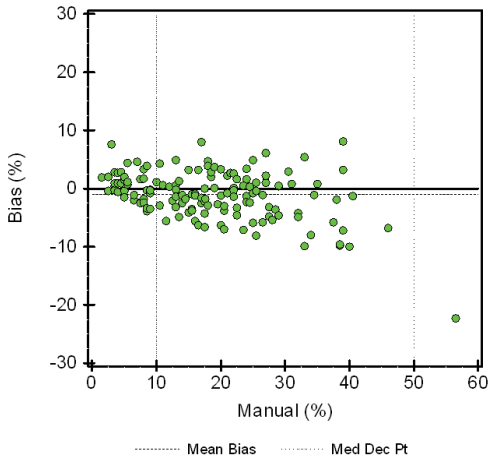
Hematology Method Comparison

X Method Manual **Y Method Eximer 100**

Scatter Plot



Bias Plot



Regression Statistics

	Slope	95% CI	Intercept	95% CI	SEE
Deming	0.985	0.923 to 1.046	-0.74	-2.06 to 0.58	4.04
Regular	0.844	0.786 to 0.901	1.86	0.64 to 3.08	3.74

Correlation Coefficient (R) = 0.9253 N = 145

Reference Interval Statistics

	Manual Entered	Eximer 100 Calculated	95% CI
Lower	10	9.1	8.2 to 10.0
Upper	50	48.5	46.4 to 50.6

Calculated by Deming Regression (R>=0.9)

Data Quality Statistics

	Manual (X)	Eximer 100 (Y)
Range	1.5 to 56.5	2.1 to 47.1
Mean	18.48	17.45
SD	10.77	9.82

Bias -1.03 (-5.6%)

Hematology (Morphology Discrepancy Page)

EP Evaluator®

User Manual -- Data Innovations, LLC

Hematology Method Comparison

X Method Manual **Y Method Eximer 100**

False Positive and False Negative Specimens

Specimen		Manual (X) Positive Parameters	Eximer 100 (Y) Positive Parameters
12031130116	FN	BANDS	--
12031130138	FN	BANDS	--
12031210300	FN	BANDS	--
12031210343	FN	BANDS	--
12031270127	FN	BANDS	--
12031270130	FN	BANDS	--
12031130064	FP	--	DIFPOS
12031130069	FP	--	DIFPOS,MORFPS
12031130076	FP	--	DIFPOS
12031130079	FP	--	MORFPS,CTPOS
12031130085	FP	--	DIFPOS
12031130091	FP	--	MORFPS,CTPOS
12031130093	FP	--	CTPOS
12031130099	FP	--	MORFPS,CTPOS
12031130112	FP	--	CTPOS
12031210119	FP	--	MORFPS
12031210257	FP	--	DIFPOS
12031210379	FP	--	MORFPS,CTPOS
12031210388	FP	--	DIFPOS,MORFPS,CTPOS
12031210427	FP	--	MORFPS
12031210443	FP	--	MORFPS,CTPOS
12031250093	FP	--	DIFPOS,CTPOS
12031260061	FP	--	MORFPS
12031270085	FP	--	MORFPS
12031270094	FP	--	MORFPS
12031270102	FP	--	DIFPOS,MORFPS
12031270103	FP	--	CTPOS
12031270106	FP	--	DIFPOS,CTPOS
12031270115	FP	--	CTPOS
12031270123	FP	--	DIFPOS,MORFPS
12031270124	FP	--	DIFPOS,MORFPS
12031270131	FP	--	MORFPS,CTPOS
12031270132	FP	--	DIFPOS,MORFPS
12031270138	FP	--	DIFPOS,MORFPS
12031270160	FP	--	MORFPS,CTPOS
12031270162	FP	--	MORFPS
12031270163	FP	--	CTPOS
12031330299	FP	--	DIFPOS,MORFPS,CTPOS
12031330352	FP	--	DIFPOS
12031330460	FP	--	CTPOS
12031330514	FP	--	DIFPOS
12031330520	FP	--	MORFPS
12031330529	FP	--	DIFPOS
12031330557	FP	--	MORFPS,CTPOS

FP = False Positive FN = False Negative

EP Evaluator 10.

HMC Example HMC Sample Study Printed: 19 Jul 2012 11:15:49 Page 1

EP Evaluator®

Hematology Method Comparison

Diff Count Data Listing: BA% to NE%

Specimen		Method	Flags	BA%	EO%	LY%	MO%	NE%
1	12031130032	Manual	BANDS	0	0	8	0	92
		Eximer 100	DIFPOS	0	0.2	6.2	0.8	92.8
		Eximer 500	DIFPOS	0	0.2	7	0.4	92.4
2	12031130052	Eximer 100	DIFPOS, CTPOS	0.2	0.7	8.9	3.7	86.5
3	12031130054	Eximer 100	DIFPOS, MORFPS, CTPOS	0.1	--	3.5	0.7	--
4	12031130057	Eximer 100	MORFPS	0.3	0.5	32.7	9.1	57.4
5	12031130062	Manual	BANDS	0	0.5	4	5	90.5
		Eximer 100	DIFPOS, MORFPS, CTPOS	--	--	3.4	7.8	--
		Eximer 500	DIFPOS, MORFPS, CTPOS	0.1	0.1	4.2	8.6	87
6	12031130063	Manual	BANDS	1	1.5	39	10	48.5
		Eximer 100	DIFPOS	0.5	0.9	42.2	15.5	40.9
		Eximer 500	MORFPS	0.2	0.9	38.9	13.3	46.7
7	12031130064	Manual		1	0.5	5	6.5	87
		Eximer 100	DIFPOS	0.4	1.1	4.6	8	85.9
		Eximer 500	DIFPOS, MORFPS	0.3	1.1	6.5	7.7	84.4
8	12031130065	Eximer 100	DIFPOS	0.1	0.6	6.1	5.4	87.8
		Eximer 500	DIFPOS, MORFPS	0.1	0.9	7.7	6.1	85.2
9	12031130066	Manual	BANDS	0	1.5	17	11	80.5
		Eximer 100	DIFPOS	0	0.9	14.5	16.1	68.5
		Eximer 500	DIFPOS	0.3	0.6	14.3	14.9	69.9
10	12031130068	Eximer 100	DIFPOS, MORFPS	0.1	0.3	3.6	--	--
11	12031130069	Manual		0	0	5.5	2	92.5
		Eximer 100	DIFPOS, MORFPS	0.1	0.1	6.2	4.9	88.7
		Eximer 500	DIFPOS	0.1	0	6.6	4.6	88.7
12	12031130071	Manual		0	0.5	32	4	63.5
		Eximer 100		0.7	2.8	27.8	7.5	61.2
		Eximer 500		0.4	2.5	30	8.1	59
13	12031130072	Manual	BANDS	0	0	17.5	8	74.5
		Eximer 100	MORFPS	0.3	0.3	13.2	6.9	79.3
		Eximer 500	DIFPOS, MORFPS	0	0.2	13.6	7.7	78.5
14	12031130074	Eximer 100		0.1	0.9	11.1	5.7	82.2
		Eximer 500	MORFPS, CTPOS	0.2	0.1	12.2	8	79.5
15	12031130075	Manual	BANDS	1	1.5	20.5	18.5	60
		Eximer 100	DIFPOS, MORFPS	0.6	1	16.7	21.6	60.1
		Eximer 500	DIFPOS, MORFPS	0.1	0.7	22.2	17.2	59.8
16	12031130076	Manual		0	0	10	7	83
		Eximer 100	DIFPOS	0	0.1	11.1	3.4	85.4
		Eximer 500	DIFPOS, MORFPS	0	0	10.4	4.2	85.4
17	12031130078	Manual		0.5	2	18.5	9.5	69.5
		Eximer 100		0.7	5.6	20.5	13.6	59.6
		Eximer 500	MORFPS	1	4.9	21.2	13.2	59.7
18	12031130079	Manual		1.5	0.5	40.5	5	52.5
		Eximer 100	MORFPS, CTPOS	0.4	0.8	39.2	12.1	47.5
		Eximer 500	MORFPS, CTPOS	0.4	1.1	40.1	10.1	48.3
19	12031130080	Eximer 100	DIFPOS, MORFPS, CTPOS	0.1	1.8	5.6	6.6	85.9
20	12031130082	Manual	BANDS, METAS, MYELO	0	0	7.5	4	88.5
		Eximer 100	DIFPOS, MORFPS, CTPOS	--	0.1	5.1	4	90.8
		Eximer 500	DIFPOS, MORFPS, CTPOS	0.2	0.1	6.8	5.8	87.1
21	12031130083	Manual		0.5	1	23.5	8	67
		Eximer 100		0.3	1.5	16.4	11	70.8
		Eximer 500	DIFPOS, MORFPS	0.3	1.3	17.4	11.2	69.8
22	12031130085	Manual		0	0	13	1	86
		Eximer 100	DIFPOS	0.3	0.1	9.8	1.6	88.2
		Eximer 500	DIFPOS	0	0	11.4	1.6	87
23	12031130086	Eximer 100		0.4	0.8	11.1	10	77.7
		Eximer 500	MORFPS	0.1	0.9	12.1	8.4	78.5
24	12031130087	Manual		0	0	27.5	2	70.5
		Eximer 100		0.1	0.7	22.7	7.1	69.4
		Eximer 500		0.2	0.8	24.5	6.8	67.7
25	12031130088	Manual	BANDS, METAS	0.5	8	20.5	22	51.5
		Eximer 100	DIFPOS, MORFPS	0.6	8.1	13.5	12.1	65.7
		Eximer 500	DIFPOS, MORFPS	0.3	8.4	16.5	16.1	58.7
26	12031130089	Manual	BANDS	0.5	4	28.5	6.5	58.7

This listing shows ALL AVAILABLE MANUAL DIFF RESULTS, regardless of whether they are used in method comparisons. 'x' indicates a specimen that was manually excluded.

EP Evaluator®

User Manual -- Data Innovations, LLC

Hematology Method Comparison

X Method Manual **Y Method Eximer 100**

Statistical Summary

	N and Result Range	Correlation Coefficient	SEE	Slope with 95% CI	Intercept with 95% CI	Lower Reference Limit Current	Lower Reference Limit Calculated with 95% CI	Upper Reference Limit Current	Upper Reference Limit Calculated with 95% CI
BA%	138 0.0 to 2.0	0.3571	0.88	2.336 1.966 to 2.706	-0.15 -0.32 to 0.02	0	0.4 * 0.3 to 0.5	--	
EO%	146 0.0 to 12.5	0.8898	1.20	1.279 1.183 to 1.375	-0.08 -0.33 to 0.17	0	0.4 * 0.3 to 0.6	7	7.3 * 6.9 to 7.8
LY%	145 1.5 to 56.5	0.9253	4.04	0.985 0.923 to 1.046	-0.74 -2.06 to 0.58	10	9.1 8.2 to 10.0	50	48.5 46.4 to 50.6
MO%	144 0.0 to 55.0	0.4399	7.24	1.526 1.299 to 1.754	-1.98 -3.88 to -0.08	0	2.5 * 1.9 to 3.1	12	11.7 * 9.5 to 13.9
NE%	141 36.0 to 96.0	0.9339	4.75	1.055 0.992 to 1.118	-5.46 -10.16 to -0.76	37	33.6 31.1 to 36.0	80	78.9 78.0 to 79.9

Summary regression statistics calculated using the Deming method.
Parameter data included if valid results exist across two methods.
* Evaluated by the Partitioned Biases Method (R< 0.900)

Clinical Utility Study

	Negative Reference	Positive Reference	Total
Negative Test	57 **TN**	6 **FN**	63
Positive Test	40 **FP**	44 **TP**	84
Total	97	50	147

	CLSI with 95% CI	Galen/ Gambino
Agreement	68.7% (60.8 to 75.6%)	
False Positive	41.2%	27.2%
False Negative	12.0%	4.1%
Sensitivity	88.0% (76.2 to 94.4%)	
Specificity	58.8% (48.8 to 68.0%)	

Chapter

17

Sensitivity (Limits of Blank)

This module provides for the determination of Sensitivity (Limit of Blank), namely the lowest concentration significantly different from zero. Two synonyms for this concept are Minimum Detectable Concentration (MDC) and Analytical Sensitivity. This type of Sensitivity is useful for methods for which low concentrations are not particularly important. Prior to Release 7 of EP Evaluator, this was called "Sensitivity (Limits of Detection).

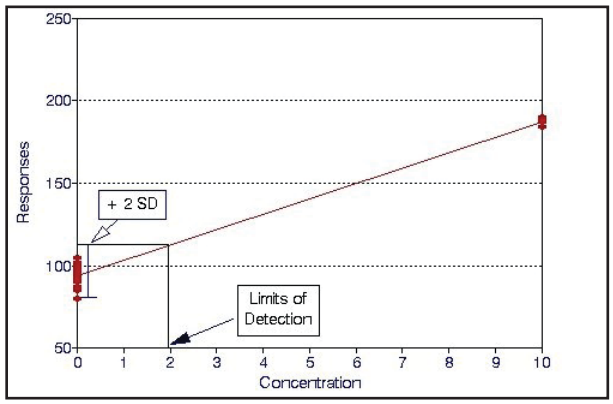
This module uses instrument **responses** (not actual **results**) for its calculations. Consequently, you must be able to get responses from your instrument in order to use this module. This approach is useful when the lowest result your instrument reports is "less than X".

If you are able to get results from your instrument which surround zero (i.e. both positive and negative), then you can use the Simple Precision module.
There are several definitions of Sensitivity which are in use in the clinical laboratory. They are discussed in detail in Lab Statistics, Fun and Easy. Sensitivity (Limit of Quantitation) has been implemented in EP Evaluator, and is discussed in Chapter 18, *Sensitivity (Limits of Quantitation)*.

Data Requirements

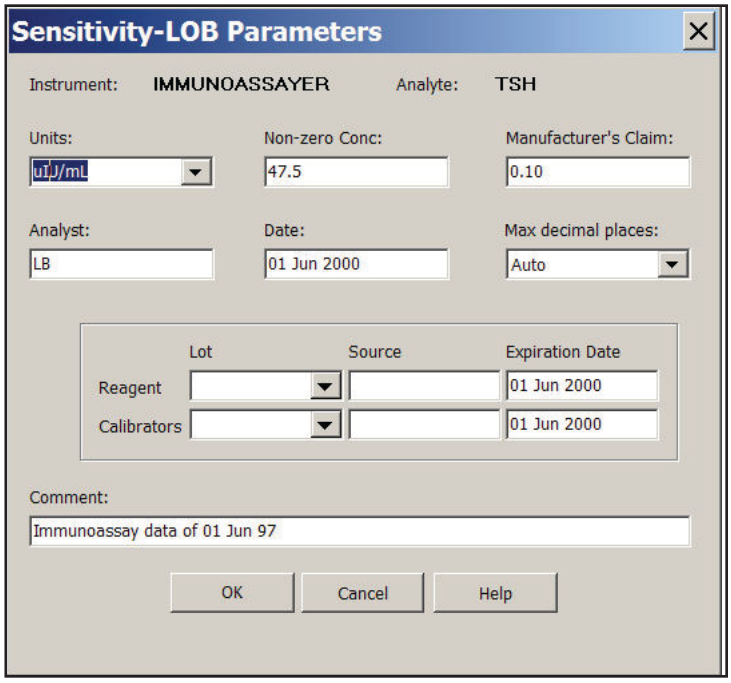
The minimum number of responses (not results) required for this module are 10 zero responses and 3 non-zero responses in EP Evaluator. The maximum number are 20 of each. Keep in mind that the data to be entered must be raw instrument values such as absorbance or fluorescence units, counts per minute or mAbs per minute units, NOT the usual analyte concentration units.

Scientific Basis



The scientific basis of the calculation is shown at right. It shows how the raw instrument RESPONSES, measured for the zero and lowest non-zero calibrators are combined to produce the Limit of Detection (LOB). A slope is calculated from the means of both sets of responses and their concentrations. The LOB is that concentration which corresponds to the response 2 SD distant from the mean of the zero responses toward that of the non-zero calibrator. If you need the lowest concentration to a 99.7% confidence level (3 SD), increase the 2 SD value by 50%.

Parameter Screen



As usual, the Parameter Screen provides for entry of various experimental details. These fields include:

Units. Required.

Max decimal places. Maximum number of decimal places for reports. "Auto" means number of decimal places is determined from the data.

This setting affects reports only; calculations are done on full-precision numbers.

Concentration of non-zero specimen must be a number. **Required**.

Manufacturer's Sensitivity claim. This must be entered to validate claim. **Optional.**

Lot number and **expiration date**. One pair for reagents and one pair for calibrators. (16 characters maximum size). **Optional**.

Analyst (12 characters maximum size). **Required**.

Experiment Date (date experiment performed). **Required**.

Comment (80 characters maximum size). **Optional**.

Experiment Detail Screen

The experiment detail screen provides for entry of the experimental responses and for real-time calculation of the detection limits. For discussion of the sensitivity and response statistics, see section on Interpretation below.
The reason for the seemingly large minimum number of responses is because the uncertainty of the SD at the zero-concentration needs to be minimized. The uncertainty of that SD will be decreased by a factor of about 1.4 if the number of responses increases from 10 to 20.

Sensitivity Report

Elements of the Sensitivity Report are discussed below. A complete example of the Sensitivity Report is shown at the end of this chapter.

Key Statistics

The most important statistics are the 2 SD Limit of Blank (95% Conf) (LOB), the Manufacturer's Claim, and a Pass/Fail declaration. If the user has entered the Manufacturer's LOB Claim, then the software will compare that value with the 2 SD LOB. If the Manufacturer's Claim equals or exceeds the 2 SD LOB, the experiment "Passes." Also included are the means and SDs calculated for the responses at the zero and non-zero concentration. If you want to determine the 3 SD LOB, simply multiply the 2 SD LOB by 1.5. That will increase the confidence of your number from 95% to 99.5%.

Sensitivity Statistics

2 SD Limit of Blank (95% Conf): 0.059 uIU/mL
Manufacturer's Claim: 0.10 uIU/mL
Passes: Pass

Response Statistics

Concentration	Mean	SD
0	10.31	0.07
47.5	120.20	5.53

Keep in mind also that the number of replicates has a significant impact on the value of your LOB. Your LOB will be better when N=20 rather than N=10.

Sensitivity Report (page 1)

EP Evaluator® — **TSH**

User's Manual -- Data Innovations — Instrument: IMMUNOASSAYER

Sensitivity-Limit of Blank

Sensitivity Statistics

2 SD Limit of Blank (95% Conf): 0.059 uIU/mL
Manufacturer's Claim: 0.10 uIU/mL
Passes: Pass

Response Statistics

Concentration	Mean	SD
0	10.31	0.07
47.5	120.20	5.53

Supporting Statistics

Analyst: LB
Analysis Date: 01 Jun 2000
Units: uIU/mL
Comment: Immunoassay data of 01 Jun 97

	Lot Number	Exp. Date
Reagents:		01 Jun 2000
Calibrators:		01 Jun 2000

Experimental Responses

Concentration: 0

10.4	10.3	10.3	10.3	10.3
10.3	10.3	10.4	10.3	10.2
10.4	10.4	10.2	10.3	10.3
10.2	10.3	10.2	10.4	10.3

Concentration: 47.5

115.3	115.4	119.1	122.8	128.4

Accepted by: _____ _____
Signature Date

EP Evaluator
Default Printed: 21 Sep 2009 19:02:36 Page 1

Chapter

18

Sensitivity (Limits of Quantitation)

This module determines the lowest concentration at which an analyte can be measured over an extended period (weeks to months). This is useful for analytes such as TSH for which low concentrations are important. A synonym for this approach is Functional Sensitivity.

Three other approaches to Sensitivity are:

Limits of Blank (Analytical Sensitivity). In this approach, the user determines the lowest concentration which is significantly different from zero. (This approach, implemented in EE, is described in Chapter 17, *Sensitivity (Limits of Blank)*.)

Limits of Detection is described in the CLSI:EP17. It is the lowest concentration for which one can be **sure** that no result which is declared as positive in fact has a zero concentration. (This approach is not implemented in EE.)

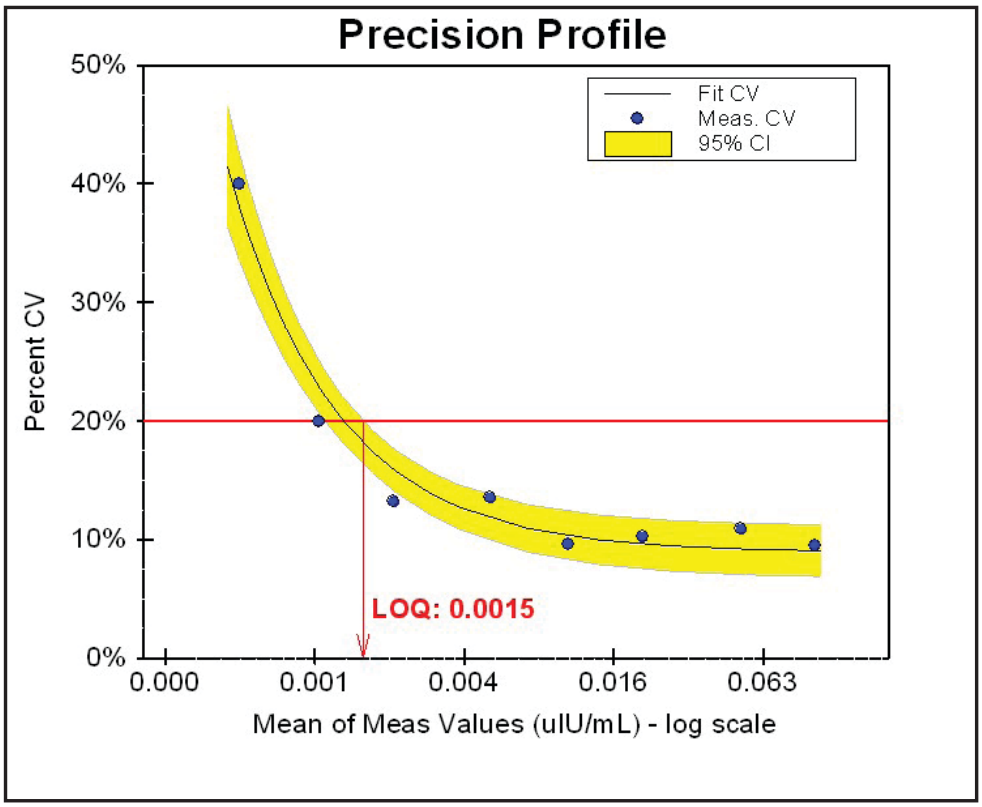
Validation of Manufacturer's Sensitivity is performed by determining the CV of a specimen with a concentration not exceeding a specified amount over a specified period of time, typically a day. If the measured CV does not exceed the manufacturer's claim during that time period, then the method is validated. (This approach is not implemented in EE.)

Experimental Design

The approach used is very pragmatic. The quick description is that it is a precision profile experiment at low concentrations. The object of the experiment is to generate a precision profile graph similar to the one shown below.

The approach used to determine functional sensitivity is to calculate the precision for each specimen over the period of the experiment. A curve is fitted to obtain an estimate of CV as a function of mean. The LOQ is the point where the upper 95% confidence limit for this curve crosses the target CV line.

Several specimens (5 to 20) are prepared which cover the range of concentrations within which the functional sensitivity concentration is expected to occur.



The specimens should be prepared so the concentrations between consecutive specimens increase logarithmically (vs. arithmetically), such as a factor of 2. In other words, the specimen concentrations should be a series like 1, 2, 5, 10 and 20 rather than 2, 4, 6, 8, 10 and 12. The problem with using an arithmetic series is that it is likely that you will have to assay many more specimens to get your result unless you have a good estimate of the final value before you begin the experiment. If the value is outside the range of your specimens, then you will have to repeat the experiment.

Once you have prepared the specimens, make 20 to 50 aliquots of each. Then freeze all of them. Perform one assay of each specimen on a given day. Expect this experiment to take a month or more to complete.

Data Requirements

The data requirements are shown in Table 18.1.

Table 18.1

Sensitivity (LOQ) Data Requirements		
	Minimum	**Maximum**
Number of specimens	5	20
Number of results per specimen	10	100+

LOQ Parameter Screen

The LOQ Parameter Screen (Figure 18.1.) provides for entry of the non-result experimental details.

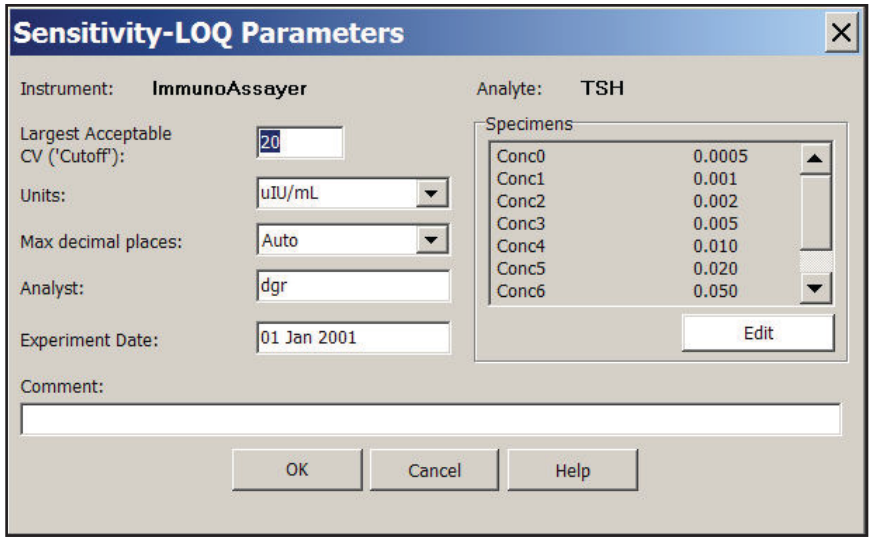
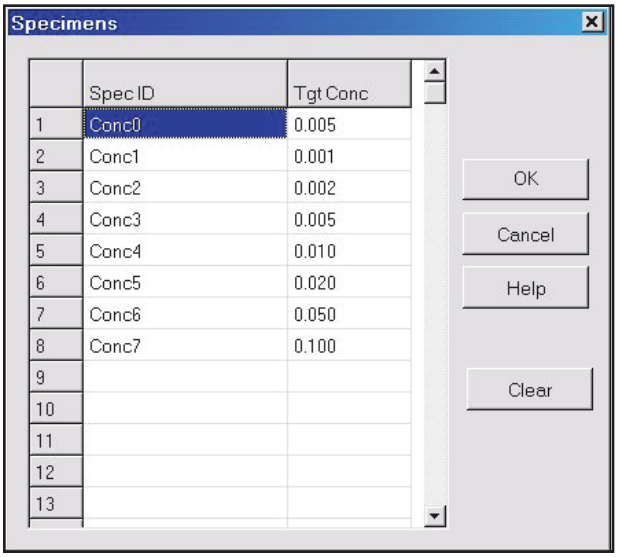


Figure 18.1. Sensitivity (LOQ) Parameter Screen

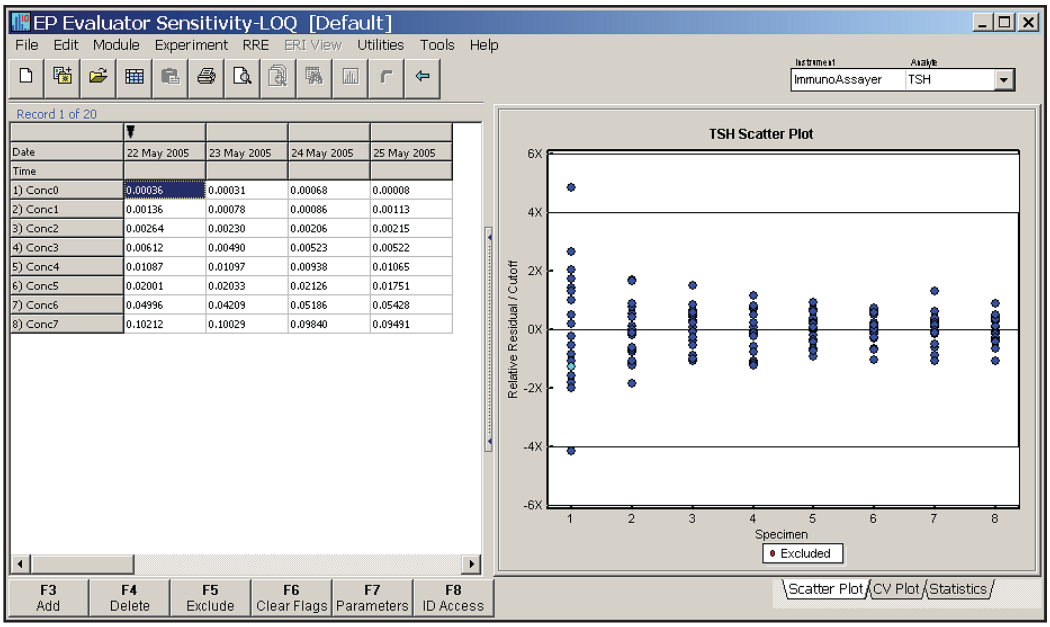
The one parameter on this screen which is not self explanatory is the Largest Acceptable CV ('Cutoff'). The point of the experiment is to find the lowest concentration that can be measured with acceptable accuracy. The cutoff defines "acceptable accuracy"—accuracy is acceptable if CV is less than the cutoff; accuracy is unacceptable if CV is greater than the cutoff.

The Specimen Description field is accessed from this screen by clicking on the Edit button of the Parameter Screen (Figure 18.1.). Up to 20 specimens can be defined. The target concentrations ('Tgt Conc') are not used in the calculations. They are the approximate concentrations of the specimen and are there for administrative purposes only.



Experiment Detail Screen

As usual, the experiment detail screen provides for entry of the experimental responses and display of the results of real-time calculations. Please note the tabs in the lower right corner of the screen which provide for access to the scatter plot, the Precision Profile plot (labeled "CV Plot") and the Statistics.
Results entry is as described in Chapter 3, *Common Operations*. The CV Plot is a plot of the point estimates of the calculated CVs, the fitted curve, and its 95% confidence interval.



Interpretation

One's reasonable expectation for this experiment is that the general shape of the precision profile will resemble that of the figure shown earlier in this chapter. If this is not the case, the validity of the experiment should be questioned. Something is not behaving as expected.

Sufficient decimal digits: Make sure that you have adequate decimal digits in your results. If you don't then your calculated SD's can be rather misleading. If your results are reported to 0.01, then you need to report your results at least for this experiment to at least three decimal digits.

Adequate N. Make sure that you have enough results. The minimum of 10 is barely enough. The observed SD may range over a factor of at least 2. Increasing N to 20 will improve the quality of the SD's significantly.

Sensitivity (LOQ) Report

A sample report is shown at the end of this chapter.

Sensitivity (LOQ) Report - Summary Page

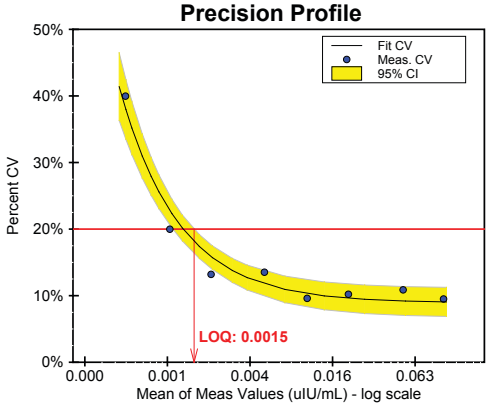
EP Evaluator® **TSH**

User's Manual -- Data Innovations

Instrument: ImmunoAssayer

Sensitivity-Limit of Quantitation

Precision Profile



Evaluation of Results

TSH was analyzed by ImmunoAssayer to determine the LOQ (lowest concentration for which CV is less than a target of 20%).

Specimens with mean measured concentration ranging from 0.00048 to 0.10078 uIU/mL were assayed. A curve was fit to estimate the relationship between Mean and CV. Based on the fitted model, the LOQ is 0.0015 uIU/mL. This is the point where the upper 95% confidence interval for the curve has a CV of 20%.

Sample	Target Conc.	N	Mean	SD	Meas. CV (%)	Fitted CV (%)	95% CI for Fitted Low	95% CI for Fitted High
Conc0	0.0005	20	0.00048	0.00019	40.0	38.1	33.6	42.7
Conc1	0.001	20	0.00102	0.00020	20.0	22.8	20.6	25.0
Estimated LOQ		--	**0.0015**	--	--	**18.2**	**16.3**	**20.0**
Conc2	0.002	20	0.00203	0.00027	13.2	15.9	14.1	17.7
Conc3	0.005	20	0.00498	0.00067	13.5	11.8	9.8	13.7
Conc4	0.010	20	0.01021	0.00098	9.6	10.3	8.3	12.4
Conc5	0.020	20	0.02039	0.00208	10.2	9.6	7.5	11.7
Conc6	0.050	20	0.05108	0.00555	10.9	9.2	7.0	11.4
Conc7	0.100	20	0.10078	0.00956	9.5	9.1	6.9	11.3

x: Excluded because either Mean or SD was zero.

Supporting Data

Analyst:	dgr
Analysis Date:	22 May 2005 to 10 Jun 2005
Units:	uIU/mL
Target CV:	20%
Comment:	

Fit Statistics

Model:	CV = A + B * (1/Mean)
A:	8.93 +/- 0.8986
B:	0.01411 +/- 0.001079
R-square:	0.9661
Std Err Est:	2.05

Accepted by: _____ _____

Signature Date

Sensitivity (LOQ) Report - Results Page

EP Evaluator® **TSH**

User's Manual -- Data Innovations

Instrument: ImmunoAssayer

Sensitivity-Limit of Quantitation

Experimental Results

Sample	Result
1) 22 May 2005	
Conc0	0.0004
Conc1	0.0014
Conc2	0.0026
Conc3	0.0061
Conc4	0.0109
Conc5	0.0200
Conc6	0.0500
Conc7	0.1021
2) 23 May 2005	
Conc0	0.0003
Conc1	0.0008
Conc2	0.0023
Conc3	0.0049
Conc4	0.0110
Conc5	0.0203
Conc6	0.0421
Conc7	0.1003
3) 24 May 2005	
Conc0	0.0007
Conc1	0.0009
Conc2	0.0021
Conc3	0.0052
Conc4	0.0094
Conc5	0.0213
Conc6	0.0519
Conc7	0.0984
4) 25 May 2005	
Conc0	0.0001
Conc1	0.0011
Conc2	0.0022
Conc3	0.0052
Conc4	0.0106
Conc5	0.0175
Conc6	0.0543
Conc7	0.0949
5) 26 May 2005	
Conc0	0.0005
Conc1	0.0009
Conc2	0.0016
Conc3	0.0039
Conc4	0.0103
Conc5	0.0201
Conc6	0.0495
Conc7	0.1189
6) 27 May 2005	
Conc0	0.0007
Conc1	0.0010
Conc2	0.0019
Conc3	0.0057
Conc4	0.0101
Conc5	0.0191
Conc6	0.0548
Conc7	0.0980
7) 28 May 2005	
Conc0	0.0004
Conc1	0.0006
Conc2	0.0017
Conc3	0.0051
Conc4	0.0098
Conc5	0.0226
Conc6	0.0643
Conc7	0.0950
8) 29 May 2005	
Conc0	0.0003
Conc1	0.0010
Conc2	0.0022
Conc3	0.0039
Conc4	0.0116
Conc5	0.0198
Conc6	0.0542
Conc7	0.1081
9) 30 May 2005	
Conc0	0.0005
Conc1	0.0012
Conc2	0.0019
Conc3	0.0057
Conc4	0.0106
Conc5	0.0231
Conc6	0.0459
Conc7	0.0789
10) 31 May 2005	
Conc0	0.0004
Conc1	0.0014
Conc2	0.0022
Conc3	0.0058
Conc4	0.0083
Conc5	0.0193
Conc6	0.0449
Conc7	0.1095
11) 01 Jun 2005	
Conc0	0.0004
Conc1	0.0008
Conc2	0.0018
Conc3	0.0048
Conc4	0.0106
Conc5	0.0207
Conc6	0.0573
Conc7	0.1075
12) 02 Jun 2005	
Conc0	0.0004
Conc1	0.0010
Conc2	0.0023
Conc3	0.0055
Conc4	0.0095
Conc5	0.0226
Conc6	0.0458
Conc7	0.1112
13) 03 Jun 2005	
Conc0	0.0005
Conc1	0.0011
Conc2	0.0019
Conc3	0.0044
Conc4	0.0103
Conc5	0.0205
Conc6	0.0551
Conc7	0.1060
14) 04 Jun 2005	
Conc0	0.0006
Conc1	0.0010
Conc2	0.0024
Conc3	0.0049
Conc4	0.0093
Conc5	0.0234
Conc6	0.0497
Conc7	0.0922
15) 05 Jun 2005	
Conc0	0.0004
Conc1	0.0008
Conc2	0.0020
Conc3	0.0047
Conc4	0.0103
Conc5	0.0178
Conc6	0.0549
Conc7	0.0931
16) 06 Jun 2005	
Conc0	0.0006
Conc1	0.0014
Conc2	0.0021
Conc3	0.0052
Conc4	0.0089
Conc5	0.0176
Conc6	0.0402
Conc7	0.1030
17) 07 Jun 2005	
Conc0	0.0009
Conc1	0.0010
Conc2	0.0018
Conc3	0.0037
Conc4	0.0121
Conc5	0.0161
Conc6	0.0533
Conc7	0.0920
18) 08 Jun 2005	
Conc0	0.0003

"X" = Excluded Results

Chapter

19

Verification of Reference Interval

The Verification of Reference Interval module (VRI) has been included to allow laboratories to meet the CLIA ‘88 requirement of verifying the reference interval.

The term **Reference Interval** has multiple definitions.

- The broadest definition refers to the range of results which define a condition of health (or lack thereof). For example, reference interval can refer to therapeutic and toxic ranges for drugs as well as panic values for various analytes.
- A second definition interprets the term as the normal range, i.e. the central 95% of results from a healthy patient population. This second definition is the one used in the CLIA ‘88 regulations and in the CLSI:C28 document. Note also another pun – that of the word normal. There are two relevant definitions of this term in this context, one referring to a healthy population, the second a more statistical one referring to a (hoped-for) Gaussian distribution.

Data Requirements

To Verify a Reference Interval: In most cases of instrument validation, it is not necessary to establish a reference interval, but only to verify the proposed one. This module allows the user to verify the proposed one. A minimum of 20 results are required.

To Establish a Reference Interval, the CLSI Reference Interval protocol (CLSI:C28) requires a minimum of 120 results to establish a Reference Interval and suggests that as many as 300 or 400 healthy individuals should be used to establish the ranges for some analytes. The minimum number required to calculate a reference interval in this module is 40. *However this small number is clearly insufficient for a reliable normal range*.

Performing a Study

Every reference interval study has three stages, pre-analytical, analytical and post-analytical. To obtain satisfactory results, attention to all three stages is critical.

Pre-Analytical is the specimen collection and preparation phase. Of the three stages, it is the most important. If a significant number of the specimens are from patients who have a disease affecting the analyte being studied, those results may be invalid. Consequently, the population from which specimens are obtained should be carefully defined. This may include a thorough screening of individuals from whom specimens are obtained for this purpose. Acceptable specimens can often be obtained from pre-employment screening patients, outpatients, etc.

Analytical phase is the analysis phase. Testing should be done on a system in good control, otherwise the results may be severely impacted.
Post-Analytical phase includes calculation and analysis of results and generation of the report.

How VRI Works

Results from at least 20 healthy individuals are entered into the module. If at least 90% are within the previously defined reference interval, the data passes the VRI test and the stated reference interval is validated.

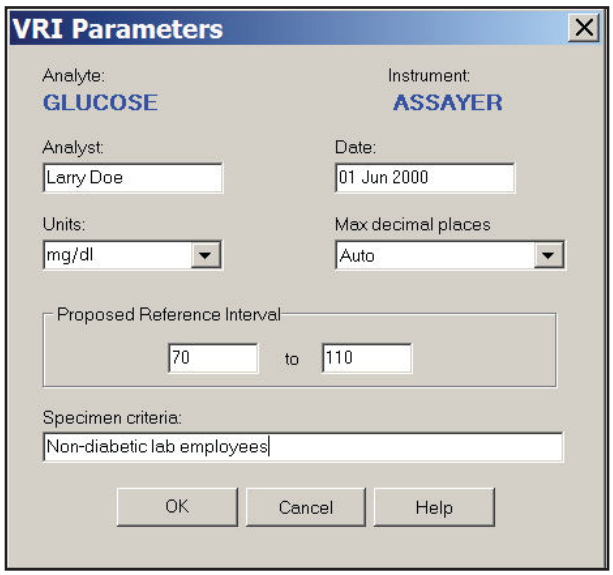
Limitation #1 is Low Statistical Power. It is possible to fail this test even on a correctly established reference interval. For a verification study with only 20 specimens, the probability of failing is 30% and 10% if one and two results respectively are outside the reference interval. (The use of 10% is used to minimize the number of failures when verifying correct reference intervals. It does lower the probability of detecting incorrect reference intervals.)

Limitation #2 is that this process attempts to validate a proposed reference interval. It is quite possible to validate a wrong reference interval. If there are significant doubts about the correctness of the reference interval, then a larger study should be done to establish it. One example of wrong reference interval is one which is too broad. For example, if the manufacturer defined a reference interval for Sodium to be from 130 to 155 mmol/L while the actual normal range is from 135 to 145, it would almost always pass this test. However it would be insensitive to a large number of abnormal Sodium values.

Limitation #3 is appropriateness. The approach used in the VRI module is applicable only for those analytes for which the reference interval is based on the central 95% rule. It will not work for drugs or other analytes with medical decision values based on pathological conditions. The drug digoxin, for example, has medical decision points for toxic and therapeutic concentrations based on medical observations of patients with enough, too little, or too much drug present in their blood.
Some laboratories handle the case with drugs by noting that the concentration of drugs in healthy individuals is zero. Therefore the reference interval is zero! If there is uncertainty whether this approach will satisfy the regulations for a lab, consult with the appropriate regulatory agency.

Parameter Screen

This screen describes essential elements of the experiment. The fields to which you have access are:



Analyst: Required.

Date: Required.

Units: Required.

Max decimal places is the maximum number of decimal places for reports. "Auto" means number of decimal places is determined from the data. Computed statistics (e.g., Mean) are usually printed with one more decimal place than the input results. This setting affects reports only; calculations are done on full-precision numbers.

Proposed Reference Interval is the upper and lower limits of the reference interval (i.e. normal range) to be verified. **Required**.

Specimen criteria notes the source of the specimens (i.e. pre-employment surveys, pre-marital testing and outpatients) or any other comment needed for documentation. **Optional**.

Sources of proposed reference intervals:

Manufacturer's package insert. A good first choice, especially for middle-class adult humans in the continental US.

Various reference books.

Several web sites contain reference intervals. For example, datainnovations.com has listings of reference intervals which reference links to other web sites with reference intervals.

VRI Report

Interpretation of the VRI Report is in the form of discussion of excerpts of the report. The data displayed in the example reports are the Standard Data which is present when the program is initially installed. A complete example of the report is shown at the end of this chapter.

The most important table in the VRI Report is the Reference Interval Table. It displays the results of the validation process for Reference Interval.

Reference Interval	
Proposed	70 to 110 mg/dl
Results (total/excluded)	23 / 0
Max/Obs outside	10.0% / 4.3%
Passes	Yes

The second most important table is the Statistical Analysis Table. Several statistics are calculated for the experiment. Keep in mind that these statistics describe a Gaussian or parametric distribution which often are not appropriate to analyze the data because of its distribution.

Statistical Analysis	
Mean	92.8 mg/dl
SD	9.8
Median	93
Range	75 to 115
Central 95% Interval	--
Central 95% Index	--

Central 95% Interval and Central 95% Index show the calculated central 95% interval for these data and the indices of the elements used to determine the central 95% interval. For example, if there are 120 results in a study, the index will be 3 and 118. In other words, the lower and upper limits of the central 95% range are defined by specimens 3 and 118 respectively.

Key Statistics

Key statistics in this module are:

Proposed RI (reference interval) shows the reference interval that is being tested.

N refers to the number of results. The first number is the number used in the calculations. The second number is the total number of results currently present for this experiment. The difference is the number of excluded results.

% Outside is the percent of results outside the proposed reference interval.

Passes? has three possible conditions after calculations are performed:

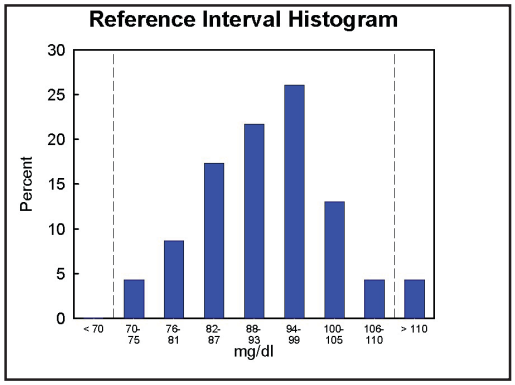
- **Pass**: no more than 10% of the results are outside the proposed reference interval.(Green dot in column 1)
- **Fail**: more than 10% of the results are outside the proposed reference interval. (Red dot in column 1)
- "**": No pass/fail determination is made since less than 20 results are available for the calculation, (White dot in column 1)

The **Result Distribution Table** shows the distribution of the results over the proposed reference interval. The significance of Percent and Count should be obvious.

Results Distribution

Interval	Percent	Count
< 70	0	0
70-75	4	1
76-81	9	2
82-87	17	4
88-93	22	5
94-99	26	6
100-105	13	3
106-110	4	1
> 110	4	1

Histogram: The ideal shape of the histogram is a bell-shaped curve. In general, the bars in the middle will have more points than those on the outer edges. The curve is not likely to be smooth unless there are hundreds of results. Keep in mind that the main point of this (verification of reference interval) experiment is not the shape of the curve, but the percent of the results that are within the specified reference interval.



One thing to check when reviewing the histogram is whether the histogram is more or less centered in the proposed reference interval. If the distribution of the points is only to one side of the proposed reference interval, then you need additional checking on whether the proposed reference interval is satisfactory. It is entirely possible that it might be too large.

Finally, the Experimental Results may be ordered either by Specimen ID or by the Magnitude of the Result. Excluded points are italicized and either gray (black and white printers) or red (color printers). The first 50 or so results will appear on the first page. Subsequent results will be printed on later pages.

Establishing a Reference Interval

While you are allowed by the software to establish a non-parametric reference interval using this module, *we strongly recommend that instead you use the Establish Reference Module to establish reference intervals*. The ERI module will calculate reference intervals more reliably over a much broader range of conditions than the VRI module.

There is substantial uncertainty in the calculated limits of the central 95% range. If the number of specimens are 20, 60, 120 and 250, the 95% confidence interval of the limits of the reference interval in one simulated study was about 20%, 15%, 10% and 8% of the overall range of the reference interval.

A minimum of 40 results must be entered before a reference interval can be calculated. Keep in mind that if only 40 results have been entered, *the low and high results in the sample define the reference interval*.

Verification of Reference Interval Report

EP Evaluator®

User's Manual -- Data Innovations

GLUCOSE

Instrument: ASSAYER

Verification of Reference Interval

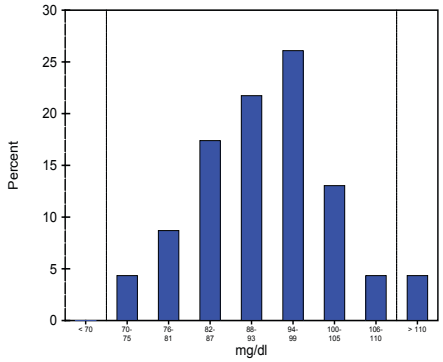
Analyst: Larry Doe
Specimen Criteria:

Date: 01 Jun 2000

Reference Interval	
Proposed	70 to 110 mg/dl
Results (total/excluded)	23 / 0
Max/Obs outside	10.0% / 4.3%
Passes	Yes

Statistical Analysis	
Mean	92.8 mg/dl
SD	9.8
Median	93
Range	75 to 115
Central 95% Interval	--
Central 95% Index	--

Reference Interval Histogram



Results Distribution

Interval	Percent	Count
< 70	0	0
70-75	4	1
76-81	9	2
82-87	17	4
88-93	22	5
94-99	26	6
100-105	13	3
106-110	4	1
> 110	4	1

Experimental Results

Spec ID	*Result*	*Spec ID*	*Result*	*Spec ID*	*Result*	*Spec ID*	*Result*	*Spec ID*	*Result*
SPEC0002	75	SPEC0022	86	SPEC0017	92	SPEC0015	95	SPEC0008	105
SPEC0013	77	SPEC0016	87	SPEC0011	93	SPEC0019	97	SPEC0009	110
SPEC0014	79	SPEC0023	88	SPEC0012	94	SPEC0021	97	SPEC0010	115
SPEC0004	85	SPEC0005	90	SPEC0018	95	SPEC0007	100		
SPEC0001	85	SPEC0003	92	SPEC0006	95	SPEC0020	102		

"X" = Excluded Results

Accepted by: _____ _____
Signature Date

Chapter

20

Establishing Reference Intervals

Reference intervals are one of the most important concepts in the clinical laboratory as all the laboratory results are judged in comparison with these values. For example, if you report a result of 23 mmol/L for "serum broccoli," that result is meaningless unless you have something to compare it to.

All laboratories use reference intervals. Manufacturers are required to provide reference intervals in their package inserts for their instruments. Manufacturers have different policies for establishing normal ranges for their instruments. Some actually establish the ranges, often based on a population of their workers, i.e. white and middle-class in a climate-controlled setting. Others get the values from the literature. Regardless of how they do it, they are providing reference intervals. Manufacturer-provided intervals are clearly unsatisfactory in some situations such as pediatric and veterinary populations, or different human populations such as working class in a tropical or desert environment.

It is the responsibility of each laboratory to make sure their intervals are satisfactory for their patient population. While many laboratories simply verify the reference intervals, others establish them on a regular basis. The latter recognize that not all methods get the same results on the same patient population.
The ERI statistical module allows the user to establish one type of reference interval – the normal range – accurately and reliably, if enough adequate results are provided.

The primary purpose of this chapter is to describe the user interface and the software for calculating reference intervals. For an extensive discussion on reference intervals including normal ranges, please see Rhoads (2012) *Lab Statistics* manual.

Definitions

Normal range: The central 95% range of results from a healthy patient population. It is important to remember that 2.5% ((100%-95%)/2) of the population results are above the upper limit of the normal range and a similar percentage are below the lower limit.

Reference Interval: A pair of medical decision points (Reference Limits) which frame the limits of results expected for a given condition. All normal ranges are reference intervals. Not all reference intervals are normal ranges. In this chapter the term reference interval refers to a normal range.

Confidence Interval (CI): It is not possible to measure the total population. We can only estimate the normal range based on a representative sample, and this estimate is subject to statistical sampling error. A confidence interval for a reference limit is a measure of sampling error. The primary factor affecting the CI width is the sample size. In fact, for a parametric reference interval estimate, the ratio of the CI width to the reference interval width does not depend on the experimental results at all. It is dependent on the sample size. For N=100 the 90% CI for each reference limit is about 15% of the reference range. For N=1000, the ratio is about 5%.

Partitioning Analysis: Suppose you have collected analyte results for a group of healthy men and women. Should you estimate a single normal range applicable to both men and women, or should you estimate separate ranges? Even if separate intervals would be clinically useful, there may be a trade-off between one's desire to have separate ranges and one's ability to acquire enough results to measure a statistically significant difference between the two groups. CLSI: C28 uses the term Partitioning of Reference Values for this decision process.

Experimental Design

In very simplistic terms, the steps required to establish a normal range are as follows:

- Collect a set of results from suitable, healthy patients.
- Enter results and calculate results. Summaries of the calculation methods are:
  Nonparametric method: Arrange the results in ascending order, and discard the highest 2.5% and the lowest 2.5%. The range of what's left – the central 95% – is an estimate of the normal range.
  Parametric method: Compute the mean and SD. Mean ± 2 SD is an estimate of the normal range. The parametric calculations may be calculated either on the original or transformed results depending on their distribution.

These steps always give a normal range estimate. But, if the patients are not both suitable and healthy, or if the sample is too small, the estimate may not be a good one. Perhaps the most significant issues of experimental design are: How many specimens do I need? And how do I obtain an adequate number of patients that are both HEATHY and SUITABLE! These issues are discussed in more detail in Rhoads (2012) *Lab Statistics* manual.

Data Requirements

There are several issues here:

- Minimum number:
  - At least 3 results are required to calculate a parametric mean and SD.
  - At least 40 results are required to calculate non-parametric statistics.

  - If there are less than 40 results present and/or less than 4 distinct (i.e. different) values, the report will be labeled PRELIMINARY.
  - Unless there are special extenuating circumstances such as great difficulty in obtaining specimens such as might be encountered with a veterinary practice working on rare animals, an experiment which uses less than 25 results is irresponsible.
- Recommended number:
  - CLSI:C28 recommends a minimum of 120 results. More are advisable under most circumstances.
- Maximum number: No software limits. We have used more than 100,000 results. We find that using more than 5,000 does not add much to the quality of the statistics.
  Calculations on large data sets are more feasible in the ERI/ROC module than in other EE modules. Analysis of 50,000 specimens usually takes a minute or less. Factors affecting performance on large data sets include:
  - Operating system and speed of the computer
  - Amount of memory (the more the better).
  - Network vs. local machine. Running large data sets over a network is significantly slower.
  - Number of columns in the data set (performance deteriorates significantly with 50+ columns).

Program Features

Some of the tasks that you can do are:

- "Plain vanilla" - type in a set of results for a one or more analytes to produce a normal range report from that set of results.
- If your database contains multiple columns of analyte results, you can get normal range reports for all the analytes with a single request.
- If your database contains patient attributes, you can perform a Partitioning Analysis. For example, partitioning by gender would give three normal range reports – for males, females, and both combined – plus a comparative report showing the statistical difference in the distributions of males and females.
- Create multiple ranges for numeric attributes such as age (i.e. infants, babies, youths, etc.).
- Use a filter to estimate a normal range for white males over 40 (if race, gender, and age attributes are in your database).
- There is a subtle difference between a partition and a filter. A partition produces a separate report for each level of the partitioning attribute – a report for males and a report for females. You can only partition on one variable at a time. You can partition by either gender or race, but not by both at once.
- With a filter, you produce a single report for all VISIBLE specimens in the database. The filter controls what specimens are visible. First you set up a filter that says "show only white males over 40" then you run a "plain vanilla" reference interval report.

Partitioning Process

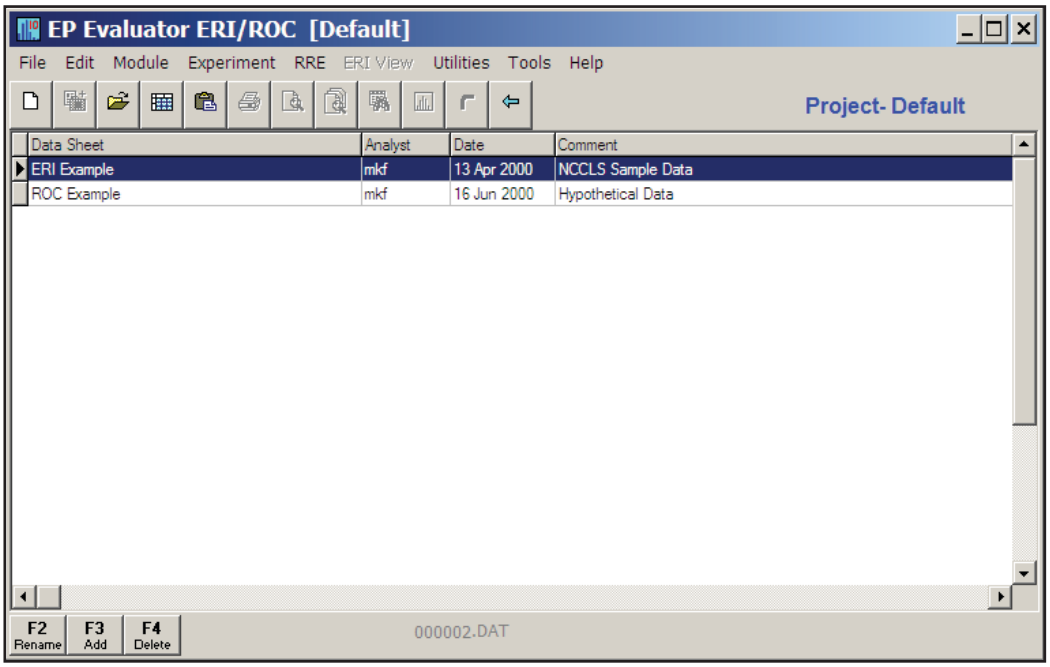
Partitioning divides the specimens into groups based on a particular attribute such as gender, race, age group or diagnosis, providing the attribute has been defined. When the report is printed, you may at that stage select which partitions to check during the analytical process.

When data are captured from a spreadsheet, the partitions are automatically established from various categories of data. If you want to create additional partitions for age ranges or the like, you must restructure the database as shown below.

If data is entered manually, then the partitions must be created using the Restructure Database Screen.

Module Overview Screen

This is the ERI/ROC version of the "Module Overview Screen." It looks a little different from the other modules because ERI and ROC operate a bit differently. Data is not organized into individual experiments for specific instruments and analytes. Instead, it is organized into Data Sheets—rather like workbook pages in Excel. A data sheet usually contains results for several analytes. It may also contain patient demographics, like gender, age, and diagnosis. The Module Overview Screen is a list of available data sheets.



What you can do from this screen

Open a data sheet to edit the data or perform calculations

- Double-click it, or highlight it in the grid and then press the Enter key.
- Go back to the main EE screen.
- Click the blue back arrow button on the tool bar, or press the Escape key.

Rename a data sheet

- Highlight a sheet in the grid and Click the F2: Rename button at the bottom of the screen, or press the F2 function key. You will get a form where you can change the data sheet name, analyst name, experiment date, or comment.

Delete a data sheet

- Highlight it and click F4: Delete, or press the F4 function key.

Add a data sheet

This assumes you want to type in all the numbers from the keyboard, which you usually don't. Often you want to import them from Excel or a CSV file. If you do want to type them in, click F3: Add, or press the F3 function key.

Import a data sheet

There are two ways to do this—cut/paste through the clipboard or import from a CSV file.
Before you Add or Import a data sheet, you must structure it so the program can tell which columns contain test results and which ones contain demographics. See next section on how to create a data sheet.

Creating a data sheet

There are three ways you can bring data into an ERI/ROC Data Sheet:

- Create it in Excel and transfer it through the clipboard.
- Create it in Excel, save it to a CSV file, and import the CSV file. Or, closely related, create a CSV file by another means—perhaps directly from your LIS—and import that.
- Type it into EE.

Regardless of the means chosen, you must code the data so EE can tell which columns contain test results and which ones contain demographics.

Data Sheet Structure

A Data Sheet is a grid of rows and columns. A row represents a patient. A column represents either a test result or a demographic (like diagnosis, age, race, or sex).

	A	B	C	D	E
1	**SpecID**	**L:Diagnosis**	**N:Age**	**D:State**	**Glucose**
2	Jon Doe	Pos	42	Icteric	143
3	Mary Roe	Neg	27		86

You must tell the program what type of data is in each column. The types are:

Type	Description
A	Numeric Test Results. ('A' stands for Analyte)
N	Numeric demographics, like age or weight. ('N' for Numeric)
L	Coded demographics, like Diagnosis, Sex or Race. ('L' for List)
D	A very short descriptive comment, with a maximum of 10 characters. ('D' for Description) The program won't use comments in calculations, but you can sort on them.
C	A list demographic computed from a numeric demographic. ('C' for Computed.) For example, age groups Child, Teenager, Adult computed from Age.

Pasting from Excel

There are two major elements to the pasting process, defining the column headers (the first row) and then pasting the spreadsheet contents into EE.

- The columns are coded to indicate what type of data they contain. The first row defines the use of each column by use of headers.
  - **Column header**: "SpecID". The first column contains the specimen ID. This is the primary sort order for the data sheet. If present, they must be unique. However they are not required. The program numbers the specimens automatically if these are not provided. The automatically generated specimen IDs will start with "S00001" and then be incremented to "S0002" and so on.
  - **Blank column header**: This column will be skipped.
  - **Blank column header identifier**: This column will be assumed to contain test results if it contains numbers. Example "Sodium".
  - **Test result column header identifier**: "A:". The column contains a test result. Example: "A:Sodium". This identifier is not required and will be assumed for all columns with numbers if not identified as a demographic.
  - **Demographic column header identifier**: "N:" (numeric - "N:Age")," L:" (list - "L:Gender" or "L:Diagnosis"), or "D:" (demographic). An identifier is required for the demographic columns if ERI data is to be partitioned by age, gender or ethnicity.

ROCNote: In order to calculate an ROC curve, you must have at least one Type L demographic to represent the true diagnosis: Positive or Negative. The column header must be something like "L:Diagnosis". Just "Diagnosis" will not work.

- Highlight the data cells in Excel and select Edit/Copy from the Excel Menu. Switch to EE, go to the ERI/ROC Module Overview Screen, and select Edit/Paste from the EE menu.
  The program will read the file and then take you to the Data Definition Screen. There you can confirm that the column types were read correctly and define computed demographics.
  Note: If your file is very large, it may be too big to transfer through the clipboard. Excel will warn you if there is not enough memory to copy to the clipboard. In that case, save the file as a CSV file and use the CSV import procedure below.

Importing a CSV File

- The first step is exactly the same as if you were transferring through the clipboard. Prepare your file with column headings, coded to indicate what type of data the column contains.
- From the Excel Menu, choose File/Save As, and enter a name for the output file. Set the Save as type combo box at the bottom of the file save dialog to CSV (Comma delimited).
- Close Excel. When Excel saves a file, it does not allow other programs to use it.
- Switch to EE and go to the ERI/ROC Module Overview Screen. Select File/Import from the EE Menu. When asked for the file name, select the file you saved in step 2.

  EE will read the file, then take you to the Data Definition Screen (see below), where you can confirm that the column types were read correctly, and define computed demographics.

Typing the data into EE

- Go to the ERI/ROC Module Overview Screen. Select Experiment/New from the menu. This takes you to the Data Definition Screen, where you define a data type for each column.

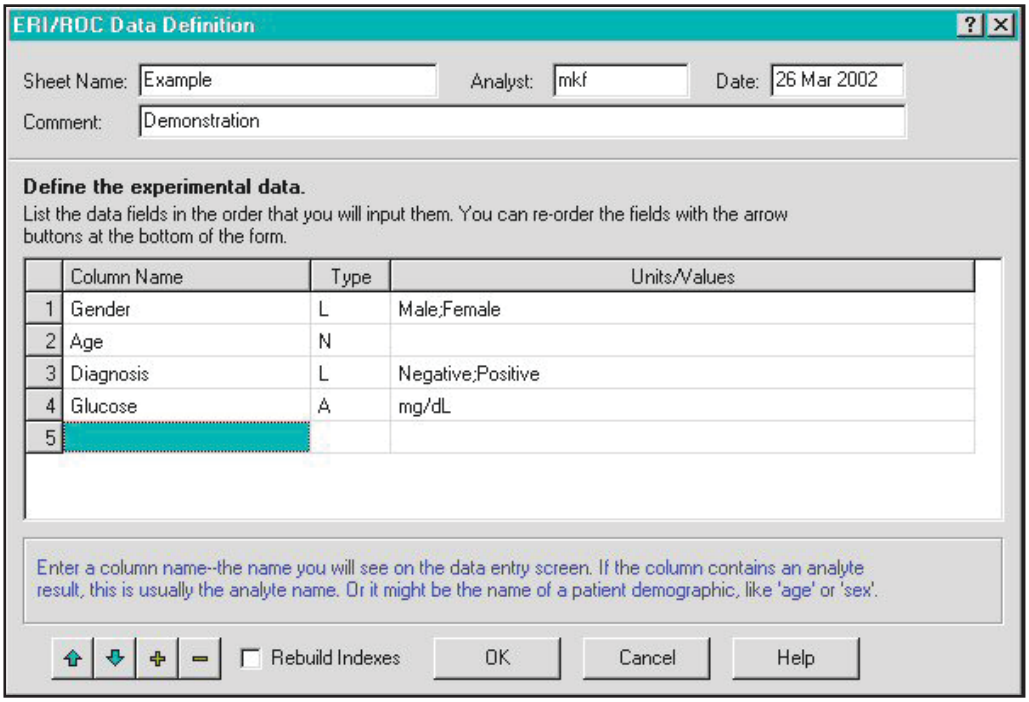
  When you complete and accept the Data Definition, you have a blank grid where you can enter the data.

Data Definition Screen

The program shows the screen seen below when you create a new data sheet, restructure an existing one, or import a file. In the latter two cases, the form is pre-filled with structure information for the existing file.

Experiment Description: The Sheet Name, Analyst, Date, and Comment fields at the top of the form contain descriptive information for the Module Overview. These fields appear only when you create a new experiment or import a file.

Variables (Test Results and Demographics): Enter a line in the grid for each variable (column) in your data sheet. The program will list variables in the data entry form in the order that you define them here. Use the Up/Down buttons at the bottom of the screen to re-arrange the variables in the order you prefer. Also, the – button deletes a variable, and the + button inserts a blank row where you can define a new variable.



Column Name specifies the name of the variable. Each variable must have a unique name.

Type specifies the variable type (A:test result, L:list demographic, etc.). When the cursor is in this column, press the spacebar or click the left mouse button to show a pick list of valid types.

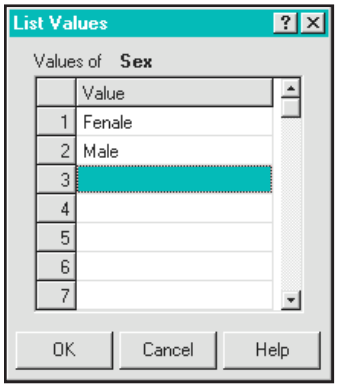
Units/Values specifies the variable type. It will show units or the elements of the list for List and Calculated variables. When you place the cursor on this column, the hint window at the bottom of the screen explains what input the program expects:

- **Test Result**: Units/Values column contains the units (optional). The program remembers the last 16 values entered. Press the F8 key for a pick list.
- **Numeric demographic or common**: Blank.
- **List or Computed demographic**: The Units/Values column contains the list of possible values. Click on the cell for a separate screen to edit them ("Defining 'List' Demographic Values" and "Defining Computed Demographic Values" below).

Rebuild Indexes: Most of the time you will leave this box unchecked. If you notice that the data is not sorting correctly, you may need to request ERI View/Restructure from the menu bar, check the Rebuild Indexes box, and click OK to rebuild the file.

Defining 'List' Demographic Values

Only for manually entered data

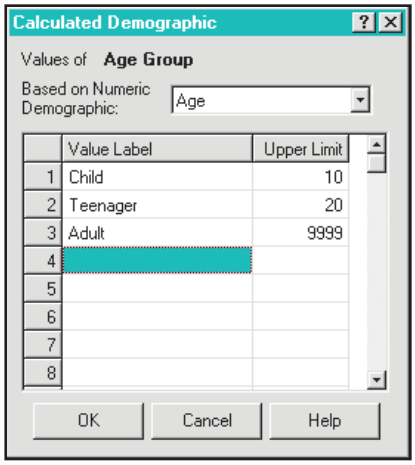


- Enter the values, one value per row.
  - If you are creating a new data sheet, you may enter the values in any order. They will appear in reports in the order in which you define them.
  - If you are restructuring an existing sheet or importing a file, you may change the spelling, but DO NOT CHANGE THE ORDER. For example, if you put Male on the first line and Female on the second line in the example here, you would change all the males to females and vice versa.
- Click **OK** to apply your changes or **Cancel** to close the form without changing anything.

NOTE: This process only needs to be done when the data is entered manually. When the source of your data is a spreadsheet, the various demographic values are read from the actual names

Defining Computed Demographic Values

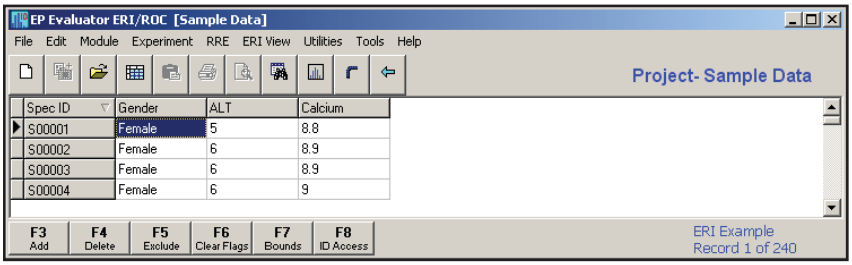
ROC and Reference Interval procedures work only with List demographics that have a discrete number of values—like Gender (Male/Female) or Ethnicity (Black, Caucasian, Hispanic). In order to analyze a continuous demographic like age, you must define bins that convert it to discrete ranges. There is no programmatic limit on the number of bins. However, some analyses may be meaningless if the bins are too narrow.



- First, select the numeric demographic that the bins are based on (e.g., Age). If the pull-down list of choices is empty, your data sheet has no numeric demographics, and you can't define a computed demographic.
- Enter a descriptive Value Label for each bin (Child, Teenager, Adult).
- Enter the Upper Limit value of each bin. You must define the bins in increasing value order, and the upper limit for the last bin must be a large number. In the example above, subjects with Age 10 or under would be classified 'Child'. Subjects between 11 and 20 would be 'Teenager', and those older than 20 would be 'Adult'.
- Click **OK** to apply your changes, or **Cancel** to close the form without changing anything.

Experiment Detail Screen (Data Sheet)

This screen is the ERI/ROC version of the Experiment Detail Screen. It shows only experimental results, with no statistical analysis. You can change a value in the grid by highlighting the cell and typing over the number.



Edit Buttons

Buttons at the bottom of the screen function as in the other statistical modules:

- **F3: Add:** Click the button (or press the F3 function key) to add a blank line at the end of the grid.
- **F4: Delete**: Permanently deletes the highlighted specimen.
- **F5: Exclude:** Excludes the value the cursor is on (or, if the value is already excluded, removes the exclusion flag). An excluded value remains in the file, but is not used in any calculations. The exclude function works only when the highlighted cell is an analyte result or the Spec ID. You cannot exclude an attribute (like age or gender). When you exclude the Spec ID you are, in effect, excluding ALL ANALYTES for that specimen. Excluded cells have an 'x' mark to the right of the number.
- **F6: Clear Flags**: Clears the exclusion flags for everything in the data set— all analytes and all specimens—even if some of the specimens or analytes have been filtered out of the display.
- **F7: Bounds**: This function works only when the cursor is on an Analyte column. It brings up the Bounds dialog, where you can change the analytes's bounds, or clear bounds for all analytes in the file. Results below the lower bound or above the upper bound are totally ignored during statistical analysis. They do not appear in the Results Listing, nor are they counted in the total N.
- **F8: ID Access**: Click this button (or press the F8 function key) to toggle whether the Spec ID is editable. When the Spec ID is editable, it appears in two separate columns—a non-editable gray column and an editable white column. The gray column is there only to make sure the Spec ID never scrolls out of view. When you change the white column, the gray column changes also.

Suggested Spec IDs

When you enter a new specimen, the program makes a guess at what Spec ID it should have. The guess is one higher than the last ID you entered. When you enter results with Spec ID access off, the program automatically creates all Spec IDs. This may occasionally cause a Duplicate Spec ID error. To correct the problem, press F8 to enable ID access and change the ID to a unique value.

Sorting

You can sort the grid on any column by clicking its column header (or request **ERI View/Sort By** from the menu bar). Test results and numeric demographics sort in numeric order – with invalid or missing values at the top. List demographics sort in the order in which you defined the value list. Spec ID and comments sort alphabetically.

CAUTION: When entering new data, you usually want the data sorted by Spec ID. For example, suppose you have the grid sorted by Glucose. Every time you enter a new record, it moves to the correct sort position on Glucose. You then have to scroll to the bottom again to add another record. This does not happen when the data is sorted by Spec ID, even when you are entering your own Spec IDs.

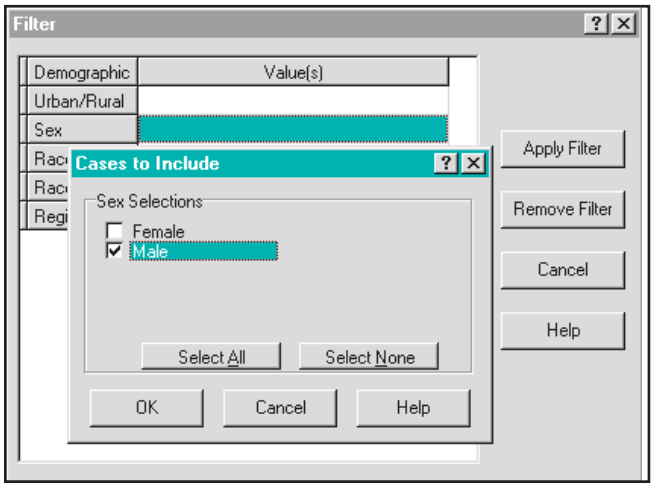
Hiding columns

Suppose your data set contains 50 columns, but you only want to edit the Glucose and ALT columns. **ERI View/Hide Columns** lets you temporarily remove the other 48 columns from the display.

- Check the variables you want to show in the data grid. Select **All** checks all variables. Select **None** unselects all variables.
- Click **OK** to apply your changes, or **Cancel** to close the selection form without changing anything.

Filtering

The **ERI View/Filter Specimens** function determines what specimens are displayed in the editor. It also controls what enters into the calculations. When a filter is in effect, the word FILTERED appears in large red letters at the bottom of the screen to remind you that any reports you run will not use the full data set.



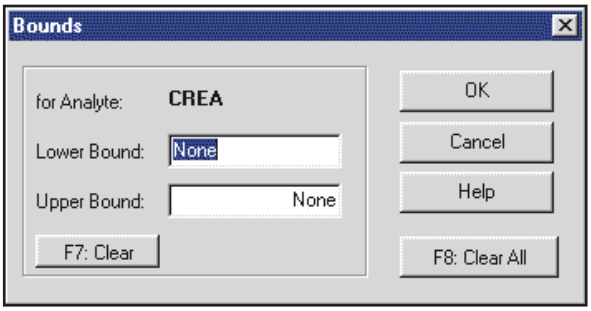
To apply a filter: Select View/Filter Specimens from the menu bar. The program will show the List and Computed demographics and their current filter conditions.

To change a filter condition: Click in the Value column. The program shows a second dialog, where you check the specimens to include. The example shown selects only males for analysis.

After defining your filter conditions, click **Apply Filter** to apply them (or click Cancel to close the form without changing anything).

To remove a filter: Select **ERI View/Filter Specimens** from the menu bar. Click Remove Filter in the filter dialog.

Setting Bounds



Bounds provide an alternative way of excluding extremely high (or low) results without marking them one at a time. Values above the upper bound and below the lower bound are considered to be Outliers. These values are marked by a small 'o' to the right of the number. In the explore screen, you set bounds by dragging a bounding line on a graph. To set or clear bounds from the data entry grid, press the **F7** key to show the dialog illustrated above.

To set the bounds for a single analyte: Enter the lower and upper bound numbers and click OK. A blank value for a bound is equivalent to None.

To remove bounds for a single analyte: Click **F7**: **Clear**.

To remove bounds for all analytes: Click **F8: Clear All.**

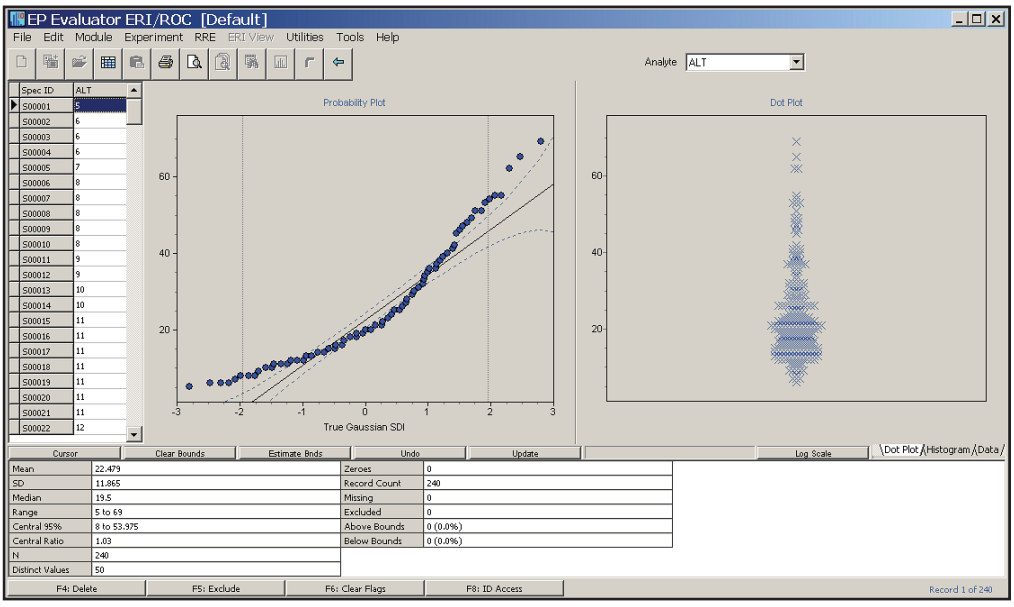
To close the form without changing anything: Click **Cancel**.

Exploring Reference Interval Experiments

Tasks which can be done during the exploration process include:

- Previewing the data
- Editing the data by excluding results
- Edit the data by cutting off results at either or both ends.

The screen to explore Reference Interval results is accessible by clicking on ERI View, Explore.



The six major components on this screen are:

- Listing of results for the specified analyte.
- The probability plot.
- The figure in the window on the right of the screen. The user has control over the content of this window. Choices for content are controlled by the tabs in the lower right portion of the screen. They include a histogram, a dot plot and the listing of results for the currently selected specimen.
- Statistics table (at the bottom of the screen).
- Cutoff control buttons (just above the statistics table).
- Control buttons at the bottom of the screen (see Chapter 3, *Common Operations* for their use).

Statistics Table

This table contains several items which may need definition:

Central Ratio: The central 95% interval divided by the 4 SD range. The value expected is 1.0 if the data have a Gaussian distribution. Just because the value is 1.0 does not mean that the distribution is Gaussian.

Distinct Values: The number of unique values of results. For example, there might be 904 total results, but the number of different results (i.e. 53 vs. 54 vs. 75) is only 46. In other words, it counts the 14 specimens which have the same result of 55 as one unique value.

Zeroes: The number of zero results. For many analytes, a zero result is impossible. In this circumstance those values should be excluded.

Above/Below bounds: The number of results above (or below) a cutoff value.

Cutoff Control Buttons

These buttons just above the table of statistics are used to define the cutoff point(s) for the results.

Cursor: Clicking on this button allows you to establish upper and lower cutoffs for the data. A line appears on the screen just below and above the lowest and highest points respectively. You may move these points up and down to exclude data from the calculation. See discussion on Cutoff lines below.

Clear bounds: Restores the system so that all points cutoff by use of the cursor may now be included in the calculation.

Estimate Bnds: Sets the bounds using a very conservative filter, namely it excludes all results more than 9 robust SD's from the mean.

Undo: Reverses an action with the Cursor.

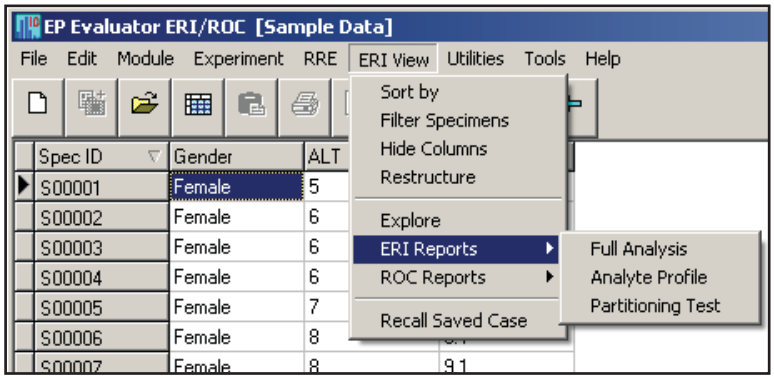
Update: Performs calculations on the data, updates the statistics table and replots the graphs.

Cutoff lines

The behavior of the cutoff lines can be a little confusing until one understands what is going on. The initial position of the low-end cutoff line will be at the value of the lowest point visible on the probability plot. After you move the line and release it, it will move so it has the value of the first result above the release point. All those results below the cutoff line will be excluded from the calculation. Each such result will be marked with an "o". The upper cutoff line operates in similar fashion except that all results above it are excluded.

Generating Reports

When you command EE to generate a report, a menu drops down which provides you the opportunity to select one of three options:

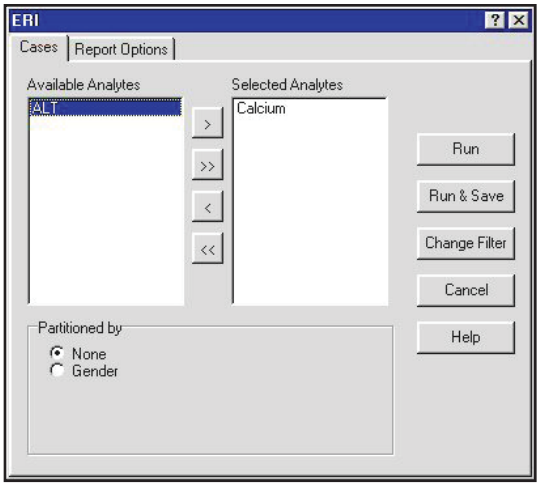


Full Analysis generates the standard report giving the 95% confidence intervals by the various methods and includes the calculated reference intervals as well as an optional results listing. The report pages generated by this selection include the Summary Page, the Statistics Page, and the Results Listing.

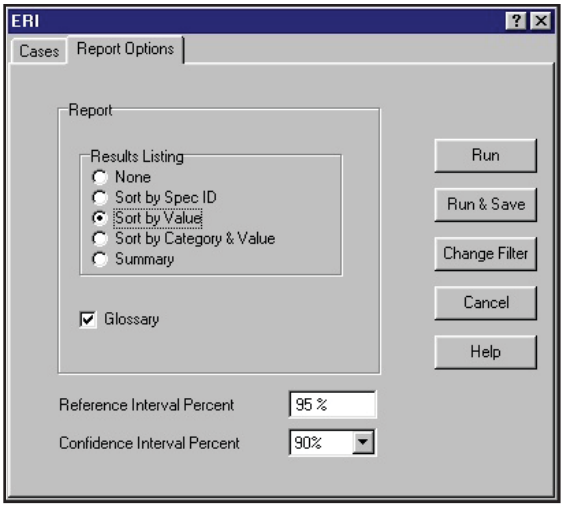
Analyte Profile performs an analysis of the data. It calculates basic statistics such as counting numbers of points of various types, and calculation of basic statistics such as N, mean, median and central 95% interval on each selected set of data. It is designed to give the investigator a quick overview of their results. The report page generated by this selection is entitled Analyte Profile.

Partitioning Test evaluates the data for whether it should be partitioned into the various categories such a gender or ethnic group. The report page generated by this selection is entitled Partitioning Test.

After selecting a type of report to generate, the Cases to Analyze screen appears. This screen allows you to define two things: (1) the analytes for which the analysis is to be done; and (2) what partitioning (if any) is to be done. To move an analyte from the left panel to the right panel, highlight the analyte in the left panel, then click on the right arrow button. Click on the double right arrow to move all analytes from the left panel to the right panel. To deselect analytes, use parallel operations but with the left arrows instead.



The Report Options Tab, available only for the Full Report, defines which type of results listing is to be generated, whether a glossary is to be included in the report, the percent of the reference interval to be used, and the confidence interval percent to be selected (choices: 90 and 95%). For interpretation of the Establish Reference Interval report shown below, please see Rhoads (2012) *Lab Statistics* manual.



Establish Reference Interval Report (Summary)

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Reference Interval Summary

Central 95% Interval

	Meth	N	Lower Limit Value	Lower Limit 90% CI	Upper Limit Value	Upper Limit 90% CI	Confidence Ratio
HGB	NP	904	12.3	12.0 to 12.5	16.9	16.8 to 17.0	0.08
RBC	NP	904	3.90	3.82 to 3.96	5.51	5.46 to 5.56	0.07
WBC	NP	904	4.1	3.9 to 4.2	10.7	10.3 to 11.9	0.14

NP: Nonparametric P: Parametric TP: Transformed Parametric X: Confidence Ratio > 0.30
Confidence Limits for Nonparametric NCCLS C-28A method computed by exact formula.

Filter: None

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Establish Reference Interval Report (Statistics Page)

EP Evaluator — **HGB**

User's Manual

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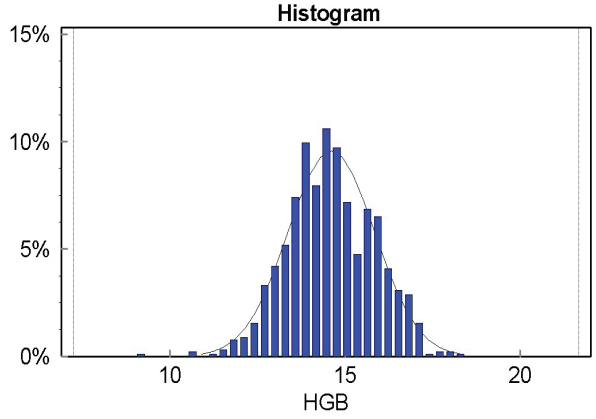
Reference Interval Estimation: Combined

Central 95% Interval
(N = 904)

	Lower		Upper		Confidence
	Value	*90% CI*	*Value*	*90% CI*	*Ratio*
Nonparametric (NCCLS C28-A)	**12.3**	**12.0 to 12.5**	**16.9**	**16.8 to 17.0**	**0.08**
Alternatives:					
Parametric	12.2	12.1 to 12.3	17.0	16.9 to 17.1	0.05
Transformed Parametric	--	--	--	--	--

Confidence Limits for Nonparametric NCCLS C-28A method computed by exact formula.

Histogram



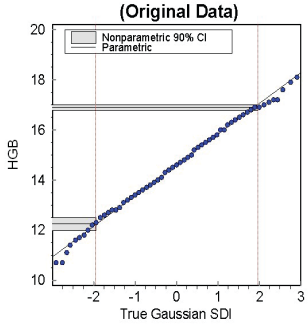
Selection Criteria:

Bounds	None
Filter	None

Statistics:

Mean	14.60
SD	1.22
Median	14.60
Range	9.1 to 18.3
N	904 of 904
Distinct values	67
Zeroes	0
Central 95% Index	22.6 to 882.4
Analyst	dgr
Expt. Date	07 May 2002

Probability Plot (Original Data)



Probability Plot (Transformed Data)

No transformation found that significantly improves fit to Gaussian distribution.

Normalizing Transformation

Exponent	--
Constant	--

Accepted by: _____ _____

Signature Date

Establish Reference Interval Report (Results Listing)

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HGB

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Results Listing

Spec ID	HGB	Spec ID	HGB	Spec ID	HGB
XX000122M	9.1	XX000447G	12.8	XX000130D	13.3
XX000762Y	10.7	XX000641W	12.8	XX000132T	13.3
XX000776L	10.7	XX000696T	12.8	XX000176B	13.3
XX000376N	11.1	XX000705G	12.8	XX000463O	13.3
XX000608Y	11.4	XX000795R	12.8	XX000504M	13.3
XX000257B	11.5	XX000835H	12.8	XX000572T	13.3
XX000615H	11.6	XX000091V	12.9	XX000575R	13.3
XX000326E	11.7	XX000224I	12.9	XX000703Q	13.3
XX000403Y	11.7	XX000352T	12.9	XX000839N	13.3
XX000230J	11.8	XX000399Z	12.9	XX000029K	13.4
XX000253V	11.8	XX000404G	12.9	XX000062I	13.4
XX000724M	11.8	XX000420O	12.9	XX000184S	13.4
XX000017N	11.9	XX000421W	12.9	XX000258J	13.4
XX000441K	11.9	XX000431D	12.9	XX000350D	13.4
XX000807C	12.0	XX000459D	12.9	XX000469K	13.4
XX000008O	12.1	XX000574J	12.9	XX000491T	13.4
XX000693V	12.1	XX000596N	12.9	XX000506C	13.4
XX000802O	12.1	XX000603K	12.9	XX000534H	13.4
XX000169S	12.2	XX000674P	12.9	XX000542Y	13.4
XX000243O	12.2	XX000695L	12.9	XX000552F	13.4
XX000382O	12.2	XX000711H	12.9	XX000598D	13.4
XX000774V	12.2	XX000731V	12.9	XX000602C	13.4
XX000215J	12.3	XX000005Q	13.0	XX000605A	13.4
XX000317F	12.3	XX000292P	13.0	XX000626W	13.4
XX000545W	12.3	XX000364Q	13.0	XX000747Y	13.4
XX000866K	12.3	XX000411P	13.0	XX000808K	13.4
XX000172V	12.4	XX000533Z	13.0	XX000811N	13.4
XX000282I	12.4	XX000778B	13.0	XX000815T	13.4
XX000714F	12.4	XX000831B	13.0	XX000832J	13.4
XX000013H	12.5	XX000840A	13.0	XX000833R	13.4
XX000040E	12.5	XX000080G	13.1	XX000883A	13.4
XX000041M	12.5	XX000150R	13.1	XX000068E	13.5
XX000449W	12.5	XX000179Z	13.1	XX000251F	13.5
XX000649I	12.5	XX000186I	13.1	XX000336L	13.5
XX000736J	12.5	XX000198F	13.1	XX000406W	13.5
XX000753Z	12.5	XX000199N	13.1	XX000423M	13.5
XX000010J	12.6	XX000219P	13.1	XX000432L	13.5
XX000106E	12.6	XX000245E	13.1	XX000453H	13.5
XX000281A	12.6	XX000302K	13.1	XX000490L	13.5
XX000625O	12.6	XX000559J	13.1	XX000530B	13.5
XX000713X	12.6	XX000668O	13.1	XX000544O	13.5
XX000775D	12.6	XX000678V	13.1	XX000549C	13.5
XX000061A	12.7	XX000716V	13.1	XX000550P	13.5
XX000175T	12.7	XX000822C	13.1	XX000595F	13.5
XX000266A	12.7	XX000069M	13.2	XX000634N	13.5
XX000379L	12.7	XX000115D	13.2	XX000638T	13.5
XX000446Y	12.7	XX000216R	13.2	XX000698J	13.5
XX000497P	12.7	XX000268Q	13.2	XX000742K	13.5
XX000613R	12.7	XX000288E	13.2	XX000772F	13.5
XX000656R	12.7	XX000370R	13.2	XX000792T	13.5
XX000844G	12.7	XX000401I	13.2	XX000801G	13.5
XX000022G	12.8	XX000511V	13.2	XX000812V	13.5
XX000049Y	12.8	XX000576Z	13.2	XX000857L	13.5
XX000085U	12.8	XX000612J	13.2	XX000012Z	13.6
XX000119J	12.8	XX000623Y	13.2	XX000072P	13.6
XX000151Z	12.8	XX000627E	13.2	XX000109C	13.6
XX000185A	12.8	XX000743S	13.2	XX000123U	13.6
XX000247U	12.8	XX000848M	13.2	XX000301C	13.6
XX000290Z	12.8	XX000889W	13.2	XX000328U	13.6
XX000325W	12.8	XX000067W	13.3	XX000338B	13.6

Values marked with an "X" were excluded from the calculations.

Establish Reference Interval Report (Analyte Profile)

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Analyte Profile

Analyte	Units	N	Missing or Excl	Zero	Mean	Median	SD	Central 95%		Min	Max	Width Ratio
WBC		904	0	0	6.7	6.4	1.8	4.1	10.7	2.6	19.6	1.1
RBC		904	0	0	4.7	4.7	0.4	3.9	5.5	2.92	6.12	1.0
HGB		904	0	0	14.6	14.6	1.2	12.3	16.9	9.1	18.3	1.1

TOTAL RECORDS 904

The "width ratio" is 4 x SD / Central 95% interval. It should be in the vicinity of 1.0. "X" indicates a width ratio > 2.

Filter: None

Establish Reference Interval Report (Partitioning Analysis)

EP Evaluator®

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Partitioning Test: SEX

Analyte	Units	N	Mean	SD	Central 95%		Diff from Overall	Max Z	Crit Z	SD Ratio	
HGB		*904*	*14.6*	*1.2*	*12.3*	*16.9*		*18.4*	*5.8*	*1.2*	*x*
M		376	15.4	1.1	12.8	17.2	0.09				
F		526	14.1	1.0	12.1	16.0	0.11				

"X" items may warrant separate reference intervals. Either Z max > critical Z or SD Ratio > 1.5. Partitions with N<10 are not included.

Filter: None

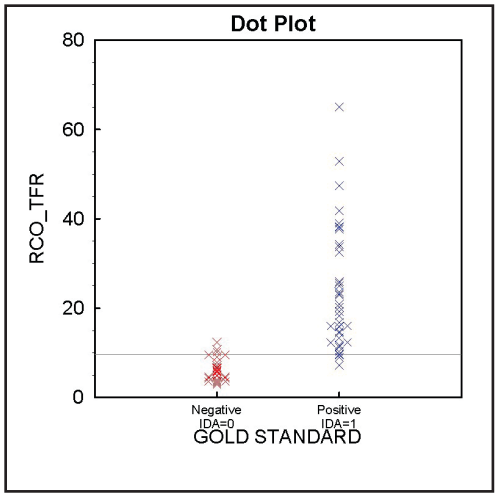
Chapter

21

ROC Curve Analysis

There are two major types of medical decision points. The most familiar one is associated with normal ranges, namely that range of results which is associated with good health. The less familiar one is used as a cutoff value in which all results greater than (or in some cases less than) a value is associated with a specified diagnosis. For example, one of the cutoff values for glucose is 126 mg/dL. If one's repeated fasting blood glucose is greater than this value, the American Diabetic Association has found that the patient has diabetes.

Two statistical modules (ROC Curve Analysis and Establishing Reference Intervals) share the same database and some of the same user interface.



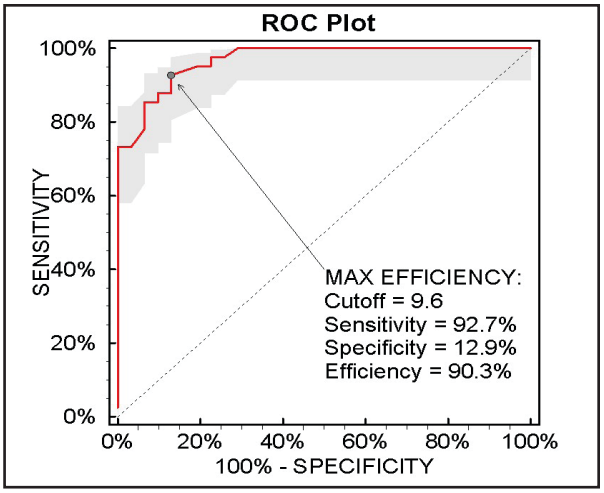
ROC Curve Analysis needs a minimum of two items of information on each specimen: (1) a numerical result; and (2) a gold standard diagnosis. Given this information, it can calculate the probability that a patient with a given result will have that condition.

The dot plot presents the data in a very clear way as shown here. Note that the left and right columns of points consist of results from patients without and with the specified condition respectively.

We have drawn two lines on the graph.

- Line A is set at the top of the left bar. If a patient's result is greater than that value, then they have the condition. In other words, the condition is **ruled in**.
- Line B is set at the bottom of the right bar. If a patient's result is less than that value, then the patient does NOT have that condition. In other words, the condition is **ruled out**.

The region between the two lines is that region of results for which a patient could be either positive or negative. In this region, the ROC plot itself is used to establish probabilities that a given result corresponds to a certain probability that the patient has a condition or not. In this example, the dot corresponds to the point of maximum efficiency when most results (77.8% of the total) are correct.



Purpose of ROC Curve Analysis

To define cutoff points so that a condition can be ruled in or ruled out. For example, a repeatable fasting blood glucose greater than 126 mg/dL is presumptive evidence for the presence of diabetes. (American Diabetic Association). In this case, diabetes is ruled in.

- To associate a probability that a condition exists with a certain magnitude of results.
- For example, in one study in which the level of cholesterol was evaluated as an indicator of coronary artery disease (CAD), a cholesterol result greater than 200 mg/dL correlated with CAD 47.2% of the time in the population they studied (S. Levinson, unpublished results).
  In another study of iron deficient patients to differentiate between iron deficiency anemia (IDA) and anemia of chronic disease (ACD), a TIBC (total iron binding capacity) greater than 315 ug/dL was ruled in IDA. A TIBC less than 284 ug/dL ruled in ACD. (F. Wians, unpublished results)
- To compare the diagnostic efficiencies of multiple tests.

Definitions

Sensitivity is the probability that a test will be positive in a population in which everyone has the disease. The ideal sensitivity is 100%.

Specificity is the probability that a test will be negative in a population in which no one has the disease. The ideal specificity is 100%.

Efficiency measures the ability of the test to make the correct evaluation of the condition. The ideal efficiency is 100%.

AUC (Area under the Curve) is a calculation of the area under the ROC curve. This number varies between 0.5 (diagnostic efficiency no better than a coin flip) to 1.0 (perfect diagnostic efficiency). Clearly the ideal is 1.0.

Cutoff is the value at which the diagnosis changes between a negative and positive value. Note that a negative value is not always the lower number. For example, if the purpose of a test for iron is to detect iron deficiency anemia, then the positive diagnosis will be at values less than the cutoff and the negative diagnosis will be at values greater than the cutoff.

True Negative is the number of cases in which a negative result correctly corresponds to the absence of the condition.

True Positive is the number of cases in which a positive result correctly corresponds to the presence of the condition.

False Negative is the number of cases in which a negative result was observed for a patient in which the condition did exist. In hematology differential cell count testing, it is important that this number be minimized because you want to detect every case in which cancer exists.

False Positive is the number of cases in which a positive result was observed for a patient in which the condition did not exist. In drug testing, it is important that this number be minimized because persons found to be positive may experience legal problems.

Likelihood Ratios are ratios between probability of t test result when the disease is present and when it is absent:

Positive Likelihood ratio is the ratio of probability of a positive test when the disease is present to probability of a positive test when the disease is absent. The Positive Likelihood Ratio at a give cutoff point is the slope of the ROC curve at that point. Likelihood ratios can be used to combine the results of several independent tests into an overall post-test probability.

Negative Likelihood ratio is the ratio of probability of a negative test when the disease is present to probability of a negative test when the disease is absent.

The next two items include the prevalence of the disease in the calculation.

Predictive Value of a Positive is the percent of positive tests which accurately diagnose the presence of disease.

Predictive Value of a Negative is the percent of negative tests which accurately diagnose the absence of disease.

The Truth Table below illustrates the relationships of several of the fundamental concepts in ROC Analysis where the data are shown in the Truth Table and the calculations are shown in the Truth Table Example just below.

Truth Table (MCV cutoff = 80.9 fL)			
	Negative Test	**Positive Test**	**Total**
Negative Reference	27	7	34
Positive Reference	37	29	66
Total	64	36	100

Truth Table Example

Specificity = TN / (Total Negative References)
= TN / (TN + FP)
= 27 / (27 + 7) = **0.79**

Sensitivity = TP / (Total Positive References)
= TP / (TP + FN)
= 29 / (29 + 37) = **0.44**

Experimental Design

The experimental design for ROC analysis must be planned in advance. A primary requirement is an accurate diagnosis. Any uncertainty in the diagnoses will significantly degrade the quality of the statistical conclusions. Often users collaborate with clinicians in order to obtain accurate diagnoses.

As with the Reference Interval studies discussed in Chapter 20, *Establishing Reference Intervals*, the numbers of patients included in the study are important. Up to a limit, the more patients, the better the study. The minimum number recommended is 120. EE can handle a maximum of 2000 specimens.

Data Entry Process

Data is entered into the ROC module using the same processes described in detail in *Import a data sheet* in Chapter 20, Establishing Reference Interval.

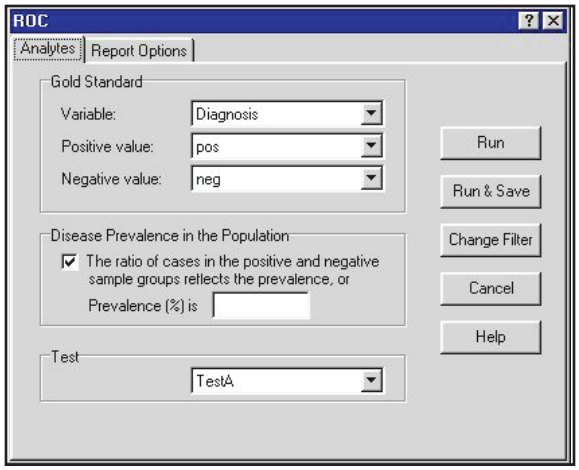
ROC Curve Analysis

The ROC Curve Analysis includes several elements: a ROC plot, a dot plot, a table of appropriate statistics, a list of results with sensitivity, specificity and efficiency at each point. If multiple tests are compared, then the statistics from the various tests are compared.
ROC Curve Analysis starts when you click on the ROC icon. At this point, you get a menu which allows you to select which type of calculation is to be done. Your choices are:

- **Single Test** (user display) analyzes the results for a single test.
- **Compare Two Tests** (user display) displays the results for two user-selected tests and provides for easy comparison between them.
- **Batch** (output to print preview or to print option) outputs a report analyzing a set of tests to the print preview facility.

Single Test Analysis

After selecting the Single Test Analysis option, a dialog box appears which allows you to specify the analytical process. Your options include:

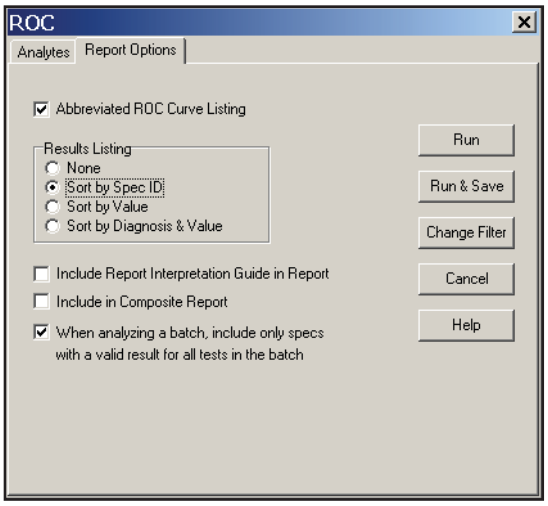


Gold Standard. Specification of the variable which defines whether the condition is present or not. The variable is selected along with which of its values constitutes a positive result and which constitutes a negative result.

Test. The test to be evaluated. In this example, it is "TestA."

Disease Prevalence in a relevant population is specified. This number is used to calculate the predictive value of a positive and negative test. If this value is left empty, then EE assumes that the prevalence in the sample is the same as that in the population.

A second tab "Report Options" is also available. This allows you to define various elements to appear on the reports. While this tab is included for all three options, it is applicable only for the Batch case in which a report is printed.



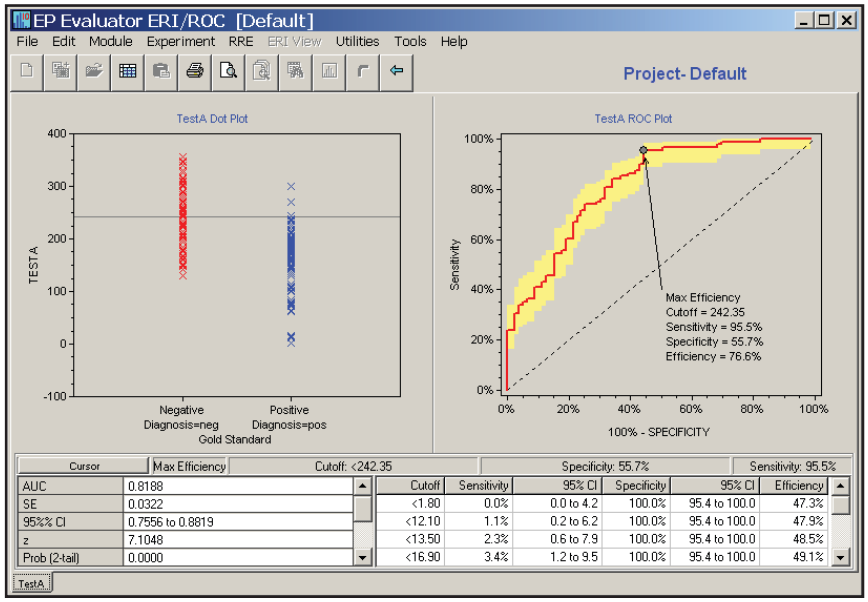
Abbreviated ROC Curve Listing controls the number of lines in the ROC Curve Listing. In most cases you want to check this box. When it is unchecked, every level of the test generates a cutoff point report line, When it is checked, only the important points are listed. If you look carefully at the plot, you will see that it moves in stair steps, vertical lines rep-resenting a range of sensitivities for the same specificity. The "important" point that shows up in the abbreviated ROC listing is the corner point, or highest sensitivity.

Results Listing defines the sort order, if any, of the results.

Include Glossary in Report specifies whether several pages of a glossary discussing the meaning of the results is to be included in the printed output.

When analyzing a batch: Always check this option because then all your analytes will be assayed using an identical set of patients. Otherwise your analytes may be tested using a different set and will not be directly comparable.

After clicking on **OK**, the screen appears showing two plots and a set of statistics for the selected evaluation. A dot plot appears in the top left panel, an ROC plot in the top right panel, overall statistics in the table in the lower left and a series of statistics for each unique value in the table in the lower right. The interpretation of these elements will be discussed later.



One important feature of this screen is that the user can click on the **Cursor button** to move the cutoff line so they can evaluate several different scenarios. For example, if the cutoff line were moved to the point just below the lowest point in the positive line of dots, that would indicate a result below which that the diagnosis could be ruled out. Similarly, if the cutoff line were located just above the highest result in the negative line of dots, that would indicate a result above which would rule in a given diagnosis.

Two Test Comparison

After selecting the Two Test Comparison option, a dialog box appears which allows you to specify the analytical process. This box is very similar to the one shown above except that it provides for selecting a pair of tests to be compared. The ROC comparison plot (left half of figure) is the most important element on this screen. Note also the statistics in the lower right corner which provide an evaluation of whether the one method is significantly better than the other, and if so, by how much. Interpretation of these results will be discussed below.

Batch Analysis

After selecting the Batch option, a dialog box appears which allows you to specify the analytical process. As before, the box is similar to the one shown above except that it provides for selecting a group of tests to be compared with one another. After clicking OK, the program generates several pages of reports and then shows them to you using the Print Preview feature. An excerpt of a sample report is shown at the end of this chapter.

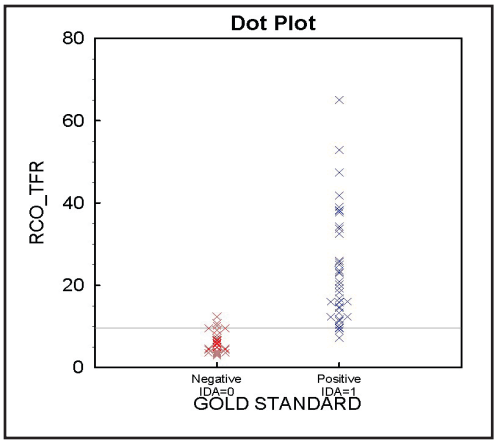
Interpretation

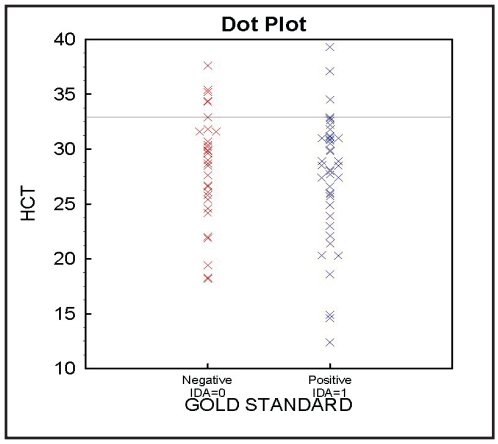
ROC curves are designed to evaluate the ability of a method to diagnose a given condition. Two types of graphs are used to illustrate the data. The first is the dot plot; the second is the ROC plot.

Dot Plot

Dot plots are very useful because they give an intuitive evaluation of the results. The reason is that the two sets of results, one for the positive condition and one for the negative condition, are lined up side by side. The less the overlap between the two sets of results, the better that test will distinguish between the two conditions. Two dot plots are shown.

The first one shows good separation between the two conditions. The second leaves much to be desired.





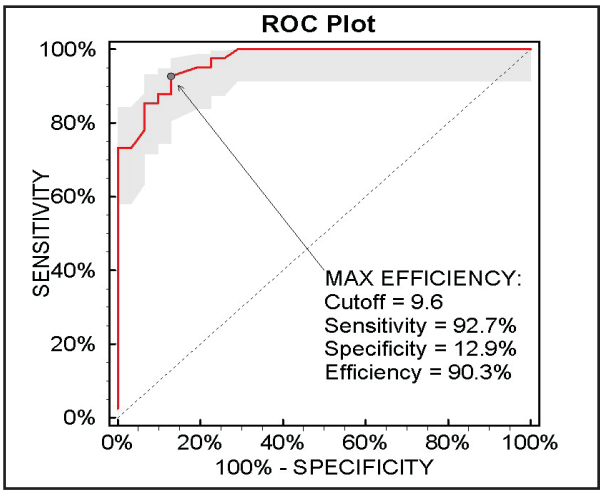
Unfortunately, a significant number of clinical laboratory tests resemble the second one much more closely than they do to those in the first.

One very important group of tests with a much too close a resemblance to the second one are the lipid profile tests (cholesterol, triglyceride, HDLC, etc.).

Editorial Note
One important goal of the clinical laboratory industry should be to dramatically improve the diagnostic efficiency of the tests commonly in use. Development of an awareness of the efficiencies of the present tests hopefully will provide a significant stimulus toward this improvement.

ROC Plot

An ROC plot from the Report Summary illustrates the important features of this type of plot.



Note that a diagonal line splits the figure from the lower left corner to the top right corner. This line represents an even probability that a test will diagnose the condition. This is the worst a test can be. It is in fact equivalent to a coin toss. Such a test will have an area under the curve (AUC) of 0.5.

As the tests have better diagnostic efficiency, they will be further and further removed from the diagonal line. The best tests will have an AUC of 1.0.

It is very difficult to get an intuitive grasp of what actually is getting plotted. What actually is happening is that the region of overlap between the two sets of results are getting plotted using calculated units. The actual results are not a visible part of this plot.

The most important thing to look for in this plot is the degree of separation of the line from the diagonal. The more the separation, the better the diagnostic efficiency.

Area Under the Curve

The most important single statistic is the Area Under the Curve (AUC). As indicated above, this number will vary between 0.5 and 1.0, where 0.5 indicates a value no better than a random coin toss, and Interpreting AUC Values Discrimination Ability AUC Range Perfect Excellent Good Fair Poor No better than a coin toss 1.00 0.95 to 1.00 0.85 to 0.95 0.70 to 0.85 <0.70 0.50 1.0 a perfect value.

Interpreting AUC Values	
Discrimination Ability	**AUC Range**
Perfect	1.00
Excellent	0.95 to 1.00
Good	0.85 to 0.95
Fair	0.70 to 0.85
Poor	<0.70
No better than a coin toss	0.50

This table provides guidance in the weighting of AUC ranges relative to their interpretative reliability.

Significance of ROC Curve Statistics

Many of the statistics in the report are either self-explanatory, or they have been discussed above, or they were defined at the beginning of this chapter. The few important remaining ones are discussed below:

From the Summary Statistics Page

AUC Std Err (AUC Standard Error) and AUC 95% CI (Confidence Interval)
These numbers indicate the uncertainty in the AUC. The less the uncertainty, the better.

Maximum Efficiency Point is that cutoff value at which in the current sample, most diagnoses will be correct.

ROC Curve Analysis (Summary Page)

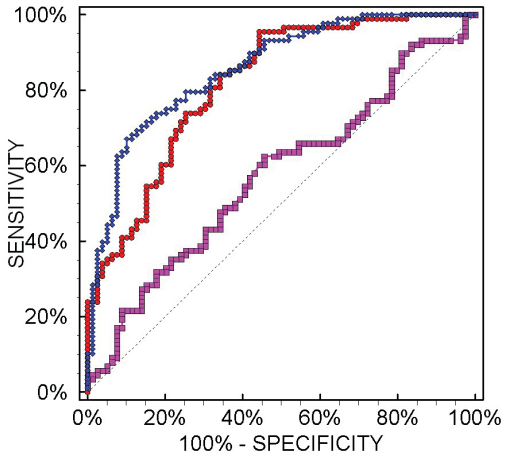
EP Evaluator

User's Manual -

ROC Example

Multiple Test Comparison

Comparative ROC Plots



Summary Statistics

	Test	Units	AUC	Std Err	95% CI	Max Efficiency Point Cutoff	Efficiency	Sensitivity	Specificity
	TestB		0.857	0.028	0.80 to 0.91	>=300.35	77.8	73.9	82.3
	TestA		0.819	0.032	0.76 to 0.88	<242.35	76.6	95.5	55.7
	TestC		0.575	0.044	0.49 to 0.66	>=49.7	58.7	62.5	54.4

Supporting Statistics

Sample Size	167
Positive Cases	88
Prevalence	52.7%
Positive Definition	Diagnosis=pos
Negative Definition	Diagnosis=neg

Prevalence is calculated

ROC Curve Analysis (Test Statistics Page)

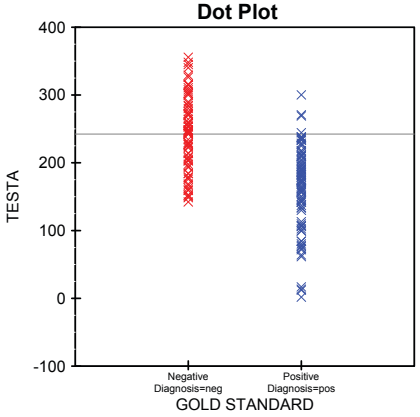
EP Evaluator® — **TestA**

User's Manual -- Data Innovations,

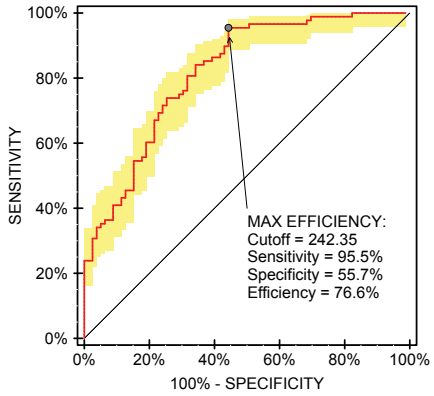
ROC Example

Single Test ROC Analysis

Dot Plot



ROC Plot



Statistical Analysis

Area under the ROC curve (AUC)	0.819
Asymptotic Std Error of AUC	0.032
Asymptotic Gaussian 95% CI	0.76 to 0.88
AUC significantly better than chance?	
Z	7.10
Probability (2-tail)	<0.001

Probability > 0.05 means the test is not significantly better than chance.

	Negative Cases	Positive Cases
Mean	239.556	162.852
SD	56.897	61.424
Range	117.05 to 355.70	1.80 to 300.20
Sample Size	79	88
Prevalence	47.3%	52.7%
Units		

Prevalence is calculated

Analyst: mkf
Expt Date: 16 Jun 2000
Filter: None

Abbreviated ROC Curve

Cutoff	Sensitivity %	Sensitivity 95% CI	Specificity %	Specificity 95% CI	Number of Specimens True Pos	Number of Specimens False Pos	Number of Specimens True Neg	Number of Specimens False Neg	Likelihood Ratio Pos	Likelihood Ratio Neg	Predictive Value Pos %	Predictive Value Neg %	Eff %
<1.80	0.0	0.0 - 4.2	100.0	95.4 - 100.0	0	0	79	88	--	1.00	--	47.3	47.3
<129.35	23.9	16.2 - 33.7	98.7	93.2 - 99.8	21	1	78	67	18.85	0.77	95.5	53.8	59.3
<133.25	25.0	17.1 - 35.0	97.5	91.2 - 99.3	22	2	77	66	9.87	0.77	91.7	53.8	59.3
<144.25	30.7	22.0 - 41.0	96.2	89.4 - 98.7	27	3	76	61	8.08	0.72	90.0	55.5	61.7
<150.00	34.1	25.0 - 44.5	94.9	87.7 - 98.0	30	4	75	58	6.73	0.69	88.2	56.4	62.9
<150.50	35.2	26.1 - 45.6	93.7	86.0 - 97.3	31	5	74	57	5.57	0.69	86.1	56.5	62.9
<152.45	36.4	27.1 - 46.8	92.4	84.4 - 96.5	32	6	73	56	4.79	0.69	84.2	56.6	62.9
<156.25	37.5	28.1 - 47.9	91.1	82.8 - 95.6	33	7	72	55	4.23	0.69	82.5	56.7	62.9
<159.95	40.9	31.2 - 51.4	89.9	81.3 - 94.8	36	8	71	52	4.04	0.66	81.8	57.7	64.1
<161.85	42.0	32.3 - 52.5	88.6	79.7 - 93.9	37	9	70	51	3.69	0.65	80.4	57.9	64.1
<163.65	43.2	33.3 - 53.6	87.3	78.2 - 93.0	38	10	69	50	3.41	0.65	79.2	58.0	64.1
<168.75	45.5	35.5 - 55.8	86.1	76.8 - 92.0	40	11	68	48	3.26	0.63	78.4	58.6	64.7
<170.80	46.6	36.5 - 56.9	84.8	75.3 - 91.1	41	12	67	47	3.07	0.63	77.4	58.8	64.7
<177.80	54.5	44.2 - 64.5	83.5	73.9 - 90.1	48	13	66	40	3.31	0.54	78.7	62.3	68.3
<179.35	55.7	45.3 - 65.6	82.3	72.4 - 89.1	49	14	65	39	3.14	0.54	77.8	62.5	68.3

95% confidence intervals for sensitivity and specificity calculated by the "Score" method.

Accepted by: _____ _____

Signature Date

ROC Curve Analysis (Results Listing)

Results Listing

Spec ID	Diagnosis	TestA	Spec ID	Diagnosis	TestA	Spec ID	Diagnosis	TestA
S00001	pos	80.4	S00057	pos	150.5	S00113	neg	204.7
S00002	pos	218.05	S00058	pos	270.8	S00114	neg	230.25
S00003	pos	235	S00059	pos	73.65	S00115	neg	316
S00004	pos	64.15	S00060	pos	137.15	S00116	neg	272.95
S00005	pos	165.65	S00061	pos	102.6	S00117	neg	142.3
S00006	pos	182.85	S00062	pos	214.9	S00118	neg	159.95
S00007	pos	202.75	S00063	pos	145	S00119	neg	179.35
S00008	pos	199.85	S00064	pos	188.4	S00120	neg	275.75
S00009	pos	183.25	S00065	pos	161.85	S00121	neg	307.65
S00010	pos	13.5	S00066	pos	109.9	S00122	neg	288
S00011	pos	195.35	S00067	pos	228.9	S00123	neg	283.65
S00012	pos	191.35	S00068	pos	194.65	S00124	neg	224
S00013	pos	269.1	S00069	pos	233.65	S00125	neg	227.15
S00014	pos	173.45	S00070	pos	150	S00126	neg	264.2
S00015	pos	163.65	S00071	pos	233.2	S00127	neg	226.55
S00016	pos	99.45	S00072	pos	175.05	S00128	neg	129.35
S00017	pos	209.9	S00073	pos	71.85	S00129	neg	304.85
S00018	pos	209	S00074	pos	61.65	S00130	neg	234.25
S00019	pos	160.85	S00075	pos	134.25	S00131	neg	252.95
S00020	pos	105.95	S00076	pos	210.55	S00132	neg	242.35
S00021	pos	16.9	S00077	pos	204.8	S00133	neg	175.75
S00022	pos	194.15	S00078	pos	84.35	S00134	neg	348.25
S00023	pos	175.45	S00079	pos	224.9	S00135	neg	166.5
S00024	pos	179.4	S00080	pos	1.8	S00136	neg	302.2
S00025	pos	113.1	S00081	pos	144.25	S00137	neg	222.3
S00026	pos	181.6	S00082	pos	156.25	S00138	neg	248.35
S00027	pos	173.95	S00083	pos	169.05	S00139	neg	228.75
S00028	pos	129.95	S00084	pos	77.9	S00140	neg	214.35
S00029	pos	190.5	S00085	pos	172.85	S00141	neg	300.05
S00030	pos	107.3	S00086	pos	212.25	S00142	neg	280.15
S00031	pos	237.6	S00087	pos	300.2	S00143	neg	243.8
S00032	pos	84.2	S00088	pos	237.8	S00144	neg	329.25
S00033	pos	76.2	S00089	neg	259.65	S00145	neg	259.6
S00034	pos	227.25	S00090	neg	242.6	S00146	neg	152.4
S00035	pos	141.9	S00091	neg	345	S00147	neg	148.65
S00036	pos	238.5	S00092	neg	193.2	S00148	neg	184
S00037	pos	156.2	S00093	neg	270	S00149	neg	117.05
S00038	pos	12.1	S00094	neg	246.2	S00150	neg	245.4
S00039	pos	147.1	S00095	neg	314.7	S00151	neg	302.25
S00040	pos	99.65	S00096	neg	253.25	S00152	neg	209.15
S00041	pos	158.6	S00097	neg	326.25	S00153	neg	184.45
S00042	pos	236.3	S00098	neg	197.85	S00154	neg	242.55
S00043	pos	217.35	S00099	neg	290	S00155	neg	213.75
S00044	pos	133.25	S00100	neg	203	S00156	neg	248.95
S00045	pos	174.15	S00101	neg	162.85	S00157	neg	243.25
S00046	pos	186.45	S00102	neg	203.1	S00158	neg	194.85
S00047	pos	189.5	S00103	neg	270.85	S00159	neg	355.7
S00048	pos	197.8	S00104	neg	227.5	S00160	neg	310.85
S00049	pos	106.95	S00105	neg	284.7	S00161	neg	207.3
S00050	pos	209.55	S00106	neg	150.3	S00162	neg	168.75
S00051	pos	170.8	S00107	neg	245.65	S00163	neg	247.85
S00052	pos	185.2	S00108	neg	315	S00164	neg	255.3
S00053	pos	178.7	S00109	neg	340.35	S00165	neg	152.45
S00054	pos	244.45	S00110	neg	272.35	S00166	neg	177.8
S00055	pos	142.05	S00111	neg	245.35	S00167	neg	159.25
S00056	pos	158.45	S00112	neg	257.75			

Values marked with an "X" were excluded from the calculations.

Chapter

22

Coag

INR (International Normalized Ratio) is a system established by the World Health Organization (WHO) and the International Committee on Thrombosis and Homeostasis for reporting the results of blood coagulation tests. The INR result should be the same even if different thermoplastics and instruments are used. This international standardization permits a patient on warfarin to use different laboratories and still obtain comparable test results.

Definitions

ISI (International Sensitivity Index) - The available thermoplastins used for measuring the Prothrombin Time (PT) vary in their sensitivity to coagulation factor depletion. The ISI value indicates how a particular reagent analyzes an internationally standardized sample. The ISI usually between 1.0 and 1.4, is provided in the reagent's package insert.

Normal Patient Mean - the geometric mean PT value in healthy subjects. The geometric mean of N results is the Nth root of the product of the individual values.

INR - INR is calculated from the PT value, normal patient mean and ISI:

$$INR = \left(\frac{PT}{\text{Normal Patient Mean}} \right)^{ISI}$$

INR Validation Requirements

With each new lot number of PT reagent, certain tasks must be done.

- Establishing a new normal patient mean and verifying the reference interval (*INR Geometric Mean and VRI*).
- Comparing results from the new and old lot numbers of PT reagent. (*PT/INR Method Comparison*)
- Programming the ISI and normal patient mean into the coagulation analyzer.
- Documenting the manual check of the INR calculation. (*Manual INR Check*)

INR Geometric Mean and VRI

This module computes the Normal Patient Mean. In addition, it verifies proposed reference intervals for both PT and INR.

- A minimum of 20 PT results for healthy subjects is required.
- The Normal Patient Mean is the geometric mean of the PT results.
- The proposed PT reference interval is verified by the same procedure used in the standard VRI module – the reference interval is verified if no more than 10% of the observed PT values fall outside the interval.
- INR is computed for each PT result based on ISI from the package insert and Normal Patient Mean. The proposed reference interval is verified if no more than 10% of the computed INR values fall outside the interval.

PT/INR Method Comparison

INR Method Comparison compares PT and INR values from the two reagent lots using linear regression. Data for this analysis should include 20-40 PT values distributed across the full range of expected results. (The quality of the analysis depends more on the range of the results than on the number of values.) Only PT values are input; INR values are computed by EP Evaluator. Two method comparison studies are performed: one for PT and a second for INR.

Manual INR Check

This process verifies that the coagulation analyzer is programmed to compute correct INR values. Up to five PT/INR pairs from the analyzer are entered to EP Evaluator. The program then calculates INR, compares the computed value to the measured value and flags incorrect calculations.

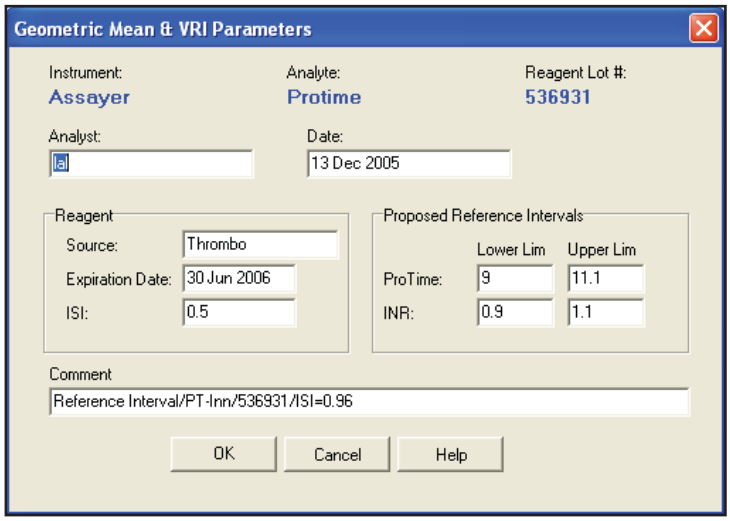
Factor Sensitivity

This statistical module is discussed in Chapter 23, *Factor Sensitivity Studies*.

INR Geometric Mean and VRI

Parameter Screen

Unique fields on this screen include:



Reagent Source. Source of the reagent (usually the vendor). Note that the reagent Lot Number at the top of the screen was chosen when the experiment was created and is not editable from the Parameters screen.

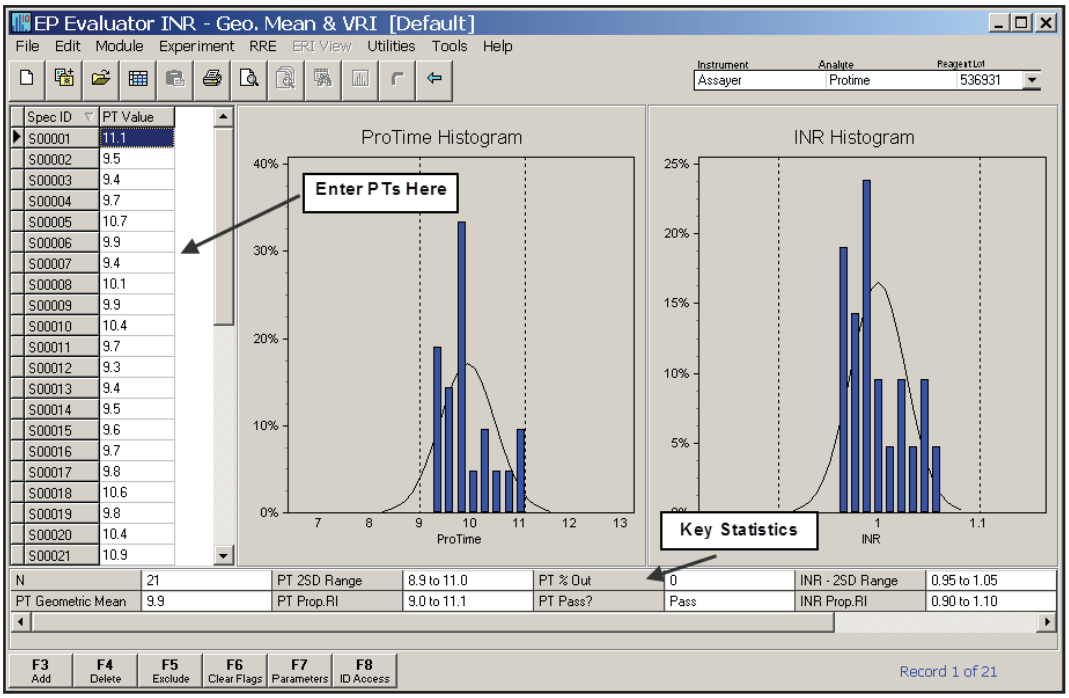
Reagent Expiration Date. For documentation purposes.

Reagent ISI. From the reagent package insert. This value is used to calculate INR values for verification of the INR reference interval.

Proposed Reference Intervals for PT and INR. One purpose of the experiment is to verify these reference intervals.

Note that this screen does not provide for specifying number of decimal places. Decimal places for PT and INR are specified on the Preferences Screen. See the Preferences section in Chapter 3, *Common Operations*.

Experiment Detail Screen



Enter at least 20 “normal” PT results in the grid on the left. One thing to note about this screen is that you enter only PT results — you do not enter INR results. INR results are computed in the program.

EP Evaluator first calculates the geometric mean of your PT results. This is the “Normal Patient Mean” that is used to calculate Nears and verify the INR reference interval. You will also need to program the Normal Patient Mean (and also the ISI) for this reagent lot into the analyzer before the analyzer can report out INR values.

Key statistics are shown in the grid at the bottom of the screen

N. Number of results

N	21	INR - 2SD Range	0.95 to 1.05
PT - Geometric Mean	9.9	INR - Prop.RI	0.90 to 1.10
PT - 2SD Range	8.9 to 11.0	INR - % Out	0
PT - Prop.RI	9.0 to 11.1	INR - Pass?	Pass
PT - % Out	0		
PT - Pass?	Pass		

PT-Geometric Mean. The Normal Patient Mean

PT-2SD Range. Ordinary mean +/- 2 SD of PT results.

PT-Prop RI. the PT Proposed Reference Interval (interval to be validated) as entered on the Parameters Screen.

PT-% Out. Percent of PT results that fall outside the proposed reference interval.

PT-Pass? Pass if no more than 10% of the PT results are outside the proposed reference interval.

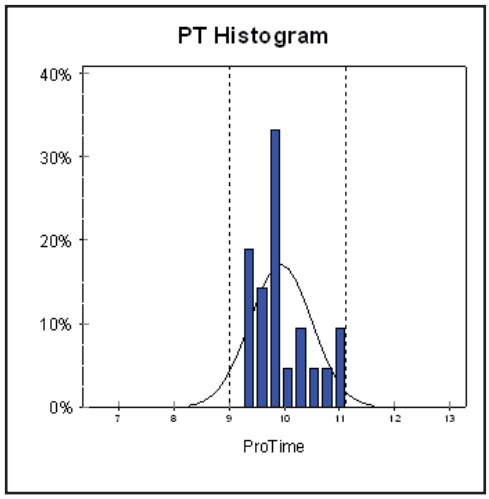
INR-2SD Range. Ordinary mean +/- 2 SD of computed INR values.

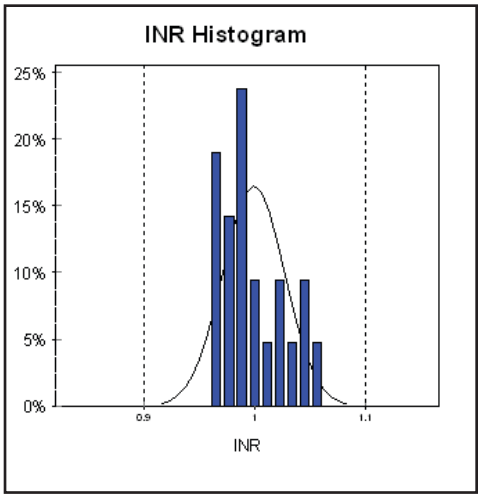
INR-Prop RI. The INR Proposed Reference Interval (interval to be validated) as entered on the Parameters Screen.

INR-% Out. Percent of computed INR values that fall outside the proposed reference interval.

INR-Pass? Pass if no more than 10% of the INR values are outside the proposed reference intervals.

The histograms in the main body of the screen show the relationship between the data points and the proposed reference intervals.





- The first thing to check is whether a large percent (more than 10%) of the data falls outside the proposed reference interval. In this case the verification test will fail.

- The second thing to check is the spacing of the reference limits and the data. A lot of space at one or both ends of the histogram may indicate the existence of problems.

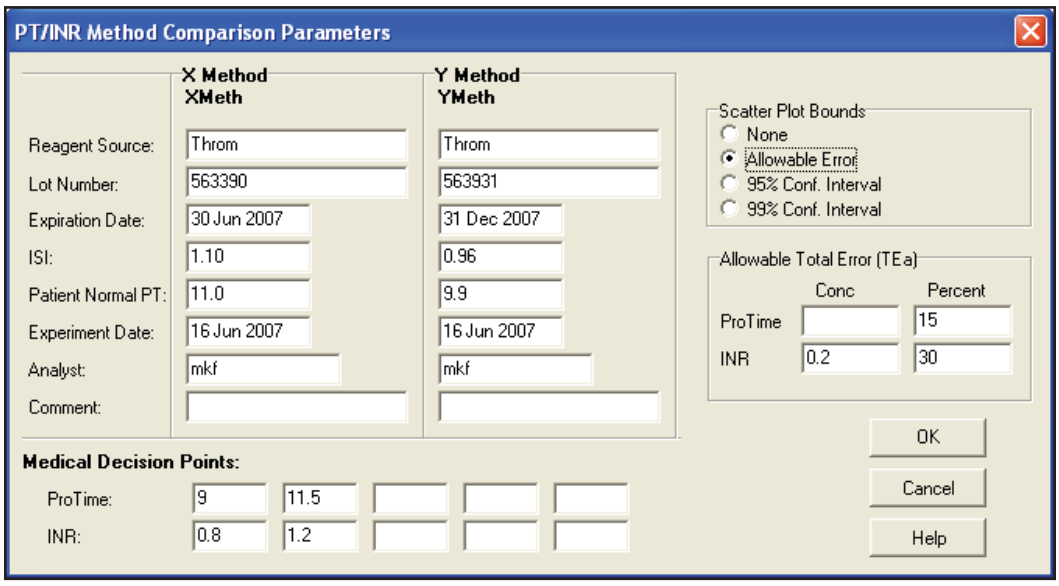
- The third thing to look for is consistency of pattern between the PT and INR histograms. Remember that INR is a mathematical calculation on PT. The illustration above suggests that perhaps the INR and PT intervals are not consistent since the PT values fit tightly in their proposed reference interval while the INR values are much further from their limits.

PT/INR Method Comparison

PT/INR Method Comparison is virtually identical to Alternate Method Comparison (AMC) module. The main reason to have a separate PT/INR method comparison module is that the program can calculate INR results from PT results so you don't have to enter the data twice.

In this chapter we will focus on the program inputs and differences from AMC. Interpretation of method comparison experiments is discussed in the Lab Statistics Manual, Chapter 9, *Interpreting Method Comparison Experiments*.

Parameter Screen



Fields on this screen include the usual Analyst, Experiment Date and comment, plus:

Reagent Source. Source of the reagent (usually the vendor) for each method

Reagent Expiration Date for each method.

Reagent ISI for each method.

Patient Normal PT for each method. These values are experimentally determined (e.g. from the Geometric Mean and VRI module). ISI and Patient Normal PT are used to calculate INR values from input PT results.

Medical Decision Points. Up to five MDPs may be specified for PT and INR. Bias is evaluated at these levels.

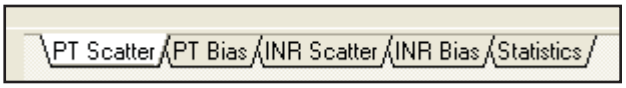
Scatter Plot Bounds. The basis for the envelope lines drawn around the data on the scatter plot. In the PT/INR method comparison module, a corresponding envelope is also drawn on the bias plot. Allowable Error bounds require specification of TEa for both PT and INR.

Note that this screen does not provide for specifying number of decimal places. Decimal places for PT and INR are specified on the Preferences Screen. See the Preferences section in Chapter 3, *Common Operations*.

Experiment Detail Screen

The PT/INR Method Comparison experiment detail screen is almost identical to the AMC screen. Data requirements are identical to those for AMC. A few things to note:

- Tab pages at the bottom of the screen look like this:

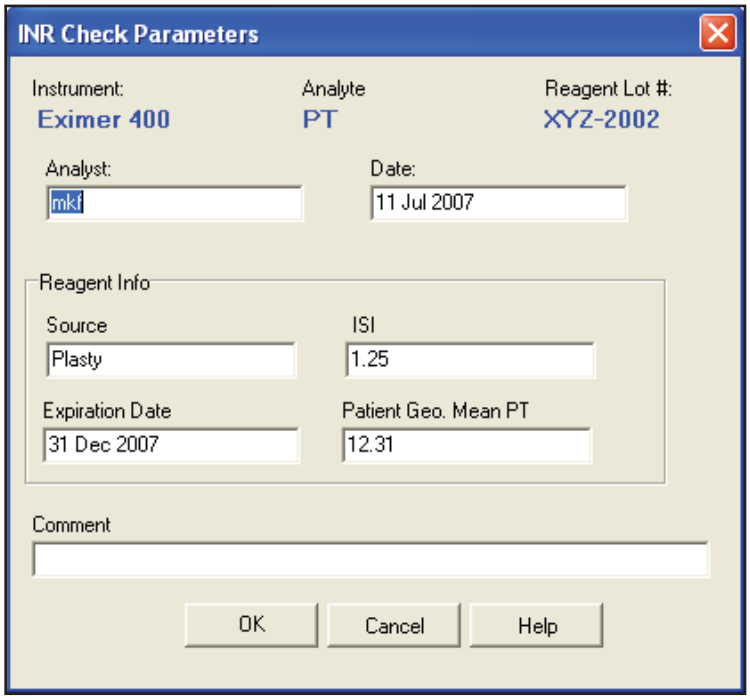


  There are two tabs for PT (scatter plot and bias), two tabs for INR (scatter plot and bias) and a page of key statistics for both PT and INR. When a PT tab or the Statistics tab is selected, you can enter PT X-Y values in the grid on the left as you would in AMC. However, when one of the INR tabs is selected, the X-Y values are INR values. You can inspect them but not edit them.

- PT/INR Method Comparison like AMC, has a Subrange capability. Click the **Subrange** button at the lower right to define or edit a subrange. When you switch to subrange mode, EP Evaluator automatically shows the PT scatter plot; you cannot define a subrange on the INR plot. (However, data plotted on the INR plots does reflect any subrange defined for PT).

Parameter Screen

Fields on this screen include the usual Analyst, Experiment Date, Comment, plus:



Reagent Source. Source of the reagent (usually the vendor). Note that the reagent Lot Number at the top of the screen was chosen when the experiment was created and is not editable from the Parameters screen.

Reagent Expiration Date. For documentation purposes.

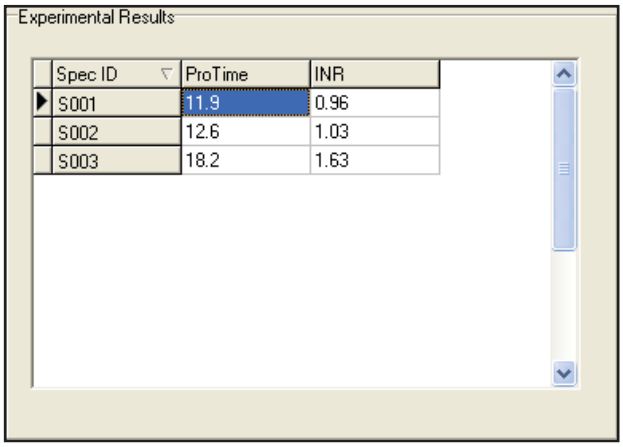
Reagent ISI. From the reagent package insert and as programmed into the analyzer.

Patient Geo. Mean PT. Geometric mean Prothrombin Time for "normal" patients determined experimentally (e.g. from the Geometric Mean and VRI module) and programmed into the analyzer.

Experiment Detail Screen

Make sure that the ISI and Geometric Mean for the reagent lot have been programmed into the analyzer *before* collecting data for this experiment. The whole point is to verify that the analyzer is correctly programmed.

Collect both PT and INR results for a handful of specimens. Since all we are doing here is checking your data, you don't need a lot of results. The program accepts a maximum of five specimens and requires a minimum of three. It is a good idea to include at least one low value, one normal and one high.



This module does not use the INR decimal place settings from the Preferences screen. Enter PT and INR with the **same number of decimal digits** reported by your analyzer.

You won't see any pass/fail indication until you print or print preview the report. The report compares the INR reported by the analyzer to the INR calculated within the program:

Specimen	*Analyzer Results for: PT*	*INR*	*Calculated INR*	*Correct?*
S001	11.9	0.96	0.96	Correct
S002	12.6	1.03	1.03	Correct
S003	18.2	1.63	1.63	Correct

The INR is considered correct if the analyzer INR is either identical to the calculate INR or differs by no more than 1 in the least significant decimal place (a difference due to rounding). For example, for a calculated INR is 0.96, reported values of 0.95, 0.96 or 0.97 are considered correct.

INR Geometric Mean and VRI Report

EP Evaluator®
Users Manual -- Data Innovations

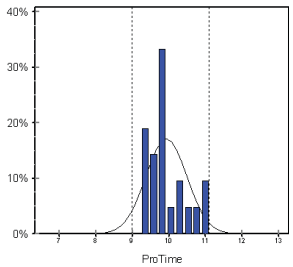
Protime
Instrument: Assayer

Geometric Mean and VRI

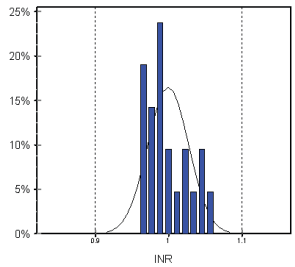
Statistical Analysis

	Geometric Mean	2 SD Range	Proposed Ref. Interval	N	%Out	Pass?
Protime	9.9	8.9 to 11.0	9.0 to 11.1	21 of 21	0	Pass
INR	1.00	0.95 to 1.05	0.90 to 1.10	21 of 21	0	Pass

PT Histogram



INR Histogram



Reagent: Thrombo
Lot Number: 536931
Expiration: 30 Jun 2006
ISI: 0.5
Patient Normal PT: 9.9

Supporting Data

Analyst: lal
Experiment Date: 13 Dec 2005
Comment:

Experimental Results

Spec ID	*PT*	*INR*	*Spec ID*	*PT*	*INR*	*Spec ID*	*PT*	*INR*
S00012	9.3	0.97	S00011	9.7	0.99	S00008	10.1	1.01
S00013	9.4	0.97	S00016	9.7	0.99	S00020	10.4	1.02
S00003	9.4	0.97	S00004	9.7	0.99	S00010	10.4	1.02
S00007	9.4	0.97	S00019	9.8	0.99	S00018	10.6	1.03
S00014	9.5	0.98	S00017	9.8	0.99	S00005	10.7	1.04
S00002	9.5	0.98	S00006	9.9	1.00	S00021	10.9	1.05
S00015	9.6	0.98	S00009	9.9	1.00	S00001	11.1	1.06

x: Excluded F: Outside Proposed Ref Int; INR values are computed (not measured) assuming ISI=0.5, Normal PT=9.9

Accepted by: _____ _____
Signature Date

Default Printed: 24 Mar 2011 09:57:29 Page 1

EP Evaluator®

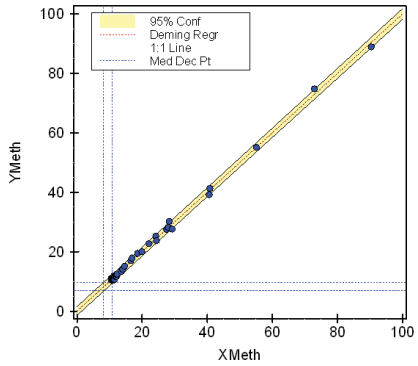
Users Manual -- Data Innovations

ProTime

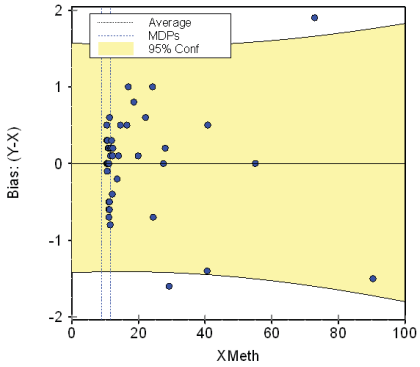
Method Comparison

X Method: XMeth **Y Method: YMeth**

Scatter Plot



Bias Plot



Deming Regression Statistics

Correlation Coeff (R)	0.9991
Slope	0.999 (0.986 to 1.013)
Intercept	0.08 (-0.27 to 0.43)
Std. Err of Estimate	0.73
N	43 of 43
Subrange	None

Medical Decision Point Analysis

X MDP	Predicted Y	95% Conf. Lim. Low	95% Conf. Lim. High
9.0	9.1	8.80	9.34
11.5	11.6	11.32	11.82

Experiment Description

	X	Y
Reagent Source:	Throm	Throm
Reagent Lot:	563390	563931
Expiration Date:	30 Jun 2007	31 Dec 2007
ISI:	1.1	0.96
Patient Normal PT:	11.0	9.9
Result Ranges:	10.5 to 90.4	10.4 to 88.9
Mean ± SD:	20.17 ± 17.00	20.23 ± 16.99
Units:	Seconds	Seconds
Rep SD:	1	1
Experiment Date:	16 Jun 2007	16 Jun 2007
Analyst:	mkf	mkf
Comment:		

Accepted by: _____ _____

Signature Date

EP Evaluator®

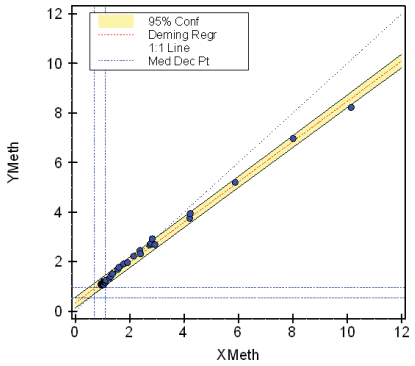
INR

Users Manual -- Data Innovations

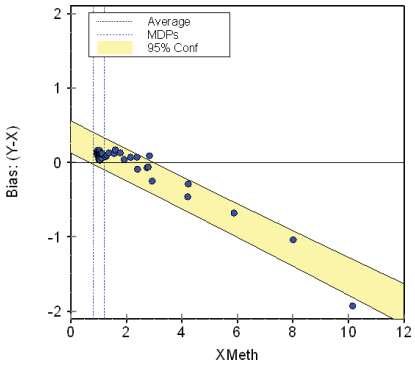
Method Comparison

X Method: XMeth **Y Method: YMeth**

Scatter Plot



Bias Plot



Deming Regression Statistics

Correlation Coeff (R)	0.9977
Slope	0.813 (0.796 to 0.830)
Intercept	0.342 (0.294 to 0.389)
Std. Err of Estimate	0.106
N	43 of 43
Subrange	None

Medical Decision Point Analysis

X	Predicted	95% Conf. Lim.	
MDP	Y	Low	High
0.80	0.99	0.954	1.030
1.20	1.32	1.282	1.352

Experiment Description

	X	Y
Reagent Source:	Throm	Throm
Reagent Lot:	563390	563931
Expiration Date:	30 Jun 2007	31 Dec 2007
ISI:	1.1	0.96
Patient Normal PT:	11.0	9.9
Result Ranges:	0.95 to 10.15	1.05 to 8.22
Mean ± SD:	2.001 ± 1.923	1.968 ± 1.564
Units:	None	None
Rep SD:	1	1
Experiment Date:	16 Jun 2007	16 Jun 2007
Analyst:	mkf	mkf
Comment:		

Accepted by: _____ _____

Signature Date

EP Evaluator

Default Printed: 24 Mar 2011 10:02:05

Page 1

EP Evaluator®

Users Manual -- Data Innovations

Method Comparison

X Method: XMeth **Y Method: YMeth**

Experimental Results

Specimen	PT (Seconds) X	PT (Seconds) Y	PT (Seconds) Bias	INR X	INR Y	INR Bias
S00001	14.6	15.1	0.5	1.37	1.50	0.13
S00002	12.2	12.3	0.1	1.12	1.23	0.11
S00003	16.9	17.9	1.0	1.60	1.77	0.17
S00004	18.6	19.4	0.8	1.78	1.91	0.13
S00005	40.6	39.2	-1.4	4.21	3.75	-0.46
S00006	55.1	55.1	0.0	5.88	5.20	-0.68
S00007	72.9	74.8	1.9	8.01	6.97	-1.04
S00008	90.4	88.9	-1.5	10.15	8.22	-1.93
S00009	14	14.1	0.1	1.30	1.40	0.10
S00010	11.3	10.8	-0.5	1.03	1.09	0.06
S00011	24.4	23.7	-0.7	2.40	2.31	-0.09
S00012	11.1	11.3	0.2	1.01	1.14	0.13
S00013	11.5	10.7	-0.8	1.05	1.08	0.03
S00014	11.6	11.8	0.2	1.06	1.18	0.12
S00015	12.3	12.5	0.2	1.13	1.25	0.12
S00016	10.8	10.8	0.0	0.98	1.09	0.11
S00017	10.5	10.5	0.0	0.95	1.06	0.11
S00018	10.6	10.6	0.0	0.96	1.07	0.11
S00019	16.5	17	0.5	1.56	1.68	0.12
S00020	24.2	25.2	1.0	2.38	2.45	0.07
S00021	11.8	12	0.2	1.08	1.20	0.12
S00022	40.8	41.3	0.5	4.23	3.94	-0.29
S00023	10.6	10.5	-0.1	0.96	1.06	0.10
S00024	10.9	11.1	0.2	0.99	1.12	0.13
S00025	11.3	10.7	-0.6	1.03	1.08	0.05
S00026	11.1	11.1	0.0	1.01	1.12	0.11
S00027	19.9	20	0.1	1.92	1.96	0.04
S00028	11.1	10.4	-0.7	1.01	1.05	0.04
S00029	28	28.2	0.2	2.79	2.73	-0.06
S00030	11.1	10.6	-0.5	1.01	1.07	0.06
S00031	12.1	11.7	-0.4	1.11	1.17	0.06
S00032	11.1	10.5	-0.6	1.01	1.06	0.05
S00033	29.2	27.6	-1.6	2.93	2.68	-0.25
S00034	27.5	27.5	0.0	2.74	2.67	-0.07
S00035	22.1	22.7	0.6	2.15	2.22	0.07
S00036	10.5	10.8	0.3	0.95	1.09	0.14
S00037	10.5	11	0.5	0.95	1.11	0.16
S00038	10.7	11	0.3	0.97	1.11	0.14
S00039	11.3	11.9	0.6	1.03	1.19	0.16
S00040	11.9	12.2	0.3	1.09	1.22	0.13
S00041	11.6	11.7	0.1	1.06	1.17	0.11
S00042	13.6	13.4	-0.2	1.26	1.34	0.08
S00043	28.3	30.2	1.9	2.83	2.92	0.09

Values with an "x" were excluded from the calculations. INR Values are calculated (not measured)

EP Evaluator®

Users Manual -- Data Innovations

Eximer 400

Analyte: PT

Manual INR Check

$$INR = (PT / Mean\ Normal\ PT)^{ISI}$$

Specimen	Analyzer Results for: PT	INR	Calculated INR	Correct?
S001	11.9	0.96	0.96	Correct
S002	12.6	1.03	1.03	Correct
S003	18.2	1.63	1.63	Correct

Reagent:	Plasty	ISI:	1.25
Lot Number:	XYZ-2002	Mean Normal PT:	12.31
Expiration:	31 Dec 2007		

Analyst: mkf
Expt. Date: 11 Jul 2007
Comment:

Explanation

The purpose of this analysis is to verify that correct ISI and Mean Normal PT values are programmed into a coagulation analyzer. The **Analyzer Results** columns of the report show PT and INR values reported by the analyzer. The **Calculated INR** column shows the correct INR, based on ISI and Mean Normal PT values listed below the table. A specimen is flagged as INCORRECT if the analyzer INR does not match the calculated INR. A tolerance of one unit in the last decimal place is allowed for rounding error. Thus 0.98 "matches" 0.97, 0.98, or 0.99.

Calculations are performed using numbers with exactly the same number of decimal places that you type on the program's input screen. The calculated INR is rounded to the same number of decimal digits as the analyzer INR.

Accepted by: _____ _____

Signature Date

Chapter

23

Factor Sensitivity Studies

Use this module to determine the factor sensitivity of a given coagulation reagent to the various factors involved in the reaction cascade it measures. This module provides for selection of a coagulation reagent based on that reagent's ability to detect when the activity of a factor is significantly diminished.

Principle

Coagulation in blood occurs because of a cascade of chemical reactions which culminate in the coagulation process. The faster these reactions happen, the shorter the time it takes for coagulation to occur.

There are two major pathways for the coagulation process. Each is evaluated by its own assay. They are:

- **Prothrombin Time (PT)**
- **Activated Partial Thromboplastin Time (aPTT)**

The major components of these two cascades of reactions are called *Factors*. Each pathway is controlled by its own set of factors. The factors most importantly associated with each are:

- **PT Factors: II, V, VII and X**
- **aPTT Factors: VIII, IX, XI and XII**

If the activity or concentration of any of these factors is sufficiently diminished, then the coagulation process is slowed down and the coagulation time is prolonged. The purpose of both of these assays (PT and aPTT) is to detect diminished activities for one or more of these factors.

The purpose of a Factor Sensitivity experiment is to determine the lot numbers of PT or aPTT reagents that are best suited to identify reduced factor activities for each of the specific factors. The output of the experiment will reveal the threshold percent activity of an individual factor that will produce an abnormal clotting time. See *Definition of Factor Sensitivity*.

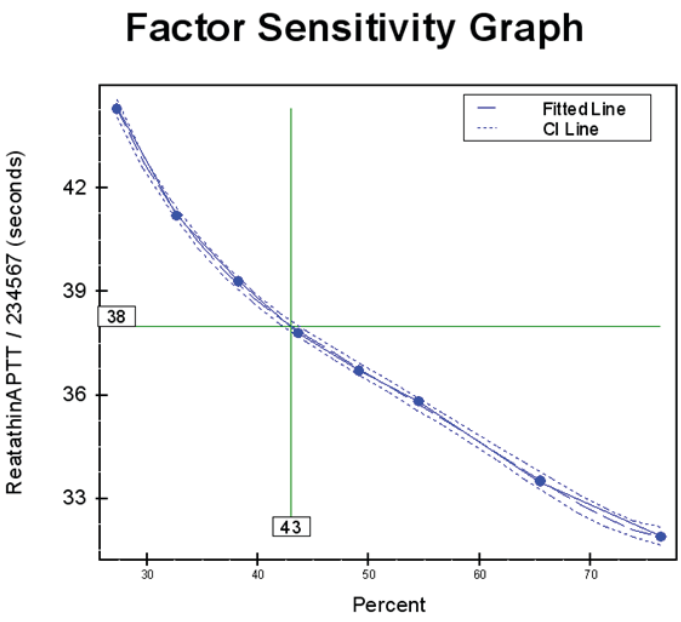
Three major components are needed for a Factor Sensitivity (FS) study:

Reagent: The proposed reagent, one for PT and/or one for aPTT. In many cases there will be multiple reagents tested for each assay.

Reference Plasma (RP): This behaves like a normal patient specimen which contains multiple factors, but the activity of each factor is determined and close to 100%.

Factor Deficient Plasma (FDP): Commercially available factor deficient plasmas with an activity of zero for the single specific factor being evaluated.

A factor sensitivity graph illustrating the decrease in coagulation time with increasing concentration of a factor (as a percentage of normal) is shown below for aPTT and a specific test reagent.



Specimen dilutions for each factor experiment are prepared by combining appropriate volumes of RP and FDP to give dilutions covering the expected range at which the reagent becomes sensitive to a given factor. Dilutions are expressed as a percent. For example, a 35% dilution specimen (total volume of 1 mL) will contain 0.35 mL of RP and 0.65 mL of FDP. Default dilutions are 25%, 30%, 35%, 40%, 45%, 50%, 60%, and 70%.

Definition of Factor Sensitivity (FS):

Factor Sensitivity is defined as that percentage of a single factor that produces an aPTT or PT above the Upper Limit of the Normal reference range (ULNR).

Typically the best fit curve representing the clotting time versus the Percent Factor will be a logarithmic, or a 2nd order or 3rd order regression, with the smallest Percent Factor dilutions exhibiting extended clotting times. Higher dilutions eventually cross the ULNR threshold. The highest dilutions are expected to reach a stable clotting time near the ULNR with variability due to assay imprecision and dilution accuracy.

EP Evaluator calculates Factor Sensitivity in two ways:

First abnormal dilution: The highest dilution which is abnormal. For example, suppose two of the dilutions were 35% and 40% and had aPTTs of 46 and 42 seconds respectively. If the ULNR is 43 seconds, then the FS by this definition would be 35%.

Calculated Sensitivity: Where a curve fitted to the data intersects with the ULNR.

Data Requirements

Number of dilutions: 3 to 15.
Numbers of replicates: 1 to 4.

The word PRELIMINARY printed diagonally across the report indicates that the data is incomplete and that the report is not acceptable as a final report. Some or all of the statistics may be missing. The Factor Sensitivity report is preliminary if there are fewer than 3 dilutions selected for inclusion in the regression calculations.

1. The experiment design has two parts.
   Normal Range Study: The normal range for the assay (PT or aPTT) must be established for each reagent being tested, if it hasn't been done previously. The ULNR for each reagent lot is needed in the FS calculation. A Normal Range Study can performed using EE's Histogram and Descriptive Stats module. For PT, it can also be performed in the INR-Geometric Mean module.
2. **Factor Sensitivity Study**: For each Factor to be studied, a series of dilutions with a range of factor activities are assayed. The default range of dilutions is 25% to 70%.

Factor Sensitivity Study

Specimen Dilution Preparation

We recommend preparing a minimum of 8 dilutions, with unadjusted factor percentages of 25%, 30%, 35%, 40%, 45%, 50%, 60%, and 70%. Below is a table of suggested dilutions. Total volume for each specimen is 1.00 mL.

Factor Percent Dilutions	Reference Plasma (mL)	Factor Deficient Plasma (mL)
70	0.70	0.30
60	0.60	0.40
50	0.50	0.50
45	0.45	0.55
40	0.40	0.60
35	0.35	0.65
30	0.30	0.70
25	0.25	0.75

Specimen Naming Convention

If entering data manually into a FS study, the specimen name (SpecID) is defined based on the dilutions provided on the Parameters screen. If data is to be copied and pasted, the format is "Dffdd" where "D" can be any single letter, "ff" is the two digit factor number, and "dd" is the dilution percent. The name of the specimen for Factor IX with a 40% dilution would be "D0940". The FS module can also accommodate decimal points in the specID. For example: **Dffdd.d**

Specimen Analysis

Assay each dilution. If feasible, assay multiple replicates of each dilution. EE can accommodate up to four replicates for each dilution. The purpose of an increased number of replicates is to reduce the imprecision of the means.

Data Analysis

Create experiments and enter the dilution data on the Parameters screen. See the *Parameters* section for more detail.

Create a new experiment

Experiment>New opens the create experiment window. Three items must be, and one additional item may be, entered into this screen:

Factor, Reagent name, Reagent lot number (optional), and Instrument. If the two Reagent items are entered, use the same line. Separate them with a / as shown in the figure where the Reagent is **Rgt-APTT** and the lot number is **234567**.

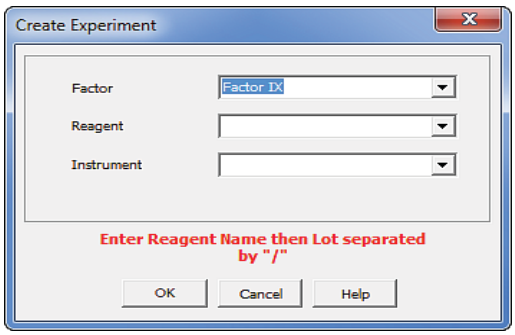


FIG 23.1: Create Experiment window - Warning

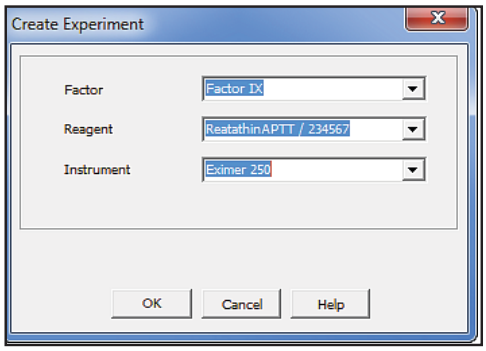
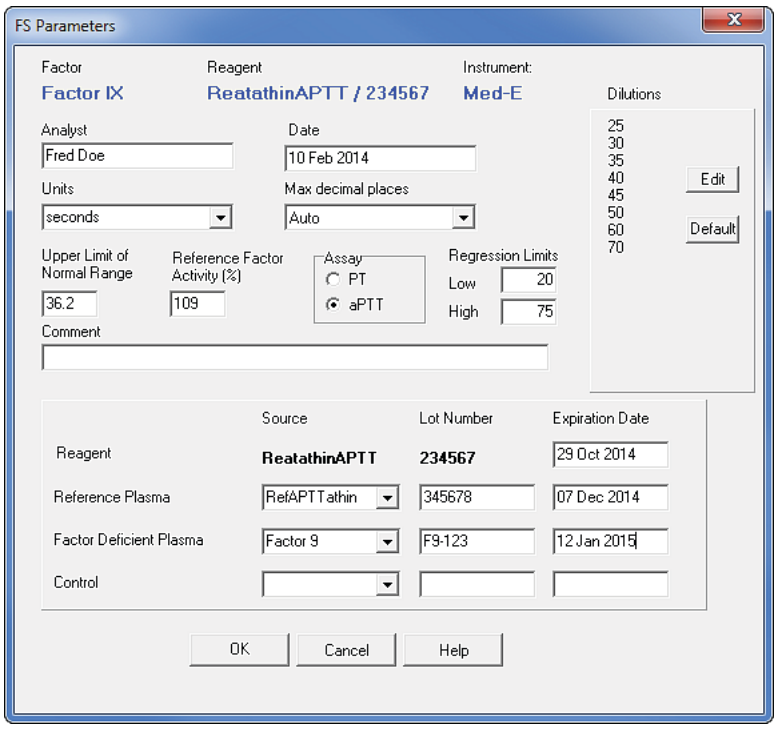


FIG 23.2: Create Experiment Window

Parameters

The Parameter screen is similar to most EE Parameter screens.
Fields unique to FS are:

- **Upper Limit of Normal Range (ULNR)**: This is the calculated upper limit for this test in your normal range study. It is specific for this reagent lot number.

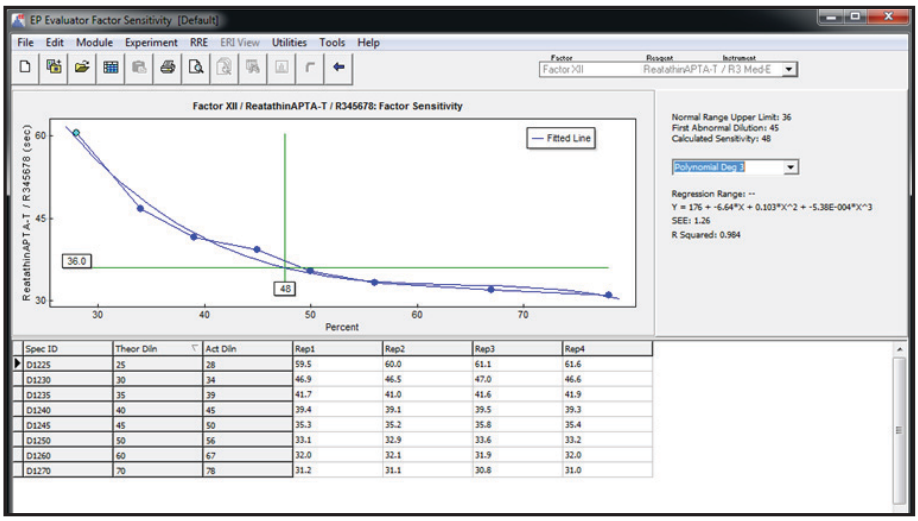


- **Reference Factor Activity (%)**: This specifies the factor activity in the reference plasma. The package insert provide a value for the specific factor tested in this experiment. The range for this number is 50% to 150%.
- **Assay:** Either PT or aPTT.
- **Regression Limits**: Limit the data that is used to perform the regression, while retaining additional data to document your experiment. We recommend that you only use Actual Dilutions between 20% and 75% for the regression calculations.
- **Dilutions**: The default dilutions are: 25%, 30%, 35%, 40%, 45%, 50%, 60% and 70%. Click the Edit button to change the dilution values. Note that these dilutions are theoretical dilutions, based on the percents of Reference Plasma.

NOTE: Once data is entered into a FS experiment, the theoretical dilutions cannot be edited.

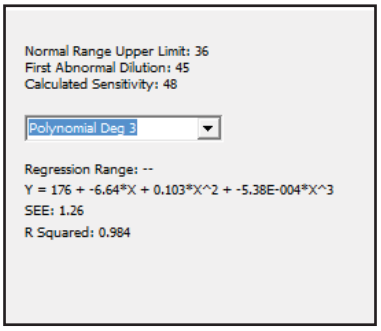
- **Source**, **Lot Number**, and **Expiration Date** for the reagent, the reference plasma and the factor deficient plasma. These parameters for controls are not required.

Experiment Detail Screen



You can manually select logarithmic or 1st, 2nd, or 3rd order polynomial regression to specify how Factor Sensitivity calculates the best fit curve. The default for new experiments is Polynomial Degree 2.

All of the replicates are used to calculate the regression. The polynomial equation, the SEE, and the R-squared value are displayed on the Experiment Detail Screen.



Specimen ID, Theoretical Dilution, and Actual Dilution are displayed in the Results Table. EE calculates **Actual Dilutions** by multiplying **Theoretical Dilutions** by the **Reference Factor Activity**. Note that if logarithmic regression is selected, any Actual Dilution of zero is omitted from the calculated regression line.

Calculated Sensitivity Calculations

EP Evaluator uses unweighted standard polynomial or logarithmic regression, using all of the replicate values, to determine the best curve fit for selected Percent Factor Dilutions.

In the **Parameters** screen, you can enter the lowest and highest actual dilutions to define the range of points to be used when calculating the regression curve.

- Dilutions that are not used to compute in the regression curve are still displayed in gray on the graph for informational purposes.
- However, dilutions that are manually excluded in the Experiment Detail screen do not appear on the graph.
- Using very low dilutions to compute the regression curve can adversely skew the accuracy of the best fit curve in the ULNR crossover region.

In the **Experiment Detail** screen, you can select the regression type (polynomial degree or logarithmic). The regression equation, SEE, and R-squared value are displayed to help you determine the best fit curve.

- While the dilution profile is expected to follow a logarithmic or 2nd order regression, in some cases a straight line or a 3rd order curve can offer the most useful interpolation of the FS threshold region.
- If logarithmic regression is selected, any Actual Dilution value of zero is omitted from the regression.
- The standard error of the estimate statistic (SEE) and R-squared are also provided to help you pick the best fit curve. As a general rule, a low SEE and high R-squared are important clues to selection of the most useful curve.

NOTE: The calculations for the polynomial and logarithmic regressions, as well as the SEE and R-squared are the same as those used in Microsoft Excel 2010.

Interpretation

The key statistic provided is the value of Factor Sensitivity (FS). When calculated Factor sensitivity can be determined using one of the regression choices, there are three possible outcomes.

NOTE: A result of "--" means that the calculation cannot be determined mathematically.

- **Calculated Factor Sensitivity**: The ULNR is within the range of the clotting times of the typical specimen dilutions of 25% to 75%.
- **Insensitive**: If the ULNR is above all of the plotted data, then the experiment is Insensitive. In this case, **Calculated Sensitivity** cannot be determined.
- **Hypersensitive**: If the ULNR is below all of the plotted data, then the experiment is Hypersensitive. In this case, **Calculated Sensitivity** cannot be determined.

The First Abnormal Dilution is also provided because that is the traditional approach.

Optimizing the quality of the Factor Sensitivity Calculation

Calculated sensitivity is an estimate of the most representative point at which the recovery of the series of dilutions will intersect the ULNR. Failure to produce a numerical result for Calculated Factor Sensitivity in EE can have several causes, including the very real possibility that the reagent under evaluation is not suited for use in determining Factor deficiency in suspected patients. In addition, this evaluation does not produce a highly precise result, and several factors contribute the uncertainty of the calculated sensitivity outcome.

Factors affecting the uncertainty of the experiment:

1. Uncertainty of the limits of the normal range

The ULNRs for PT and aPTT are expected to be different from each other. However, all the reagent lots within each reagent type (PT or aPTT) should be similar, and generally within 10% to 15% of one another. If there are dramatic differences between reagent ULNRs, consider increasing the number of subjects included in the normal range study, particularly if that number is small, e.g. less than 60. The uncertainty of the normal range limits decreases significantly as the number of subjects increases.

2. Uncertainty in the measurement of the diluted FS specimens

A well planned series of dilutions and their replicate instrument measurements should follow a logarithmic or 2nd order regression. Low factor percent dilutions should recover well above the ULNR and results for high factor percent dilutions should decline to a stable level below the ULNR, with variability due to assay imprecision and dilution accuracy.

If one or more of the assayed results don't appear to follow the expected kinetics, this could be due to errors in dilution preparation or in the instrument analysis. If repeated measurement of a dilution continues to give the same answer, prepare a new full set of specimens and repeat the experiment.

3. Quality of Dilution preparation

Good analytical technique is important when preparing dilutions, as inaccurate pipetting is a major source of error. If serial dilutions are used, an error in one dilution will be perpetuated to the rest of the series.

4. Number of dilutions and replicates

Assuming no pipetting errors, uncertainty can be decreased by increasing the number of specimens used to determine the normal range and/or by increasing the number of replicates assayed for each of the diluted specimens in the FS experiment. Increasing the number of replicates reduces random error. Increasing the numbers of dilutions near the expected crossover point can improve the "goodness of fit" of the selected regression.

One point of a Factor Sensitivity study is to determine the FS for each factor using two or more coagulation reagents. The reagent with the superior performance for the most factors will be selected.

Before performing an FS experiment, consider the following question:

What differences in FS are significant?

- For all the reasons cited above, Factor Sensitivity is only reported to the nearest percent.
- In general, when comparing different reagents lots for the same factor, differences not exceeding 2 units are considered to be insignificant.

Acknowledgements

We are indebted to the coagulation group at Beckman Coulter for providing us support during our development of this module. In particular, Pat Hudson has made herself readily available to answer our questions and to patiently explain coagulation and FS. Dana Conner has helped us understand how this module would benefit field installation staff and customers alike. We have based this implementation on Beckman's FS protocol (2009).

References:

Beckman FS Protocol (2009). Factor Sensitivity Study, Hemostasis Performance Verification Manual, pages 3-5. (PN 7222768A – December, 2009). Beckman Coulter, Inc, Miami, FL.

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Clinical Laboratory -- Kennett Community Hospital

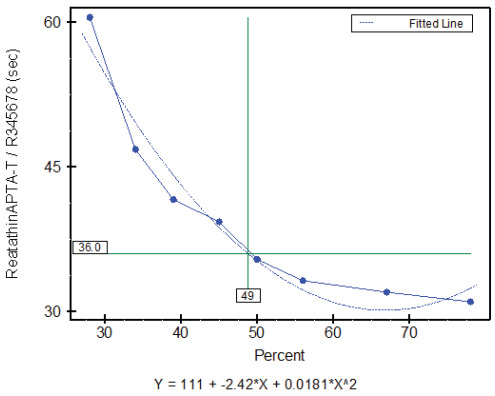
Factor XII

Reagent ReatathinAPTA-T / R345678

Instrument Med-E

Factor Sensitivity

Factor Sensitivity Graph



Y = 111 + -2.42*X + 0.0181*X^2

Factor Sensitivity (%)

First Abnormal Dilution	**45**
Calculated Sensitivity	**49**

Supporting Data

Analyst	jon
Date	30 Sep 2011
Assay	aPTT
Upper limit - Normal Range	36
Reference Factor Activity	112
Number of Specimens	32
Regression Range	--
SEE	2.12
R-Squared	0.952

Comment

Materials

	Source	*Lot Number*	*Exp. Date*
Reagent	ReatathinAPTA-T	R345678	03 Jan 2012
Reference Plasma	RefAPTTathin-A	RP45678	01 Mar 2012
Factor Deficient Plasma	Factor 12	F12-123	09 Apr 2012
Control			

Experimental Results

	Dilutions		*Coagulation Times (sec)*				
Specimen ID	*Theoretical*	*Actual*	*Mean*	*Rep1*	*Rep2*	*Rep3*	*Rep4*
D1225	25	28	60.5	59.5	60.0	61.1	61.6
D1230	30	34	46.8	46.9	46.5	47.0	46.6
D1235	35	39	41.6	41.7	41.0	41.6	41.9
D1240	40	45	39.3	39.4	39.1	39.5	39.3
D1245	45	50	35.4	35.3	35.2	35.8	35.4
D1250	50	56	33.2	33.1	32.9	33.6	33.2
D1260	60	67	32.0	32.0	32.1	31.9	32.0
D1270	70	78	31.0	31.2	31.1	30.8	31.0

Accepted by: _____ _____

Signature Date

EP Evaluator [illegible]

Default Printed: 14 Mar 2014 10:10:13 Page 1

Chapter

24

CLSI EP10 Preliminary Evaluation of Methods

The CLSI:EP10 Protocol evaluates linearity, recovery, drift, carryover and precision at three concentrations: low, medium and high.

CLSI has published a second document (CLSI:EP15) on the evaluation of clinical laboratory methods. It has not been implemented in EP Evaluator, Release 11. There are two parts to this protocol, one for the linearity and accuracy components, and one for a multi-day precision analysis. For those interested in performing experiments using this protocol, the Linearity and Complex Precision modules are adequate to this task.

Data and Specimen Requirements

A minimum of 5 runs with 10 results per experiment are required. CLSI recommends that each run be on a different day. The maximum number of runs allowed is large (50+). (The current version of this program provides for 11 results per run. The extra result is the first primer. Just enter a zero or leave it blank.)

Aliquots of the same original specimens are to be assayed each day. Specimen preparation should be done carefully. Select two specimens which have concentrations reasonably near the extreme ends of the reportable range. A mid-level specimen is prepared from a 1:1 dilution of the low and high specimens.

Order of assay is critical. Three specimens are assayed a total of 10 times on each day in the required order of Mid, High, Low, Mid, Mid, Low, Low, High, High, and Mid. The initial Mid specimen is a primer. The remaining 9 daily results are used in the statistical calculations.

Experimental Design

This experiment has been cleverly designed to produce several different elements, all from the same set of 50 results.

The order of specimens when used correctly, provides information on carryover. Only one analyte can be assayed at a time on *multi-channel instruments, otherwise the assumptions for carryover are invalid*.

The specimens are assayed repeatedly at three concentrations to provide both within-day and total precision statistics. The total precision statistics are often a much better estimate of the total instrument performance than the within-day because it includes the day-to-day variation.

The fact that the specimens have defined concentrations allows analysis of accuracy and linearity.

If the concentrations of the low and high specimens challenge the ends of the reportable range, then the reportable range can be evaluated as well.

Parameter Screen

The Parameter Screen (Figure 24.1.) provides for entry of the critical descriptive data for each experiment. The key elements of this screen are:

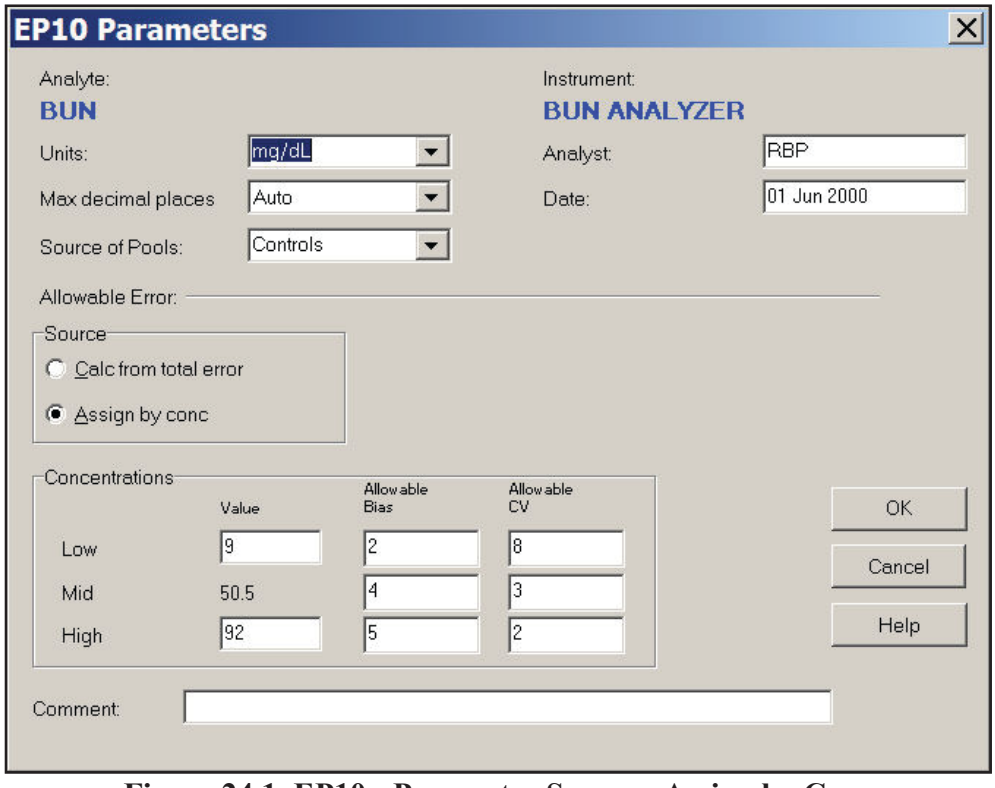


Figure 24.1. EP10 - Parameter Screen - Assign by Conc

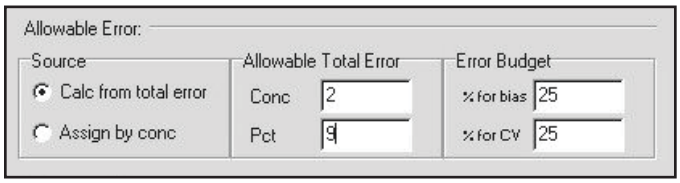
Max decimal places is the maximum number of decimal places for reports. "Auto" means number of decimal places is determined from the data. Computed statistics (e.g., Mean) are usually printed with one more decimal place than the input results. This setting affects reports only; calculations are done on full-precision numbers.

Concentrations: Note that only the low and high concentrations can be entered. The concentration of the mid value is the average of the other two because it is prepared as a 1:1 dilution of the other two.

Allowable Error can be assigned two ways, by calculation from Allowable Total Error or by Assignment at Each Concentration.

- **Assignment at Each Concentration** is assigned in the form of allowable bias and allowable cv for each specimen (as shown in Figure 24.1.)

- **Calc from total error** is checked, then the Allowable Total Error section of the screen changes to what is shown at left. In this instance, Allowable Total Error can be entered in the usual way. In addition, it can be budgeted for both systematic error (% for bias) and random error (% for CV).



- **% for bias** is the maximum allowable systematic error. If the error of any mean value exceeds this number, then the experiment fails. The same rules apply for assignment of % for bias here as in the linearity module. % for bias should be in the range of 25 to 50%.

- **% for CV** defines the maximum allowable value for 1 SD. For example, if the allowable total error is 20 and the "% for CV" is 25%, then the maximum value for 1 SD will be 5 (25% of 20). The value of this variable should be in the range of 17 to 33%, with the usual value being 25%.

Experiment Detail Screen

As usual, most of the elements in the Experiment Detail Screen were discussed in Chapter 3, *Common Operations*.

The primary unique element is the display of the experimental results with the mean and CV of the results for that run. Any exclusion in a given run excludes the whole run and none of the points from that day are used in any of the calculations. The symbols for excluded points are displayed in a different form than any unexcluded points.

EP10 Report

The report consists of two different types of pages: (1) a page displaying the statistical information; and (2) a page containing the experimental results. Both are shown at the end of this chapter.

Interpretation

Interpretation of the experiment is straight forward. For each day and for the whole experiment, the slope, intercept, carryover, linearity and drift are evaluated. For the whole experiment only, precision and bias are evaluated. See the glossary for definitions of the terms. Elements of the report include:

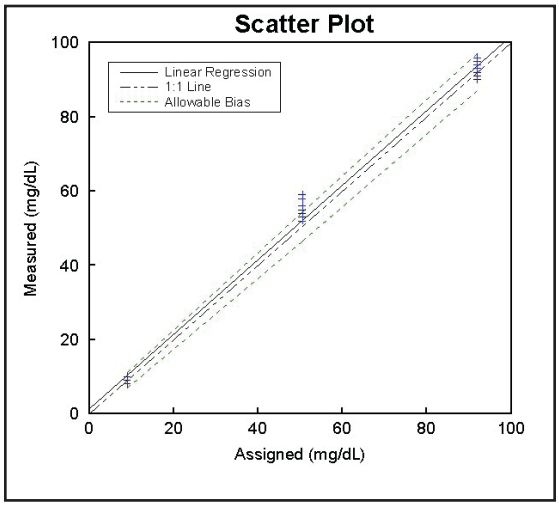


Figure 24.2. EP10 Scatter Plot

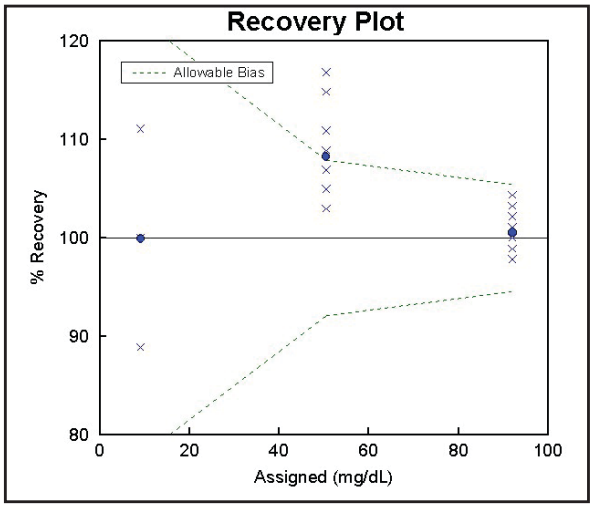


Figure 24.3. EP10 Recovery Plot

Scatter plot

A graphic indication of the degree of linearity of the data (Figure 24.2.).

Recovery plot.

A graphic display of the accuracy of the data (Figure 24.3.). There is a pair of dashed lines (envelope) centered around the 0 bias line. This indicates the amount of allowable bias at each concentration. Points outside the envelope exceed the amount of allowable bias.

Precision and Bias Table

This compares the observed precision and bias against the user-defined allowable bias and allowable CV's. If a value exceeds the allowable amount, it is flagged with an X.

Precision and Bias

	Low	Mid		High		Low	Mid		High
Assigned Values	9	50.5		92	Within-Run SDs	0.4	1.9		1.6
Grand Mean	9.0	54.7		92.6	Total SD	0.4	2.0		1.6
Bias	***0.0***	***4.2***	***x***	***0.6***	***Total CV***	***4.2***	***3.6***	***x***	***1.7***
Allowable Bias	2	4		5	Allowable CV	8	3		2

X indicates unacceptable bias or CV

Linearity, Carryover and Drift Table

This shows the amount of these three items as well as the slope and intercept. Any given value is significant (i.e. the probability of the value being outside the statistical limits <0.01) if the absolute value of the *t* value exceeds 4.6.

Linearity, Carryover, and Drift

	Intercept			Slope			% Carryover			Nonlinearity			Drift			
Run	Value	t		Value	t		Value	t		Value	t		Value	t		sy.x
All	**1.33**	**3.6**		**1.005**	**0.5**		**1.63**	**1.5**		**-0.00220**	**-4.9**	**X**	**0.17**	**1.2**		**1.09**
1	***2.20***	***11.4***	***X***	***1.004***	***0.6***		***2.77***	***4.8***	***X***	***-0.00290***	***-12.1***	***X***	***0.36***	***4.7***	***X***	***0.58***
2	***1.19***	***6.3***	***X***	***1.000***	***-0.1***		***1.56***	***2.8***		***-0.00260***	***-11.2***	***X***	***0.04***	***0.5***		***0.56***
3	***1.34***	***4.3***		***1.016***	***1.8***		***2.80***	***3.0***		***-0.00224***	***-5.8***	***X***	***0.30***	***2.4***		***0.94***
4	1.11	1.9		0.999	-0.1		-0.11	-0.1		-0.00181	-2.5		0.09	0.4		1.74
5	0.80	2.0		1.007	0.6		1.12	1.0		-0.00143	-2.9		0.06	0.4		1.18

X: ABS(t) exceeds 4.6 (probability <0.01) -- review for possible problems.

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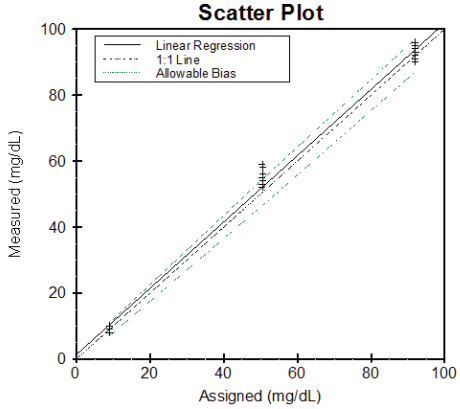
User Guide -- Data Innovations

BUN

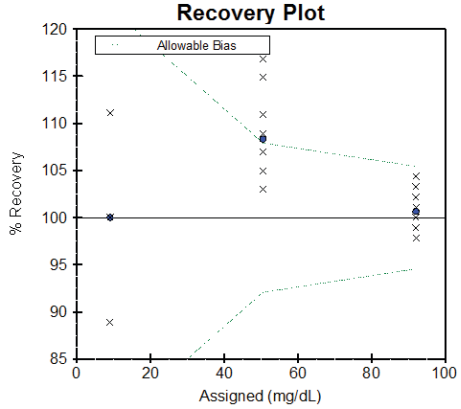
Instrument BUN ANALYZER

EP10 Preliminary Evaluation

Scatter Plot



Recovery Plot



Precision and Bias

	Low	Mid		High
Assigned Values	9	50.5		92
Grand Mean	9.0	54.7		92.6
Bias	***0.0***	***4.2***	***X***	***0.6***
Allowable Bias	2	4		5

	Low	Mid		High
Within-Run SD	0.4	1.9		1.6
Total SD	0.4	2.0		1.6
Total CV	***4.2***	***3.6***	***X***	***1.7***
Allowable CV	8	3		2

X indicates unacceptable bias or CV

Linearity, Carryover, and Drift

	Intercept			Slope			% Carryover			Nonlinearity			Drift			
Run	Value	t		Value	t		Value	t		Value	t		Value	t		sy.x
All	**1.33**	**3.6**		**1.005**	**0.5**		**1.63**	**1.5**		**-0.00220**	**-4.9**	**X**	**0.17**	**1.2**		**1.09**
1	***2.20***	***11.4***	***X***	***1.004***	***0.6***		***2.77***	***4.8***	***X***	***-0.00290***	***-12.1***	***X***	***0.36***	***4.7***	***X***	***0.58***
2	***1.19***	***6.3***	***X***	***1.000***	***-0.1***		***1.56***	***2.8***		***-0.00260***	***-11.2***	***X***	***0.04***	***0.5***		***0.56***
3	***1.34***	***4.3***		***1.016***	***1.8***		***2.80***	***3.0***		***-0.00224***	***-5.8***	***X***	***0.30***	***2.4***		***0.94***
4	1.11	1.9		0.999	-0.1		-0.11	-0.1		-0.00181	-2.5		0.09	0.4		1.74
5	0.80	2.0		1.007	0.6		1.12	1.0		-0.00143	-2.9		0.06	0.4		1.18

X: ABS(t) exceeds 4.6 (probability <0.01) -- review for possible problems.

Supporting Data

Expt Date	01 Jun 2000	Source of Pools	Controls
Analyst	RBP	Units	mg/dL
		Scale Factor	41.5
Comment			

User's Specifications

Allowable bias and CV assigned by concentration

Accepted by: _____ _____

Signature Date

Sample Data Printed: 31 Dec 2013 15:40:14 Page 1

EP Evaluator®

Users Manual -- Data Innovations

BUN

Instrument: BUN ANALYZER

EP10 Preliminary Evaluation

Results Listing

Run No.	1	2	3	4	5	
Date	26 May 2000	27 May 2000	28 May 2000	29 May 2000	30 May 2000	
00. Mid	51	51	51	51	52	
01. High	92	92	93	90	92	
02. Low	9	9	9	9	9	
03. Mid	54	54	54	54	52	
04. Mid	56	54	54	55	55	
05. Low	10	9	9	9	9	
06. Low	9	8	9	9	9	
07. High	92	91	92	92	92	
08. High	95	92	96	94	94	
09. Mid	59	56	58	52	53	
Low Mean	9.3	8.7	9.0	9.0	9.0	
Low SD	0.6	0.6	0.0	0.0	0.0	
Low CV	6.2	6.7	0.0	0.0	0.0	
Mid Mean	56.3	54.7	55.3	53.7	53.3	
Mid SD	2.5	1.2	2.3	1.5	1.5	
Mid CV	4.5	2.1	4.2	2.8	2.9	
High Mean	93.0	91.7	93.7	92.0	92.7	
High SD	1.7	0.6	2.1	2.0	1.2	
High CV	1.9	0.6	2.2	2.2	1.2	

'X' indicates an excluded run

Chapter

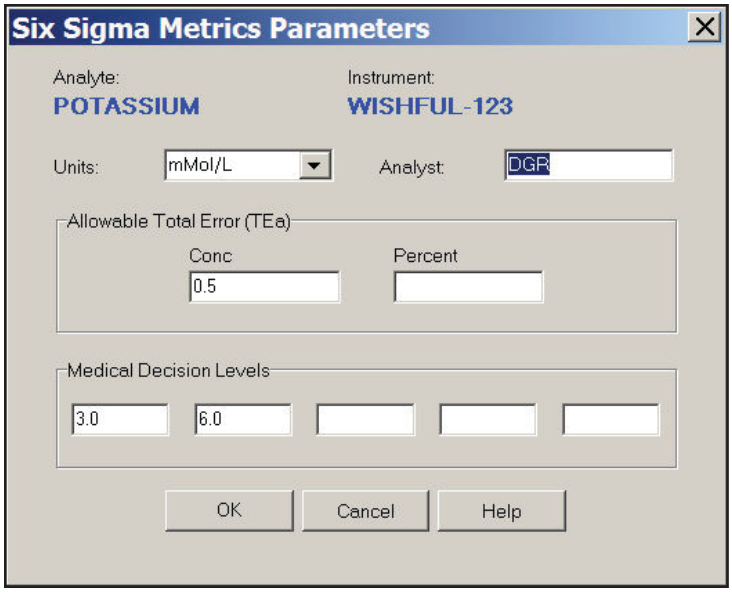
25

Six Sigma Metrics

This module calculates total analytical error (TAE) from random and systematic errors. Then it makes a judgement about whether the risk level for a given combination of random and systematic error is satisfactory or not based on comparing the total analytical error to the allowable total error. Elsewhere, the concepts are known as **"Sigma metrics."** "Sigma" is the statistician's term for "SD".

Parameter Screen

The Parameter Screen is shown at right. The unique data to be entered in this dialog box are:

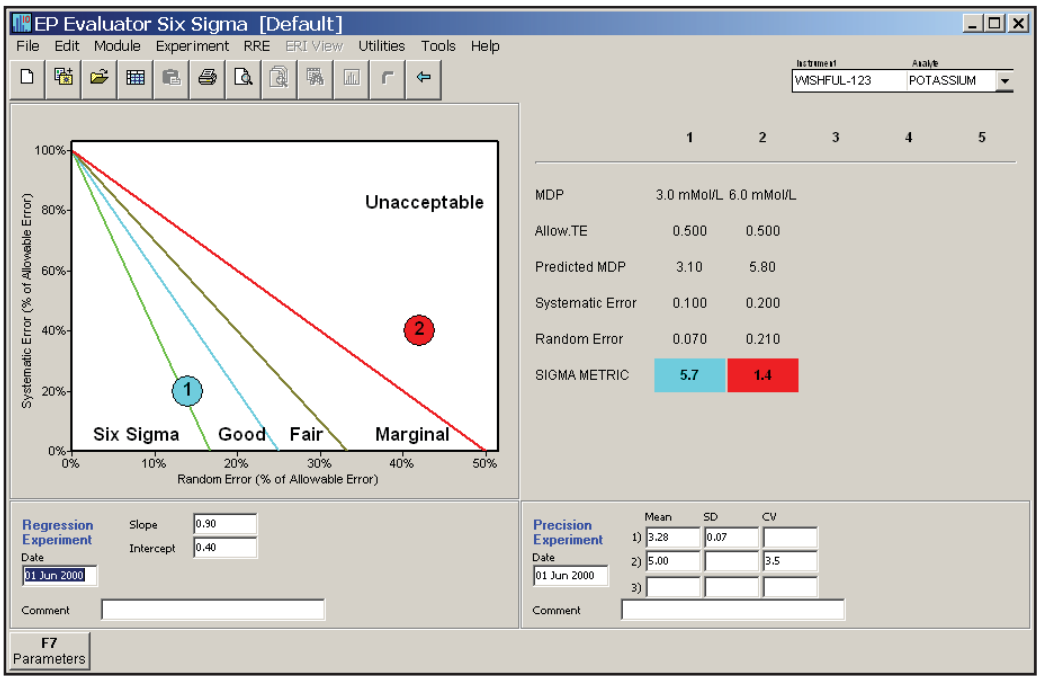


Medical Decision Points (MDP's) Up to 5.

Allowable Total Error defined as a concentration or as a percent or both. See discussion in the Rhoads (2012) *Laboratory Statistics* manual for more detail.

Experiment Detail Screen

The Experiment Detail Screen is shown below. After entry of the Regression Experiment statistics (slope and intercept) and the Precision Experiment statistics (mean, SD and CV), the points are displayed on the graphs. Note that the color of the plotted points match the color of the Random Error Factor.



Precision Experiment Statistics

These statistics are used to define a precision profile. These statistics should be an accurate representation of the random error of a method. Good sources include:

- One or more Complex Precision experiment, with two replicates per run, two runs per day for at least 20 days.

- Routine QC results for at least one month, preferably two or more.

Especially poor sources of these statistics include:

- A Simple Precision experiment calculated from results collected in one day.

The reason that precision statistics need to be collected over an extended period is that the results then reflect a more realistic value for precision than if they were collected for only a brief period. For most laboratory instruments, an SD calculated from results obtained over a period of 30 days is almost always substantially larger than one calculated from results obtained on one day.

A precision profile is calculated from the Precision Experiment data as follows:

- If precision data for one concentration has been entered, the SD or CV is assumed to apply across all concentrations. If both the SD and CV have been entered, the one that is larger at the Medical Decision Point (MDP) applies.
- If an MDP falls between two precision means, the CV's are interpolated between the two values based on the observed SD's at each. If the precision data is expressed as both a CV and an SD, the effective SD's are calculated both ways and the larger of the two is used. Outside the range of the precision means, the value calculated from the nearest precision mean applies.

Regression Experiment Statistics

There are several possible sources of the slope and intercept. The best sources are linearity experiments (as defined in Chapter 4, *Linearity and Calibration Verification*). Data from method comparison experiments are not nearly as good especially if the X method is a routine production method.

Interpretation

The graphs are based on the concepts of Six Sigma. The graph is divided into 5 sectors depending on the number of SDs that will fit into the total allowable error space left after subtracting the observed systematic error.

Six Sigma Metrics Analysis Table			
Color	**Label**	**Random Error Factor**	**Error Rate (ppm)**
Green	Six Sigma (excellent)	>6	<3
Blue	Good	4 -6	3 - 300
Yellow	Fair	3-4	300-1500
Orange	Marginal	2-3	1500 - 22,750
Red	Unacceptable	<2	>22,750

The reason that the system with the number of SDs of 3 is only marginal is that if there is a shift in systematic error of 1 SD, it would be difficult to pick it up using many QC rules. This would then result in a relatively high probability of failing proficiency testing. (Carey, 2001, unpublished)

Acknowledgment:

We thank Drs. Carl Garber, R. Neill Carey, David Koch and James O. Westgard for their leadership with respect to this issue of Six Sigma Analysis. These men have been major factors in the development of the theory and application of experimental error to the clinical laboratory for many years. We are indebted to them for their efforts.

Six Sigma Metrics Report

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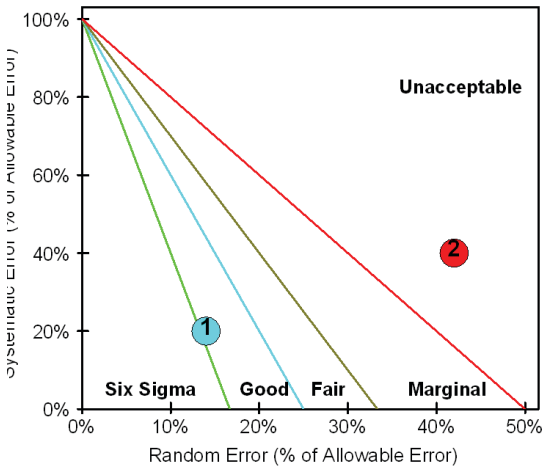
POTASSIUM
Instrument: WISHFUL-123

Six Sigma Metrics



Medical Decision Points	1	2	3	4	5
MDP	3.0 mMol/L	6.0 mMol/L			
Allowable Total Error (TEa)	0.500	0.500			
Predicted MDP	3.10	5.80			
Systematic Error	0.100	0.200			
Random Error	0.070	0.210			
SIGMA METRIC	5.7	1.4			
	Good	**Unacceptable**			

Regression Experiment

Slope:	0.90
Intercept:	0.40
Expt. Date:	01 Jun 2000

Precision Experiment

Mean	SD	CV
3.28	0.07	
5.00		3.5
Expt. Date:	01 Jun 2000	

Supporting Data

Allowable Error	0.5 mMol/L
Units	mMol/L
Analyst	DGR

Accepted by: _____ _____
Signature Date

Chapter

26

Carryover

This module is designed to determine specimen to specimen carryover. The experiment has a traditional design in which specimens with very high results are followed by specimens with very low results. If the results for the High-Low sequence are statistically identical to the results for the Low-Low sequence, then it passes the Carryover test.

Experimental Design

The design of this experiment is:

- Two specimens are prepared, one with a very high concentration and one with a very low concentration. A total of 21 samples are prepared, 11 with the low concentration, 10 with the high concentration.

  The high concentration should be such that a carryover in the range of 0.1% to 0.01% will be detected. For example, the decision point for HCG is about 5. A 0.01% carryover after a specimen with a 100,000 result (+10 units) would change a result of 2 (negative) to 12 (positive).

- While assaying these 21 samples, no other specimens or tests should be assayed in the instrument. If any other tests or specimens are run on the instrument during this experiment, the experiment is invalid.

- The 21 samples are assayed in the following order. The order is assumed by the calculations. Any other order invalidates the experiment. After the tests have been done, the results are entered into EE and the calculations performed.

  - 3 Low specimens
  - 2 High specimens
  - 1 Low specimen
  - 2 High specimens
  - 4 Low specimens
  - 2 High specimens

- 1 Low specimen
- 2 High specimens
- 1 Low specimen
- 2 High specimens
- 1 Low specimen

Key Statistics

The most important statistics are:

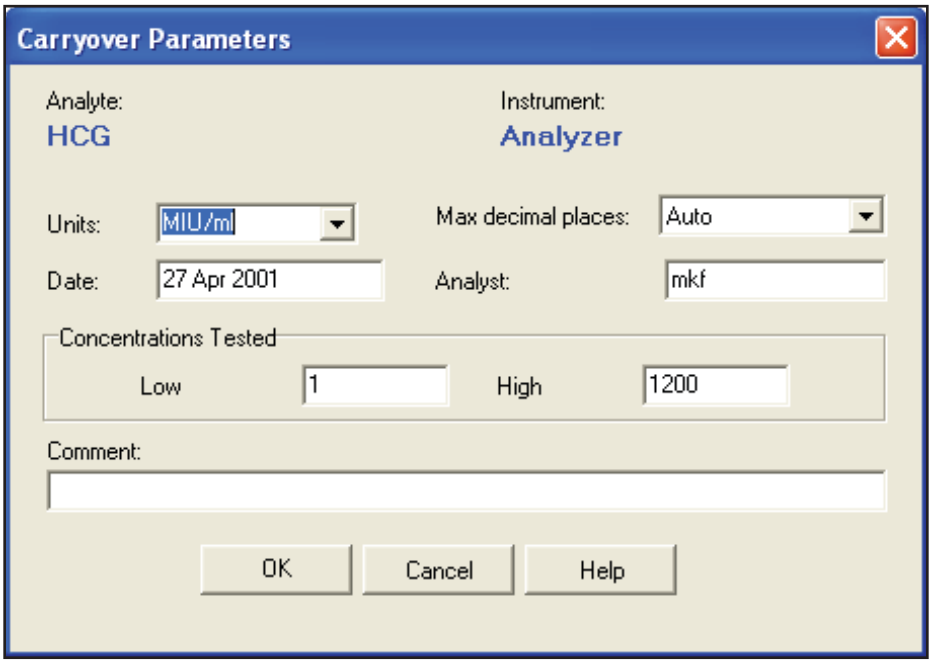
Carryover: The mean of the low results after the high-low transition less the mean of the low results after the low-low transition.

Error Limit: Three times the SD of the results after the low-low transition.

Pass: If the carryover is less than the error limit, then the experiment passes.

Parameter Screen

The Parameter Screen provides for entry of the elements which describe the experiment. These elements are listed below.



- **Units**

- **Max decimal places** is the maximum number of decimal places for reports. "Auto" means number of decimal places is determined from the data. Computed statistics (e.g., Mean) are usually printed with one more decimal place than the input results. This setting affects reports only; calculations are done on full-precision numbers.

- **Analyst**
- **Date**
- **Concentrations** of the low and high specimens.
- **Comment**. A descriptor up to 80 characters in length.

Interpretation

Interpretation is very simple. The table shown is taken from the report. Notice columns 3 and 4. These two columns represent the difference between two transitions, the low-low transition (Col. 3) and the high-low transition (Col. 4). The means and SDs of these numbers are listed at the bottom of the table.

Carryover is calculated from the difference between the High-Low and Low-Low means.

Error Limit is calculated from 3 times the Low-Low SD.

If Carryover does not exceed the Error Limit, then Passes is "Yes," otherwise it is "No."

Experimental Results

Sample	Result	Low-Low Samples	High-Low Samples
L1	0		
L2	0	0	
L3	1	1	
H1	1205		
H2	1210		
L4	1		1
H3	1201		
H4	1218		
L5	2		2
L6	0	0	
L7	0	0	
L8	1	1	
H5	1224		
H6	1204		
L9	1		1
H7	1221		
H8	1218		
L10	0		0
H9	1209		
H10	1217		
L11	0		0
Mean		**0.4**	**0.8**
SD		**0.5**	**0.8**

Carryover Report

This report has several components. All have been discussed above or are self-explanatory.

Acknowledgment

We are indebted to **Loretta Stanley** of Holmes First Regional Medical Center in Melbourne, FL for providing us with the algorithm for this statistical module.

Carryover Report (page 1)

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HCG
Instrument: Analyzer

Carryover

Carryover Analysis			
High-Low Mean	0.8	Error Limit	1.6
Low-Low Mean	0.4	Passes?	Yes
Carryover	0.4		

Experimental Results

Sample	Result	Low-Low Results	High-Low Results
L1	0		
L2	0	0	
L3	1	1	
H1	1205		
H2	1210		
L4	1		1
H3	1201		
H4	1218		
L5	2		2
L6	0	0	
L7	0	0	
L8	1	1	
H5	1224		
H6	1204		
L9	1		1
H7	1221		
H8	1218		
L10	0		0
H9	1209		
H10	1217		
L11	0		0
Mean		**0.4**	**0.8**
SD		**0.5**	**0.8**

Supporting Data

Units:	MIU/ml
Analyst:	mkf
Expt. Date:	27 Apr 2001
Low Conc:	1
High Conc:	1200
Comment:	

Accepted by: _____ _____
Signature Date

Chapter

27

Performance Standards

Performance Standards (PS) for many labs are an under-appreciated element in the practice of Clinical Laboratory Medicine. They define the quality of the results that are produced. Performance Standards are expressed in this industry in terms of Allowable Error as applied to instrument performance. This issue is discussed at length in Chapter 6, *Defining Performance Standards*, in our book Lab Statistics, Fun and Easy (LSFE).

PS is a synonym for Total Allowable Error (TEa). We prefer to use the term PS in non-technical environments because PS is easily understood by people without technical backgrounds such as vice presidents and many lab directors. Furthermore, TEa is a highly technical term with negative connotations.

The approach taken in this module to calculate TEa is identified in LSFE as the Approach for Established Methods. We expect this to be useful except on those relatively infrequent occasions (for most labs) when a lab is introducing a "homebrew" method.

There are three sources of statistics used with the Approach for Established Methods are:

- **Medical Requirements.** Performance. The source of medical requirements used by most labs will be the national medical requirements coming from working groups at NIH. Presently (October, 2007), there are values established for 5 analytes, namely four lipids and creatinine. Some academic institutions have established their own medical requirements.

- **Regulatory Requirements** such as the CLIA '88 Proficiency Testing (PT) limits in the United States. Other jurisdictions or regulatory agencies have also established requirements.

- **Achievable Requirements** which is based on the actual performance of clinical laboratory methods in the field. In general, TEa's can be easily calculated from PT Survey results. Furthermore these values are generally available for almost all the tests routinely performed in most hospital laboratories.

Several things to note:

- In most cases, values are available from only a limited number of these sources.
- The fundamental purpose is to obtain a TEa which is both **achievable and defensible**. It is counter-productive to use a TEa which is either too large or too small.
- For most analytes, there is no single correct TEa. In fact, it can be anywhere in a range of values.
- In many cases, two numbers need to be calculated, for both higher and lower concentrations. The higher number is expressed as a percent of concentration while the lower number is expressed as a concentration. (See the discussion of Precision and Error Profiles in LSFE for details.)

Parameter Screen

Enter one or more of the items into the Parameter Screen (Figure 27.1.) It is important to realize that for many analytes, data will be present for only one or two of these categories.

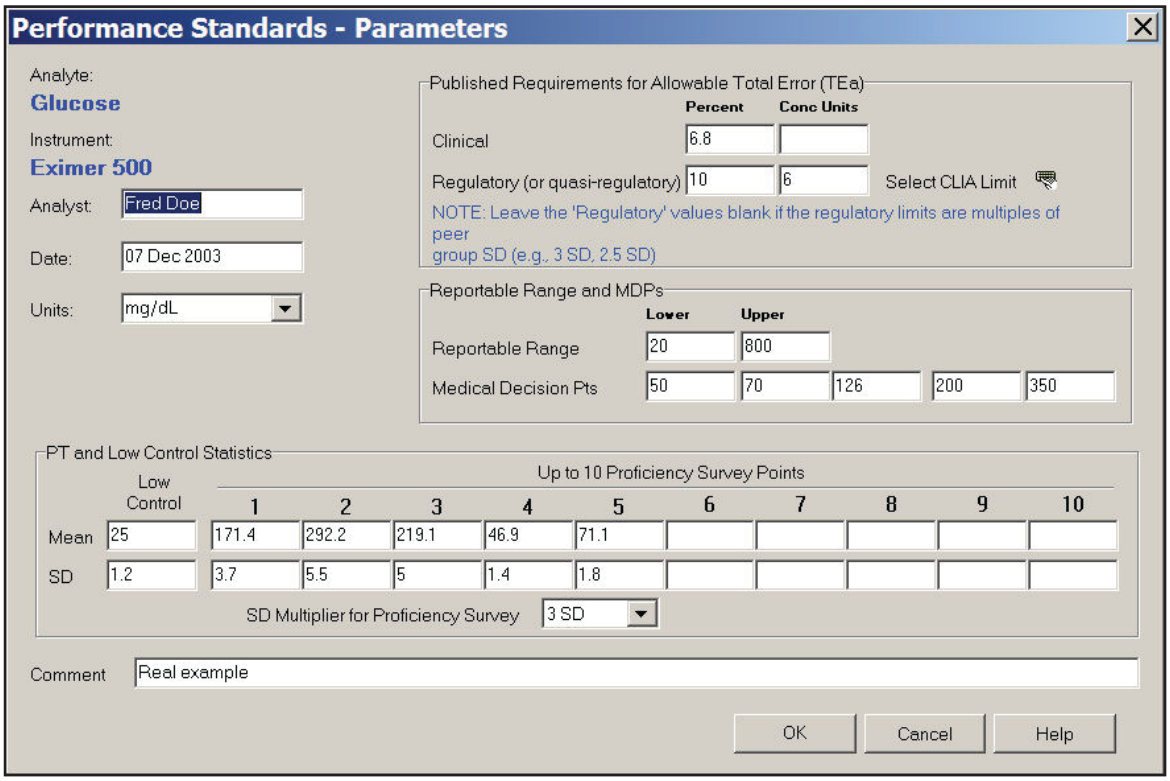


Figure 27.1. Performance Standards Parameter Screen

The fields unique to Performance Standards in this module are:

- Published requirements for Allowable Total Error.
  - **Clinical**: Here is where medical requirements are entered. There are several sources. Nationally established medical requirements exist, now for 5 analytes. If your institution has established its own medical requirements, enter them here.

  - **Regulatory**: If the test is subject to regulatory requirements, those values go here. Click on the little button to the right of this field to get the CLIA '88 PT limits.

- Enter the **reportable range** (required field).

- Enter **medical decision points** if any.

- Enter up to 10 results from two or more recent proficiency testing surveys. We recommend that you use a minimum of six results (two specimens per survey), nine results (three specimens per survey) or ten results (five specimens per survey).

- **For low concentrations**: Enter the SD and its associated mean for a specimen assayed at a low concentration.

  The calculated SD will be 3 * (the entered SD). Often there will be no data available for this point. As long as the value you select is clinically insignificant, you can enter whatever value you choose. Keep in mind the process: namely that your entered SD is tripled to give you the low end TEa. Then that value is multiplied by your systematic error budget (25 - 50%) to get the allowable systematic error which you will need for the linearity module.

- Select the Number of SDs required for Proficiency Surveys. This references the PT requirement specified for some analytes of a PT limit based on the observed results for a given method. This PT requirement usually is 3 SDs, but may in some cases be 2 or 2.5. Unless you have a good reason to do otherwise, select 3 SD. One good reason to select 2 or 2.5 is that the resulting TEa calculated using 3 SDs is too large (i.e. over 30%).

Interpretation

The data are all entered into the Parameter Screen (Figure 27.1.) and then calculations are performed. The results are displayed in four ways. These ways are:

Allowable total error is calculated for each contributing approach for which data has been entered. The percent value is calculated for each approach. The concentration for the Peer Group approach is calculated from the Low Specimen.

Based on Approach	Allowable Total Error is the greater of: Percent	Concentration
Clinical Requirements	6.8%	--
Regulatry (or quasi-regulatory) Limit	10%	6 mg/dL
Peer Group SD-Based	6.4% 3 x Peer CV	3.6 mg/dL 3 x Low Ctrl SD

Allowable total error concentrations, for each medical decision point;

MDP Analysis

MDP	TEa Range Lowest	Highest	CLIA
50 mg/dL	3.40 mg/dL	6.00 mg/dL	6.00 mg/dL
70	4.76	7.00	7.00
126	8.57	12.60	12.60
200	13.60	20.00	20.00
350	23.80	35.00	35.00

Reportable Range: 20 to 800 mg/dL

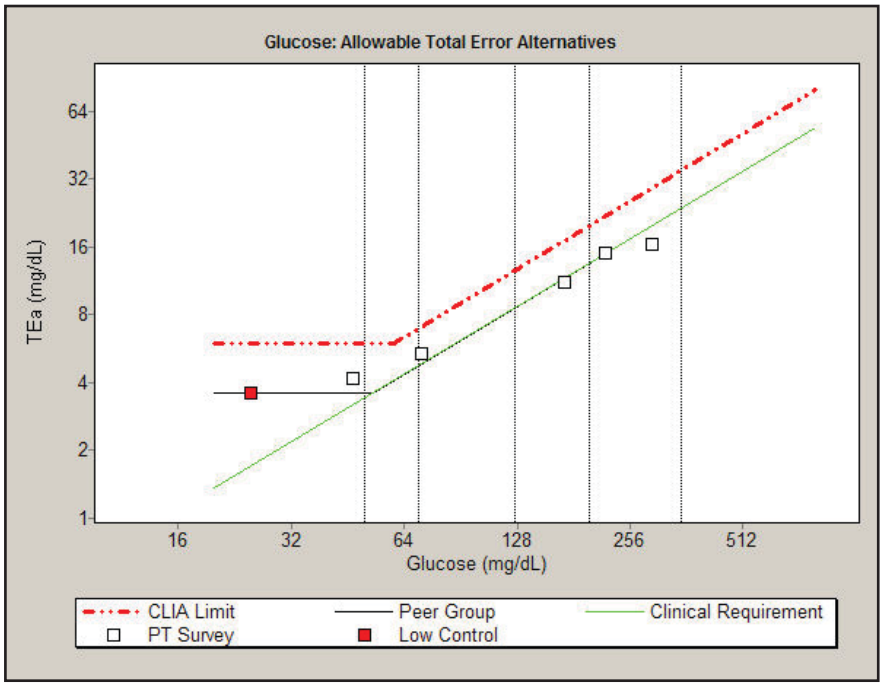
Supporting data (i.e. the PT Survey results) which is a listing of the Proficiency Testing means, SD's and CV's.

Supporting Data

	Low Conntrol	PT Survey 1	2	3	4	5
Mean	25	46.9	71.1	125.6	171.4	219.1
SD	1.2	1.4	1.8	2.2	3.7	5
CV (%)	4.8	3.0	2.5	1.8	2.2	2.3

	6	7	8
Mean	292.2	385.2	486.2
SD	5.5	8.1	10.4
CV (%)	1.9	2.1	2.1

A graph showing the relationships of the various values. For interpretation, note the following:



- The vertical lines represent the medical decision points.
- A higher location on one of these vertical lines indicates more error than a lower location.
- The diagonal lines on the right correspond to error expressed in percent terms, the horizontal lines on the left correspond to error expressed in concentration terms.

Your decision is to decide which TEa to use. Keep in mind that there is no single correct TEa. In fact, any value in an appropriate range can be selected. That said, whatever value you choose must be achievable and defensible.

- Your TEa cannot exceed one specified by Regulatory Requirements.
- The TEa defined by Peer Group Survey results is definitely achievable.
- However if a Clinical Requirements TEa is available, we recommend that you choose that value. That value will most definitely be defensible and more than likely will be achievable.

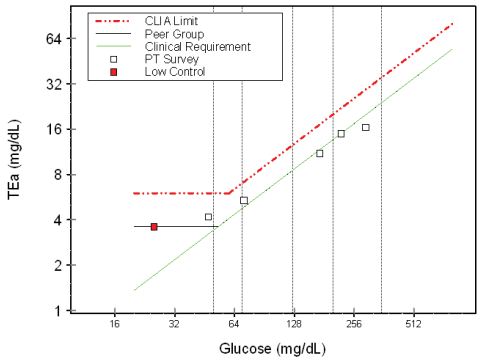
Performance Standards Report

EP Evaluator®
Users Manual -- Data Innovations

Glucose
Instrument: Eximer 500

Allowable Total Error Alternatives

Based on Approach	Allowable Total Error is the greater of: Percent	Concentration
Clinical Requirements	6.8%	–
Regulatory (or quasi-regulatory) Limit	10%	6 mg/dL
Peer Group SD-Based	6.8% 3 x PeerCV	3.6 mg/dL 3 x Low Ctrl SD



Allowable Total Error Range (mg/dL)			
MDP	Lowest	Highest	Regulatory
50	3.40	6.00	6.00
70	4.76	7.00	7.00
126	8.57	12.60	12.60
200	13.60	20.00	20.00
350	23.80	35.00	35.00

Reportable Range: 20 to 800 mg/dL

Note: Both axes of the graph are shown on a logarithmic scale.

Peer Group Statistics

	Low Control	Peer Group Statistics from PT Survey 1	2	3	4	5
Mean	25	46.9	71.1	171.4	219.1	292.2
SD	1.2	1.4	1.8	3.7	5	5.5
CV (%)	4.8	3.0	2.5	2.2	2.3	1.9
	6	**7**	**8**	**9**	**10**	
Mean	--	--	--	--	--	
SD	--	--	--	--	--	
CV (%)	--	--	--	--	--	

Supporting Data

Reportable Range: 20 to 800 mg/dL
SD Multiple: 3 SD
Analyst: Fred Doe
Date: 07 Dec 2003
Comment: Real example

Accepted by: _____ _____
Signature Date

Chapter

28

Average of Normals

Average of Normals (AON) is a method of patient-based Quality Control. Its purpose is to detect shifts in the analytical process by monitoring trends in reported patient results. AON is most useful when data is collected regularly (every week or every month), and for relatively high-volume tests (50+ samples per day).

The Traditional AON Procedure

The traditional implementation of AON, as originally described by Hoffman and Wald in 1965, is as follows:

- Patient results are acquired in some approximation of real time. Results that fall outside a user-defined "truncation range" are discarded; the remaining results are averaged. The truncation range is often set to the normal range, hence the name Average of Normals.
- When a predetermined number of normal patients has been collected, the average is compared to previously established control limits. If the average is within these limits, the process is considered to be in control.
- AON makes the fundamental assumption that the patient population does not vary over time.

The EP Evaluator Procedure

The EP Evaluator implementation differs from the traditional implementation in that:

- Data is not collected in real time. Results are extracted from the LIS at regular time intervals and analyzed retrospectively. In this context, calenderized charts and reports are more readable than are reports for constant-size blocks of patients.
- Medians are used instead of averages. This makes it unnecessary for the user to define a truncation range, since extremely high or low results (outliers) have very little effect on the median.

- Control limits are set from (computed) intra-day variation in the data, rather than being predefined by the user. The user may define a target value, but the program sets the width of the Control Limits around that target.

Each point on the control chart represents the median of one calendar day of patient results. 3-sigma Control Limits are shown on the chart. A point above or below the Control Limit lines indicates that the process is out of control. Light gray bars at the bottom of the chart show the daily patient volume on which the medians are based.

Overview of the Operating Procedure

1 Periodically, extract all patient results from the LIS.

No results are typed into the AON module—data may be entered only by importing files (or perhaps by pasting, but usually file import is more convenient). Raw input is all patient results. The import process reduces the raw input to daily summary statistics. Only the summary statistics are stored in EE.

The import file contains the standard information that one usually finds in an LIS extract: Analyte, Date, and Test Result, one result per line. Multiple analytes can either be mixed in the same file or put in separate files. The format is described in detail in the document LIS Export File Formats which may be found in the EE Resources folder (see Appendix B, *EP Evaluator Resources* for additional details).

The reason file import is usually more convenient than pasting is that you might easily have too many results to fit in Excel. Also, each analyte must be pasted separately. There is a Paste example in the PasteModOview.xls file in the EE11\Resources directory.

2 Use the **AON Data Manager** to load the LIS extract into EE.

Data Manager will create experiments if they don't exist, or update them if they do exist. Thus no separate "Create Experiment" step is necessary.

3 Re-calculate all analytes using the **Module/Recalc All** menu command.

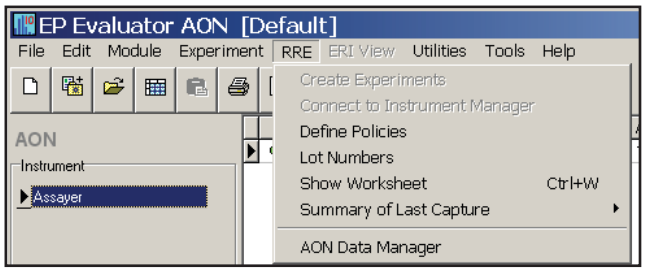
4 Check for Out-Of-Limit Flags.

Analytes for which an out-of-limit condition occurred during the latest 30 days are identified by red icons on the Module Overview Screen. Double-click an analyte name to review its results in detail.

AON Data Manager

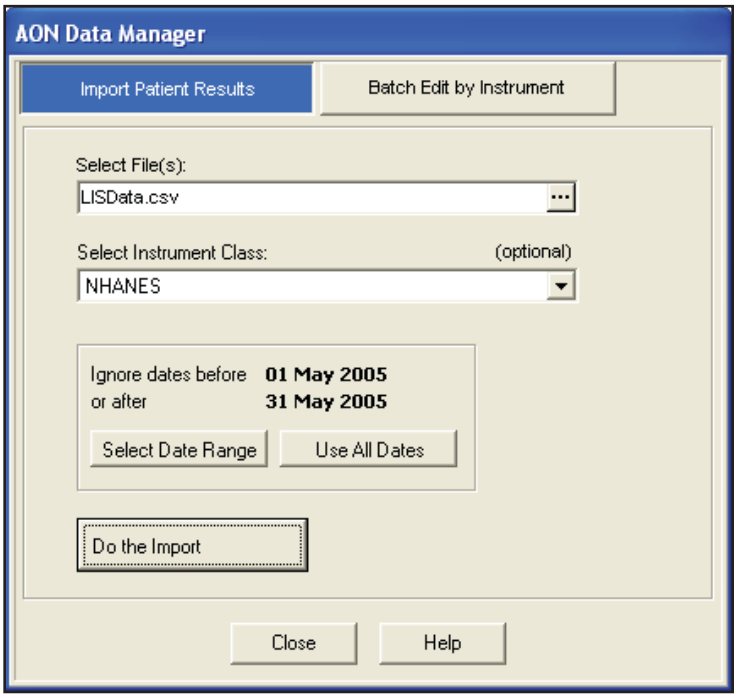
To start AON Data Manager**,** first open the AON module. Then select AON Data Manager from the RRE Menu.

AON Data Manager performs two functions:



- Importing data extracted from your LIS, either to create new experiments or to update existing ones.
- Batch-editing AON experiments—for example, to set a target period for a complete instrument at once, or to delete old data.

Import Patient Results



Select File(s): Click the dots on the right to select the file (or files) to import. This takes you to a popup screen where you both choose a file name and give some information about its format (see *Defining the Import File Layout*).

Select Instrument Class: If you select an instrument class, EE can set up the units and weekend exclusion option when it creates a new experiment. Otherwise you will have to manually edit each experiment to supply the units. This option is available only if you have defined Policies (see Chapter 37, *Policy Definition*.)

The instrument class setting has no effect when you update experiments, only when you create them. The time to define AON policies is before your first use of AON.

Date Range: You might select a specific date range to prevent a "short" day at the end of the data. EE cannot sum two days from separate imports. It can only replace old data with new data.

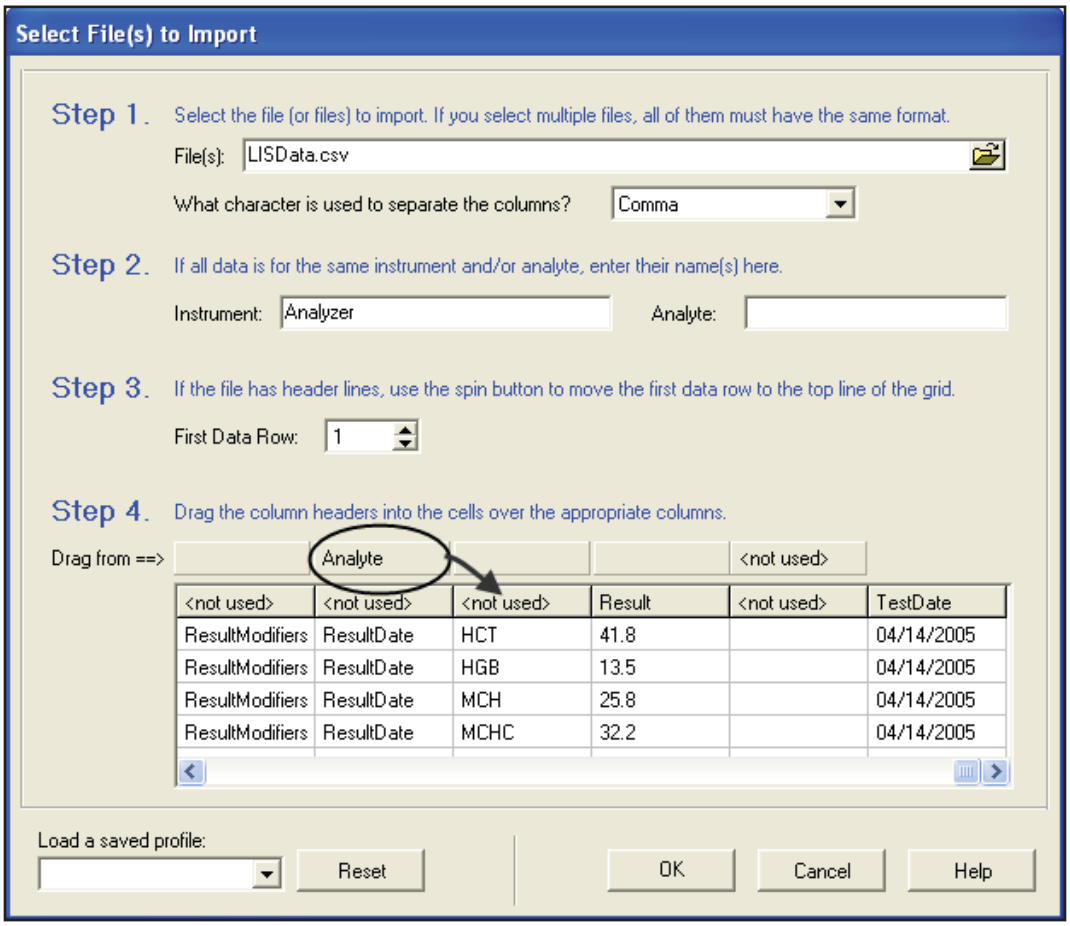
Do the Import: Reads the file, condenses it to daily summary statistics, and stores the summary in the AON database. If you did not supply instrument and analyte names when defining the file layout, the program prompts you for them as needed. Suppose, for example, you are importing multiple files that do not contain analyte names. The program will ask for the analyte name as it reads each file.

EE will update existing experiments by adding days that are not already its database. It will replace a day only if the number of patients in the new data is greater than the number of patients in the existing record.

After completion of the import you may either select another file to import or **Close** AON Data Manager and return to the Module Overview Screen.

Immediately after completing an import session, use the **Module/Recalc All** menu command to update the AON summary statistics on the Module Overview Screen. They show at a glance which analytes need closer review (see the section *Module Overview Screen* in this chapter).

Defining the Import File Layout



Step 1. Select one or more files to import. You can't type a file name—click the folder icon to the right of the field to pick files from a directory list. You can select more than one file as long as they are in the same format. For example, if your LIS produces a separate file for each analyte, you can import all of them at once.

Once you select a file, the first few lines are displayed in the grid at the bottom of the screen. If everything shows up in the first column, use **What character is used to separate the columns?** to change the column separator.

Step 2. Usually all the data is for the same instrument, and the instrument name is not a field in the file. In this case, type the instrument name in the **Instrument** box.

Enter the analyte name in the **Analyte** box only if the entire file is for the same analyte, and the analyte name is not a field in the file. Otherwise leave the Analyte box blank.

Step 3. If there are headers at the top of the file, adjust **First Data Row** so the first line of data you want to import is at the top of the grid.

Step 4. This is where you define the contents of the columns. Drag the headers into the gray blocks above the data in the grid. Your LIS extract may have extra columns in it (like the text fields on the left side of the example screen). A "<not used>" header over a column means EE will ignore that column.

If you make a mistake, you can drag a title out of the grid—either into a different column, or to a blank area of the form (to remove it altogether).

When the file format is defined, select **OK** to return to the main Data Manager screen.

Using Profiles

When you select **OK**, the program asks whether you want to save the file definition for future use. If you want to save it, you are asked for a name and description. In the future, you can use the **Load a saved profile** combo box at the lower left of the screen to recall the saved profile.

It is not necessary to create a profile if your data format is always the same. The program automatically remembers the settings you last used.

Use the **Reset** button to remove the current settings and start the definition over from a scratch.

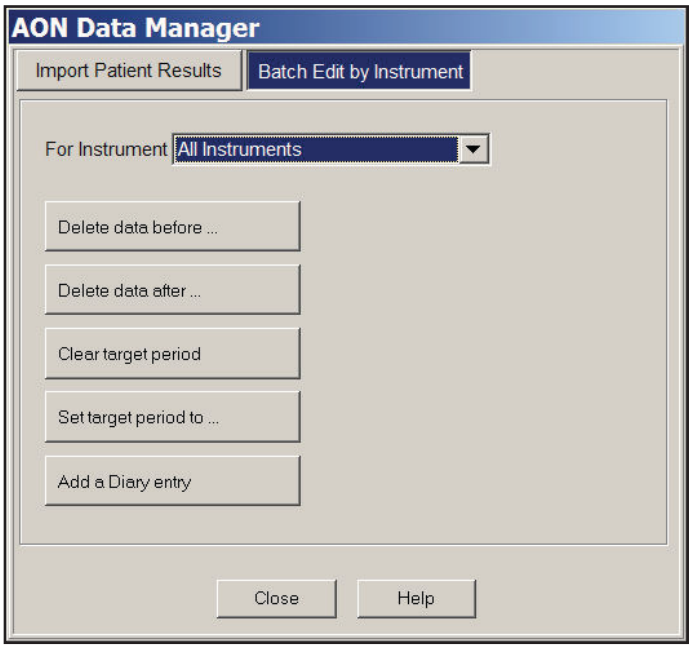
Batch Edit by Instrument

The second page of AON Data Manager lets you apply edits to all analytes within an instrument with a single command. You might want to do this if:

- You import a week's results for 30 analytes. Then you realize the data was faulty, and you need to delete it.
- You accidentally imported partial results for the last day, and need to delete that one day.
- You want to remove "ancient history."
- You want to mark a specific date on the charts for all analytes.
- You want to define a target period for an entire instrument.

Without batch edit capability, you would have to edit the analytes one at a time to make these changes.

The Batch Edit screen is quite straight-forward:



For Instrument selects whether edits apply to all instruments or to one specific instrument.

Delete data before removes data earlier than a date you specify. You might want to do this every 6-12 months to keep the chart display readable.

Delete data after removes data later than a date you specify. You might want to do this if you captured incorrect data due to a problem in the file extracted from the LIS.

Set target period defines start and end dates that determine target values for the chart.

Add a Diary entry creates an event marker on the charts.

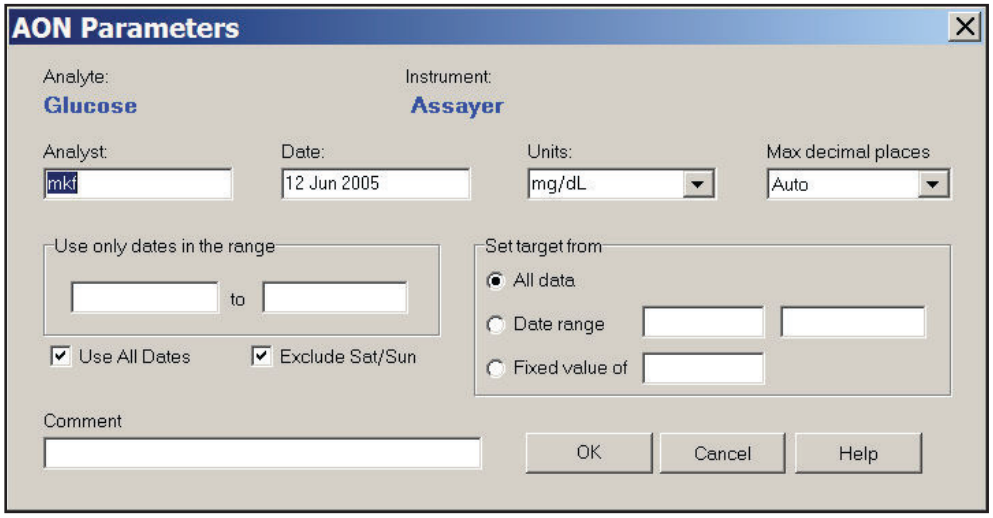
Parameter Screen

You will see the Parameter Screen in two situations:

- You created a new experiment through AON Data Manager with no Policy definition. When you try to open the experiment, EE will tell you that you can't calculate until you define required parameters. You must go to the Parameters Screen and enter Units before you can see any statistics.

- You ask for it from the Experiment Detail Screen.

Fields on the Parameter Screen are described below.



Analyst, Date, and Units, Max decimal places, Comment: As usual.

Use only dates in the range: If you enter a start and end date, analysis will be performed only on dates in that range. Blank start date means earliest available date; blank end date means latest available date.

If you have several months of data, the chart may begin to look cramped. You might set a date range to see only the latest month.

Use All Dates: Checking this box clears the "Use only dates in the range" fields so analysis is performed on all dates.

Exclude Sat/Sun: Checking this box excludes data for Saturdays and Sundays. Weekends often have an atypical patient mix. In most cases you should exclude them.

Set Target From: A "Target Value" is the center line for the control chart. This setting defines how the target value is determined. Choices are:

- All Data - target is the median of the daily medians (the default).
- Date Range - target is the median of daily medians in a specified time span. Enter the start and end dates.
- Fixed Value - target is a fixed value. This option is available, but it is unlikely that you know where to set a target value for patient medians. Unlike QC materials, patients don't come with a Package Insert attached.

Module Overview Screen

AON Interpretation starts at the Module Overview screen (Figure 28.1), before you even look at a report. Scenario: You just ran AON Data Manager to capture results for the latest week, and did **Recalc All** to update experiment status on the Module Overview Screen.

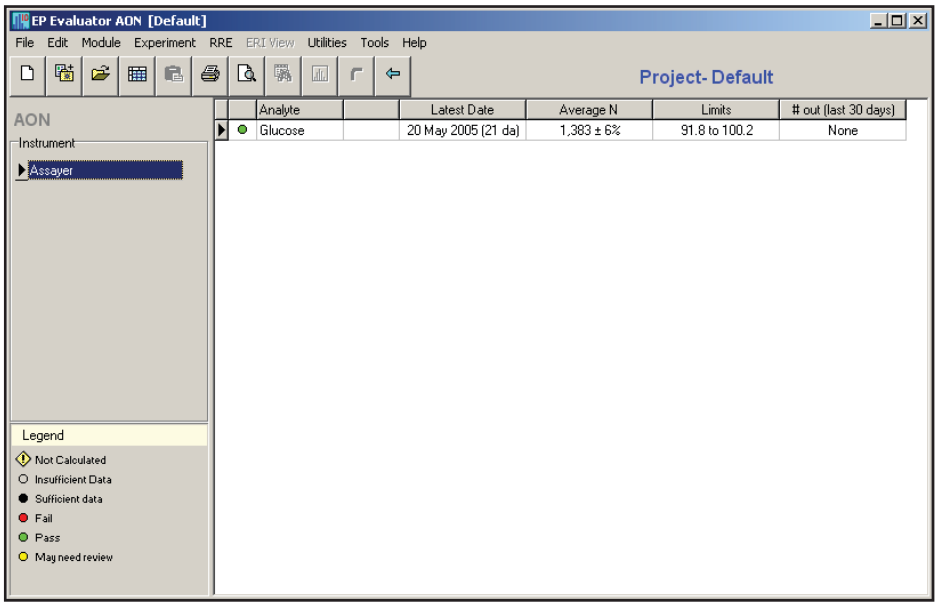


Figure 28.1 AON Module Overview Screen

- Analytes with green circles in the status column have been within control limits for the last 30 days.

- Analytes with red circles were out of control on at least one of the last 30 days. You need to review these analytes in more detail.

- Analytes with white circles have a data problem—control limits for these analytes are shown on the chart but are probably too wide to be useful. White circles mean that either the average number of patients per day is less than 20, or the CV of patients per day is greater than 25%. Sometimes the CV is high because you forgot to exclude weekends. Another possibility is that you captured only a partial day's worth of data on the last day.

For example, the example shows that HDLB has a high CV. Scanning through the day counts, you see that HDLB has 6 days of data. The other analytes have only 5 days. Data for the 6th day is probably incomplete.

Experiment Detail Screen

There are a few unique things about the AON Experiment Detail Screen. The most obvious is that you can't edit the data, nor can you exclude points. You can delete, but only the first or last day in the dataset. You can't delete an interior day. The most likely scenario is that you need to delete the last day—because you accidentally captured only a handful of patients on that day.

There are two check boxes above the graph:

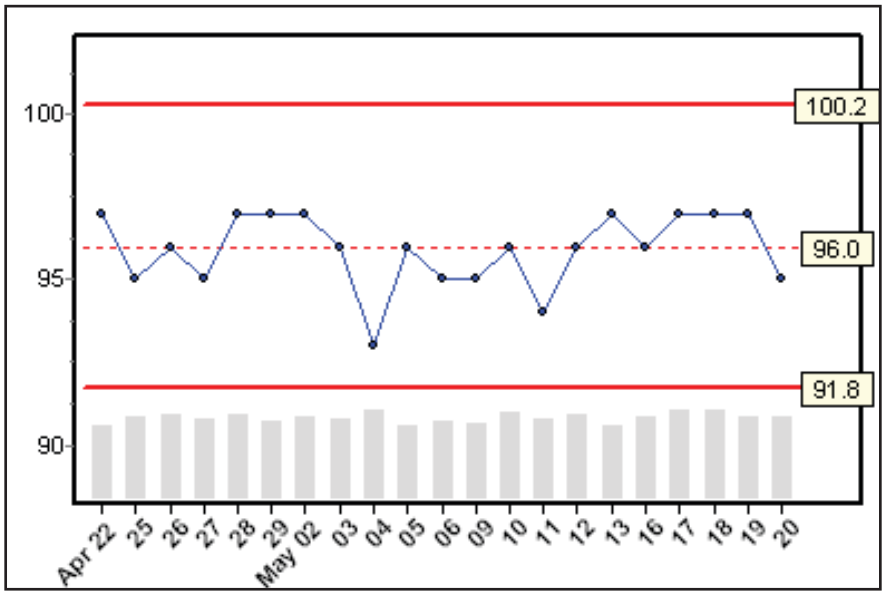
- The **Legend** box shows or hides the legend. (The chart is rather wide, and the legend takes up quite a bit of space.) This setting affects only the screen display. The printed report always includes the legend.

- The **Cursor** box enables a vertical line that makes it easier to match a plot point with a date on the X axis.

The central element of the screen is the Control Chart and the statistics below it. They are discussed in the Interpretation section below.

Interpretation

If you don't try to "over-analyze" the report, interpretation is very simple. The most important thing on the report is the Control Chart. The points (circles) are the daily medians of patient results. The dashed line in the middle is the target. The solid lines are the control limits. You want the points to remain inside the control limits. That's all there is to it.



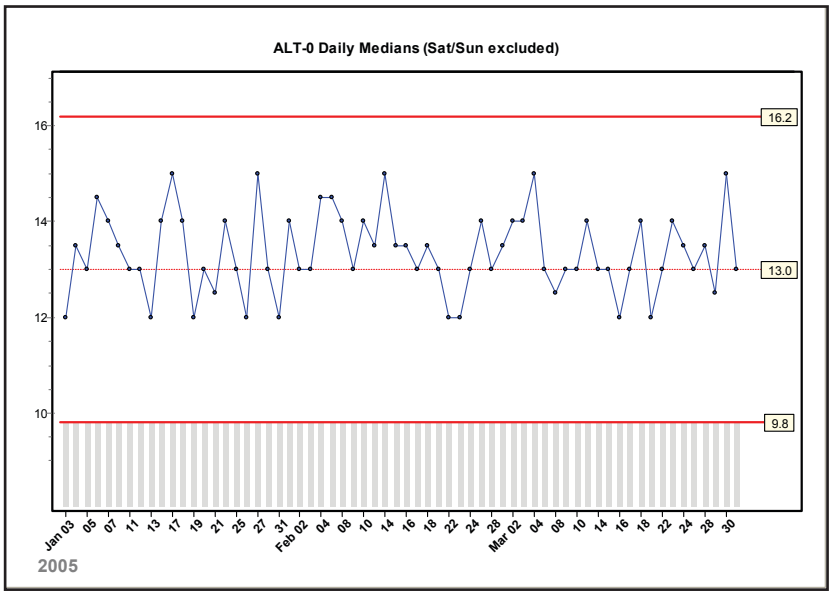
Two more comments about the chart:

- The bars below it represent the number of patients on each day.
- The control lines are usually red. Yellow control lines means either the average patients per day is small or its CV is large. The control limit range may be too wide to be useful. If you print a report with yellow control lines, it will be stamped PRELIMINARY.

Before spending any more time on statistics, let's look at some case studies.

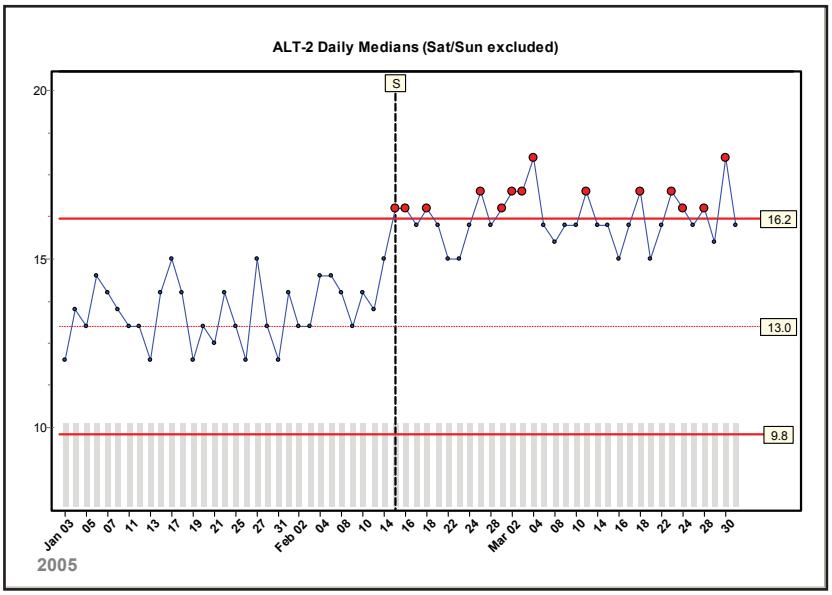
In Control Case

This chart shows data for ALT. Here is what it looks like when the process is in control. The entire chart is within its control limits, and it fluctuates randomly up and down around the target line.



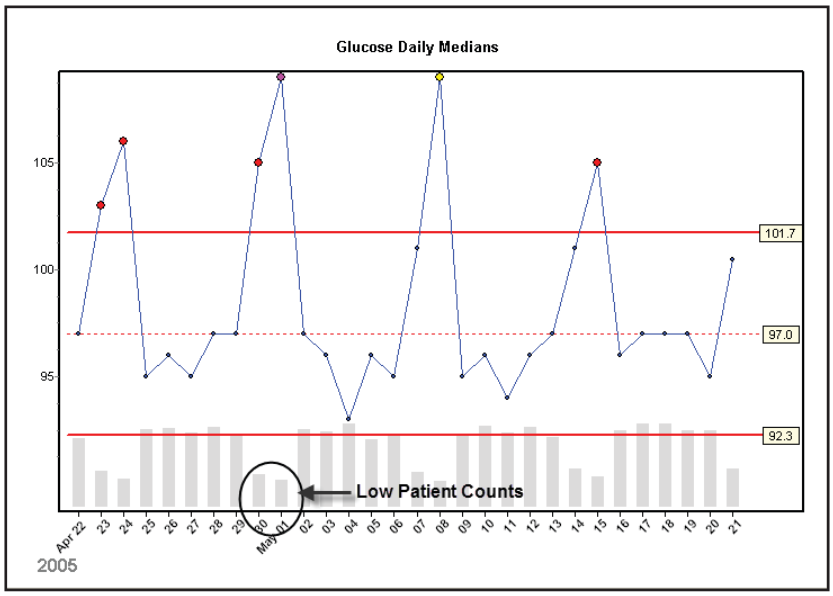
Shifted Case

This is the same data as the In Control case above except that, starting on February 15, every patient's ALT result is increased by 3 U/L. Much of the data is now above the upper control limit. (Note that the target for this example was set based on January data only).



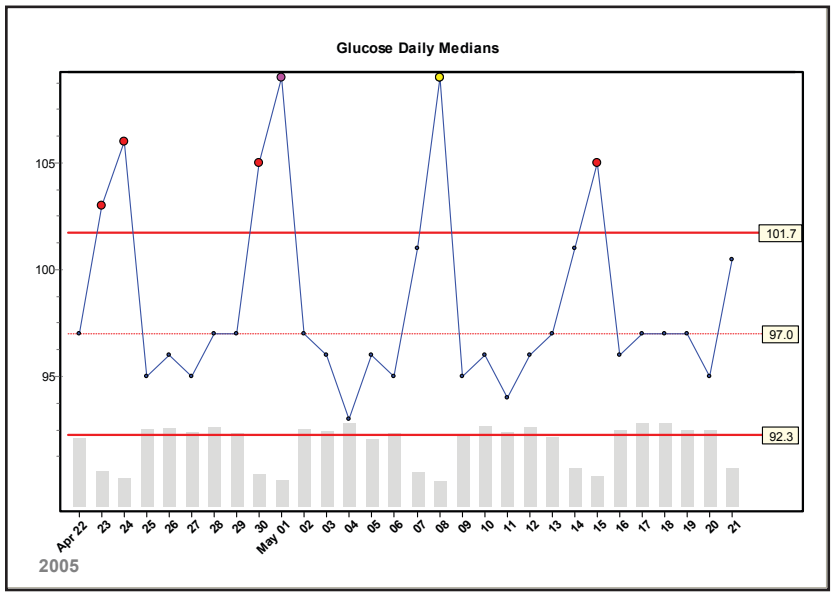
The Weekend Effect

Here is a 1-month chart for Glucose. This is real data from a large regional medical center.



Notice that the days where the chart is above the upper control limits occur in a regular cyclical pattern. They are also days where the patient count is unusually low. All of these days are Saturdays and Sundays. A chart can be out of control for two reasons: 1) the measurement process is out of control, or 2) the mix of patients on which the measurements are made is not the same as it is on most days. In this example, the patient mix seems to be different on weekends.

Here is what the same data looks like with weekends excluded.



What size shift can AON detect?

A fundamental rule when using control charts to detect shifts in the mean—either in AON or in ordinary QC—is that you can't reliably detect a shift that is "small" relative to the typical random variation of the process. For example, if your process CV is 10%, you can't expect QC to detect a 5% shift in the mean. That 5% shift is indistinguishable from the background noise.

The **SD of the Median** statistic shown on the AON report measures the background noise present in AON. So don't expect the control chart to detect smaller than SD of the Median.

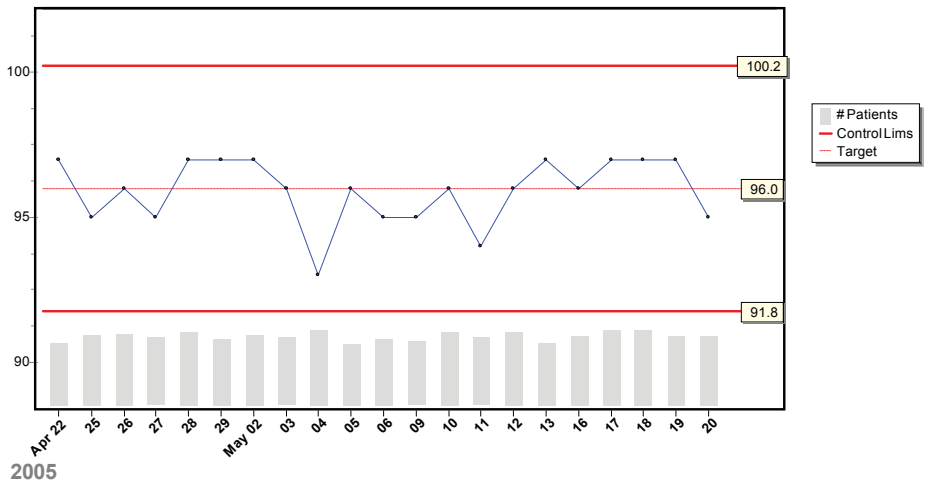
Average of Normals Report

EP Evaluator®
Users Manual -- Data Innovations

Glucose
Instrument: Assayer

Average of Normals

Glucose Daily Medians (Sat/Sun excluded)



Evaluation of Results

Average of Normals analysis was performed for Glucose on Assayer for medians of all daily patient results over the period 22 Apr 2005 to 21 May 2005. Weekends were excluded from analysis. Each plot point represents the median of one day's patient results, with an average of 1,383 patients per day. The target value is the median of all daily medians. 3 SD control limits around the target (91.8 to 100.2 mg/dL) were determined from the intra-day population variance. The test PASSED. None of the latest 30 fell outside the control limits.

Experiment Statistics

Target Value:	96.0 mg/dL
from	Median of all daily medians
Control Limits:	91.8 to 100.2 mg/dL
# Out-of-Limit Days:	None
Total # Pt Results:	29,036
Average Results/Day:	1,383 ± 6%
Robust Population SD:	42.0 mg/dL or 40.1%
SD of Daily Median:	1.4 or 1.5%

Supporting Data

Date Range:	22 Apr 2005 to 21 May 2005
Weekends excluded?	Yes
Analyst:	mkf
Units:	mg/dL
Expt. Date:	12 Jun 2005
Comment:	

Accepted by: _____ _____
Signature Date

Default Printed: 24 Mar 2011 10:20:13 Page 1

EP Evaluator®

User Manual -- Data Innovations, LLC

Glucose

Instrument Assayer

Average of Normals

Daily Medians

*	Date	# Patient Results	Median Value	%CV of Median
	22 Apr 2005	1,239	97	1.4
X	23 Apr 2005	653	103	2.0
X	24 Apr 2005	516	106	2.2
	25 Apr 2005	1,414	95	1.2
	26 Apr 2005	1,433	96	1.4
	27 Apr 2005	1,355	95	1.2
	28 Apr 2005	1,452	97	1.4
	29 Apr 2005	1,326	97	1.4
X	30 Apr 2005	588	105	2.0
X	01 May 2005	492	110	2.6
	02 May 2005	1,417	97	1.4
	03 May 2005	1,361	96	1.3
	04 May 2005	1,512	93	1.4
	05 May 2005	1,236	96	1.5
	06 May 2005	1,320	95	1.3
X	07 May 2005	643	101	2.1
X	08 May 2005	478	110	2.3
	09 May 2005	1,285	95	1.4
	10 May 2005	1,464	96	1.3
	11 May 2005	1,344	94	1.4
	12 May 2005	1,449	96	1.3
	13 May 2005	1,260	97	1.5
X	14 May 2005	695	101	2.0
X	15 May 2005	544	105	2.3
	16 May 2005	1,386	96	1.3
	17 May 2005	1,503	97	1.3
	18 May 2005	1,508	97	1.2
	19 May 2005	1,383	97	1.4
	20 May 2005	1,389	95	1.4
X	21 May 2005	694	101	1.8

x: Excluded L: Below limits H: Above limits N: Unusual N Limits: 91.8 to 100.2 mg/dL

Chapter

29

Interference

The CLSI:EP7 document deals with two issues, the first to determine whether interference exists, the second to determine the maximum concentration of interfering material can be present without causing a clinically significant change in the assayed result. This module was originally written to deal with the second part. However it has been modified to also deal with the first issue, but not exactly as described in CLSI:EP7.

The design of the experiment is the same in both cases. The difference lies in the calculations done. Control which calculations are done are specified in the Parameter Screen (Paired Difference -> Existence of Interference; Dose-Response -> Degree of Interference).

Experimental Design

The design of the experiment is defined by CLSI:EP7.

- Select an interferent. Prepare a solution of the interferent such that when mixed with the specimen, you will have a concentration (100%) which will ideally exceed the expected cutoff value by a factor of about two. However you can get by with a range of 110% to 1000% of the expected cutoff value.
- Prepare two specimens so they will have the concentrations of the interferent of 0% and 100%. Set up the dilutions so that the concentration of the analyte is the same in both.
- Prepare three additional specimens by mixing various proportions of these two materials so the interferent concentrations will be 25%, 50% and 100%.
- Assay these materials at least three times. For the first series, assay the specimens in increasing order of interferent. Each successive series, reverse the order of the previous series. Three series is generally adequate.
- Enter the test parameters and test results into EE, perform the calculations, and print the report.

Specimen Preparation Example

Suppose that the interferent, “SuperBlood Interferent” (SBI), is available in a concentration of 10 g/dL. From elsewhere, you have learned that the expected cutoff SBI concentration will be about 500 mg/dL. Your analyte, “serum asparagus” (SA) has a reportable range of 5 to 1000 umol/L. The reference interval is from 30 to 150 umol/L. Fortunately, you can prepare up to a 100-fold dilution of SA using your favorite diluent and still recover all the expected analyte. (In other words, the dilution process does not deactivate the analyte.)

Your analytical process requires a specimen size of 100 uL. Consequently, you will need to put 200-250 uL of specimen in each of the three tubes for each specimen. Prepare the five specimens with a volume of at least 1 mL each.

As you perform your routine work on patients, you look for an SA specimen with a relatively high concentration, preferably at least 2 to 5 fold higher than the highest SA concentration you are going to test. You find one with a concentration of 1200 umol/L.

Preparation of 100% SBI specimen

- SA concentration of 400 umol/L
- SBI concentration of 1000 mg/dL
- Total volume needed: 3.0 mL.

Preparation of 100% SBI specimen		
Solution	Volume (mL)	Calculation
SA	1.0	$vol_{SA} = FV * TC_{SA} / OC_{SA}$ $vol_{SA} = 3.0 * 400 / 1200$
SBI	0.3	$vol_{SBI} = FV * TC_{SBI} / OC_{SBI}$ $vol_{SBI} = 3.0 * 1000 / 10,000$
Diluent	1.7	$vol_{dil} = FV - vol_{SA} - vol_{SBI}$ $vol_{dil} = 3.0 - 1.0 - 0.3$
FV = final volume TC = target concentration OC = original concentration		

Preparation of 0% SBI solution

- SA concentration of 400 umol/L
- Total volume needed: 3.0 mL

Preparation of 0% SBI specimen		
Solution	Volume (mL)	Calculation
SA	1.0	$vol_{SA} = FV * TC_{SA} / OC_{SA}$ $vol_{SA} = 3.0 * 400 / 1200$
Diluent	2.0	$vol_{dil} = FV - vol_{SA}$ $vol_{dil} = 3.0 - 1.0$
FV = final volume TC = target concentration OC = original concentration		

Preparation of 25%, 50% and 75% SBI solution

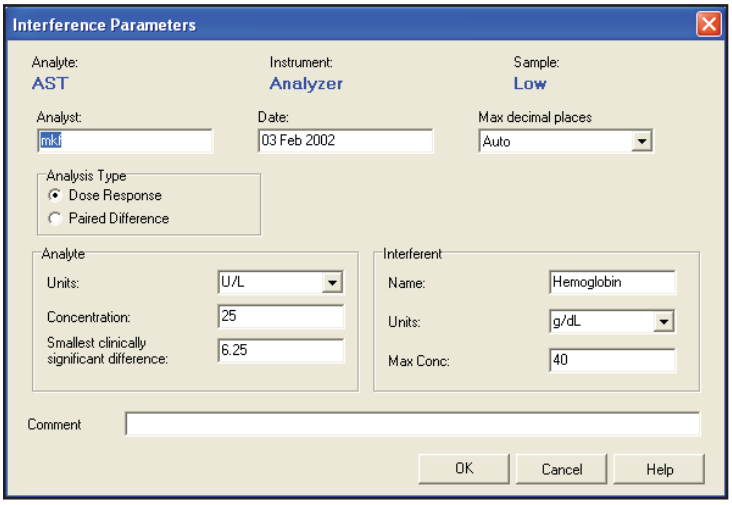
- Final volume needed of each: 1.0 mL
- 50% SBI: 1.0 mL 0% SBI + 1.0 mL 100% SBI
- 25% SBI: 0.5 mL 0% SBI + 0.5 mL 50% SBI
- 75% SBI: 0.5 mL 100% SBI + 0.5 mL 50% SBI

Data Requirements

- Five specimens assayed at least three times.
- The analyte concentration in each of these specimens is identical.
- Interferent concentrations are 0%, 25%, 50% 75% and 100%.
- Order of analysis is important. In each run, each specimen is assayed one time.
- Run 1: interferent concentration runs from 0 to 100%
- Run 2: interferent concentration runs from 100% to 0%.
- Run 3 and later: reverse sequence from previous series.

Parameter Screen

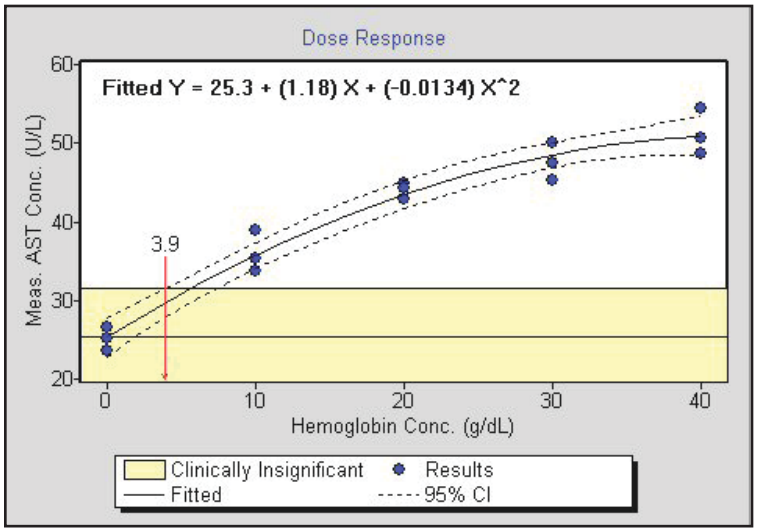
The fields unique to this module are:



- **Analyte concentration:** Enter a nominal value. The actual value may be different.
- **Analysis Type**. The setting to establish the degree of interference is **Dose Response**. The setting to establish the existence of interference is **Paired Difference**.
- **Smallest clinically significant difference**: Different values can be justified ranging from 50 to 100% of the Total Allowable Error. The difference between them relates to the issue of how to account for systematic error. If your "within-run" SD is actually obtained from your daily QC, then use of the larger value is justified.
- **Max Conc**: Enter the interferent concentration of the 100% specimen.

Interpretation of Results

The core concepts of this module expressed in the graph as generated by EE are:



- Zone of results for which the change is clinically insignificant (yellow band).
- In this graph at a Y value of about 32, a horizontal line is drawn. This line, in fact the Y intercept, represents the 0% response.

- Line (labeled 3.9 in this example) which represents the maximum interferent concentration which can be in the specimen and still generate a valid result.

- Regression line drawn through the data. This may be either a linear or quadratic equation.

- 95% confidence interval band drawn around the regression line.

Experiment Declared to be Preliminary

The expectation is that the graph resulting from this experiment will resemble that shown just above. However if all of the results are in the clinically insignificant region, then the analysis by the Dose Response approach will declare the experiment to be preliminary. This is because the CLSI:EP7 Dose Response protocol assumes that the highest interferent concentration causes clinically significant interference. CLSI places great emphasis on using a sufficient number of replicates so that this point is statistically distinguishable from "background noise" (normal imprecision). If the dose response curve does not cross the clinically significant difference line, EP Evaluator concludes that the crossover point is not distinguishable, and classifies the experiment as preliminary.

If the Dose Response experiment is found to be preliminary, then it is trivial to check the Paired Difference button. That then triggers a different type of evaluation of the results and allows you to determine whether interference exists in that analytical system.

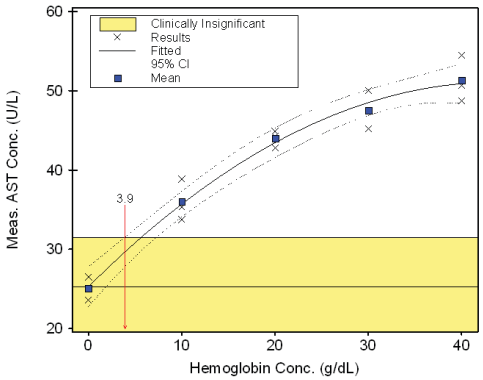
Interference Report (Dose Response)

EP Evaluator®
Users Manual -- Data Innovations

AST
Instrument: Analyzer
Sample: Low
Interferent: Hemoglobin

Interference Dose Response

Dose Response Curve



Evaluation of Results

AST at a concentration of 25.07 U/L was evaluated for interference on Analyzer according to CLSI document EP7-A. Bias exceeding 6.25 U/L is considered clinically significant.

The interference of Hemoglobin up to 40 g/dL was tested. Over this range, the bias can be approximated from the relationship

Fitted Y = 25.3 + (1.18) X + (-0.0134) X^2

with a standard error of 2.12 g/dL. Bias at interference level X is the difference between the Fitted Value at X and the Fitted Value at zero. At Hemoglobin concentrations less than 3.9 g/dL, the upper 95% confidence limit for predicted bias is not clinically significant.

Expected increase in measured analyte concentration due to interference

Interfer. Conc	Analyte Conc. Meas. Mean	Meas. SD	Fitted	Interfer. Bias	95% CI
0	25.07	1.45	25.30	0	-2.50 to 2.50
3.9	--	--	*29.70*	*4.40*	*2.55 to 6.25*
10	36.00	2.62	35.71	10.41	8.79 to 12.04
20	43.97	1.07	43.45	18.15	16.30 to 20.01
30	47.53	2.40	48.51	23.21	21.59 to 24.84
40	51.30	2.95	50.90	25.60	23.10 to 28.10

Fitted Y = 25.3 + (1.18) X + (-0.0134) X^^2 SEE = 2.12 U/L
Clinically Significant Difference = 6.25 U/L

Experimental Results

Rep	Interferent (% of maximum) 0%	25%	50%	75%	100%
1	23.6	33.8	44.9	45.2	54.5
2	26.5	38.9	44.2	47.4	50.7
3	25.1	35.3	42.8	50.0	48.7

'X' indicates an excluded replicate.

Supporting Data

Analyst:	mkf
Analysis Date:	03 Feb 2002
Analyte Units:	U/L
Nominal Analyte Conc:	25 U/L
Number of replicates:	3
Clinically Significant Diff:	6.25 U/L
Interferent Units:	g/dL
Max Interferent Conc:	40 g/dL
Comment:	

Accepted by: _____ _____
Signature Date

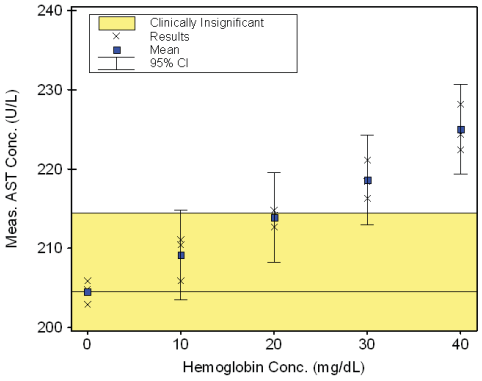
Interference Report (Paired Difference)

EP Evaluator®
Users Manual -- Data Innovations

AST
Instrument: Analyzer
Sample: High
Interferent: Hemoglobin

Interference Dose Response

Paired Difference SD Chart



Evaluation of Results

AST at a concentration of 204.53 U/L was evaluated for interference on Analyzer . Bias exceeding 10 U/L is considered clinically significant.

The interference of Hemoglobin up to 40 mg/dL was tested. The 95% CI for Interference effect is clearly outside the Clinically Significant Difference at a Hemoglobin concentration of 40 mg/dL

Paired Difference Statistics

Interfer. Conc.	Analyte Conc. Meas. Mean	Analyte Conc. Meas. SD	Difference from Zero Pool	Bonferroni 95% CI (1)
0	204.53	1.52		
10	209.13	2.82	4.60	-1.04 to 10.24
20	213.87	1.07	9.33	3.69 to 14.98
30	218.60	2.41	14.07	8.42 to 19.71
40	225.00	2.95	20.47	14.82 to 26.11

(1) Based on pooled, within-level SD of 2.275 (10 df)
Clinically Significant Difference = 10 U/L

Experimental Results

Rep	Interferent (% of maximum) 0%	25%	50%	75%	100%
1	204.8	205.9	214.8	216.3	228.2
2	205.9	211.1	214.1	218.4	224.4
3	202.9	210.4	212.7	221.1	222.4

'X' indicates an excluded replicate.

Supporting Data

Analyst:	mkf
Analysis Date:	03 Feb 2002
Analyte Units:	U/L
Nominal Analyte Conc:	200 U/L
Number of replicates:	3
Clinically Significant Diff:	10 U/L
Interferent Units:	mg/dL
Max Interferent Conc:	40 mg/dL
Comment:	

Accepted by: _____ _____
Signature Date

Chapter

30

Stability

The Stability module is designed to evaluate measurand (i.e. analyte) recovery over time (i.e. drift). The Stability report reflects observed change for aliquots of a single specimen under specified storage conditions. A comprehensive stability study will typically include several reports covering specimens near the upper and lower limits of the reportable range, and may also include multiple storage conditions. Specimen analyte stability can be determined for storage variables of temperature or type of storage container, such as draw tube. Reagent stability can be evaluated for various storage conditions, such as refrigerated shelf life or open life on the instrument.

Drift is evaluated by the regression analysis of the observed value (Y-axis) vs. time (X-axis). Stability duration is the earliest time at which the 95% confidence interval for the fitted curve crosses a predetermined allowable drift threshold.

Experiment Design

The specimen is aliquotted into tubes for assay at a later time. One aliquot is assayed at the beginning of the experiment (time=0). At appropriate times, additional aliquots are assayed. The total duration of the experiment should extend past the product's expected stability duration. Within this total duration, at least five time points should be evaluated. Increasing the frequency will increase confidence in the result. To reduce the effects of imprecision, it is recommended that each sample be assayed in duplicate or triplicate.

> **Example**: The claimed or expected shelf life is 5 days. The experiment is run for 7 days. The sample is assayed in triplicate at the beginning of the experiment (day zero), and again on days 1, 2, 3, 6, and 7.

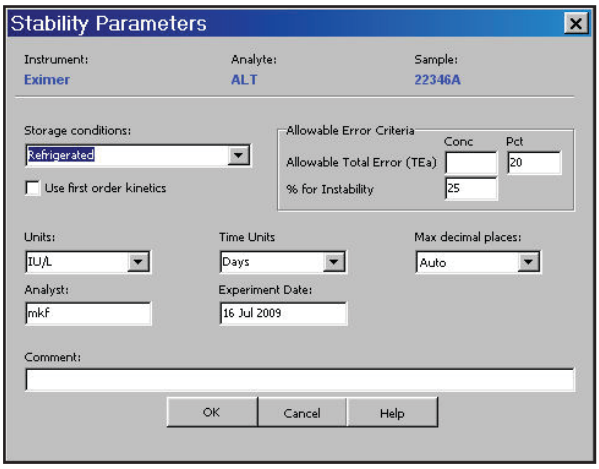
Data Requirements

Number of specimens: Minimum of 5. No upper limit is specified by EE.

Number of replicates: 1 to 5.

Parameter Screen

The Parameter Screen is similar to many of the other Parameter screens.



The fields include:

- **Storage conditions**: Text description of storage conditions for this experiment
- **Use first order kinetics**: If this box is checked, the program will fit a logarithmic curve to the data; otherwise it will fit a linear curve
- **Allowable Error Criteria**: EE uses an error budget to define allowable instability: first define Allowable Total Error, then budget some percent of the total for instability -- usually between 20% and 50%. In the U.S., CLIA rules are often used to define Allowable Total Error. For example, the CLIA limit for Glucose is 6 mg/dL or 10%. You may enter the value in concentration units, in percent, or both.
- **Units**: Analyte measurement units.
- **Time Units**: Units in which time is measured.
- **Date**: Date on which the experiment was run.
- **Max decimal places**: Maximum number of decimal places for reports. “Auto” means number of decimal places is determined from the data. Computed statistics (e.g., Mean) are usually printed with one more decimal place than the input results. This setting affects reports only; calculations are done on full-precision numbers.
- **Analyst**: Person responsible for doing the experiment.
- **Experiment Date**: Date on which the experiment was run.
- **Comment**: Text describing the experiment.

Allowable Instability

A predetermined allowable instability (allowable drift) must be specified in order to perform the analysis. The results are acceptably stable as long as the 95% confidence interval for the regression line remains within allowable instability bands. In EP Evaluator®, allowable instability is specified as a percent of Total Allowable Error (TEa). The Instability Budget is typically 20% - 50%.

> **Example**: Based on CLIA limits, TEa for AST is 20%. Assuming a 50% Instability Budget, Allowable Instability is +/- 10% of the concentration at time=0.

Imprecise. If Allowable Instability is too small, no conclusion can be drawn because the data is Imprecise. Imprecise means the confidence interval for the regression line is outside the acceptable stability range even at time=0. Approaches for dealing with this problem include:

- Increase the number of replicate measurements to reduce the width of the regression confidence interval.
- Increase Instability. If Allowable Instability is less than 2 times routine CV, a large number of replicates will be required.

Evaluating the Fitted Curve

The curve fit is a regression line determined from the observed data. In most cases an ordinary regression line is used, and the fitting equations is:

Y = Intercept + Slope x Time.

When the duration of the experiment is much longer than the expected stability duration, you may choose to use first order kinetics that will fit an exponential curve:

Log(Y) = Intercept + Slope x Time.

Not Significant. If the 95% confidence interval for the Slope includes 0.0, then the slope is not statistically significant. This means that there is no systematic upward or downward trend in the data over the duration of the experiment. You may conclude that there is no drift. Note that this statistic only tests for drift; it does not test for other forms of instability, such as increases in imprecision.

Estimated Stable Concentration and **Acceptable Range**. The intercept of the fitted curve is an estimate of the stable concentration at time=0. The Acceptable Range is set relative to the Estimated Stable Concentration. For example, suppose Allowable Instability is +/- 10%, and the Estimated Stable Concentration is 50 units. Then the Acceptable Range is 50 +/- 10%, or 45 to 55 units.

Bad Fit. Regression analysis assumes that the fitted curve is a good estimate of the overall behavior of the process over time. If this assumption is true, there are three values that might be used to estimate the stable concentration:

- A predetermined Target Value for the sample, established from an independent source.
- The mean measured value of the sample at time=0.
- The intercept of the fitted curve.

EP Evaluator® uses the intercept of the fitted curve as its estimate of the stable concentration. If the mean measured value at time=0 does not lie within the 95% confidence interval for the intercept, the curve is not a good fit to the observed data, and conclusions about stability duration are questionable. You might consider increasing the frequency of measurement time periods, inspecting observed data for outliers, or increasing the number of replicate measurements.

Pass or Fail

This experiment is not intended as a Pass/Fail test for stability. Instead, its purpose is to determine the rate of drift and, given that rate of drift, the time interval over which the process will produce acceptable results. The expected outcome is that the experiment duration is longer than the shelf life, so the crossover point can be determined. If the duration of the experiment is too short, the report will classify instability as “Not Significant”.

Preliminary Report

The word PRELIMINARY printed diagonally across the report indicates that the data is incomplete, and the report is not acceptable as a final report. Some or all of the statistics may be missing. The Stability report is preliminary if:

- There are no measurements with time=0.
- There are fewer than five time periods with valid data.
- The data is “imprecise”, or a “bad fit” as defined earlier in this chapter.

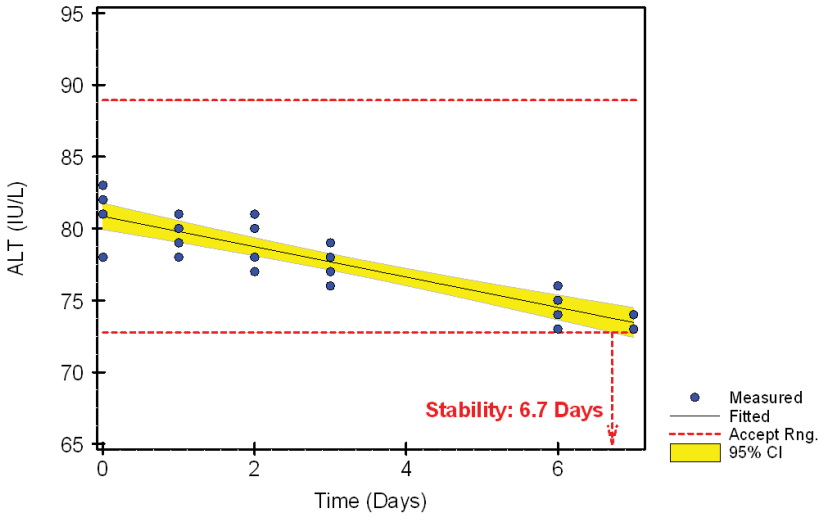
Stability Report (Page 1)

EP Evaluator®

User Manual -- Data Innovations, LLC

ALT
Instrument Eximer
Sample Name 22346A
Refrigerated

Stability



Evaluation Stability estimate: 6.7 Days

Evaluation Criteria

Allowable Total Error (TEa)	20.0%
% for Instability	50%
Allowable Instability	10.0%
Est. Stable Concentration	81 IU/L
Acceptable Range	73 to 89 IU/L

Fit Statistics

Model	Y = (80.8) + (-1.056) * Time
Slope and 95% CI	-1.056 (-1.283 to -0.829)
Intercept and 95% CI	80.8433 (79.9223 to 81.7644)
R	0.900
SEE	1.4
Experiment Duration	7.0 Days
# Meas. Periods	6
# Data Points	24

Supporting Data

Expt Date	16 Jul 2009
Analyst	mkf
Analyte Units	IU/L
Time Units	Days
Comment	

Accepted by: _____ _____
Signature Date

EP Evaluator®

User Manual -- Data Innovations, LLC

ALT
Instrument Eximer
Sample Name 22346A
Refrigerated

Stability

Results Listing

Time	Mean	SD	CV	Fitted	95% CI		Measured Values			
0	81.0	2.2	2.7	80.8	79.9	81.8	78	81	82	83
1	79.5	1.3	1.6	79.8	79.0	80.5	78	79	80	81
2	79.0	1.8	2.3	78.7	78.1	79.4	77	78	80	81
3	77.5	1.3	1.7	77.7	77.1	78.3	76	77	78	79
6	74.5	1.3	1.7	74.5	73.6	75.4	73	74	75	76
7	73.5	0.6	0.8	73.5	72.4	74.5	73	73	74	74

Values marked with an "X" were excluded from the calculations.

Chapter

31

Histogram and Descriptive Statistics

The Histogram and Descriptive Statistics Module does not answer any specific research question. Instead, it computes a few not-so-common statistics that you sometimes need, but can't easily compute in Excel, or even in a full-fledged statistical package.

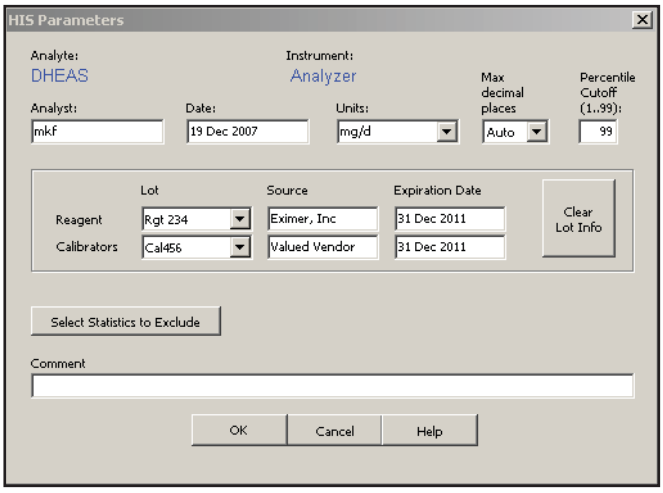
In this module, no experimental design is specified. Interpretation of results is totally in the user's hands and depends on an understanding of the appropriate statistics which are described extensively below.

A minimum of 10 unexcluded results are required. With any less, the report will be marked "Preliminary."

Parameter Screen

The Parameter Screen requests the same sort of information as most of the other screens.

Note that the **Select Statistics to Exclude** button allows you to select statistics to be excluded from the final report. Sometimes it is advisable to exclude certain statistics from the report because then fewer questions will need to be answered.



Interpretation of Results

Mean, SD, CV, N. Nothing unusual about these.

Range. Lowest and highest values in the dataset.

2 SD Range. Mean +/- two standard deviations. If the data represents test results for healthy patients, this is a quick estimate of the Reference Interval (Normal Range).

Mean/SD. Ratio of the Mean to the SD. This measures how many SDs the mean is from zero.

Geometric Mean. Definition – n'th root of the product of n values. Computation – compute the average of the natural logs (Excel ln function) of the numbers, then exponentiate the result. The geometric mean is not computed when any value is zero or negative.

Geometric SD. This is rather like a CV. It measures spread of the data around the geometric mean, as a percent.

Geometric 2 SD Range. Geometric mean +/- 2 x Geometric SD. For a log-normal distribution, 95% of the values lie within the Geometric 2 SD Range.

Delta. Delta is the ratio of Mean/SD for the logarithms of the data. This is used in Serology to assess the effectiveness of HIV and other assays.

Median. Midpoint of the data. Half of the results are above the median, and half are below it. The median is an alternative measure of central tendency that is less likely to be distorted by outliers than is the mean.

SMAD. Scaled Median Absolute Deviation. Median difference (absolute value) between the data points and the median, multiplied by a scaling factor of 1.483.

Central 95% Range. Rank the values in size order, and remove 2.5% of the results from each end. What's left is the central 95%. This is the nonparametric Reference Interval. It cannot be calculated for $N < 39$.

Is Gaussian? The program does an Anderson-Darling test for normality (Gaussianness) and reports "No" if the data is clearly non-Gaussian, and "Maybe" otherwise. As is often the case with statistics, you can never prove that the data really is Gaussian; you can only prove that it isn't. The decision is based on the p-value printed beside the conclusion. $p<0.05$ means the data is non-Gaussian. The smaller the p value, the more certain you are. $p<0.001$ and you are really, really sure; $p=0.049$ means it is a borderline case.

Robust Mean, SD, CV, and 2 SD Range. "Robust" is a statistical term indicating that an estimate is less sensitive to outliers than some alternative estimate. For example, the sample median is a robust estimate of the population mean.

Tolerance Interval. There is a 95% probability that 99% of the population lies within the Tolerance Interval. The calculation assumes a Gaussian distribution, and is computed from Mean +/- K SD. K is not a simple number like 2 or 3, but is a complex calculation based on the size of the sample. The larger the sample, the narrower the Tolerance Interval.

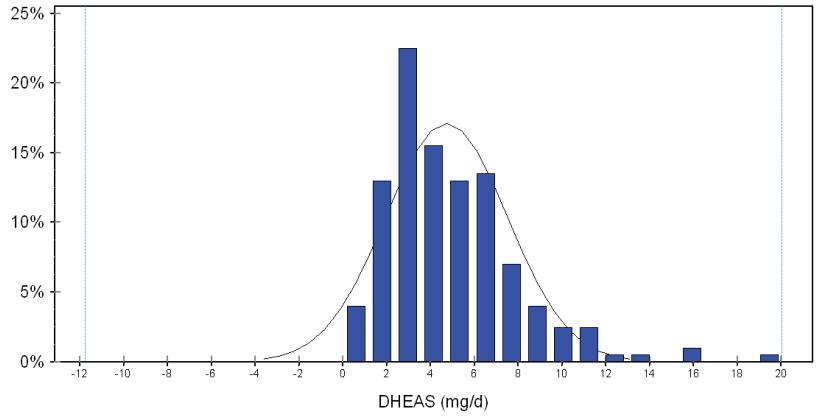
Cutoff. With the percentile cutoff set at x %, then it will identify the point at which x % of the data will be at or below the cutoff value. The default value is 99%.

Histogram and Descriptive Statistics (Page 1)

EP Evaluator®
Users Manual -- Data Innovations

DHEAS
Instrument: Analyzer

Histogram and Descriptive Statistics



Statistic	Value	95% Confidence Interval
Mean	4.97	4.56 to 5.38
Standard Deviation (SD)	2.96	2.69 to 3.28
Coefficient of Variation (CV)	59.5%	52.2% to 67.5%
Range of Data	1.1 to 19.3	
2 SD Range	-0.94 to 10.89	
Mean/SD	1.68	1.48 to 1.92
Geometric Mean	4.21	3.88 to 4.57
Geometric SD	80.3%	71.0% to 92.2%
Geometric 2 SD Range	1.30 to 13.68	
Mean/SD of Logs ("Delta")	2.44	2.19 to 2.74
Median	4.10	
SMAD	2.52	
Central 95% Range	1.2 to 12.4	
Is Gaussian?	No (p<0.001)	
% < Mean - 2SD	0.0%	0.0% to 1.9%
% > Mean + 2SD	4.5%	2.4% to 8.3%
Robust Mean	4.72	
Robust SD	2.73	
Robust CV	57.9%	
Robust 2 SD Range	-0.75 to 10.19	
95% Tolerance Int. for 99% of population	-3.36 to 13.30 (±167.6%)	
N	200 of 200	
Cutoff (99%)	10.7	
Units	mg/d	

Reagent Lot: --
Calibrator Lot: --

Analyst: mkf
Date: 19 Dec 2004

Accepted by: _____ _____
Signature Date

Histogram and Descriptive Statistics (Summary Report)

EP Evaluator®
Users Manual -- Data Innovations

DHEAS
Instrument: Analyzer

Results Summary

Result	Count	Result	Count	Result	Count	Result	Count
1.1	3	3.5	6	5.8	2	8.2	1
1.2	5	3.6	4	5.9	1	8.3	1
1.3	1	3.7	4	6	2	8.4	1
1.4	2	3.8	4	6.1	5	8.6	2
1.5	1	3.9	2	6.2	3	8.9	3
1.6	2	4	6	6.3	2	9.2	1
1.8	2	4.1	2	6.4	2	9.6	1
1.9	2	4.2	3	6.5	1	9.7	1
2	6	4.3	1	6.6	1	9.9	2
2.1	3	4.4	1	6.7	3	10.3	1
2.2	2	4.5	1	6.8	3	10.7	1
2.3	5	4.6	1	6.9	2	11.1	1
2.4	1	4.7	2	7	3	11.3	1
2.5	5	4.8	1	7.2	1	11.6	1
2.6	6	4.9	2	7.3	2	11.7	1
2.7	3	5	3	7.4	1	12.4	1
2.8	1	5.1	2	7.5	1	13.4	1
2.9	1	5.2	1	7.6	1	15.4	1
3	4	5.3	3	7.7	2	16.1	1
3.1	4	5.4	3	7.8	1	19.3	1
3.2	5	5.5	2	7.9	1		
3.3	3	5.6	5	8	1		
3.4	6	5.7	1	8.1	2		

Shows only valid, unexcluded results

A MAXIMUM OF 2000 LINES WILL BE LISTED

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Chapter

32

Cost per Test

Cost per Test is the first of the many Lab Management modules we will include in EP Evaluator. It is designed to provide the capability of calculating cost per billable test (BT) for a wide variety of situations ranging from a "quick and dirty" calculation to a complete calculation which includes all relevant costs.

Overview

One major element of operating a clinical laboratory is being aware of what the various costs are. These costs are of several major types. Some of these types are relatively fixed, others are incurred every time a specimen is assayed. This program is designed to deal with all these types.

Indirect Expense is a fixed cost. Elements of overhead are listed below. In order to input this item, they need to be all totaled together as one item as they will remain relatively constant as long as test volume does not change much.

- Administrative salaries
- Building costs such as cost of construction, janitorial services
- Utilities
- Waste removal
- Computer services
- Support services
- Indirect labor costs
- Courier services

Labor, specifically direct labor costs. These are defined as being associated with production of test results. Examples are:

- Instrument setup
- Instrument calibration
- Test performance
- Sample preparation
- Performance of QC

Supplies are associated directly with performance of tests. Items included are:

- Reagents, test strips and slides
- Pipette tips
- Wash solutions
- Tubes and disposable cuvettes
- Equipment obtained under a reagent rental plan

Equipment expenses can be any of several types. If the instrument is purchased, it is depreciated over its lifetime. On the other hand, if it is obtained using a reagent rental plan, then those costs need to be treated as "supplies."

Parameters define the key accounting details for each calculation. Items included are:

- Test volume of the current test
- Test volume of all tests
- Use of calibrators and controls
- Approach to calculating indirect costs
- Approach to calculating profits

Test volume is a major item. It appears in the program two ways:

- Overall test volume: i.e. total number of tests performed by the lab.
- Test volume for a specific test.

There are a large number of potential costs involved in operating a clinical laboratory. This program provides for itemizing your direct costs and to estimate your indirect costs. Consequently, the number that you calculate is an estimate of the costs for each test. If you set it up correctly and enter good estimates, the estimate will be reasonably accurate.

Starting a New Estimate

To calculate costs on a "new" method, perform the steps below. If you have already developed a estimation for a test, and the new test is similar, see the section later in this chapter on cloning tests.

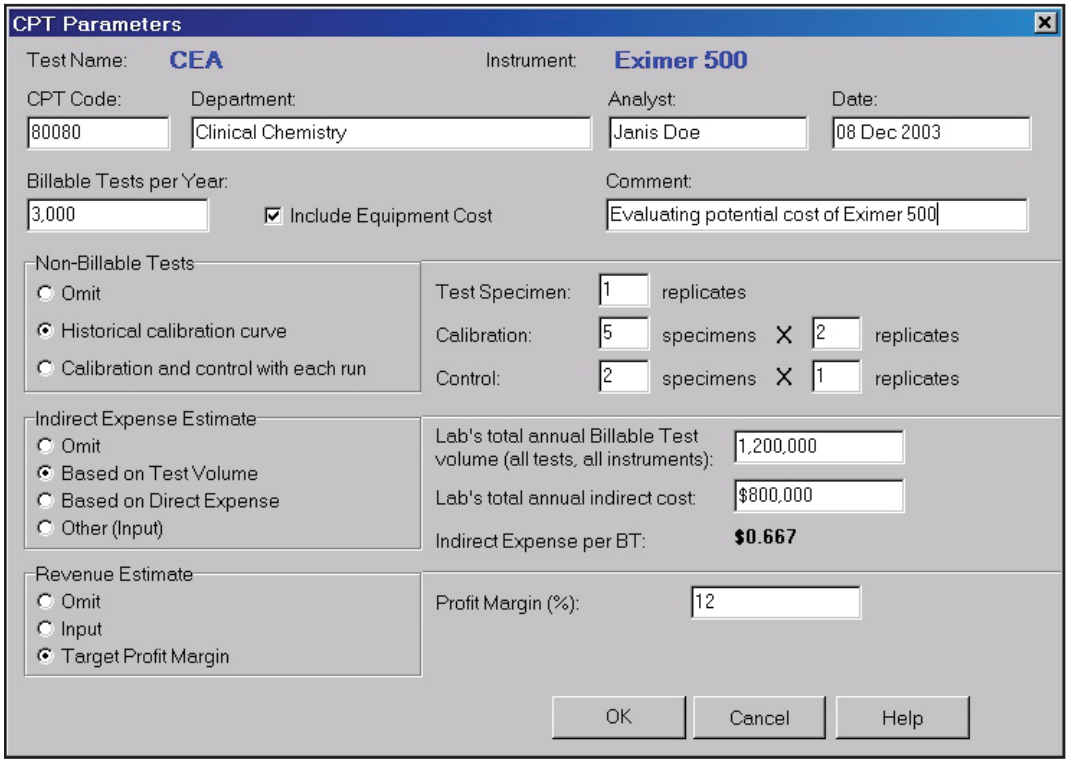
- Click on Experiment (horizontal menu), then click on New.

- Enter the names of the instrument and the test. At this point, the Parameter Screen will be displayed.

Parameters Screen

This screen comes up immediately after defining a new instrument and test. It also comes up on clicking the "F3-Edit button" near the bottom left of the Experiment Detail screen.

The fields on this screen are:



CPT Code: Enter a CPT code or reasonable facsimile thereof.

Department: Use this field to identify the department which controls the instrument.

Analyst and **Date**: The person entering the data and the date the analysis was started.

Billable tests per year: This refers to the number of tests for this analyte per year which are generated using this instrument(s).

Include Equipment Cost: Checking this item makes the "Equipment" tab visible so you can define equipment costs.

Comment: Use this as a place to say something about this calculation, such "Evaluating the potential cost of an Eximer 500 analyzer."

Non-Billable Tests: Select one of three options to specify how to account for calibrations and controls with respect to this test.

- **Omit**: No provision is made for calibrations and controls. Examples in this category might be a process such as phlebotomy or an operation not using calibrators and controls such as the manual differential in hematology.

- **Historical Calibration Curve**: The number of calibrators and controls is calculated from an estimate of the number used each month. An example of this might be a VITROS 950 instrument which might be calibrated a few times every three months or a Hitachi 747 which is calibrated daily and has a variable number of controls performed each day.

- **Calibration and control with each run**: In this case, the number of calibrators and controls are fixed with respect to each run. The number of runs per week is estimated. Examples of this are an RIA experiment with a fixed number of calibrators and controls for each run.

For the latter two cases, you will need to define several elements so the numbers of calibrators and controls can be calculated:

- Number of replicates for each test specimen
- Number of calibrations specimens with the number of replicates for each.
- Numbers of control specimens with the numbers of replicates for each

The values you've just entered will be displayed at the top of the supplies tab for your reference during data input there.

Indirect Expense Estimate defines the way indirect expenses are associated with the costs for each test.

- **Omit**. Indirect expenses are not to be included in this calculation. This might be used when you are comparing different costs involved in the acquisition of an instrument such as purchase vs. reagent rental.

- **Based on Test Volume**. In this case, the costs are allocated based on the fraction the current test volume is of the total test volume. For example, if total number of tests performed by the lab is 1,000,000 and the number of glucose tests are 50,000, then 5% of the indirect costs would be allocated to glucose.

- **Based on Direct Expense**. Indirect expense is a user-specified fraction of the direct expense. In other words, if the direct expense for a test is $20,000 and the user specified fraction is 50%, then the allocated indirect expense is $10,000.

- **Other**: Input for this case is very simple–enter the amount of indirect expense to be included in the cost of each billable test.

Revenue Estimates come in three types:

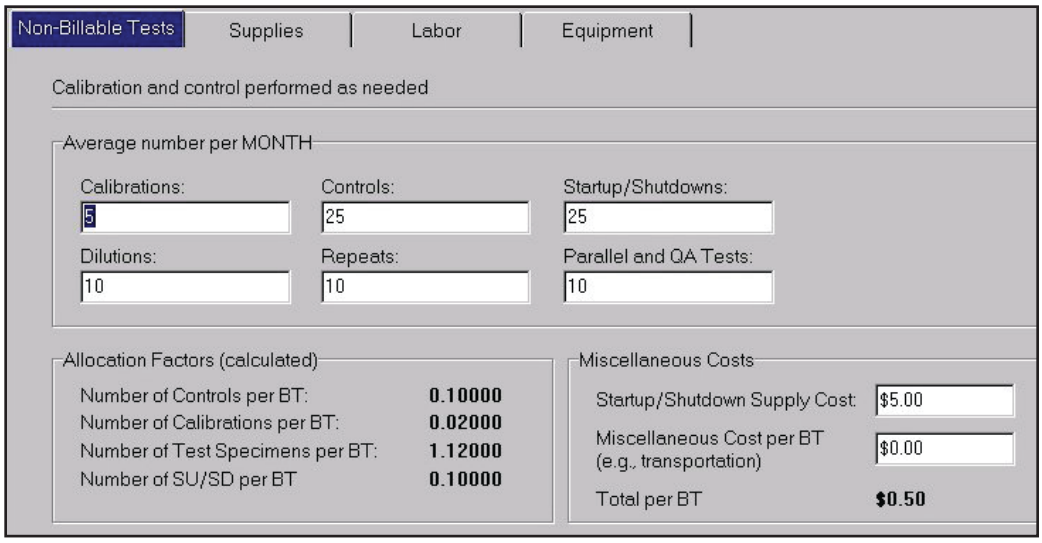
- **Omit**. Ignore income for this calculation.

- **Input**. Enter the expected revenue from one billable test. This is the amount a given provider such as Medicare is paying for that test.
- **Target Profit Margin**. Enter the profit margin you expect for that test (i.e. 10%). This will be a percent of the final price for that test. For example, if a given test costs you $3.60 and you specify a profit margin of 10%, the revenue from that test will be calculated to be $4.00 for a $0.40 profit per test.

Non-Billable Tab

The form available on this tab is used to describe how many of each of the non-billable tests are performed each month. Numbers are needed for:

- Calibrations
- Controls
- Startups and shutdowns
- Dilutions
- Repeats
- Parallel and QA tests

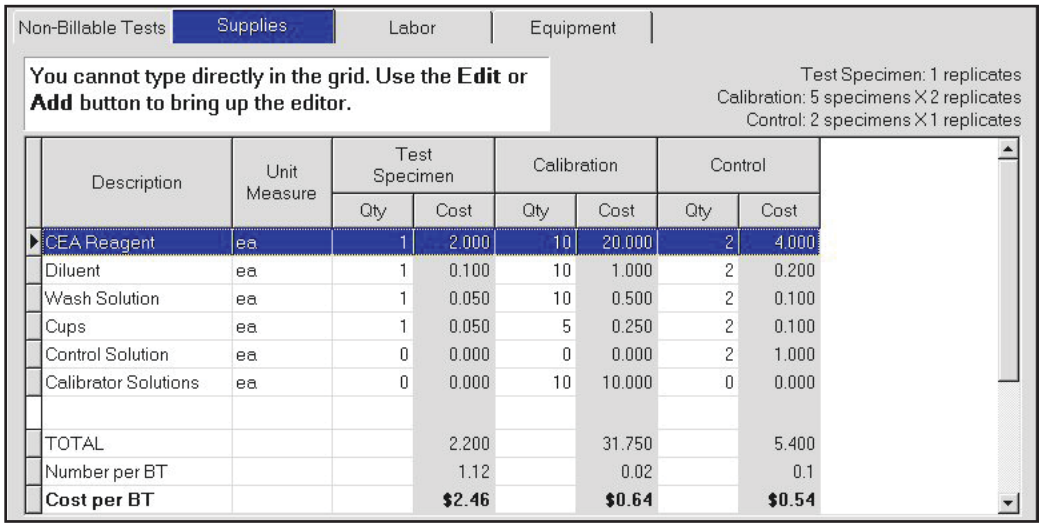


Some additional information about the costs of two additional items is also needed. The total of these two items per BT is added to the total for Supplies.

- Materials cost for a startup/shutdown
- Miscellaneous costs per BT (from other sources). This item provides for an adjustment for costs not accounted for elsewhere in this statistical module.

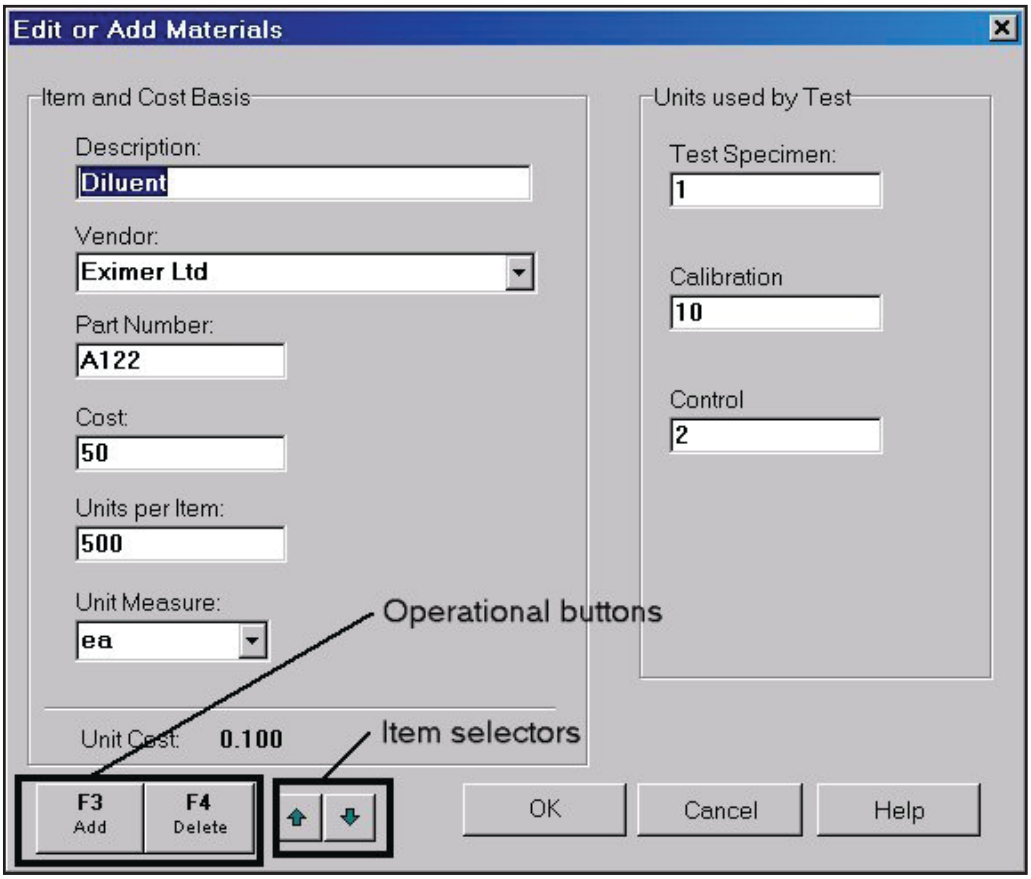
Supplies Tab

Entries under this section are for supply items such as reagent costs, diluents, wash solutions, control and calibration materials and the like.



Description	Unit Measure	Test Specimen		Calibration		Control	
		Qty	Cost	Qty	Cost	Qty	Cost
CEA Reagent	ea	1	2.000	10	20.000	2	4.000
Diluent	ea	1	0.100	10	1.000	2	0.200
Wash Solution	ea	1	0.050	10	0.500	2	0.100
Cups	ea	1	0.050	5	0.250	2	0.100
Control Solution	ea	0	0.000	0	0.000	2	1.000
Calibrator Solutions	ea	0	0.000	10	10.000	0	0.000
TOTAL			2.200		31.750		5.400
Number per BT			1.12		0.02		0.1
Cost per BT			**$2.46**		**$0.64**		**$0.54**

A fragment of the Supplies Screen is shown above. To create an entry, click on the F2-Add button (not shown in fragment). This brings up the Edit or Add Materials Screen. Items include:

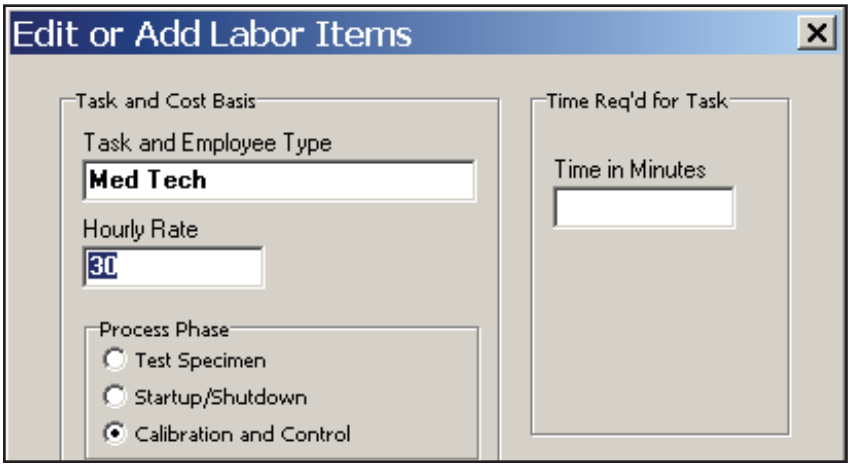


- Description - name or description of the supply item (**required**)
- Vendor - supplier (optional)
- Part Number - supplier's identifier (optional)
- Cost - cost of one standard purchase amount, or "batch" (**required**)
- Units per item - number of units in a batch (**required**)
- Unit measure - what is a unit? (**required**)

In addition, three additional numbers are required to relate amounts of these supplies to the various types of testing being done (on specimens, controls and calibrators). The numbers entered should be for one set of each type. In this example, a total of ten tests are required to calibrate the system. Consequently, ten tests are performed to calibrate the system one time.

Labor Tab

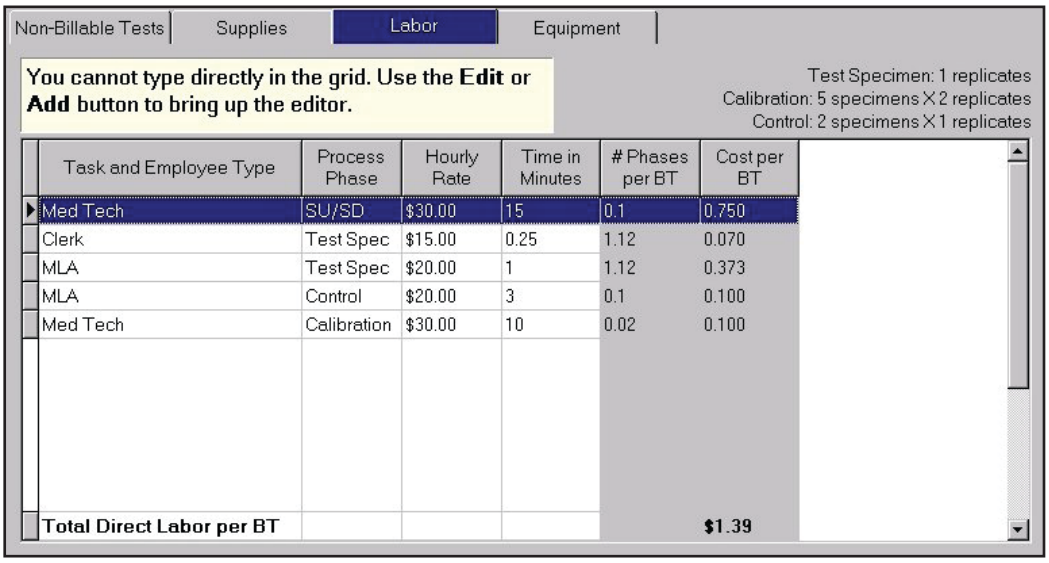
In this section, labor costs for each step in the process are entered into the Edit or Add Labor Items Screen which is very similar functionally to the corresponding screen for Materials above:



- Worker description (i.e. Med Tech, MLA, Clerk)
- Hourly rate
- Number of minutes for each task
- Type of task (see 4 categories below)
  - Test specimens
  - Controls
  - Calibrators
  - Startup/ Shutdown

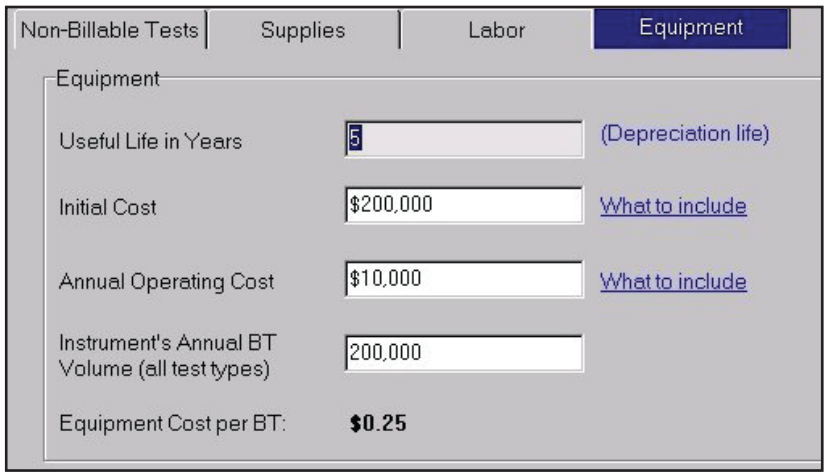
This section works by calculating the cost for each item displayed in the Labor Tab screen and then summing them across all the various items.

All your entries are displayed on the Labor Tab Screen (fragment shown).



Equipment Tab

This tab provides for calculating equipment costs. If the instrument is purchased or leased, enter those data in this screen. The purpose of this screen is to calculate the cost per billable test. The components of this calculation are:



- Number of useful years of instrument life.
- Initial cost of the instrument. The cost of the instrument per year is calculated by dividing the total cost by the number of years of useful life. Consequently, if the instrument is leased, the annual payments each year should be entered as the initial cost with the number of useful years being set to 1. Alternatively, the total cost of the lease over its life can be calculated and the useful number of years is then specified.
- Annual Operating cost should include things such as maintenance contract.

- Number of billable tests per year. Obvious.

At the bottom of this page is shown the calculated instrument cost per billable test.

Cloning Tests

In many cases, multiple analytes are assayed on the same machine. In some cases, instrument menu can be over 50 tests. The issue is how to create additional related tests without having to re-enter those data. The steps needed are:

- Get the first analyte to be as accurate as possible. If there are any changes, you will have to make changes in all the clones.

- Go to the Module Overview Screen. Click on the instrument (in the list on the left). Right-click on the test. Click on the bottom item on the drop down menu ("Clone"). Enter the name of the new test in the box that will appear. A new entry with that name will appear in the grid of the Module Overview Screen.

- Change the data as appropriate. In many cases, you will only need to change the test name and items relating to the reagent.

Cost per Test Report (Summary Page)

EP Evaluator®
Users Manual -- Data Innovations, LLC

CEA
Instrument Eximer 500

Cost per Test

Summary

	Cost per Billable Test	Annualized Cost	Percent of Total
Reagents & Supplies:			
Test Specimens	2.46	7,392	36
Calibration and Control	1.28	3,840	19
Other	0.50	1,500	7
Total	4.24	12,732	63
Direct Labor	1.63	4,880	24
Equipment Expense	0.25	750	4
Indirect Expense	0.67	2,000	10
Total Cost	**$6.79**	**$20,362**	**100%**
Revenue	7.71	23,139	114
Net Profit	**$0.93**	**$2,777**	**14%**
Number of Billable Tests		3,000	

Detail may not add to total due to rounding

NonBillable Tests

Calibration and Control frequency	As needed
Average # calibrations per Month	5
Average # controls per Month	25
Average # startup/shutdown per month	25
Average # dilutions per month	10
Average # repeats per month	10
Average # parallel and QA tests per month	10
# Replicates per test specimen	1
# Specimens for calibration	5 x 2 reps
# Specimens for control	2 x 1 reps

Equipment Expense

Initial equipment cost	200,000
Useful life	5 years
Annual operating expense	10,000
Annual BT volume (all tests)	200,000
Equipment Expense per BT	$0.25

Supporting Data

CPT Code	80080
Comment	Evaluating potential cost of Eximer 500
Department	Clinical Chemistry
Billable Tests per Year	3,000
Analyst	Jane Doe
Analysis Date	11 Nov 2011
Options	
Non-Billable Tests	Include
Equipment Expense	Include
Indirect Expense	Based on lab annual total of $800,000 per 1,200,000 BT
Revenue	12% Profit Margin

Accepted by: _____ _____
Signature Date

EP Evaluator®

Users Manual -- Data Innovations, LLC

CEA
Instrument Eximer 500

Cost per Test

Labor

Task	Phase	Hourly Rate	Time in Minutes	# Phases per BT	Cost per BT
Med Tech	SU/SD	$30.00	15	0.1	0.750
Clerk	Test Spec	$15.00	0.25	1.12	0.070
MLA	Test Spec	$20.00	1	1.12	0.373
MLA	Control	$20.00	10	0.1	0.333
Med Tech	Calibration	$30.00	10	0.02	0.100
Total					**$1.63**

Reagents and Supplies

Vendor	Part Num	Description	Cost per Item	Units per Item	Unit Measure	Cost per Unit	# Units	Extended Cost
Calibration								
Eximer Ltd.	A122	CEA Reagent	$2.00	1	ea	2.000	10	20.000
		Diluent	$0.10	1	ea	0.100	10	1.000
		Wash Solution	$0.05	1	ea	0.050	10	0.500
		Cups	$0.05	1	ea	0.050	10	0.500
		Caibrator Solutions	$1.00	1	ea	1.000	10	10.000
							Total Cost	$32.00
							x # per Billable Test	0.02
						Calibration Cost per Billable Test		**$0.64**
Control								
Eximer Ltd.	A122	CEA Reagent	$2.00	1	ea	2.000	2	4.000
		Diluent	$0.10	1	ea	0.100	2	0.200
		Wash Solution	$0.05	1	ea	0.050	2	0.100
		Cups	$0.05	1	ea	0.050	2	0.100
		Control Solution	$1.00	1	ea	1.000	2	2.000
							Total Cost	$6.40
							x # per Billable Test	0.1
						Control Cost per Billable Test		**$0.64**
Test Specimens								
Eximer Ltd.	A122	CEA Reagent	$2.00	1	ea	2.000	1	2.000
		Diluent	$0.10	1	ea	0.100	1	0.100
		Wash Solution	$0.05	1	ea	0.050	1	0.050
		Cups	$0.05	1	ea	0.050	1	0.050
							Total Cost per Performed Test	$2.20
							x Performed Tests per Billable Test	1.12
						Test Specimen Cost per Billable Test		**$2.46**
							Startup/Shutdown ($5.00 x 0.1 SU/SD per BT)	0.50
							Other Reagent & Supply Cost	0.00
TOTAL REAGENT AND SUPPLIES COST PER BILLABLE TEST								**$4.24**

Chapter

33

Simple Inventory System (SIS)

The Simple Inventory System (SIS) is a stand-alone materials management program, included with EP Evaluator. Its primary purpose is to keep track of the Quantity on Hand (QOH) of items in the store room (reagents, controls, office supplies, etc.).
SIS does the four general tasks listed below.

- Count items for Physical Inventory, manually or with a barcode scanner
- Receive items into Inventory
- Check items out of Inventory, manually or with a barcode scanner
- Create a Shopping List

Overview of Inventory Tasks

This section describes the basic tasks and concepts underlying SIS, more from the standpoint of what needs to be done than how to do it. Details of how to do it are described elsewhere.

Setup Tasks

Before you can use SIS, there are a few one-time setup tasks:

- **Hardware Setup** - connecting the barcode scanner to your computer; setting up a label printer to print barcode labels. While SIS can be run over a network (if you have a network license for EP Evaluator), the typical installation will use a single workstation for reading the barcode scanner and printing barcode labels.

  An SIS Starter Kit is available from Data Innovations. It contains three bar code scanners and a box of labels. A file exists in the EE Resources folder describing these items.

- **Database Creation** - think of a "database" as a folder on your hard drive that holds files of inventory data. One of these databases is the Example that we ship with the software. You will have at least one database for your lab. If ordering is not centralized across departments, you may choose to create a separate database for each department.

Access to a database is restricted by a login. There are three classes of users: Administrators, Operators, and Guests. Administrators can do anything. Guests can see the data, but are not allowed to change it. Operators are somewhere in between – they can enter inventory transactions, but may not define inventory items and users.”Creating” a database includes the process of assigning user names and passwords and assigning each user to the appropriate class.

Note that if you set up separate databases for each department, the user administration process must be done for each department.

- **Defining Inventory Items** - making a list of the items you want to count. If you currently use a spreadsheet to keep track of inventory, you can reformat that spreadsheet in a form to paste into SIS.

  Each inventory item has an item name (30 characters), an item group (32 characters), and a part number (10 characters), all of which are printed on the barcode label. The name, group and part number are on the label for human readability. The part number is also on the label in the form of a barcode. Vendor part numbers may be used for barcodes if they are short enough and contain no special characters.

  As each inventory item is added to the Items screen, it is assigned to a **Count Sheet**. The point of a count sheet is to make sure every item gets counted when you do physical inventory. Suppose John is responsible for physical inventory for some of the items, and Mary is responsible for the rest. For example, John is responsible for a stock room and Mary for a refrigerated area. John’s items are assigned to Count Sheet 1, and Mary’s to Count Sheet 2. When it is time to do physical inventory, you can use SIS’s **Make Count Sheets** function to produce separate lists for John and Mary to show what they need to count and the expected quantities in stock.

  Another important data field on the Items screen is the **Divisor**. This field applies when you order the item in whole boxes, but want your staff to check out a partial box when it is removed from the store room. For example, you might order reagent in boxes, where a box contains 5 bottles. In this case, the divisor is 5 – 5 bottles per box.

Ongoing Tasks

There are four main ongoing operations you will perform with SIS:

- **Physical Inventory** - counting all the items on the shelves. You must do this once to establish the initial stock. You will also do periodic physical inventories on a recurring basis to confirm that the check in/check out process is working satisfactorily.

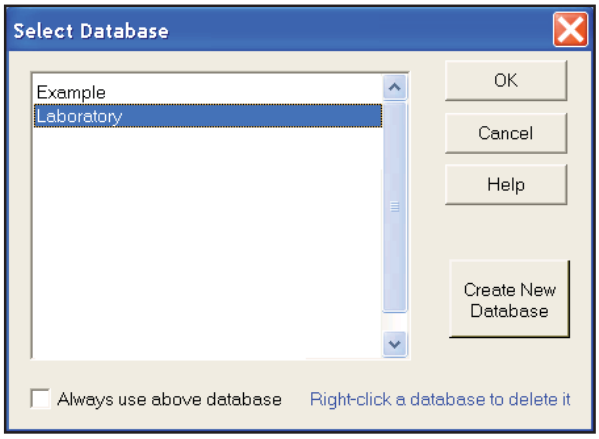
- **Receiving** - adding items to inventory when an order arrives at the lab. Bar-code labels are printed and attached to the boxes as they are placed in the store room so subsequent checkouts can be performed with a barcode scanner.

- **Check Out** - subtracting items from inventory as they are removed from the store room. A barcode scanner is placed in the store room, and employees are instructed to scan each item as they remove it. The scanner is not connected "live" to the computer – it is simply a memory device that holds a record of what items were scanned. Once a day (or perhaps once a shift) the scanner is collected from the store room and its contents are uploaded to the computer. Scanner memory holds about 350 barcodes.

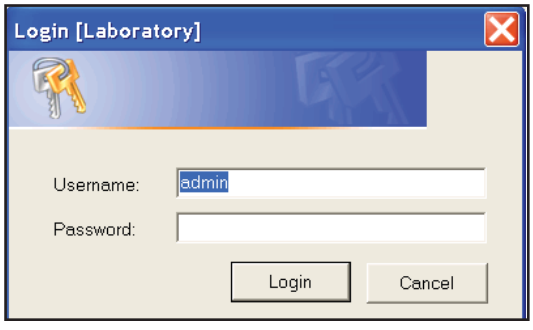
- **Making a Shopping List** - looking at the Inventory Status (QOH) and deciding what items need to be ordered. The items can be selected into a separate, permanently stored "list" within SIS. The first thing you will do with this list is to print a Shopping List Report to serve as a basis for ordering. When the order arrives, you can use the shopping list to print barcode labels. The process of attaching these labels to the packages is a way of confirming that you received what you ordered – if you have extra labels, the order was incomplete. Once you have confirmed that the order is correct (or corrected the quantities in your shopping list to agree with what you received), you can add the shopping list to inventory.

Creating a New Database

You can start SIS from the **Tools** menu in EE. For the long term, you probably want to create a separate desktop icon for SIS, so you can start it directly, with no need to launch EE each time. You can use **Tools, Create Desktop Icon for . . .** in the EE menu to create a SIS icon.



When you start SIS, the first screen asks you to select a database. Click on the database you want, then select OK. If you want to bypass this screen and always open the same database each time, check the **Always use above database** box at the bottom of the screen before clicking OK. If you select **Cancel** instead of OK, the program will terminate. If you want to delete a database, right-click it and select **Delete** from the popup menu.



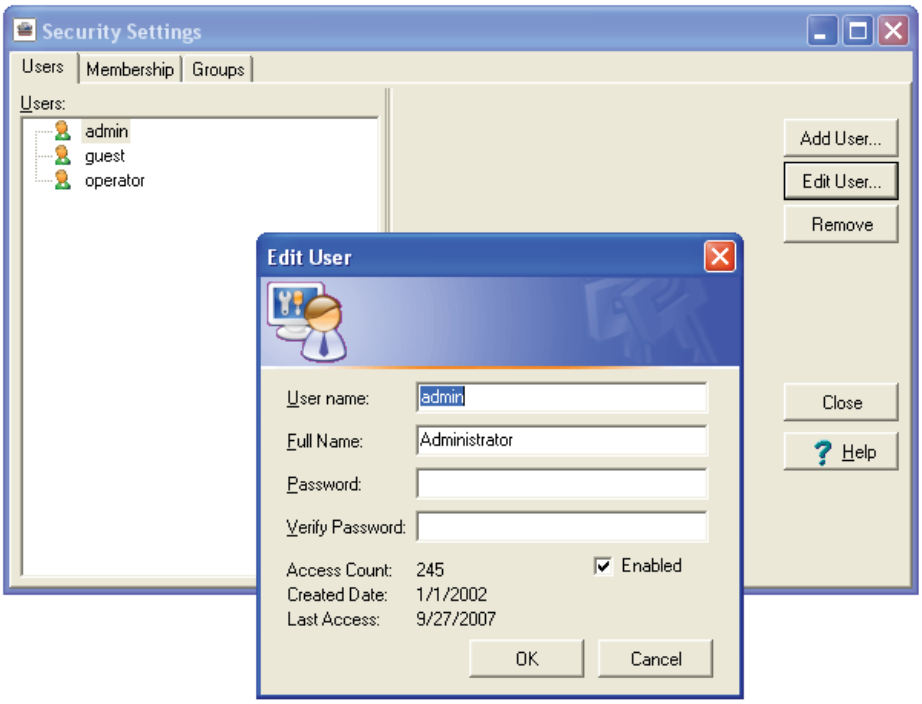
We recommend that you explore the Example database first, before creating your own. When you are ready to create your own data-

base click the **Create New Database** button. SIS will first create a folder for the database, and a default set of users: admin, operator, and guest. These users have no passwords. Before you can use the database, you will be asked to log in. Enter admin for the Username, leave the Password field blank, and select Login. The first thing to do, after login, is set up your users. (Alternatively, if you don't need a secure system, you can instruct everyone to log into the system as "admin" with no password.)

User Administration

User Administration starts by selecting **File, User Administration** from the SIS menu to show the **Security Settings** screen. This screen has three tab pages: **Users** (for adding people), **Membership** (for specifying which group each user belongs in, and **Groups** (for specifying what rights the groups have).

Adding and Editing Users (Users Tab)



The Users pane on the left shows valid "User Names" to enter in the login screen. A new database is created with three users: admin, guest, and operator. Use the Add **User**, **Edit User**, and **Remove** buttons to set up users for your system. You should:

- Edit the admin user and uncheck the Enabled box. We recommend that you do not delete admin or change its user name or right to do user administration functions. If you leave the disabled admin account in the system, you can re-gain access to your database with a call to Data Innovations support if all your administrators lose their login information.

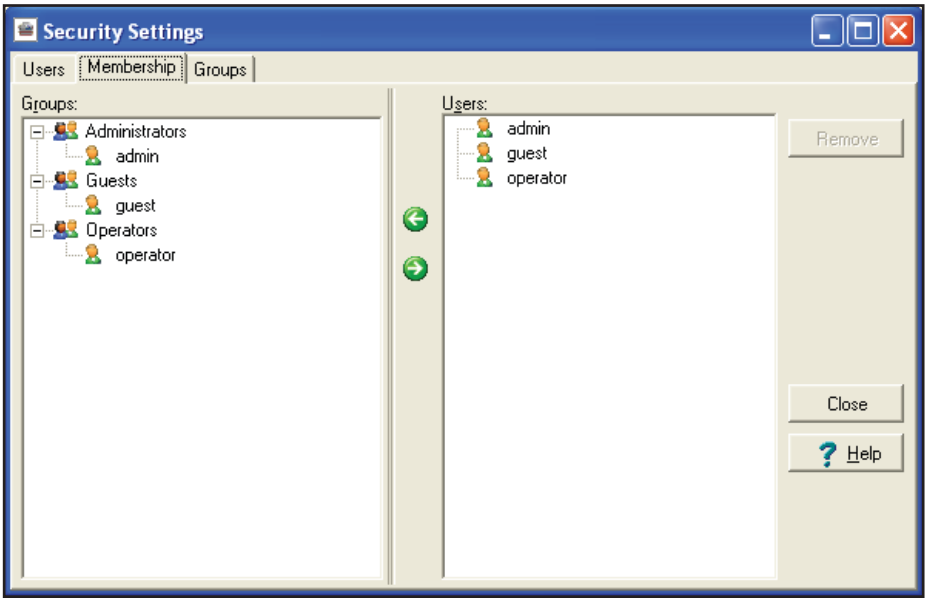
- Add a new user(s) to serve as administrator.

- Delete the operator account. Add a new account for each user who will enter inventory transactions.

- Leave the guest account as-is. Anyone can log in as guest, with no password, and see the data, but s/he can't edit it.

Assigning Users to Groups (Membership Tab)

A Group defines what users can do in SIS. Users in the Administrators group can do anything. Users in the Guests group can look at screens and reports, but they can't edit anything. Users in the Operators group can enter routine transactions and make lists, but they cannot do things like changing inventory part numbers, User Administration, hardware setup, or restoring backup files.



Anyone who uses SIS must log in, and his/her username determines which menu items are visible. For example, if you login as operator or guest, you will not see the **File, Administer Users** menu item.

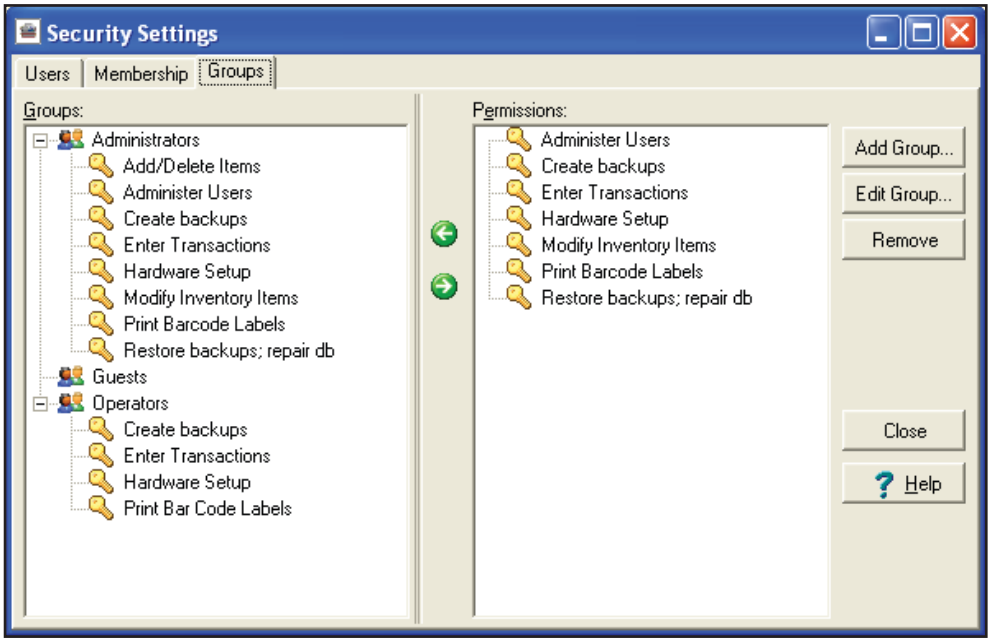
To assign a user to a group, first click the group name in the left pane to highlight it. Then select the user in the right pane and click the green left-pointing arrow. You can also use the mouse to drag a user name into a group.

To remove a user from a group, highlight the user name in the left pane, then click the **Remove** button.

Each user should be assigned to exactly one group. If you forget to add a user to a group, that user implicitly belongs to the Guests group.

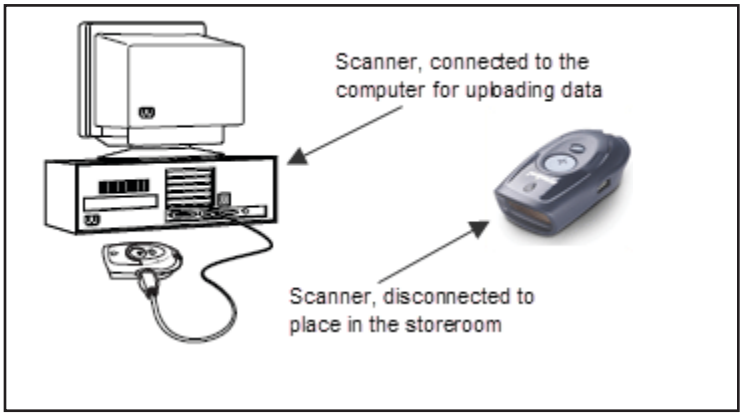
Defining Group Privileges (GroupsTab)

The Groups tab gives you limited ability to change what functions the groups may perform and to add or delete groups. In most cases you should leave the group permissions at their default values.



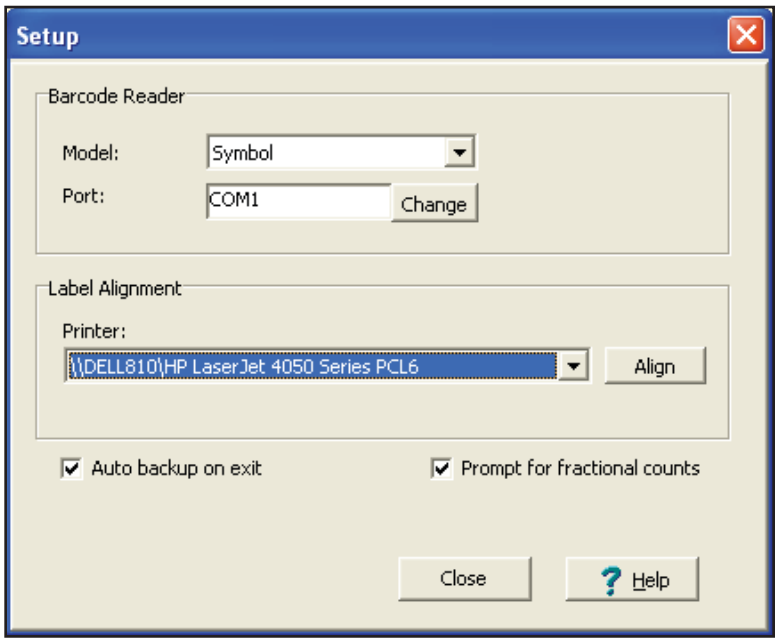
Connect the Barcode Scanner before starting SIS

At this time (April, 2014), we support only the Symbol CS 1504 Consumer Memory Scanner. The scanner is available with either serial or USB interface. The USB version is simply the serial version with a (detachable) Serial-to-USB conversion cable.



Start by connecting the barcode scanner cable to the computer. If your computer has a free serial port, you do not need the serial-to-USB conversion cable. Just connect the scanner's 9-pin serial connector to the COM port connector on the computer. If your computer does not have a serial port, connect the scanner's 9-pin connector to the conversion cable, then connect the conversion cable to a USB port on the computer. Wait for the computer to recognize that a new USB device is present. You may be prompted to install a Windows device driver. Drivers for Windows XP-NT and Windows ME are provided on the EE installation CD in the Drivers folder. You can use the Windows XP drivers in Windows Vista and Windows 7.

After the scanner is connected, start SIS and select **Setup** to configure the scanner, label printer, and other settings.



Setting up the Barcode Scanner

In the Barcode Reader box, select "Symbol" as the model.

Click the **Change** button next to the Port and select the COM port the scanner is connected to. When you select the correct port, the green light on the scanner will flash.

Once you "Accept" the port, SIS will remember the port number (on that computer).

You may now disconnect the scanner from its cable.

Setup for Printing Barcode Labels

SIS prints barcode labels on 1-inch tall labels, either from a dedicated "strip" label printer (such as the Dymo Label Writer) or from a page printer using Avery 5160-compatible labels. In most cases, labels from the page printer are more convenient.

If you use a page printer, you may need to adjust the print alignment. If labels are printing over the creases, use the **Align** button to print a test page. Align lets you specify a top adjustment and/or a label height adjustment. If the text on every label is printing over the fold by the same amount, increase or decrease the top adjustment. If the alignment error gets progressively worse as you move down the page, increase or decrease the label height adjustment.

There are several places in the program where you can print barcode labels. Each of these ways will generate a Print dialog box giving you options for printing or print preview.

From the Items screen: Using the icon **Print/ "Print Barcode Labels"** Labels can be printed for all active Items and all unexpired lot numbers. The print dialog box allows you to print one of each, the standing order quantity if applicable, or a specified quantity of each label.

From the Items screen: Using selected items lists. **Choose "With selected items do: Print Barcode Labels"**. Labels can be printed for active Items and unexpired lot numbers. The print dialog box allows you to print one of each, the standing order quantity if applicable, or a specified quantity of each label.

From the QOH screen: Using a **Shopping List** created from the icon **Lists\ Make Shopping List**. When the list is open, labels can be printed with one lot number at a time. You can choose to print one of each, the recommended shopping list order quantity that is greater than 0, or a specified quantity of each label.

From the QOH screen: Using selected items lists. **Choose "With selected items do: Print Barcode Labels"**. Labels can be printed with one lot number at a time. You can choose to print one of each, the recommended shopping list order quantity that is greater than 0, or a specified quantity of each label.

When barcode labels are printed from the Lists screen, the user can designate the order the barcodes are printed by clicking a column header in the list so the data is sorted by the values in that column. Barcodes will be printed in this order. You may print them by Sequence order, Group order, Item Name order, Part Number order, or Quantity. Similarly, when barcodes are printed from the Items screen, they will print in the order the user has specified, including Sequence, Item Group, Item Name, Part Number, Location, and Vendor.

Other Settings

Auto backup on exit - If this box is checked, SIS will create a backup file each time you exit the program.

Prompt for fractional counts - If this box is checked, SIS will ask whether you want to divide barcode scanner counts by the divisor before posting them to the database. If unchecked, SIS assumes you will never have fractional counts.

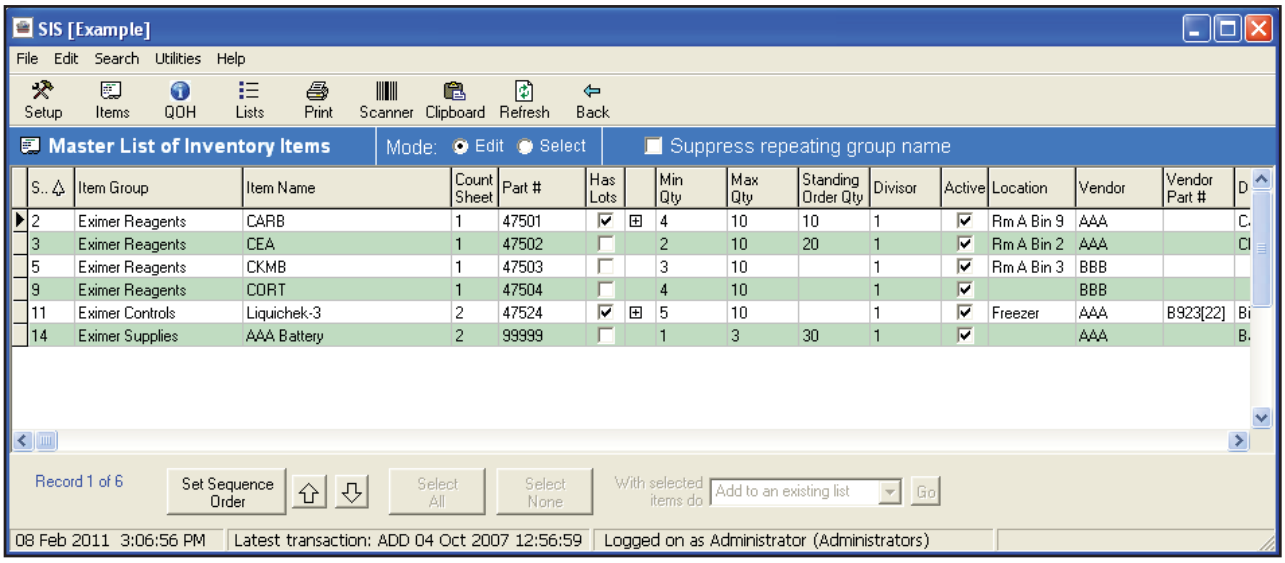
First-time Initialization of the Barcode Scanners

You can use multiple barcode scanners (one at a time) from the same computer. Simply leave the cable connected to the computer. Any scanner can be connected to the cable for data upload.

Before distributing the scanners, attach each scanner to the cable, then use the **Scanner, Clear Barcode Scanner** command to empty its memory.

Defining Inventory Items

Select the **Items** icon to open the Master List of Inventory Items. On the screen, you will define the items that you want to ensure are always available in the lab. SIS compares the data from this list to your physical inventory data to ensure you do not drop below the minimum quantity of any item.



Inventory Items Data Fields

Maximum field lengths: Item Group 32 char, Item Name 30 char, Part Number 10 char, Location 10 char, Vendor 32 char, Vendor Part Number 16 char, Description 64 char.

Seq (first column) reflects the order in which records were added. Although not directly editable, you can use the up/down arrow buttons at the bottom of the screen to re-arrange items. The sequence number is used to order items when they are printed in a count sheet. You may establish the sequence order by clicking on the **Set Sequence Order** button.

Item Group groups the items in related categories. You can type directly into the Item Group field, or you can pull down the combo box and select a previously defined group.

Item Name is a unique name for something to be ordered. This needs to be short enough to fit in 30 characters but, at the same time, descriptive enough so that the combination of Item Group and Item Name is easily recognized by the person applying labels to the boxes. The name is not case-sensitive.

Count Sheet (integer) - Every item must be assigned to a "Count Sheet." The point of a count sheet is to make sure every item gets counted when a physical inventory is done. Suppose John is responsible for physical inventory for some of the items, and Mary is responsible for the rest. For example, John is responsible for a stock room and Mary for a refrigerated area. John's items are assigned to Count Sheet 1, and Mary's to Count Sheet 2. When it is time to do a physical in-

ventory, you can use the **Lists, Make Count Sheets** function to produce separate lists for John and Mary to show what they need to count and the expected quantities in stock.

Part Number is the identifier printed in the barcode. Part numbers must be unique and may contain only letters, numbers, and the "-" (hyphen). You can use Vendor part numbers here if you do not have internal part numbers.

Has Lots - Check this box if you want to print lot number codes on barcode labels and keep track of the item by lot. When you receive a new lot, click the + next to the Has Lots column and enter the lot number and expiration date. The Lot Code is a single letter that prints on the barcode label. For example, if the Part Number of the item is 1234 and the Lot Code is A, the bar code prints as 1234.A. You can delete and re-use a lot code once its supply is exhausted. To delete a lot, right-click in the lot list and select Delete from the popup menu. Lot numbers close to or exceeding their expiration dates are color coded. Lot numbers with less than 30 days remaining before expiration are highlighted in yellow, while expired lot numbers are highlighted in gray. Lot data is highlighted in red if the expiration date has not been specified.

Min Qty - Quantity of the item that you must have in stock. When the quantity on hand drops below this level, the item is flagged in red on the Inventory Status (QOH) Report.

Max Qty - Quantity you would like to have in stock immediately after ordering.

Standing Order Qty - Quantity shipped automatically by the vendor (often zero or blank).

Divisor - This field applies when you order the item in whole boxes but want your staff to check out a partial box when it is removed from the store room.

> **Example:** You order 10 boxes of reagent, where each box contains three bottles. When you add the order to inventory, you want to add 10 (boxes), and you want inventory reports to show the quantity on hand in boxes. However, you want employees to scan the item every time they remove a bottle. In this case the Divisor is 3 (3 bottles per box). When you import the scanner memory into SIS, the scanner counts are in number of bottles – the scanner might show 2 bottles checked out. There is a checkbox on the scanner import form where you can say "Divide the counts by the divisor for the item." Check the box and SIS will deduct 2/3 items from inventory. You checked in 10 boxes, then checked out 2/3 of a box, and the Inventory Status (QOH) Report shows a quantity on hand of 9.3 boxes. When you do a physical inventory, count the number of unopened boxes plus the number of bottles left in the opened boxes.
>
> **Alternative:** If you don't want to bother with fractional boxes, set the Divisor to 1 and instruct employees to scan the item only when they open the box. When you do a physical inventory, count the number of unopened boxes only.

Active - Checked if the item is Active. The program will not import data from the barcode scanner for inactive items.

Location - You only need to enter a location for the item if you want to print it on the barcode label. If you want to print a location for the item, you may need to use less than 10 characters for part number – a 10 character part number plus a 2-character extension for lot number plus a 10 character location code in all caps may be too long to fit on the label.

Vendor - This field is used to organize the Shopping List Report. If you don't use Vendor names, the shopping list will be organized by Item Group instead.

Vendor Part Number - This field is longer than the basic Part Number field, and allows special characters. If you have entered vendor part numbers in the non-vendor Part Number field, they will appear on the barcode labels and you can leave the Vendor Part Number field blank. The Vendor Part Numbers appear on the barcodes and Shopping Lists if both Vendor and non-Vendor Part Numbers are specified. (In this situation, the Vendor Part Number supersedes the non-Vendor Part Number).

Description - Use this field to describe clearly what is to be ordered, e.g., "Tips, Pipette 200 - 1000 Blue." The point of this field is that it can be longer than the Item Name. (Item Name is constrained, since it has to be short enough to print on the barcode label.)

What you can do from the Inventory Items Screen

Administrators can . . .

- Change the data for an existing inventory item, including desired and minimum quantities to hold in inventory.
- Add items either by pasting from Excel or by typing directly into the grid.
- Add/delete/edit lot number information
- Determine the sequence order of items, which is mirrored in count sheets and reports. Items can be ordered to reflect the order they are encountered in the storeroom.
- Delete a single item (right-click and select Delete from the popup menu).
- Delete several items at once. Go to the Mode radio buttons at the top of the screen and switch to Select mode. Select the items you want to delete, then execute **With selected items do Delete** at the bottom of the screen.

Administrators and Operators can . . .

- Add items to an existing list
- Print barcode labels. In Edit mode, barcodes are printed for all items and all unexpired lot numbers. In Select mode, barcodes are printed for selected items with all unexpired lot numbers as well.
- Any Lists created from selected items have empty quantity columns, and when open in the list viewer. Lot numbers are selectable one at a time.

Administrators, Operators, and Guests can . . .

- Change the sort order of the display, by clicking the column headings. Not all columns are sortable–if you click on a sortable heading, you will see an arrow symbol in the heading indicating the sort direction.
- Drag the column headers to make the columns wider or narrower.
- For guest access, some features are grayed out, while others are simply not present.
- View the defined lot numbers (by clicking the + symbol next to the Has Lots column).
- Right-click an item and select **Full Screen View** to see the data for that item in a vertical format where no columns are clipped due to lack of space. Administrators can edit the data in Full Screen View; operators and guests can only view it.
- Copy the inventory item list to the clipboard. Administrators and operators can switch to Select mode, select a subset of items, and copy the selected items only. Guests can copy the full list only.
- Search for text, using Search, Find or Control+F. Find locates a string (or partial string) in the Item Name, Part Number, Vendor Part Number, or Description. For example, find "T3" would find "T3", "FT3" and "TT3." Find moves the cursor to the first matching record. **Find Next** (or the F3 function key) moves to the next matching record.

Pasting from Excel

From the Inventory Items screen, select **Edit**, **Copy** from the SIS menu, then open Excel and select **Edit**, **Paste** in Excel. This creates a template with valid column headings. You can then delete all the lines except the first heading line and enter your own data in its place.

NOTE: If any field values in your database contain leading zeros, pasting the data into Excel may remove the leading zeroes in numeric fields. Usually, this is only a problem with the values in the Part Number field. EP Evaluator displays a warning if your database contains field values with leading zeros. Before pasting the SIS data into Excel, format all cells in the spreadsheet as Text.

After preparing your data in Excel, copy it to the clipboard. Switch back to the SIS Inventory Items screen, and select **Edit**, **Paste** from the SIS menu. Pasted entries are added/updated based on the Part Number column. If the Part Number is not in the SIS database, it will be added to the database. If it is in the database, the data for that part number will be updated.

Edit Mode vs. Select Mode

The **Mode** radio buttons at the top of the screen toggle between **Edit Mode** and **Select Mode**. In Edit Mode, you can type in the grid cells to change inventory item data. In Select Mode you cannot edit the data, but you can select one or more records for batch operations. To select adjacent lines, click the first line of the group, then shift-click the last line. To select non-adjacent items, control-click each one individually. After items are selected, use the **With selected items do** combo box at the bottom of the screen to perform an operation on the selected items.

Ditto Key

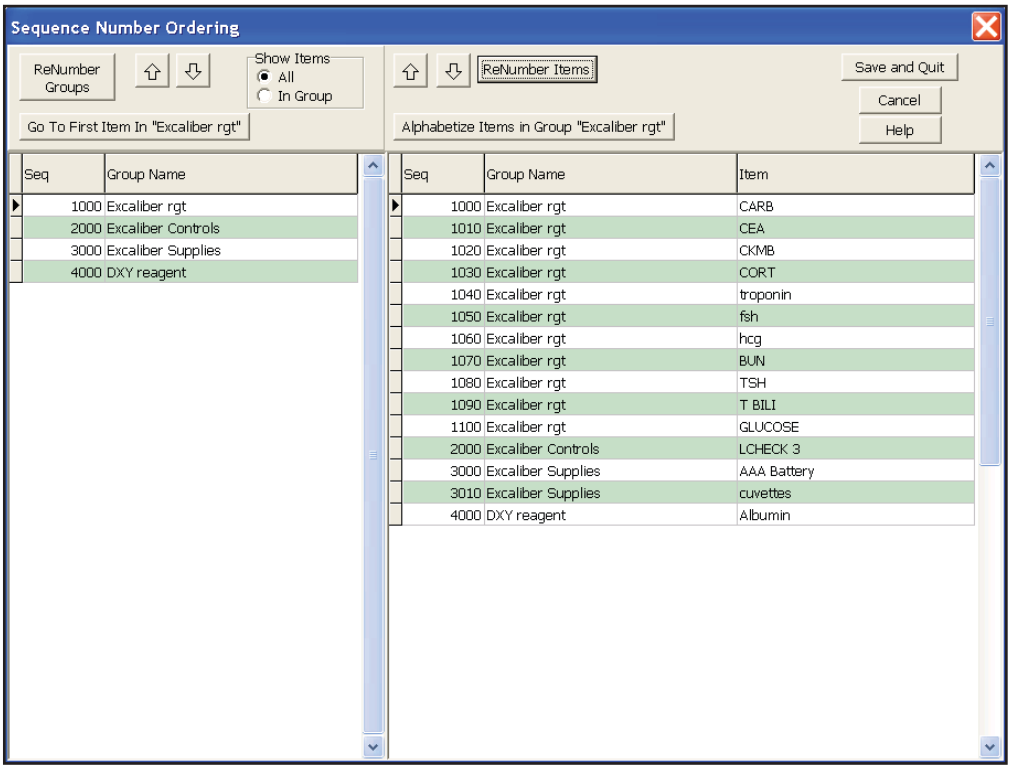
When editing a record, press Control+D to duplicate data from the previous record. When inserting a new record, Control+D duplicates data from the record that was active when you pressed Insert. Ditto operates on a field basis not on a record basis. For example, if the cursor is in the Item Group column, pressing Control+D duplicates only the Item Group, not the other values. Also, Ditto does not work on fields like the Part Number that would not commonly be repeated across multiple items.

Controlling the “Natural” Sort Order

The first column of the Inventory Items grid shows a sequence number that, by default, reflects the order in which items were added to the database. This natural sort order also determines the order in which items appear on you count sheets and other reports. Because it is useful for items on the count sheets to be listed in the order in which they are encountered in your storage area, you may find it necessary to change the sort order of inventory items. When the data is sorted on this column, you can use the up/down arrow buttons at the bottom of the screen to move the selected item up or down in the list. To insert an item at a specific location, put the cursor on a line and press the Insert key to insert a blank row above the selected line. To insert an item at the end, scroll to the bottom of the list and press the down key. Note that this works only when adding items from the keyboard. When you paste from the clipboard, new items are added at the end. The “Natural” sort order can also be changed by setting the sequence order as described in the next section.

Set Sequence Order

Count sheets are usually printed in the same order as the inventory items are encountered in your storage area. For inventories with small numbers of items, this can be achieved fairly easily using the up/down arrow buttons on the Items Inventory form. For larger numbers of items, after you have defined all of your Groups and Items, you may find it easier to click on the **Set Sequence Order** button found on the bottom of the Inventory Items screen, which will bring up the following form:



Groups Grid (left grid)

From the **Sequence Number Ordering** screen, you can change the sort order of the Group Name column by editing the number in the **Seq** column in the left grid. This changes the order in which you encounter your Groups in the store-room. If the sequence numbers start to get too close together, you can renumber them with the **ReNumber Groups** button. If you edit a Group Name, that change will be propagated to the Items grid, on the right. Minor changes in order can be made with the up/down arrow buttons. This screen also allows you to navigate to the first Item in a Group by selecting the Group row and clicking the **Go to First Item In** button. To see only the Items listed for a particular Group, select **In Group** in the **Show Items** radio-button menu.

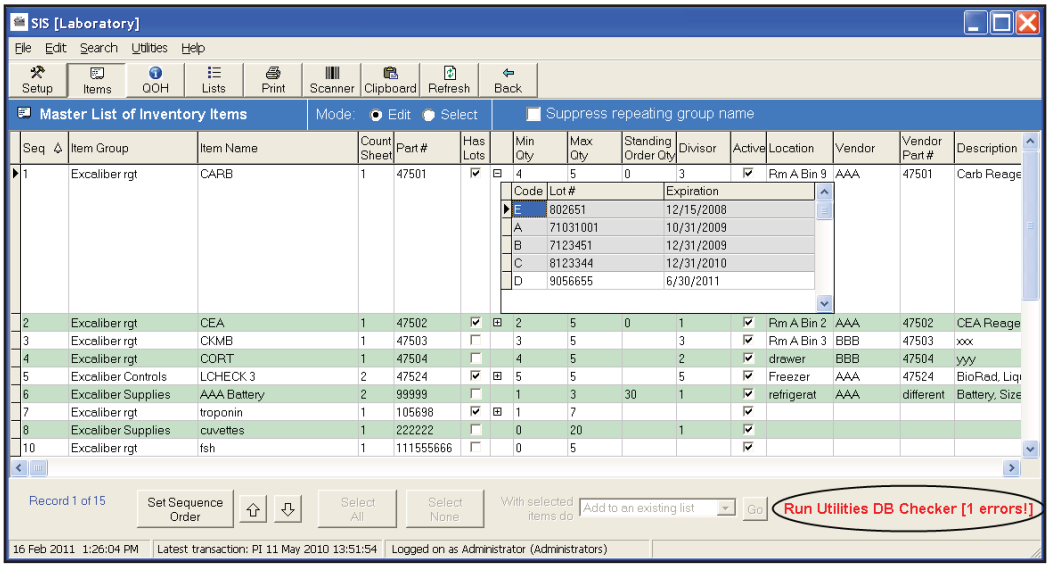
Items Grid (right grid)

Items within the Groups can be sorted in the right grid by editing the numbers in the **Seq** column**.** If the numbers get too close together, you can renumber them using the **ReNumber Items** button. Minor changes in order can be made with the up/down arrow buttons. Use the **Alphabetize Items in the Group** button to alphabetize items within a Group. It is possible to recategorize an Item by selecting the Group Name that appears next to that Item and selecting a different Group Name from the dropdown. You can also rename an Item from the Sequence Number Ordering screen.

Once you have made your changes, click **Save and Quit**. Clicking **Cancel** closes the screen without saving your changes.

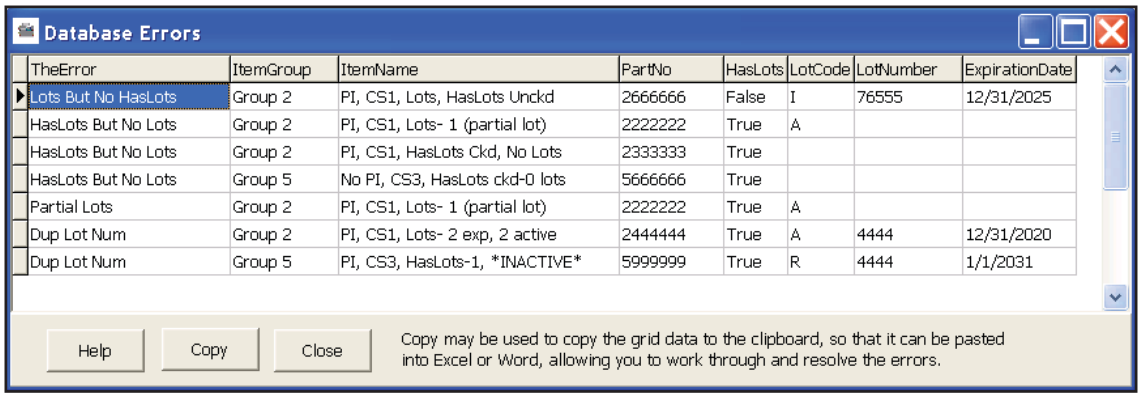
Detecting and Fixing Data Entry Errors

If the SIS database detects an error in how lot number data is entered, a **Run Utilities Database Checker** error will appear in the lower right-hand corner of the Inventory Items screen.



The consequences of handling lots incorrectly are troublesome. If the Has Lots checkbox is checked for a particular item, but no Lots are defined, the item may be omitted from your reports. If you create an Item with Lots, and accidently uncheck the Has Lots checkbox, the Item will lose its Lot-oriented features.
To find data entry errors related to Lots, go to the **Utilities, Database Check** menu.

The **Database Errors** screen appears:



The Database Errors screen reports four types of errors:

Lots But HasLots: Lots appear to be defined for this item, but HasLots is not checked.

HasLots But No Lots: The HasLots checkbox is checked, but not lots are defined. This error could result in the item being omitted from barcode printouts. Define your lots or un-check HasLots.

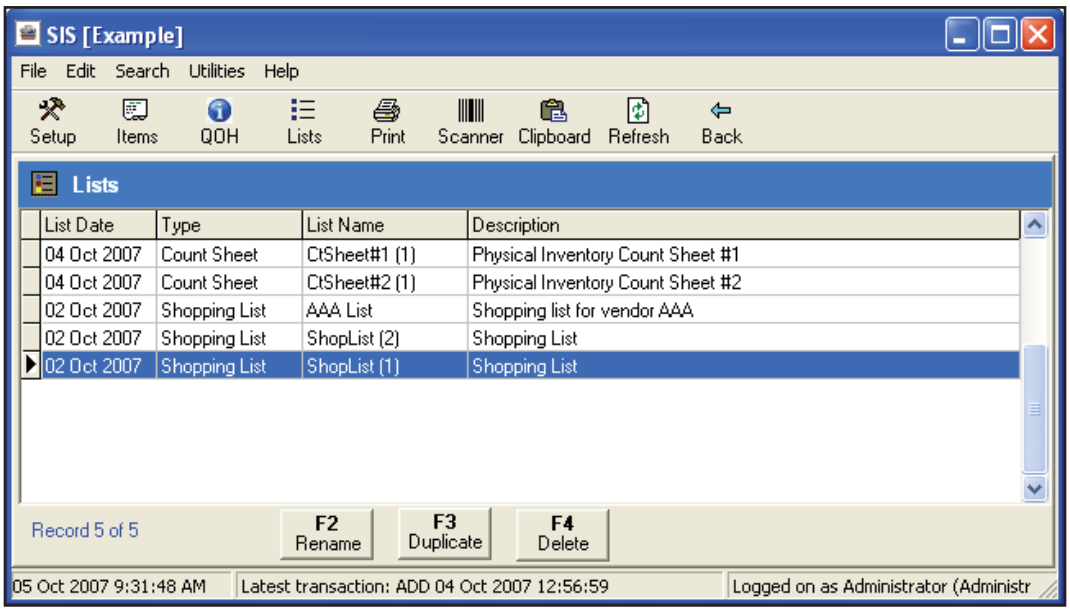
Partial Lots: Each lot should have a Lot Code, Lot Number, and Expiration Date. This error occurs when you have not defined all three of these fields for a given lot.

Dup Lot Num: Each lot number should be unique across all items. This error warns you that you have used the same lot number more than once.

Doing a Physical Inventory

Step 1. Create Count Sheets

Start by going to the QOH screen and creating Count Sheets using the **Lists, Make Count Sheets** command. This creates list(s) of items to be counted and automatically opens the List Viewer. These count sheets contain the net totals of quantities set during the last physical inventory, plus any added items, minus any subtracted items.



The List Viewer shows a catalog of all the lists you have created. A list is just a subset of items and quantities. There are three types of lists:

Count Sheet - a list of items to be counted for physical inventory. When you make count sheets, every active item is put in its count sheet. In the illustration above, the master inventory list used two count sheets - CtSheet #1 and CtSheet #2. Other count sheets created from selected items in the item screen:

- Have empty quantity column
- Lot numbers appear one at a time.
- Lot numbers sort according to expiration date

Shopping List - a list of items created for ordering.

From the List Viewer screen, you can **Rename**, **Delete**, **Duplicate**, or **Open** a list by right-clicking it and selecting the function from the dropdown menu, or by highlighting it and using the buttons at the bottom of the screen. You can also Open a list by double-clicking it.

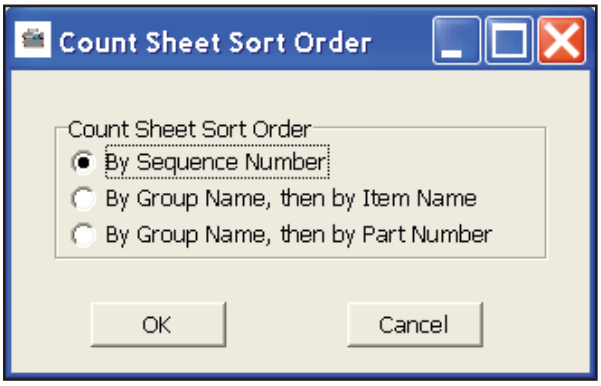
Delete and **Rename** are self-explanatory. **Duplicate** is worth a bit more discussion. Suppose you created a shopping list last month. This month you want to order the same items but with different quantities. However, you don't want to re-

move the old list. You can duplicate the old list to create a new, identical list (but with a different name). You will have a choice of carrying the quantities forward to your new list, or keeping just the items and clearing the quantities.

Step 2. Print Count Sheet Reports

A Count Sheet Report is a printout of items to be counted. You can only print this report when you are looking at the list of items you want to print (i.e., when it is "open" in the list viewer). Double-click the Count Sheet in the List Viewer to open it. Then request **Print, Manual Count Worksheet** to get the report illustrated in Figure 33.1.

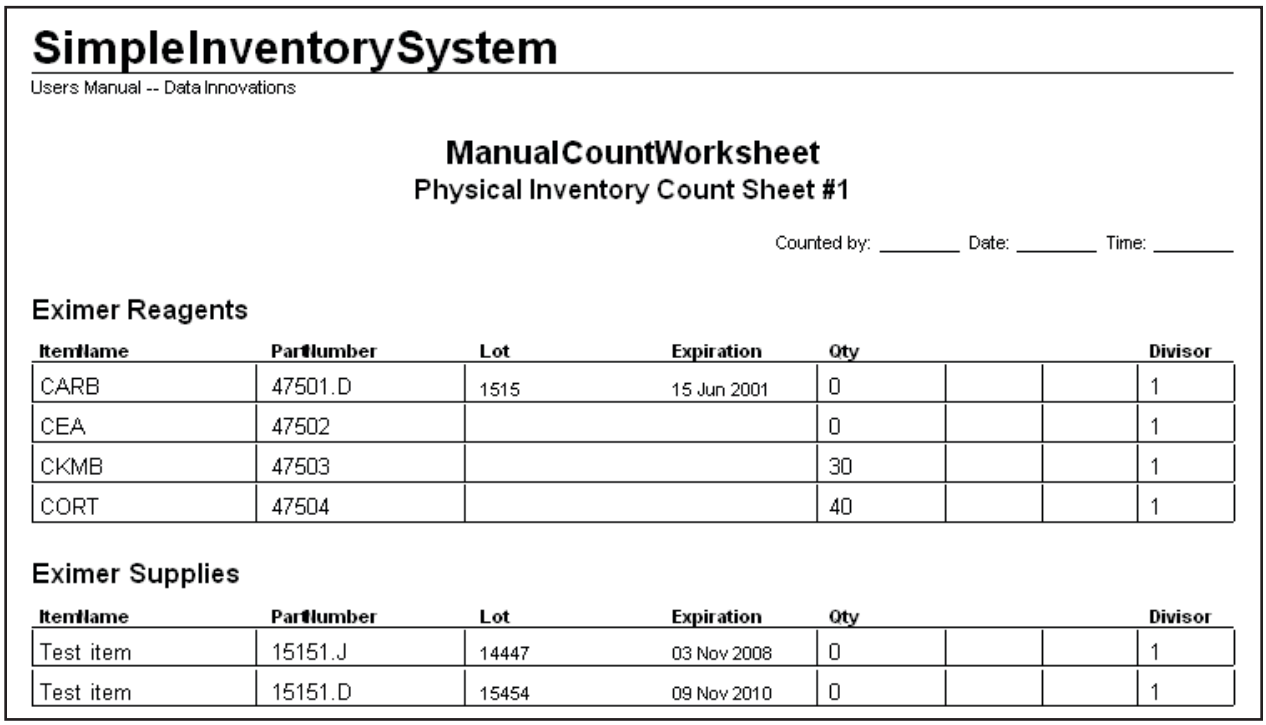
The **Count Sheet Sort Order** dialogue displays, allowing you to choose how items in the printed Manual Count Worksheet will be sorted. Once you click OK, the **Output Options** dialogue displays. From this dialogue, you can preview and print your Count Sheet Report.



Take this report to the store room and record the actual item counts. (You don't need to record anything if the actual count is the same as the Qty on the report.) Don't forget to record the date and time when the items were counted.

- In the report below, some items have a "Divisor" that is not 1. This means that users are scanning out fractional items. Record the number of unopened boxes in the first blank square, and the number of bottles in opened boxes in the second square.

- The illustration also shows an example where CARB is being tracked by lot number, while CKMB, CEA, and CORT are not.



SimpleInventorySystem

Users Manual -- Data Innovations

ManualCountWorksheet

Physical Inventory Count Sheet #1

Counted by: _____ Date: _____ Time: _____

Eximer Reagents

ItemName	PartNumber	Lot	Expiration	Qty			Divisor
CARB	47501.D	1515	15 Jun 2001	0			1
CEA	47502			0			1
CKMB	47503			30			1
CORT	47504			40			1

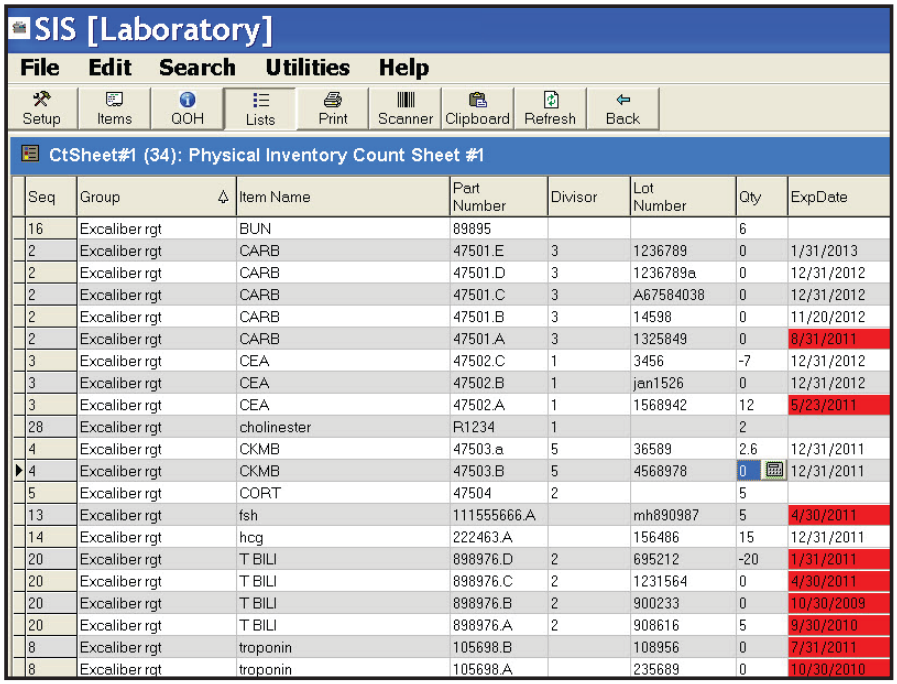
Eximer Supplies

ItemName	PartNumber	Lot	Expiration	Qty			Divisor
Test item	15151.J	14447	03 Nov 2008	0			1
Test item	15151.D	15454	09 Nov 2010	0			1

Figure 33.1: Manual Count Worksheet Report

Step 3. Enter the Corrected Counts in SIS

After completing the manual counts, go back to SIS and select **Lists, Open List Viewer**, then double-click the Count Sheet List to open it.



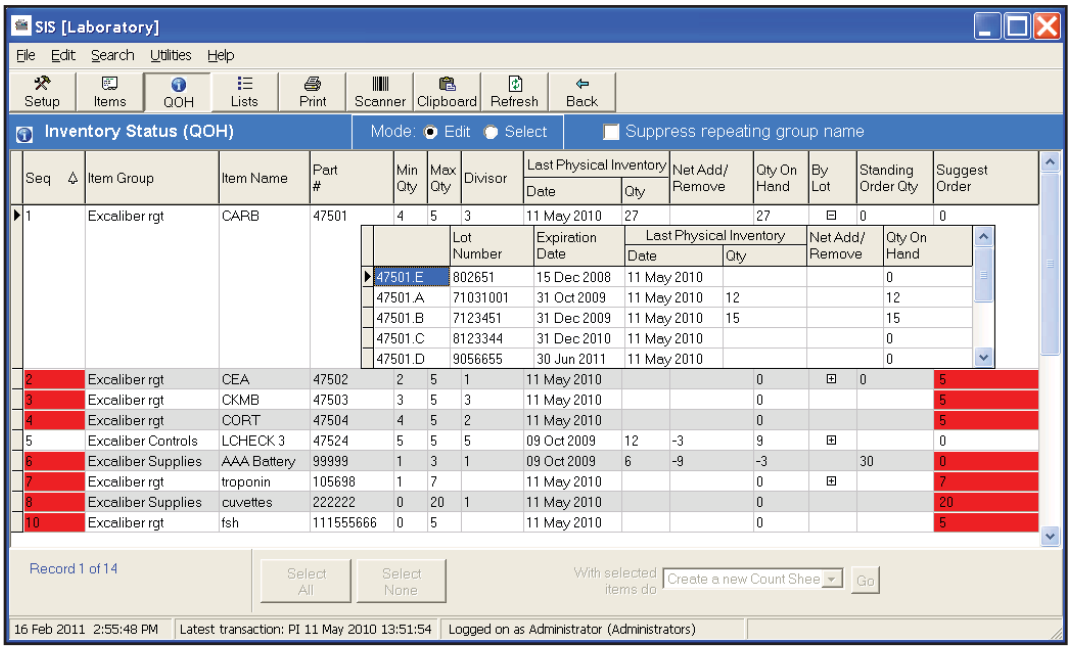
Seq	Group	Item Name	Part Number	Divisor	Lot Number	Qty	ExpDate
16	Excaliber rgt	BUN	89895			6	
2	Excaliber rgt	CARB	47501.E	3	1236789	0	1/31/2013
2	Excaliber rgt	CARB	47501.D	3	1236789a	0	12/31/2012
2	Excaliber rgt	CARB	47501.C	3	A67584038	0	12/31/2012
2	Excaliber rgt	CARB	47501.B	3	14598	0	11/20/2012
2	Excaliber rgt	CARB	47501.A	3	1325849	0	8/31/2011
3	Excaliber rgt	CEA	47502.C	1	3456	-7	12/31/2012
3	Excaliber rgt	CEA	47502.B	1	jan1526	0	12/31/2012
3	Excaliber rgt	CEA	47502.A	1	1568942	12	5/23/2011
28	Excaliber rgt	cholinester	R1234	1		2	
4	Excaliber rgt	CKMB	47503.a	5	36589	2.6	12/31/2011
4	Excaliber rgt	CKMB	47503.B	5	4568978	0	12/31/2011
5	Excaliber rgt	CORT	47504	2		5	
13	Excaliber rgt	fsh	111555666.A		mh890987	5	4/30/2011
14	Excaliber rgt	hcg	222463.A		156486	15	12/31/2011
20	Excaliber rgt	T BILI	898976.D	2	695212	-20	1/31/2011
20	Excaliber rgt	T BILI	898976.C	2	1231564	0	4/30/2011
20	Excaliber rgt	T BILI	898976.B	2	900233	0	10/30/2009
20	Excaliber rgt	T BILI	898976.A	2	908616	5	9/30/2010
8	Excaliber rgt	troponin	105698.B		108956	0	7/31/2011
8	Excaliber rgt	troponin	105698.A		235689	0	10/30/2010

If the numbers in the Qty column differ from what you counted, change the values. If you counted an integer number of unopened boxes, just type the number in the cell. If you counted something like 2 boxes + 3 bottles for CKMB, you can click the calculator icon in the cell and do the division: 2+3/5. Here the “5” is the divisor for CKMB.

Once the counts are correct, use **With this list do Set as Physical Inventory** from the combo box at the bottom of the screen.

Inventory Status (QOH)

The QOH screen is a list of the items you currently have on hand.



Inventory Status (QOH) Data Fields

(The first seven columns are descriptive fields and are described in more detail in "Inventory Items Data Fields".)

Seq - item order

Item Group - groups items for sorting

Item Name - name of the item

Part Number - unique item identifier that is printed on the bar code label. For lot numbered items, a single line represents aggregate quantities for all lots. To see detail by lot, click the + symbol in the By Lot column.

Min Qty - Quantity of the item that you must have in stock. When the quantity on hand drops below this level, the item is flagged in red.

Max Qty - Quantity you would like to have in stock immediately after the order is received.

Divisor - If you order in boxes, but check items out of inventory in bottles, the Divisor is the number of bottles per box.

Last Physical Inventory - Date and quantity counted at the last physical inventory.

Net Add/Remove - For transactions since the last physical inventory, sum of items added (received) less sum of items withdrawn (taken out of the store room).

Qty on Hand - Quantity at last physical inventory plus Net Add/Remove. Items with a Quantity on Hand less than the minimum are shown in red.

By Lot - For lot-numbered items, click the + symbol to see quantity on hand by lot number.

Standing Order Qty - Quantity shipped automatically by the vendor (often zero or blank).

Suggested Order - Order quantity that would bring the quantity on hand up to the Max Qty level: Suggested Order = Max Qty - QOH - Standing Order (but never less than zero). Items with a quantity at or below the minimum quantity are highlighted in red. Items with a quantity above the minimum quantity, but below the maximum quantity are highlighted in yellow.

Note: The only column you can edit in the Inventory Status (QOH) screen is the **Suggested Order Quantity** column. Any changes you make to this column will be reflected in a shopping list created from the QOH screen. However, once you leave the QOH screen, the value in this column resets to its original value.

What you can do from the QOH Screen

Administrators and Operators can . . .

- Make a standard Shopping List–using the **Make Shopping List** command on the Lists button. A "standard" shopping list contains all the items with non-zero Suggested Order Quantity. Here is an example where you might want to edit the suggested order quantities, even though the change is not permanent:

  You look at the QOH report and agree with all of the suggested order quantities but one. SIS suggests an order quantity of zero for item ABC, but you would prefer to order 6. Change the zero to a 6, then do Make Shopping List. The resulting shopping list will show a quantity of 6 for item ABC. Items with a suggested order quantity of zero will not appear in the list at all.

- Create a list of selected items.

  Perhaps you don't want to put everything on one shopping list. For example, you might want a list for just one vendor. To do that, use the **Mode** radio buttons at the top of the screen to switch to **Select** mode. To select consecutive items, click the first one, then shift-click the last one. To select non-consecutive items, control-click each one.

  Similarly, perhaps you do not want every item listed in a count sheet. Use the **Mode** radio buttons at the top of the screen to switch to Select mode. To select consecutive items, click the first one, then shift-click the last one. To select non-consecutive items, control-click each one. The count sheet will be labeled Manual Count Sheet and list QOH quantities.

- Add selected items to an existing list.

- Set the physical inventory for selected items to zero. For one item, right-click it. For multiple items, switch to Select Mode, select the items, then use With selected items do.

Administrators, Operators, and Guests can . . .

- Change the sort order of the display by clicking the column headings. Not all columns are sortable–if you click on a sortable heading, you will see an arrow symbol in the heading indicating the sort direction.

- Drag the column headers to make the columns wider or narrower.

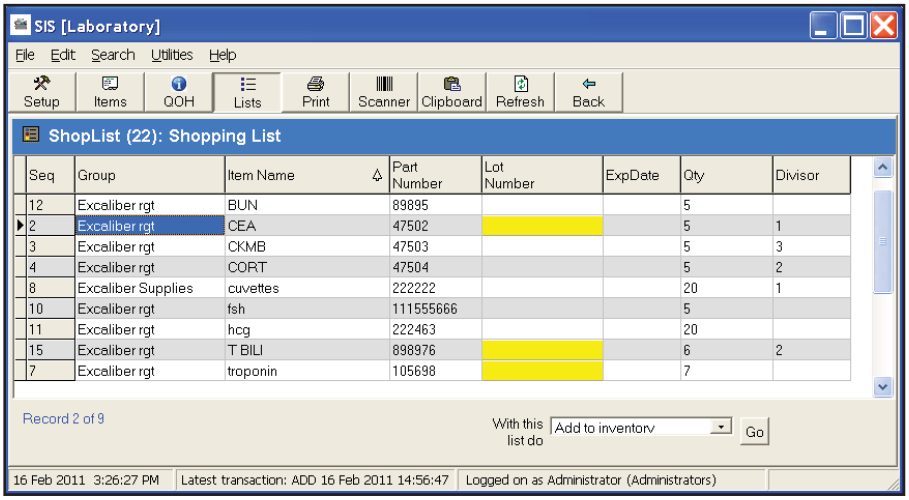
- Copy the data to the clipboard. Administrators and operators can switch to Select mode, select a subset of items, and copy the selected items only. Guests can copy the full list only.

- Review the transaction history for a single item by right-clicking the item and selecting Transaction History from the dropdown menu.

Creating Your Shopping List

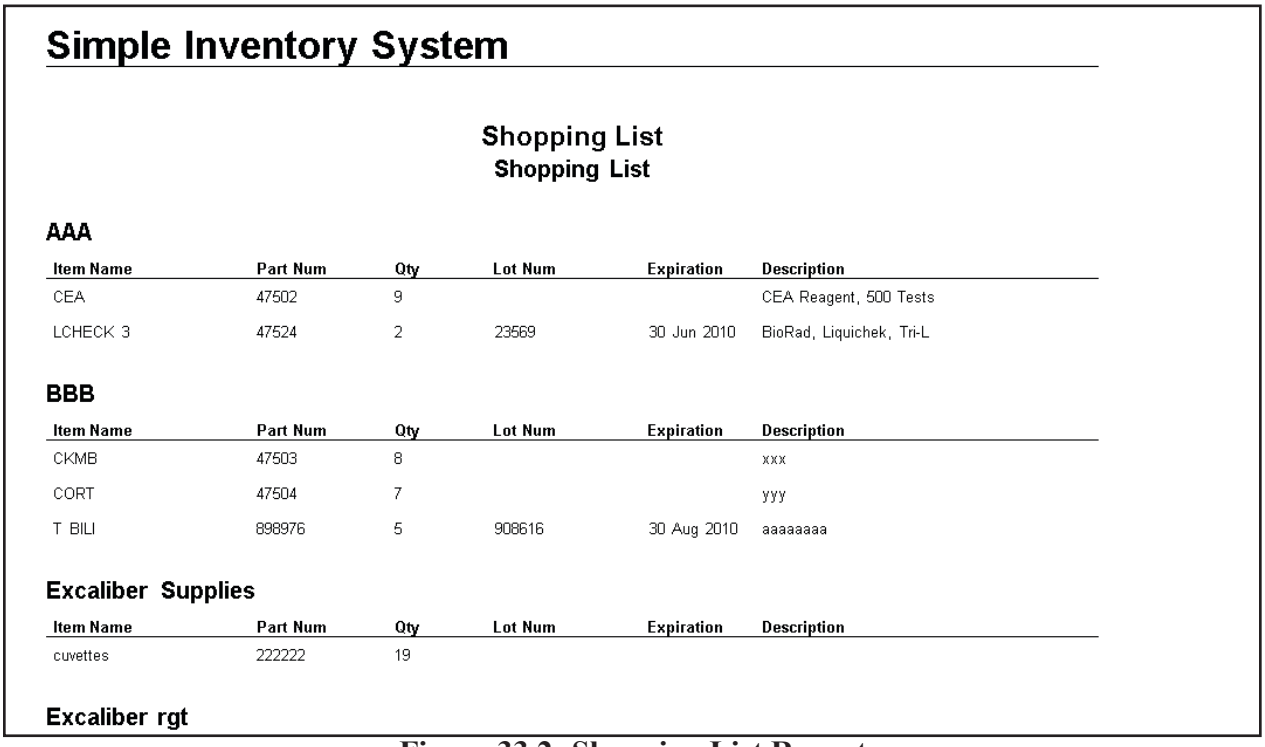
A Shopping List is any list of items to be ordered. A "Standard" Shopping List is created from the Quantity on Hand and is based on the Min, Max, and Standing Order quantities you assigned to the items when you created the master inventory list. To create a shopping list, first Select the QOH icon at the top of the screen to view the Inventory Status (QOH). Select the **Lists/Make Shopping List** command. Alternatively, switch to Select mode, select the items you want on your shopping list, and use the **With selected items do Create a New Shopping List** at the bottom of the screen.

Creating a list opens your new list in the List Viewer. A shopping list might look something like this:



Adjust the quantities if necessary, then select **Print, Shopping List**. The Shopping List Report (illustrated in Figure 33.2) contains information needed to place the order. Note that:

- Multiple lot numbers appear if more than one non-expired lot number is present for an item that needs to be ordered.
- If an Item is supposed to have lots (HasLots is checked on the Inventory Items screen) but the Lot Number is empty, the Lot Number field is flagged in yellow. If a lot number is expired, the The ExpDate field is flagged in red.
- If the Vendor Name is specified, then the Shopping List items are sorted by the Vendor Name field. Otherwise, the report is sorted by the Item Group field. Within each Item Group, items are sorted by Item Name.
- The Part Number column contains the Vendor Part Number if available. Otherwise it contains the barcode part number.
- Both a Shopping List and a Count Sheet can be created from the Inventory-Items (QOH) screen. A Shopping List will include suggested re-order quantities; a Count Sheet will include QOH quantities.



Simple Inventory System

Shopping List
Shopping List

AAA

Item Name	Part Num	Qty	Lot Num	Expiration	Description
CEA	47502	9			CEA Reagent, 500 Tests
LCHECK 3	47524	2	23569	30 Jun 2010	BioRad, Liquichek, Tri-L

BBB

Item Name	Part Num	Qty	Lot Num	Expiration	Description
CKMB	47503	8			xxx
CORT	47504	7			yyy
T BILI	898976	5	908616	30 Aug 2010	aaaaaaaa

Excaliber Supplies

Item Name	Part Num	Qty	Lot Num	Expiration	Description
cuvettes	222222	19			

Excaliber rgt

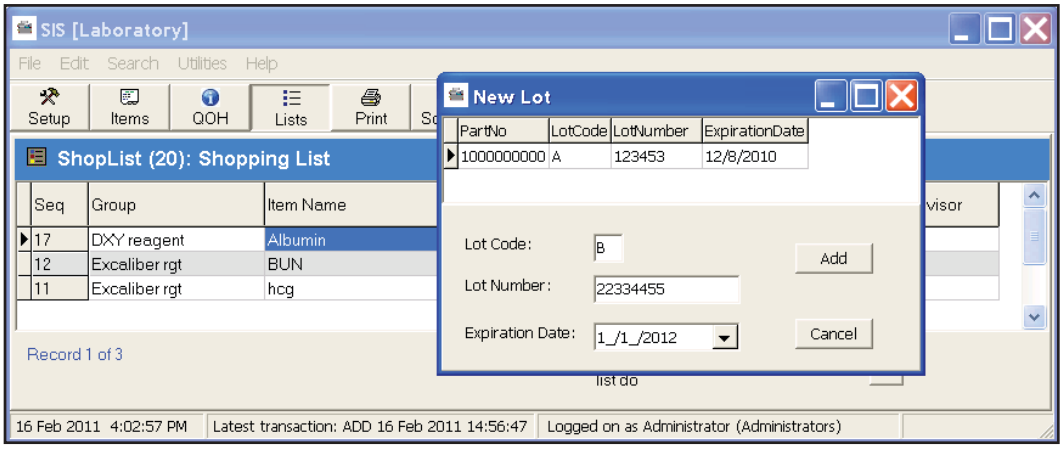
Figure 33.2: Shopping List Report

Receiving the Order

When your order arrives, you will need to confirm that the quantities you received agree with what you ordered. You will also need to print barcode labels to attach to the boxes so they can be checked out of the store room with the barcode scanner.

To print barcode labels, go to the List Viewer and open your shopping list. If you are tracking lot numbers, confirm that the lot numbers on the list match what you received.

If you receive a new lot, modify the shopping list by right-clicking on the name of the item with the new lot and select **Add New Lot**. The **New Lot** dialogue displays. Add the new lot and click **Add**. Once you see the new lot in the shopping list, you can enter the quantity received.

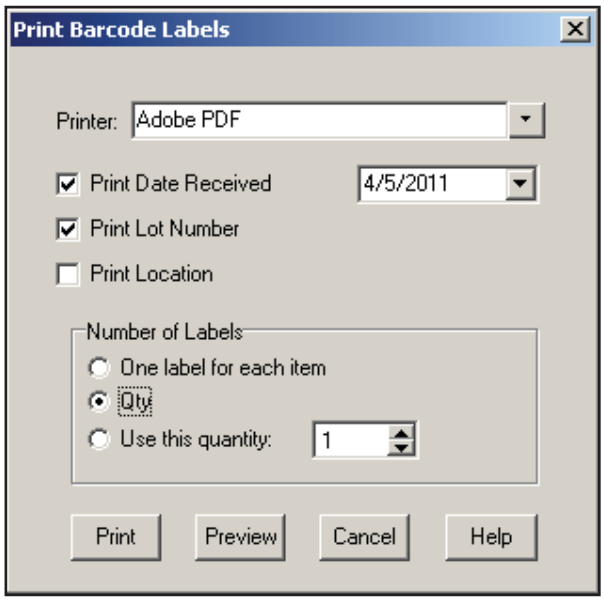


Select With this list do Print Barcode Labels from the combo box at the bottom of the screen. SIS asks for additional details:

Printer - choose the printer where the labels are to be printed

Print Date Received - check the box if you want the date printed on the label. Also enter the date in the edit field to the right of the checkbox.

Print Location - check the box if you want the location printed on the label. This assumes, of course, that you specified a location for the item in the master list of items.



Number of Labels - You can print one label for each item, some other fixed number of labels, or you can use the Qty column from the list. In most cases you want to use the Qty column.

Click **Print** to print the labels, or **Preview** to view a print preview.

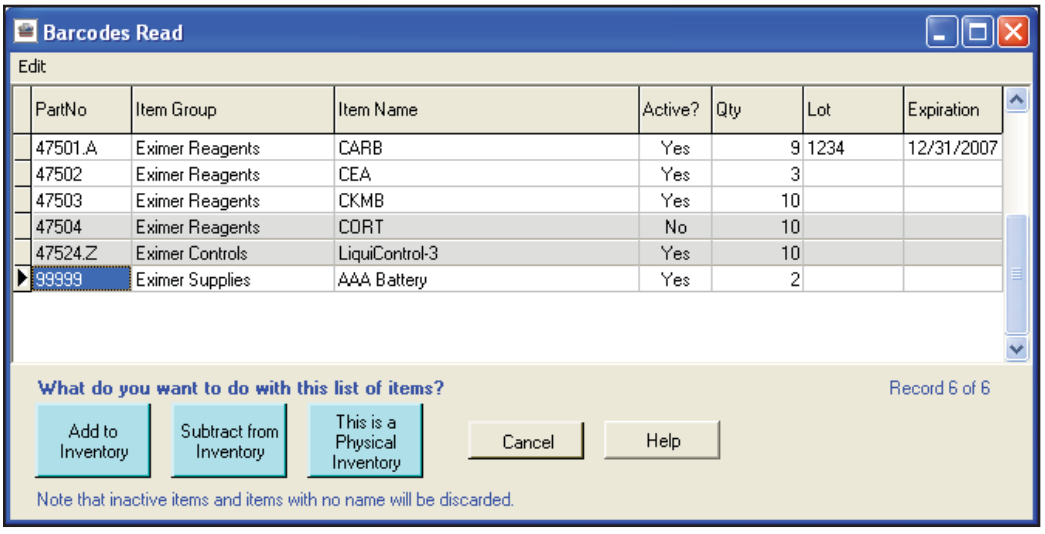
Did you receive what you ordered? Attach the barcode labels to the boxes you received. If the number of labels exactly matches the number of boxes, the counts agree. Otherwise edit your shopping list to indicate what items you actually received.

After editing the shopping list, select **With this list do Add to Inventory** from the combo box at the bottom of the screen. You will be asked for the date and time of the transaction. The important thing about times is to make sure the transactions go into SIS in chronological order.

Inventory Checkout

A barcode scanner should be available in the store room so employees can scan items out as they are removed. Periodically the scanners are collected, and their contents are uploaded to SIS. A scanner memory holds about 350 barcodes.

To upload barcodes, first connect the scanner to the computer. Then select the Scanner/Read Barcode Scanner command. The scanner should beep (if it doesn't, you may have forgotten to connect it). Then SIS shows what was read:



Before doing anything with the data, look for lines shaded in light gray. These lines represent "invalid" items, and they will NOT be sent to the database. There are three reasons this might happen:

- The barcode (part number) does not appear in the master list of inventory items. In that case the Item Group and Item Name will be blank.

- The barcode is valid, but the item is inactive (for example, CORT in the illustration above).

- The barcode is for a lot numbered item, and the lot code does not appear in the master list (for example, Liquicontrol-3 in the illustration). The ".Z" in the part number signals that this item has a lot number.

You may have simply scanned an incorrect item. In that case you can process the data normally, and the invalid items will be ignored. Alternatively, select **Cancel**. Edit the master inventory list to add the lot or activate the item; then read the data again.

There are a few changes you can make (with caution) to the data in this form before sending it to the database:

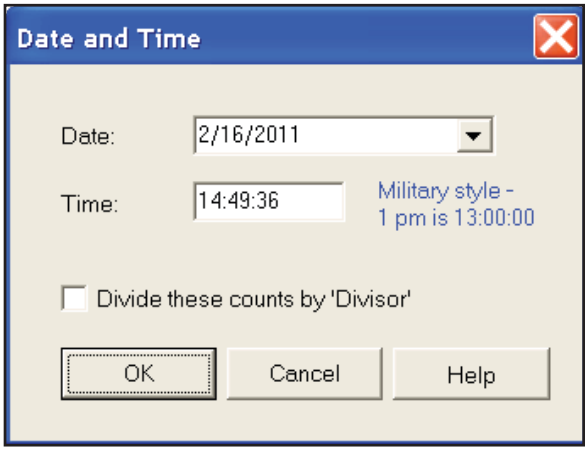
- You can edit the numbers in the Qty column.

- You can delete a line–right-click, then select Delete from the popup menu. Note that it is not necessary to delete the gray lines, since the program will automatically ignore them.

You cannot add items, and you can't change part numbers.

If you need to make more extensive changes, select **Edit, Copy** from the menu at the top of the screen, then Cancel this form, paste the data into Excel and edit it there. After correcting the data, you can import it with **Clipboard, Paste Inventory Counts**.

When the data is correct, click the **Subtract from Inventory** button at the bottom of the screen. (This assumes, of course, that the scanner memory holds items that employees have checked out of the store room.)



SIS prompts you to enter a date and time for the batch. Two important points about this form:

- The date and time don't have to be absolutely precise to the second – but the dates you assign to transaction batches must correctly reflect the order in which the events occurred in relation to the last physical inventory. Quantity on Hand is determined by summing the additions and subtractions that occurred since the last physical inventory. If an add or subtract is applied out of chronological sequence, the quantity on hand will be incorrect.

- **Divide these counts by 'Divisor'** appears on the form when you are doing a physical inventory or subtracting from inventory if you indicated on the Setup Screen that you wanted to be prompted for fractional counts.

Example: Reagent is ordered in boxes. Each box contains 5 bottles (divisor of 5), and users scan each bottle when they remove it from the store room. The scanner memory contains a count of bottles, but the inventory database stores the count in boxes. Check **Divide these counts by 'Divisor**' to tell SIS to convert the scanner counts to appropriate units.

Other Reports

This section illustrates other reports available from the SIS Print button:

- The **Inventory Item Listing** is a printable form of what you see on the Inventory Items screen. It comes in two forms: short (Figure 33.3.) and long (Figure 33.4.). If you don't need vendor names, vendor part numbers, or long descriptions, use the more compact short form. Click the Print button and select **Inventory Item Listing (Short)** or **Inventory Item Listing (Long)**.
  - This report is sorted by the Sequence order field.

- The **Quantity on Hand or Inventory Status Report** (Figure 33.5.) can be printed any time you wish to review the current status of your inventory. This report displays the data visible in the QOH screen grid. Click the Print button and select **Quantity On Hand Report**.
  - This report is sorted by the Sequence order field.

- The **Monthly Usage Report** (Figure 33.6.) shows the total number of items removed from inventory each month, for the most recent 12 months. These counts include only what was subtracted from inventory; they do not include any adjustments when the physical inventory differs from the reported quantity on hand. Click the Print button and select **Monthly Usage Report**.
  - This report is sorted by the Sequence order field.

- The **Inventory Adjustments Report** (Figure 33.7.) shows, for the last three physical inventories, the difference between the manual count and the reported quantity on hand. **Date** is the date of the physical inventory, **PI** is the physical inventory, and **Adj** is the difference between the physical count and the reported quantity on hand. Click the Print button and select **Inventory Adjustments**.
  - This report is sorted by the Sequence order field.

Simple Inventory System

Master List of All Inventory Items

Excaliber rgt

Part Num	Active?	Count Sheet	Item Name	Min Qty	Max Qty	Stand Order	Divisor	Has Lots?
47501	Y	1	CARB	4	5	0	3	Y
47502	Y	1	CEA	2	5	0	1	Y
47503	Y	1	CKMB	3	5		3	N
47504	Y	1	CORT	4	5		2	N
105698	Y	1	troponin	1	7			Y
111555666	Y	1	fsh	0	5			N
222463	Y	1	hcg	0	20			N
89895	Y	1	BUN	0	5			N
555556666	Y	2	TSH	1	6		1	N
898976	Y	1	T_BILI	2	6		2	Y

Figure 33.3. Inventory Item Listing (short)

Simple Inventory System

Master List of All Inventory Items

Excaliber rgt

Part Num	Count Sheet	Item Name	Min Qty	Max Qty	Stand Order	Divisor	Active?	Has Lots?	Location	Vendor	Vendor Part #
47501	1	CARB	4	5	0	3	Y	Y	Rm A Bin 9 Carb Reagent, 250 Tests/Box	AAA	47501
47502	1	CEA	2	5	0	1	Y	Y	Rm A Bin 2 CEA Reagent, 500 Tests/Box	AAA	47502
47503	1	CKMB	3	5		3	Y	N	Rm A Bin 3 xxx	BBB	47503
47504	1	CORT	4	5		2	Y	N	drawer yyy	BBB	47504
105698	1	troponin	1	7			Y	Y			
111555666	1	fsh	0	5			Y	N			
222463	1	hcg	0	20			Y	N			
89895	1	BUN	0	5			Y	N			

Figure 33.4. Inventory Item Listing (long)

Simple Inventory System

Inventory Status

Excaliber rgt

PartNo	Item Name	Min Qty	Max Qty	Last Phys Inventory Date	Qty	Net Add/ Remove	Quantity on Hand	Standing Order	Suggested Order
47501	CARB	4	5	11 May 2010	27		27	0	0
47502	CEA	2	5	11 May 2010			0	0	5
47503	CKMB	3	5	11 May 2010			0		5
47504	CORT	4	5	11 May 2010			0		5
105698	troponin	1	7	11 May 2010			0		7
111555666	fsh	0	5	11 May 2010			0		5
222463	hcg	0	20	11 May 2010			0		20
89895	BUN	0	5	11 May 2010			0		5

Figure 33.5. Quantity on Hand Report

Simple Inventory System

Monthly Withdrawals from Inventory
(last 12 months)

Excaliber rgt

PartNo	ItemName	Jun09	Jul09	Aug09	Sep09	Oct09	Nov09	Dec09	Jan10	Feb10	Mar10	Apr10	May10
47501	CARB	-	-	-	-	1	-	4	-	10	-	1	1
47502	CEA	-	-	-	-	3	-	2	-	11	-	2	-
47503	CKMB	-	-	-	-	3	-	-	-	14	-	1	5
47504	CORT	-	-	-	-	2	-	1	-	10	-	-	-
105698	troponin	-	-	-	-	-	-	-	-	-	-	6	-
111555666	fsh	-	-	-	-	-	-	1	-	11	-	-	-
222463	hcg	-	-	-	-	-	-	1	-	11	2	1	2
89895	BUN	-	-	-	-	-	-	-	-	11	-	-	-
5555566666	TSH	-	-	-	-	1	-	-	-	10	-	-	-
898976	T BILI	-	-	-	-	3	-	1	-	10	-	-	-

Figure 33.6. Monthly Usage Report

Simple Inventory System

Inventory Adjustments

Excaliber rgt

PartNo	ItemName	Date	PI	Adj	Date	PI	Adj	Date	PI	Adj
47501	CARB	11 May 10	0	-6	13 Apr 10	6	2	24 Feb 10	4	3
47502	CEA	01 Jan 00	0	0	01 Jan 00	0	0	11 May 10	0	-8
47503	CKMB	11 May 10	0	-4	13 Apr 10	2	0	24 Feb 10	2	-4
47504	CORT	11 May 10	0	-10	13 Apr 10	3	0	24 Feb 10	3	-7
5555566666	TSH	13 Apr 10	0	0	24 Feb 10	0	-6	14 Oct 09	6	0
898976	T BILI	11 May 10	0	-3	13 Apr 10	0	0	24 Feb 10	0	0
111555666	fsh	11 May 10	0	-20	13 Apr 10	0	0			
222463	hcg	11 May 10	0	-18	13 Apr 10	0	2			
89895	BUN	11 May 10	0	-25	13 Apr 10	3	3			
105698	troponin	01 Jan 00	0	0	01 Jan 00	0	0	11 May 10	0	-7

Figure 33.7. Inventory Adjustments

Back-up and Restore

Backups made with normal program commands are kept on the same computer and in the same folder with the database. They are intended to protect more against human error and less against computer malfunctions like a hard drive crash. It is a good idea to make periodic backups of the INV Databases folder (in the EE directory) to a different computer.

Automatic Backup

The database is automatically backed up when you exit the program. These automatic backups are also automatically "aged." The program keeps the latest 5 automatic backups for the current day, plus the last daily backup for the last 5 days on which the program was used.

You can exit without making a backup by using the **Exit without backup** command in the **Utilities** menu. You can also turn off the automatic backup feature from the Setup screen.

Manual Backup

In addition to the automatic backups, you can make manual backups with the **Utilities**, **Backup** and **Restore**, **Create a Backup File**. For example, you might want to make a manual backup just before you change the database setup. Manual backups are not automatically aged – they remain available until you delete them.

Restoring a Backup

Use **Utilities**, **Backup** and **Restore**, **Restore to an Earlier Time** to restore a backup file. Note that, if you are using the software in a network environment, you can't restore a backup if other users are using the database.

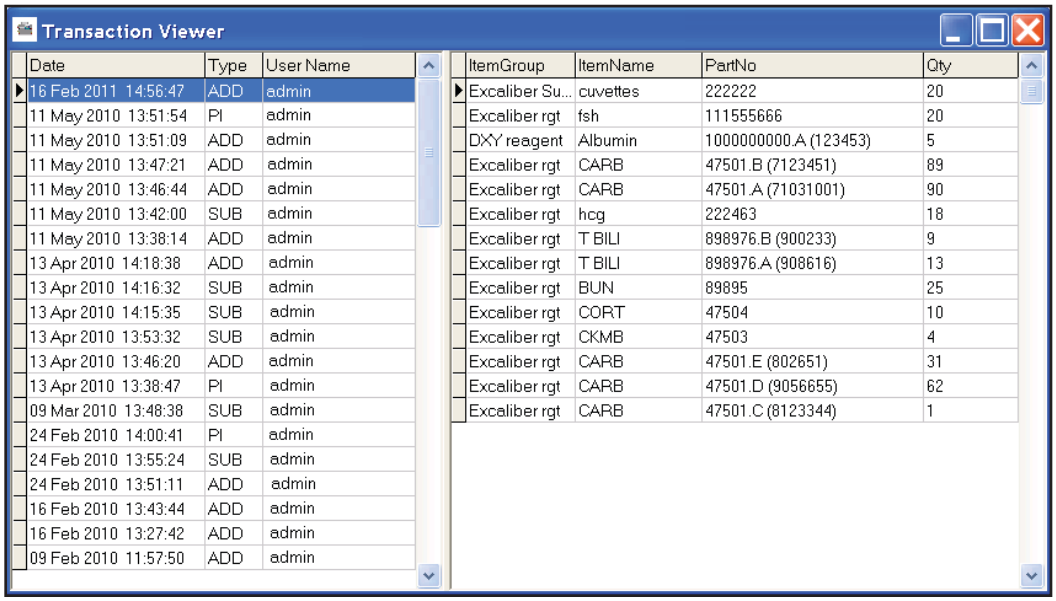
Immediately after restoring, you can undo the restore using **Utilities**, **Backup** and **Restore**, **Undo Last Restore**.

Deleting a Backup File

Use **Utilities, Backup and Restore**, **Delete Backup File(s)** to remove backups you no longer need.

The Transaction Viewer

The Transaction Viewer (**File, Transaction Viewer** command) shows the history of all transaction batches entered to the SIS database. The panel on the left shows the batch date and time, the user who was logged in at when the transaction occurred, and the transaction type: Add to Inventory (ADD), Subtract from Inventory (SUB), or Physical Inventory (PI). When you highlight a batch in the left panel, the item counts for that batch are displayed on the right.



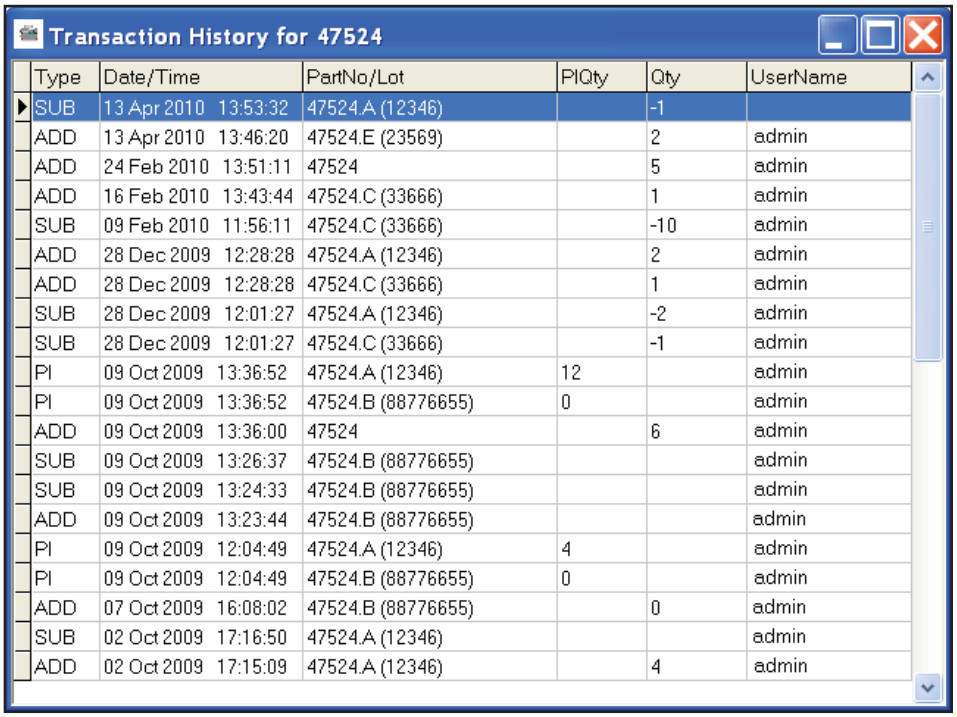
If you right-click a batch in the left panel, you can delete either just that batch, or that batch plus all earlier batches. Common uses of this function include:

- Delete the latest batch, if you accidentally posted bad data.
- Delete an older batch and all earlier ones to remove obsolete data from the database.

Transaction History

The Transaction History, requested by right-clicking an item in the QOH screen, shows all transactions for an item.

- Transaction types are PI=physical inventory, ADD=add to inventory (receive), and SUB=subtract from inventory
- All lot numbers of the item appear in the report.
- Physical Inventory counts appear in a separate column (**PIQty**) from adds and subtracts (**Qty**). Only transactions occurring since the latest physical inventory contribute to the Quantity on Hand.
- **UserName** shows the user who was logged in when the Transaction was generated.



Type	Date/Time	PartNo/Lot	PIQty	Qty	UserName
SUB	13 Apr 2010 13:53:32	47524.A (12346)		-1	
ADD	13 Apr 2010 13:46:20	47524.E (23569)		2	admin
ADD	24 Feb 2010 13:51:11	47524		5	admin
ADD	16 Feb 2010 13:43:44	47524.C (33666)		1	admin
SUB	09 Feb 2010 11:56:11	47524.C (33666)		-10	admin
ADD	28 Dec 2009 12:28:28	47524.A (12346)		2	admin
ADD	28 Dec 2009 12:28:28	47524.C (33666)		1	admin
SUB	28 Dec 2009 12:01:27	47524.A (12346)		-2	admin
SUB	28 Dec 2009 12:01:27	47524.C (33666)		-1	admin
PI	09 Oct 2009 13:36:52	47524.A (12346)	12		admin
PI	09 Oct 2009 13:36:52	47524.B (88776655)	0		admin
ADD	09 Oct 2009 13:36:00	47524		6	admin
SUB	09 Oct 2009 13:26:37	47524.B (88776655)			admin
SUB	09 Oct 2009 13:24:33	47524.B (88776655)			admin
ADD	09 Oct 2009 13:23:44	47524.B (88776655)			admin
PI	09 Oct 2009 12:04:49	47524.A (12346)	4		admin
PI	09 Oct 2009 12:04:49	47524.B (88776655)	0		admin
ADD	07 Oct 2009 16:08:02	47524.B (88776655)		0	admin
SUB	02 Oct 2009 17:16:50	47524.A (12346)			admin
ADD	02 Oct 2009 17:15:09	47524.A (12346)		4	admin

Acknowledgements

We wish to thank several individuals for giving us their time so we could better understand many of the intricacies of Inventory Management. They include: Dr. Herbert Rose of Montefiore Medical Center, Bronx, NY; Sara Diaz and Donna DeSandro of Abington (PA) Memorial Hospital; and Susan Steele of Lancaster (PA) General Hospital.

Chapter

34

Incident Tracking

Overview

On January 23, 2003, the Centers for Medicare and Medicaid Services (CMS) instituted the "Quality Assessment and Performance Improvement Conditions of Participation for Hospitals" as published in the Federal Register. In an effort to address patient safety issues and reduce medical errors in hospitals, CMS requires the development and implementation of a quality assessment and performance improvement (QAPI) program.

Under the Medicare Conditions of Participation (CoP) rule, hospitals must:

- Establish, implement, maintain, and evaluate their own QAPI program.
- Have a QAPI program that reflects the complexity of its organization and services.
- Have a QAPI program that is hospital-wide and focuses on maximizing quality of care outcomes.
- Include preventive measures that foster patient safety, such as reducing medical errors.

The Incident Tracking Database (ITRAK) represents the Error Identification phase of a QAPI program for the laboratory. Its primary purpose is to classify laboratory Incidents (a.k.a. errors, problems, mistakes, events) by cause and to identify what problems occur most frequently, are most preventable, or have the greatest potential for jeopardizing patient safety. For a quick perspective on the program's purpose, see *The Big Picture Report Example*.

Tasks

1. **Familiarization**. Before entering "live" data, experiment with the Demo/Example database to become familiar with what the program does.
2. **Setup**. After you get a feel for the program, you will need to exit ITRAK to exit the Demo/Example database, then re-enter ITRAK and click the **Live!** button to create your live database. Run **Setup** to create your live database. (See *Designing Your Input Form.*) Initially, ITRAK creates a "default" data-

base that looks just like the Demo/Example database, but it also offers many customization options. Even if you choose to use the default more or less "as-is', you still need to modify the pick lists to reflect your own organization. For example, entering your list of Investigator names and Patient Locations.

3. **Data Entry**. Once the Setup phase is complete, you can begin entering incident reports. (See *Entering Incident Reports.*) This is, of course, an on-going process. Review your Setup thoroughly before you start entering Incident Reports.

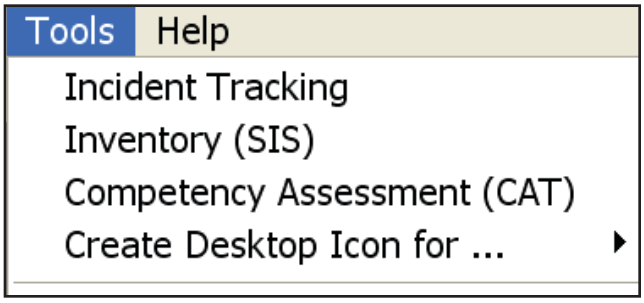
Note: **It is a lot easier to make changes before you enter data than afterwards.** For example, suppose you enter 100 Incident reports, then decide that you really need a "Shift" field. You can add the field, but it won't have a value for those first 100 incidents. Even worse, suppose you decide to change your problem classifications. You then have 100 old incidents classified according to the old system, and future ones classified by the new system.

If your LIS has the ability to capture error information, you can create an export file to import into ITRAK. (See *Importing Incident Reports.*)

4. **Analysis**. The key report is **The Big Picture**. In addition, you can produce **Breakdown** reports on various criteria. For example, you can show a distribution of problems for the Emergency Department only, or show what percent of Phlebotomy problems the lab is responsible for. You can also Browse the Incident list, sorting and filtering it to highlight problems of interest.

Starting ITRAK

ITRAK is not a Statistical Module, it is a separate program. To launch it, select Incident Tracking from the EP Evaluator Tools menu. It does not matter what project you have open, since ITRAK does not use projects. You can create a desktop icon for Incident Tracking. That way you will be able to access Incident Tracking without having statistical modules open.



You can't use ITRAK on live data until you define the database structure. In other words, you cannot list the problems you want to track and how you want to categorize them. Until you have defined your database structure, ITRAK shows the Database Startup Screen each time you launch. We recommend that you explore the Demo/Example databases before attempting to define your own. If you have

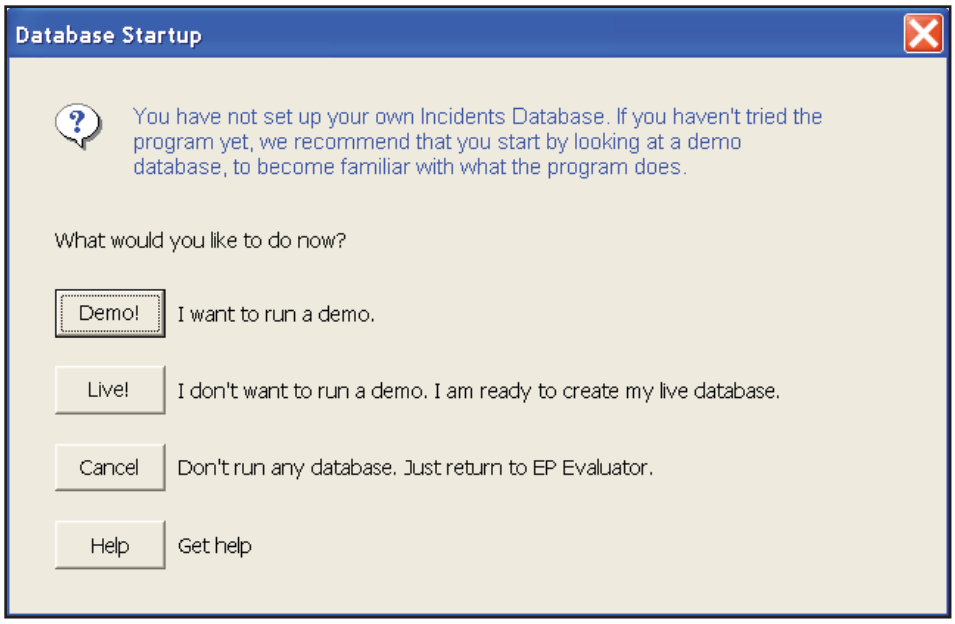
never run the program before, choose

Demo! I want to run a demo.

When you have decided what you want in your live database, choose

Live! I don't want to run a demo. I am ready to create my live database.

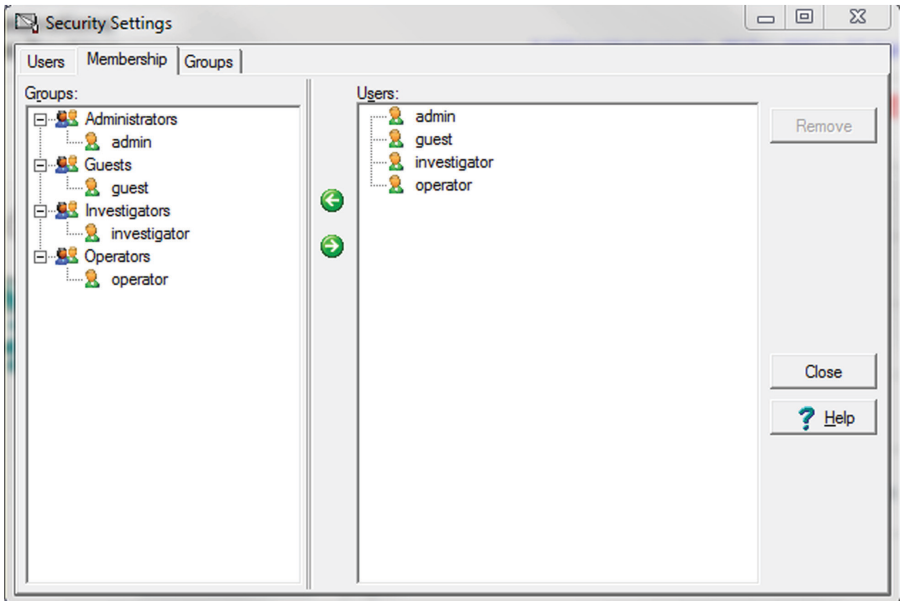
Once you have defined your live database, you will no longer see the startup screen — the program opens your live database every time you launch ITRAK.



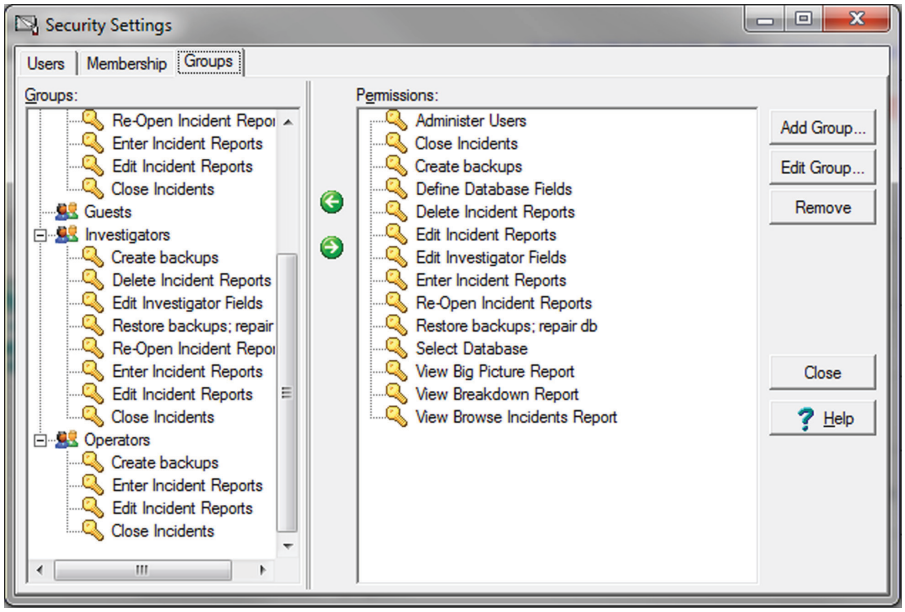
ITRAK User Administration

To configure security settings, select **File>User Administration** from the ITRAK main menu to open the Security Settings screen. This screen contains three tab pages: Users (for adding people), Membership (for categorizing users into groups), and Groups (for defining permissions for each group).

The instructions for setting up security for ITRAK can be found in the discussion of SIS User Administration. The steps are the same for both the SIS and ITRAK modules. However, unlike in the SIS module, ITRAK user administration includes an Investigators group:



Additionally, the ITRAK permissions list contains ITRAK related tasks, such as "Edit Incident Reports" or "View Breakdown Reports".

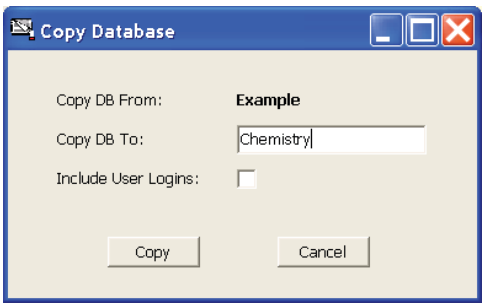


Setting up the Database

During the Setup process, you define what fields will appear on your input form, what order they appear in and, for pick list fields like Patient Location and Problem Classification, what the legal values are.

When you create the live database, ITRAK initializes it to look just like the Demo/Example database. If there are things in the Demo/Example that you aren't interested in, you can remove them from the input form so they won't confuse your users. Similarly, you may want to track things that aren't in the Demo/Example. There are ten user-definable fields that you can add for your own use. Even if you want to use the input form fields "as-is", you will need to enter your own list of operators and patient locations.

While you can keep all of the incidents for your organization in one database, it is possible that you would prefer to use separate databases for different logical or physical locations within your organization. Set up your first database carefully, and then choose the **File**, **Copy Database** menu. You will be allowed to name your new database, and optionally copy the user administration information. The new database will contain all of the field definitions from the old database, but will contain no incidents.



Designing Your Input Form

The Form Designer screen (Figure 34.1) defines the fields that appear on your input form. Each line represents a field.

- Set **Show on Form?** to *No* if you don't want to use the field. Its line will turn gray and move to the bottom.

- By default operators can edit and view any field on the form. Set **Investigator-Only** to **Yes** to make a particular field editable and viewable only by Investigators and Administrators.

  Suppose that you have a field called "Lab Responsible", which indicates whether the Investigator has determined that the Lab was responsible for the Incident. You might choose to make this an "Investigator Only" field, since it will be determined by the Investigator.

- Fields highlighted in yellow on the Form Designer screen are used in creating the Big Picture report. They may also be used for peer group comparisons at some point in the future.

- Some of the fields need a pick list of acceptable values. Click **Edit** to define the pick list. (See *Editing a One-Level Pick List* and *Editing the Problems*

Pick List in this chapter.)

Pick List fields can consist of as few as 3 alternatives (Unassigned/Yes/No) or dozens of alternatives. By default, pick lists with fewer than 8 items will always display in the drop down exactly as many lines as there are list items. Pick lists with 8 or more items must display at least 8 items in the drop down. For pick lists with more than 8 items, use the Drop Down Count column to designate the number of items that display in the dropdown.

- Change the **Descriptions** so your operators will understand what you want them to input.

- Use the **Move Up** and **Move Down** buttons to change the order of the fields on your form.

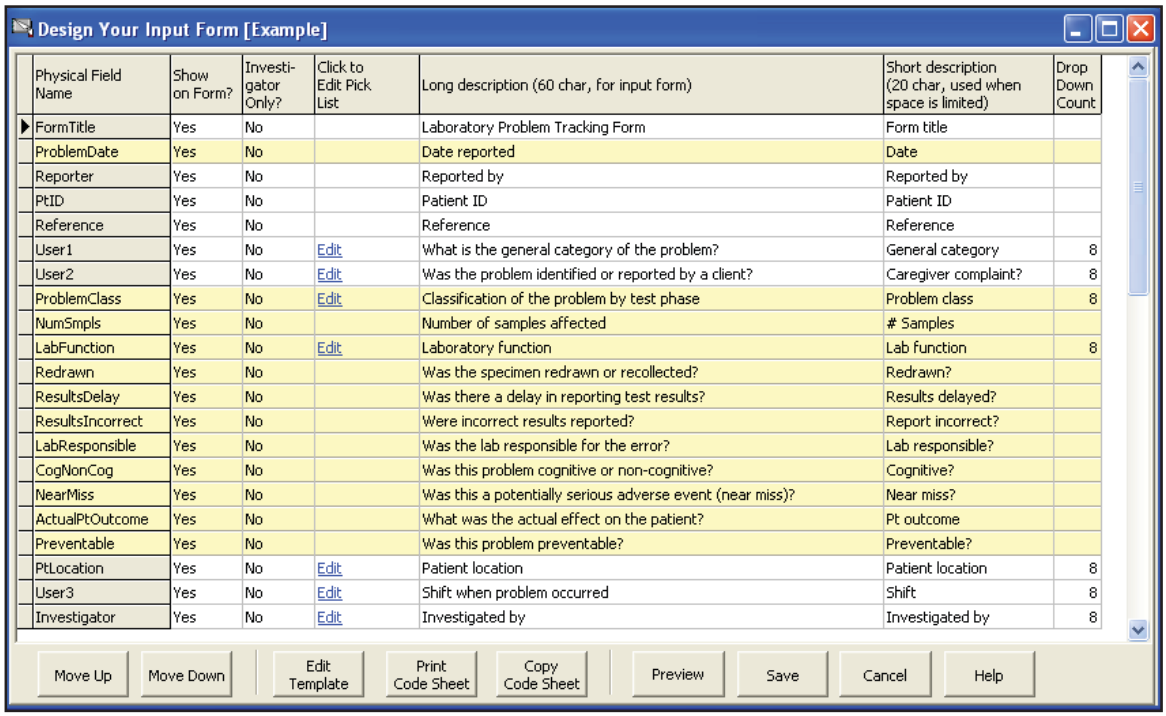
- Edit a **Template** to put boiler-plate text in the free-form text field – for example, headings to provide a guide for what information to include. (See *Defining a Template*.)

- **Preview** allows you to view the form before you save it. Preview also allows you to try out entering data. Data entered in **Preview** is not saved in the database.

- The code sheets contain two parts: 1) a blank data entry form that you can use to enter incident data in the field, and 2) a list of all of the fields, and the legal values for pick list fields, including the numeric value codes for each pick list item. This is useful when you want to create an import file that specifies field values by number instead of by name. (See *Importing Incident Reports.*) **Print Code Sheet** prints the data entry form and code sheets in two separate print jobs, while **Copy Code Sheets** puts the data entry form and code sheet data into the clipboard so that you can use programs such as Excel to create your own custom data entry forms and "cheat sheets". (See *Importing Incident Reports*.)

- **Save** exits and saves your changes; **Cancel** exits without saving.

When you first create your live database, the fields are initialized just like the Demo/Example database, except that the Investigator and Patient Location pick lists are empty. Our recommendation follows:



Physical Field Name	Show on Form?	Investi-gator Only?	Click to Edit Pick List	Long description (60 char, for input form)	Short description (20 char, used when space is limited)	Drop Down Count
FormTitle	Yes	No		Laboratory Problem Tracking Form	Form title	
ProblemDate	Yes	No		Date reported	Date	
Reporter	Yes	No		Reported by	Reported by	
PtID	Yes	No		Patient ID	Patient ID	
Reference	Yes	No		Reference	Reference	
User1	Yes	No	Edit	What is the general category of the problem?	General category	8
User2	Yes	No	Edit	Was the problem identified or reported by a client?	Caregiver complaint?	8
ProblemClass	Yes	No	Edit	Classification of the problem by test phase	Problem class	8
NumSmpls	Yes	No		Number of samples affected	# Samples	
LabFunction	Yes	No	Edit	Laboratory function	Lab function	8
Redrawn	Yes	No		Was the specimen redrawn or recollected?	Redrawn?	
ResultsDelay	Yes	No		Was there a delay in reporting test results?	Results delayed?	
ResultsIncorrect	Yes	No		Were incorrect results reported?	Report incorrect?	
LabResponsible	Yes	No		Was the lab responsible for the error?	Lab responsible?	
CogNonCog	Yes	No		Was this problem cognitive or non-cognitive?	Cognitive?	
NearMiss	Yes	No		Was this a potentially serious adverse event (near miss)?	Near miss?	
ActualPtOutcome	Yes	No		What was the actual effect on the patient?	Pt outcome	
Preventable	Yes	No		Was this problem preventable?	Preventable?	
PtLocation	Yes	No	Edit	Patient location	Patient location	8
User3	Yes	No	Edit	Shift when problem occurred	Shift	8
Investigator	Yes	No	Edit	Investigated by	Investigated by	8

Figure 34.1. Example Database - Input Form Layout

Standard Fields - Required

FormTitle is required. Its long description is the title that appears at the top of the input form — change it if you wish. The short description is never used.

ProblemDate is the date the incident occurred. (Note that the Incident ID numbers that appear at the top of the input form are not input by the user. They are unique IDs assigned automatically by the program and represent the order in which incident reports are entered.)

Big Picture/Peer Reporting Fields

Fields highlighted in yellow on the Form Designer screen are used to create the Big Picture report. They may also be used for peer group analysis in the future. While you may omit any of them (except ProblemDate), we recommend that you retain them. See *The Big Picture* for an explanation of how these fields are used.

ProblemClass, in particular, is probably the most important field on the form. This is a pick list that defines exactly what the problem is. Select Edit to examine or change its values. (See *Editing the Problems Pick List*.)

Other Standard Fields

Reporter and Patient ID - to keep track of where the incident report came from. These are both 20-character text fields. The operator can type any text (or leave them blank).

Reference - We strongly recommend using this field if you plan to import incident reports. It is a unique ID, such as the medical record number, that prevents the same incident report from being imported twice.

PtLocation - Patient location (e.g., Nursing Station). This is a pick list field – the operator cannot type into the field, s/he can only select one of the predefined values. Select **Edit** to define the pick list.

Investigator - Person who investigated the incident (i.e., the person who filled in most of the form). Like the patient location, this is a pick list. Select Edit to define the list of eligible investigators.

DateClosed - Date the investigation was completed.

Closer - Person who closed the investigation

Description - A mini-word processor, where the investigator can write a formal description of the follow-up investigation. You can define a Template to "prompt" for the what information is expected. (See *Defining a Template*.) Alternatively, if you don't need such a formal description, you could use the Comment field instead. Comment is an 80-character unformatted text field.

GeogLocation - Geographic location. Multi-national or large labs might want to use this to record which company or division the report came from. Probably not necessary for smaller labs.

User-Definable Fields

In addition to the standard fields, there are 10 user-definable fields — 7 pick list fields (**User1-7**) and 3 20-character text fields (**UserAlpha1-3**). These fields can be used for additional information that is not covered by the standard fields. The Demo/Example database uses three of the user fields.

The Demo/Example database assumes that incident reports are handled in two distinct phases: Error Identification and Error Investigation. The following explains how and why we set up the Demo/Example database:

- The person who identifies the error assigns the problem to one of five general categories: 1) Sample/Requisition, 2) Test Result(s) Questioned, 3) Delayed or unavailable test result(s), 4) Personnel problem, or 5) Billing error. S/he also enters the Reporter, Patient ID, Problem Date, and Reference. The *User1* field holds the general category information.

- Periodically, the manager reviews the database, examines open incidents that

have not been assigned to an investigator, decides whether the problem should be investigated and, if so, assigns an Investigator.

- The investigator classifies the incident to a specific test phase (**Problem-Class**), enters the detailed (yellow) fields describing the incident, and clicks the **Close Incident** button when the investigation is complete.

- Fields are arranged on the form so the Error Identification fields (ProblemDate through User2) are at the top, and the Error Investigation fields are at the bottom.

- This lab also wants to track two other pieces of information not included in the standard fields: Was the problem reported by a client? (***User2***) and the shift when the problem occurred (***User3***).

- Note that the User1-3 fields are set up like Demo/Example when you create your live database. If you don't want to use them, set their **Show on Form?** column to No. If you like the separate Error Identification step but want to use different general categories, Edit the User1 pick list. If you want to use Shift (User3) but your shift names are something other than Day-Evening-Night, Edit the User3 pick list.

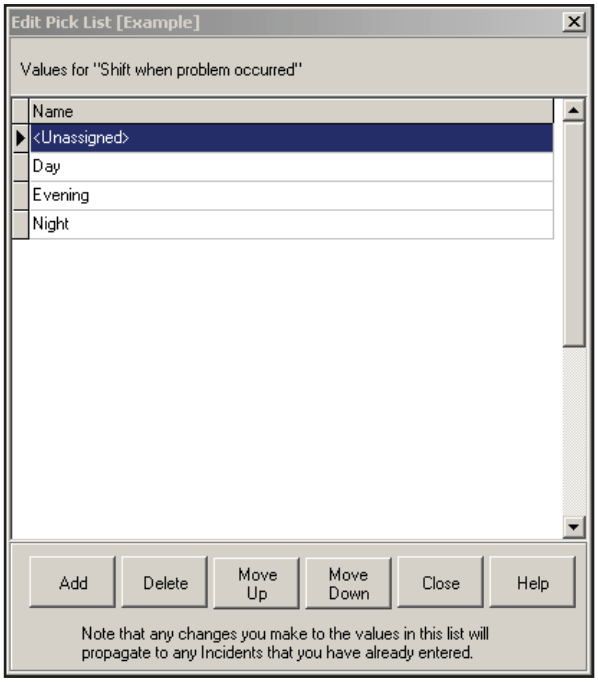
Editing a One-Level Pick List

Enter the "names" for the list, one per line. Every list must have a default item, usually "<Unassigned>." You can change the text for the default item, or move it up/down in the list, but you cannot delete it.

Add (or the Insert key) adds a blank line at the end

Delete (or the Delete key) deletes the highlighted line.

Move Up/Move Down buttons change the order of the list. These buttons do not appear when editing the Investigator and Patient Location pick lists — those lists are always shown in alphabetical order. Remember that those "alphabetical" lists are treated as text, not numbers. For example, if your Patient Locations are department numbers, you must enter them with leading zeros in order to sort correctly.



Copy to Clipboard. Right-click a list item and select **Copy list of names** to copy the entire list into the clipboard, so that you can edit the list in Excel.

Paste from Clipboard. If you have a long list (typically investigators or patient locations) in an Excel column, you can copy/paste them into the ITRAK list.

- First highlight the Excel column and select **Edit/Copy** from the Excel menu. Then right click the ITRAK list and select **Paste (append) to list of names** from the popup menu. This will add only names from the Excel column that are not already in the list; all names will be appended to the end of the list.

NOTE: Before you have entered incidents into the database, you can clear out a long lists of patient locations, department numbers, etc., by right-clicking on any item in the list and selecting **Clear** from the popup menu. This will delete the entire pick list. Once you have entered incidents into the database, you may no longer use the **Clear** function.

Editing the Problems Classification pick list

The Problem Classification pick list (Figure 34.2) is, arguably, the most important pick list in the program. It defines the specific problem. Finalize the Problem Classification pick list before you begin entering incidents into your database. Although you can change the wording or spelling of a problem class once incidents exist in the ITRAK database, changing the meaning of a problem class would change the problem classification for all existing incidents.

Problems are organized by test phase. The list contains a mix of standard and user-defined problems. You may not delete the standard problems, though you may change the wording. However, you should not change the meaning of the words. We hope to institute a peer group comparison service in the future. If you change the standard problem definitions, your data will be inconsistent with that of your peers.

You can add items to the list:
Add Parent adds a test phase (a parent item in the outline). Note that these non-standard test phases will not be included in the Big Picture report, unless you check the box in Preferences to include all classified incidents. Example: the Administrative test phase in the standard data is a user-defined item.

Add Child. Highlight a test phase, then select **Add Child** to add a problem to it. The program will continue prompting for additional children until you press the Escape key.
To change the wording of a problem or test phase, first highlight it, then type over the existing text.

Delete. To delete an item, first highlight it, then select **Delete** (or press the Delete key). You cannot delete a standard item. The program will warn you if you ask to delete an item attached to an Incident report. If you delete an item that is attached to an Incident report, that report's value will be reset to <Unassigned>.

Move Up/Move Down. Use these buttons to change the order.

Save saves your changes and returns to the main setup screen.

Cancel closes the form without saving. Note that you still have a second chance to cancel, even if you save the pick list form. The Setup facility allows you to make arbitrary changes and preview them. When you Cancel from the Setup screen, all changes made during that Setup session are undone.

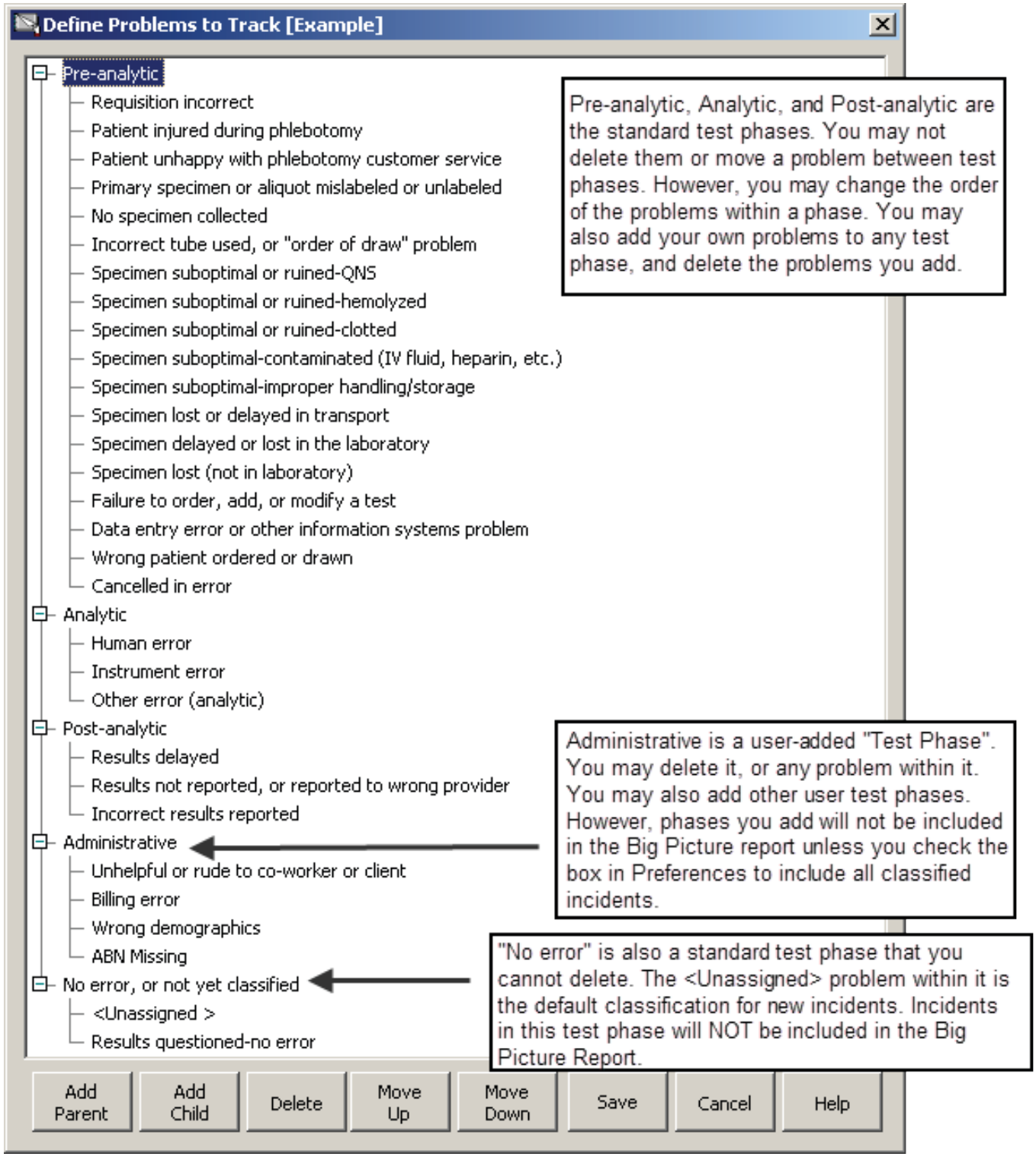
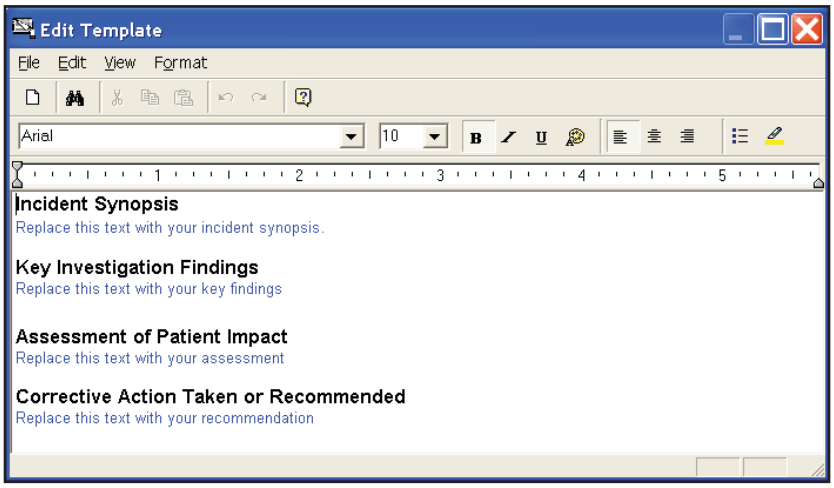


Figure 34.2. Problem Classification Pick List

Defining a Template

A Template contains boiler-plate text to guide the operator in entering the free-form text description of an incident. When a new incident report is created, its Description field is initialized from the template. The operator can then type over "instruction" text, replacing it with the appropriate content.



Entering and Editing Incident Reports

Entering Incident Reports

The input fields on the left side of the screen are user-definable. During database setup, you define what fields appear on the screen, what they are called, and what order they appear in. See *Designing Your Input Form* for a description of the available fields.

Unassigned IS NOT the same as "No"

Many of the fields are pick lists, indicated by a down arrow on the right. These fields only allow you to choose one of the predefined answers; you cannot enter arbitrary text.

Every pick list has a default value, usually called "<Unassigned>." Unassigned means "I don't know," or "the value has not been entered yet." If the correct answer is No, always select No specifically.

Example: There is a phrase on the Big Picture report that says:

> Patient safety impact was evaluated for 984 (80%) of incidents. For these incidents, the average severity of patient outcome was 1.31.

This phrase is based on the question *What was the actual effect on the patient?* on the input form. Suppose you have 100 incident reports. 5 had a serious impact on the patient, and you record those as having severity 3. The other 95 might be

a mix of "I don't know" and "No effect". Suppose you left all 95 of them unassigned. The summary phrase would say:

> Patient safety impact was evaluated for 5 (5%) of incidents. For these incidents, the average severity of patient outcome was 3.00

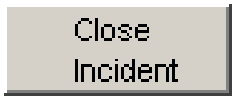
This gives the false impression that a) you have very serious problems, and b) you are not investigating them.

Edit Controls

Add (or the Insert key) appends a new, blank incident report.

The **Post** and **Undo** buttons are enabled only if you have made changes to an incident report but haven't saved them yet. Post saves the changes; Undo cancels them. Changes are saved automatically when you close the input form, or when you scroll to a different incident report.

Delete (or the Delete key) deletes the current incident report.



Closing an incident populates the current date in the Date Closed field on the Incident Tracking Form. Closed incidents may not be edited, although they may be reopened by Administrators and Investigators.

Closed incidents may be reopened with the **Re-Open Incident** button. Clicking this button will clear the date in the Date Closed field.

The "VCR" buttons scroll to the first, previous, next, or last incident report. Incidents are sorted by Incident Number (automatically assigned by the program, reflecting the order in which reports were entered), unless you use **Filter** to change the sort order.

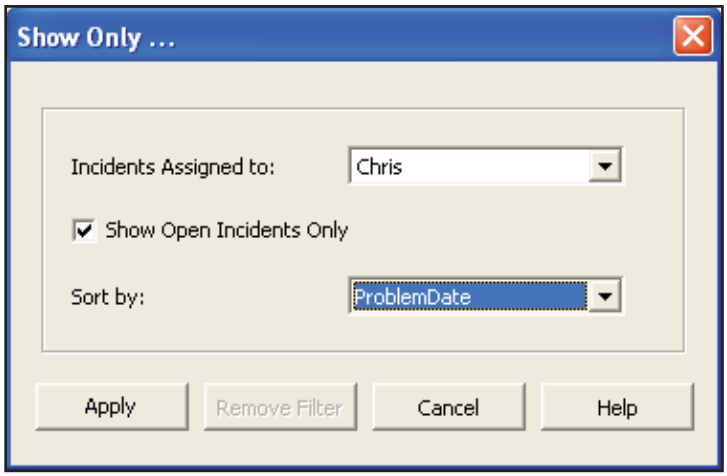
Are you an investigator and only want to see the incidents assigned to you? Are you a manager and want to see only open incidents that haven't been assigned to an investigator? Do you want to scroll through the incidents in date order instead of entry order? If so, use a **Filter.** (See *Filtering to Show Only "Your" Incidents*.)

Find shows a pop-up list of incidents – including incident number, reference number, patient ID, date reported, and date closed – and lets you go directly to a specific incident. (See *Finding a Specific Incident*.)

Back closes the Incident Editor and returns to the main screen.

Filtering to Show Only "Your" Incidents

This form applies or removes a filter on the list of Incident Reports available for editing.



Incidents Assigned to. To show only incidents assigned to a specific investigator select the person's name. To show incidents that have not been assigned to any investigator, select <Unassigned>. To show all incidents, select blank. This item is unavailable (grayed) if the Investigator field does not appear on your input form.

Show Open Incidents Only. Check the box to show only incidents for which Date Closed is blank; leave it unchecked to show all incidents. This item is unavailable if the Date Closed field does not appear on your input form.

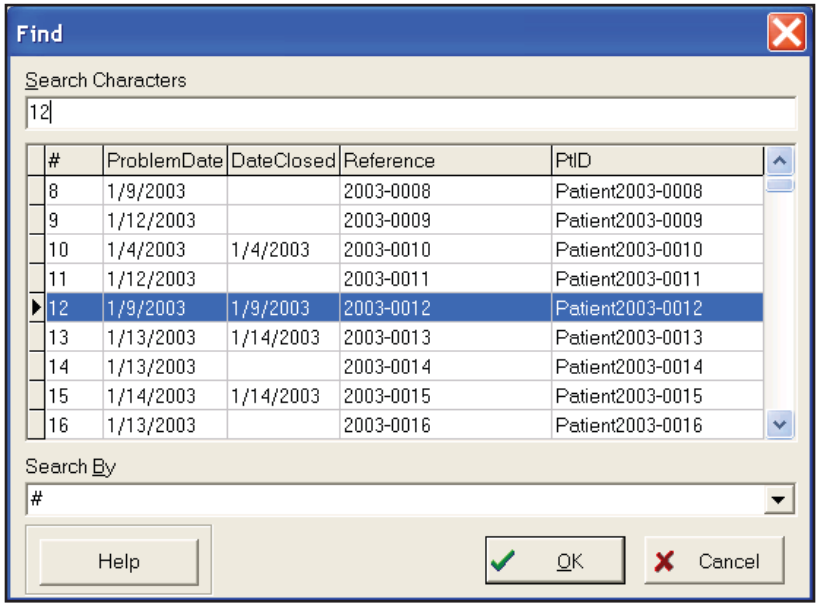
Sort by. This determines the order in which incident reports appear, for the VCR buttons on the input form.

Apply. Applies the filter.

Remove. Removes the filter.

Cancel. Closes the form without changing the filter state.

Finding a Specific Incident

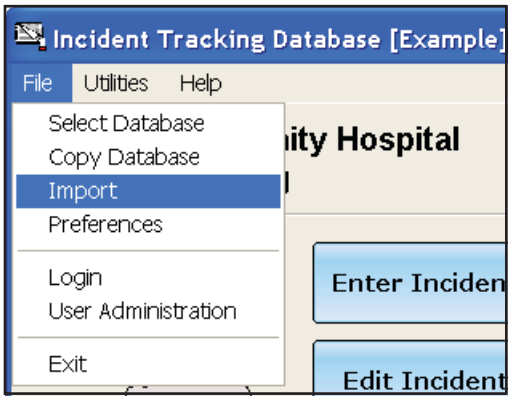


Examples:

1. Suppose you want to edit the incident with reference number 2003-0010. Select **Reference** in the **Search By** box at the bottom of the screen. Then type the first few characters of the reference number in the **Search Characters** box at the top. When the incident you want is highlighted, double-click it (or select OK).

2. Suppose you know the date of the incident you want. Select **ProblemDate** in the **Search By** box to sort the list by date. Then scroll to the date of interest.

Importing Incident Reports



- First, prepare an import file, as described below.
- From the main ITRAK screen, select **File/Import** from the menu.
- Select the text file to import.
- ITRAK will import the file and show error messages (if any).
- If there are no errors, click the **Keep Import** button. If there are errors, you have two choices:

Keep Import w/ Rejects File keeps everything that didn't have messages, and produces a "rejects file" of the others. Manually edit the rejects file, then import just the rejects.

UnDo Import discards the entire import. You will need to obtain a corrected import file. If there are a lot of errors, it is often easier and more reliable to fix the problem at the source than to do manual edits.

Searching the Error Messages

If there are error messages, the text that will be written to the rejects file prints in the "Details" panel below the buttons. Click in the panel, then press Control+F to find the first error message. F3 (Find next) finds subsequent error messages.

Import File Format

- The file is an ASCII text file. See Figure 34.3 for an example.
- First non-blank line must contain "ITRAK-Import-File."
- Each line in the file represents one field in an Incident record, in the format "PhysicalFieldName: Value", or "PhysicalFieldName#: Value". See the Setup screen for a list of physical field names.
- The "PhysicalFieldName#:Value" format applies only to pick list fields, and the Value is the number code of the pick list item. Use **Print Code Sheet** on the Setup Screen to print a list of number codes.
- When using the "PhysicalFieldName: Value" format. Value is the text to be entered. When using this form for a pick list field, the text must exactly match the text of the pick list item.
- Dates must be in yyyy-mm-dd format.
- The only required field is the **ProblemDate**. For other fields, if they don't have a value, omit the line entirely. Do not leave the line blank; a blank value will give an error message when the user imports the file.
- **Reference** is an important field for the import process. If an incident with an identical Reference number already exists in the Incident Tracking database, an error will occur upon importing the file. The File – Import process should only be used to import new incidents, not to update existing incidents.
- The record must be terminated by a "/" line.
- Lines beginning with a semi-colon are comments.
- Blank lines are ignored.

```
ITRAK-Import-File
; Lines that start with semicolon are comments (LIS doesn't
;           need to output them).
; Blank lines are ignored
; First non-blank line must contain "ITRAK-Import-File"
; Examples assume your LIS will create only the Error Identification fields
; Reference is Sample accession #
; Reporter is name of person initiating the form. If it's not a
;           person, might use "LIS". If you don't want to
;           give the field a value at all, omit the line.
; ProblemDate is Date of incident (must be yyyy-mm-dd format)
; User2 is "was the problem identified or reported by a client?".
;           Yes or No. Omit the line altogether
;           if you don't know.
; User1 is "what is the general category of the problem?"
;           The first example calls it User1#, and supplies the number
;           code for the value (from Print Code Sheet on the Setup screen)
;           The second example calls it User1, and supplies the exact
;           words on the input form.
;           Either way will work.
; Must be a / line at the end of a record

PtID: Patient2003-0001-1
Reference: 1234
Reporter: John Doe
ProblemDate: 2003-01-02
User2: No
User1#: 1
/

PtID: Patient2003-0002-2
Reference: 4567
Reporter: Jane Smith
ProblemDate: 2003-01-15
User2: No
User1: Sample/requisition
/
```

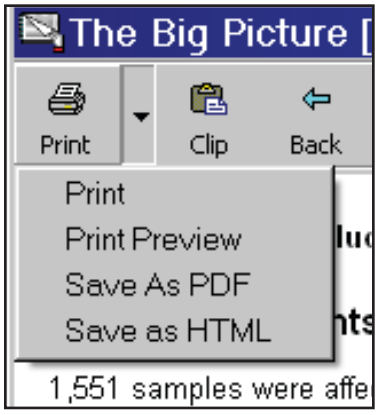
Figure 34.3. Import File Example

The Big Picture

The Big Picture report shows an overview analysis of your database. It has four sections: 1) summary statements and statistics, 2) distribution of incidents by test phase, 3) distribution of incidents by lab function, and 4) a time trend. The exact content varies depending on what fields appear on your input form.

Printing

By default, you can print Big Picture reports. However if you click on down arrow next to the Print icon, you also have the option of saving the reports as PDF files or HTML files.



Note the Clip option on the Big Picture menu. This allows you to copy a graph or section of the report to the clipboard for pasting into another document.

Summary Statements

Figure 34.4 shows an example with a description of what input fields the statement is based on. In the Source column, fields are identified by names used in the Demo/Example database – these names can be changed by the user. Physical field names are shown in parentheses.

Except where noted, the summary statement does not appear on the report if the applicable field does not appear on the input form.

Distribution by Test Phase and Lab Function

Click on a line item to browse the associated incidents. When you move the mouse over the click area, the text is highlighted in yellow.

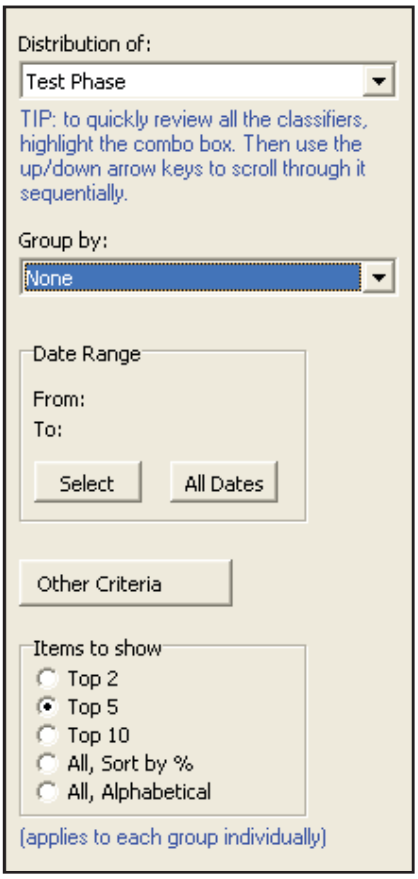
Time Trend

By default, the chart covers all data in the database. Use **File/Preference**s to change the time span.

Statement	Source
NOTE: By default, this report excludes Administrative incidents, and incidents that have not yet been classified to a test phase.	Classification of the problem by test phase (ProblemClass). The report only includes incidents classified as Pre-Analytic, Analytic, or Post-Analytic, unless you check the box in Preferences to include all classified incidents.
For 1,233 incidents reported between 06 Dec 2002 and 03 Apr 2005:	Date reported (ProblemDate). By default, the report covers the latest 90 days. You can change this with the File/Preferences menu command.
1,550 samples were affected, an average of 1.26 samples per incident	Sum of Number of samples affected (NumSmpls).If this field does not appear on your input form, the number of samples affected is the same as the number of incident reports.
Error Rate: Number of errors per 1000 samples = 1.11, assuming a typical volume of 50,000 samples/month x 27.91 months = 1,395,616 samples	The typical monthly sample volume is set with File/Preferences. If you don't set it, the error rate is omitted from the report.
This error rate is equivalent to a Sigma Metric of 4.6σ	To omit this item, uncheck Show Sigma Metric in File/Preferences. The sigma metric is the equivalent number of SDs from a Gaussian distribution. Example: an error rate of 5% = 2σ; an error rate of 1% = 3σ.
Patient Safety: Patient safety impact was evaluated for 984 (80%) of incidents.	What was the actual effect on the patient? (ActualPtOutcome) - number of incidents for which a value was assigned. In other words, <Unassigned> means patient safety impact was not evaluated.
For these incidents, the average severity of patient outcome was 1.31 (1=No Effect, 2=Minor, 3=Severe)	Total Severity divided by total number of incidents. Example: Incident 1 has severity 1, Incident 2 has severity 2, Incident 3 has severity 3. Average Severity = (1+2+3)/3.
1,149 (93%) of incidents were potentially serious adverse events (near misses)	Yes response to Was this a potentially serious adverse event? (NearMiss)
489 (40%) caused specimen to be redrawn	Yes response to Was the specimen redrawn or recollected? (Redrawn)
1,052 (85%) caused a delay in reporting results	Yes response to Was there a delay in reporting test results? (ResultsDelay)
360 (29%) caused incorrect results to be reported	Yes response to Were incorrect results reported? (ResultsIncorrect)
Lab was responsible for 693 (56%) of incidents	Yes response to Was the lab responsible for the error? (LabResponsible)
500 (72%) of incidents for which lab was responsible were preventable	Yes responses to Was this problem preventable (Preventable).
211 (30%) of incidents for which lab was responsible were cognitive (mistakes that involve misinterpretation of results, or faulty decision-making by the technologist)	Was this problem cognitive or non-cognitive? (CogNonCog)
The top 3 problems were: 1. Primary specimen or aliquot mislabeled or unlabeled - 576 (47%) 2. Requisition incorrect - 189 (15%) 3. Wrong patient ordered or drawn - 98 (8%)	Classification of problem by test phase (ProblemClass)

Figure 34.4. How the "yellow" fields affect The Big Picture

Breakdown



The Breakdown report shows the distribution of incident reports by a user-selectable classifier. Controls on the left side of the screen select the classifier, date range, and level of detail:

Distribution of, Group By. These two fields select the classifier to summarize.

- For a simple breakdown, set Group By to "None." This shows the count and percent of incidents for each value of the Distribution of variable. (Example 1, Figure 34.5)
- For a two-level breakdown, such as distribution of problems within each Lab Function, set Group By to outer level and Distribution of to the inner level. (Example 2, Figure 34.5)

Date Range. Selects the time period to report. Click Select to enter start and end dates; click All to report all incidents in the database.

Other Criteria. Filter criteria to apply in addition to the Date Range. For example: Show a distribution of problems for the Phlebotomy lab function only. A yellow circle to the right of the button indicates that additional filter conditions are in use. Note that the Value field is a free-text field which allows you to define the condition value.

Items to Show. Lets you focus on the most frequent problems and suppress detail for the less frequent ones. Suppose there are 20 possible problems. If Items to Show is set to Top 2, the report will show individual percents for the most frequent and second most frequent problem. The other 18 will be lumped together on a single line labeled "Other." Top 5 and Top 10 work in a similar fashion. All**,** Sort by % shows all items individually, sorted in descending order by percent. All, Alphabetical also shows all items, but sorted in alphabetical order. This is most useful for patient outcomes, since they are displayed in the form "n: description," where "n" is the severity rank.

Jumping Directly to the Browse Screen. Click on a line label to browse the individual incident reports for that line. For example, clicking the text "Human Error" in Example 1 takes you to the Browse screen which shows detailed information about the 24 Billing Error incidents. When you move the mouse cursor over a line label it is highlighted in yellow to remind you that it is clickable.

Example 1. Distribution of: **Problem**, Group By: **None**

Distribution of Incidents by Problem
06 Dec 2002 to 03 Apr 2005

Problem	Count	Percent
Primary specimen or aliquot mislabeled or unlabeled	576	40.5%
Requisition incorrect	189	13.3%
<Unassigned >	170	11.9%
Wrong patient ordered or drawn	98	6.9%
Human error	74	5.2%
Other	316	22.2%
Total	**1,423**	**100.0%**

Example 2. Distribution of Problem, Group By: **Lab Function**

Distribution of Incidents by Problem
06 Dec 2002 to 03 Apr 2005

Lab function: <Unassigned>

Problem	Count	Percent
Primary specimen or aliquot mislabeled or unlabeled	257	47.4%
Requisition incorrect	74	13.7%
Wrong patient ordered or drawn	54	10.0%
Specimen suboptimal-improper handling/storage	33	6.1%
Human error	24	4.4%
Other	100	18.5%
Total	**542**	**100.0%**

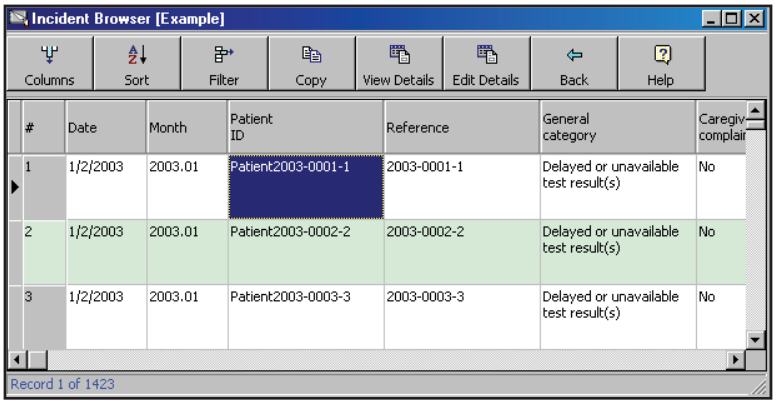
Lab function: Processing

Problem	Count	Percent
Primary specimen or aliquot mislabeled or unlabeled	133	44.5%
Requisition incorrect	44	14.7%
Human error	25	8.4%
Specimen lost or delayed in transport	22	7.4%
Specimen suboptimal-improper handling/storage	16	5.4%
Other	59	19.7%
Total	**299**	**100.0%**

Figure 34.5. Distribution of/Group by Examples

Browse

The Browse screen displays selected incident reports in an Excel-like grid. You cannot edit data directly in this grid. You can, however, click the **Edit Details** button to edit an incident.



If you arrived at this screen from Breakdown or The Big Picture, the incidents have been pre-filtered to show only the subset of interest. You can change the filter with the **Filter** button.

If you entered from the **Browse** button on the main screen, the grid shows all incidents in your database.

What You Can Do From the Browse Screen:

Columns. Select which columns to show. Perhaps you have many fields, but you are only interested in the Patient ID, Date, Problem, and Preventability. You can hide the other fields, so all the fields you want to see fit on the screen without left/right scrolling. (See *Hiding and Displaying Columns*.)

Sort. Sort the incident reports.

Filter. Limit what incidents are displayed. For example: show only incidents that occurred in March 2004, were preventable, and had cognitive causes. (See *Defining a Filter*.)

Copy. Copy the visible part of the grid to the Windows clipboard. It can then be pasted into Excel, or other Windows programs.

View Details. Show the complete incident report for the highlighted row in the grid.

Edit Details. Opens the selected incident for editing.

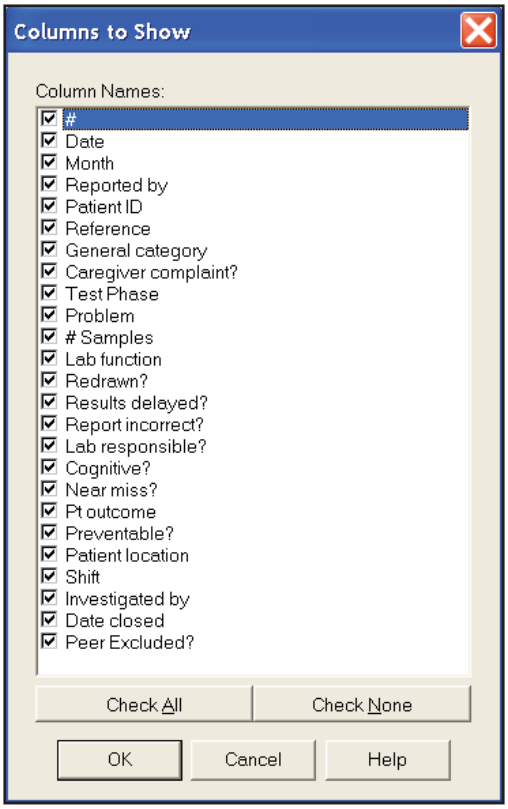
Back. Close **Browse** and return to the previous screen.

Help. Access the **Help**.

Hiding and Displaying Columns

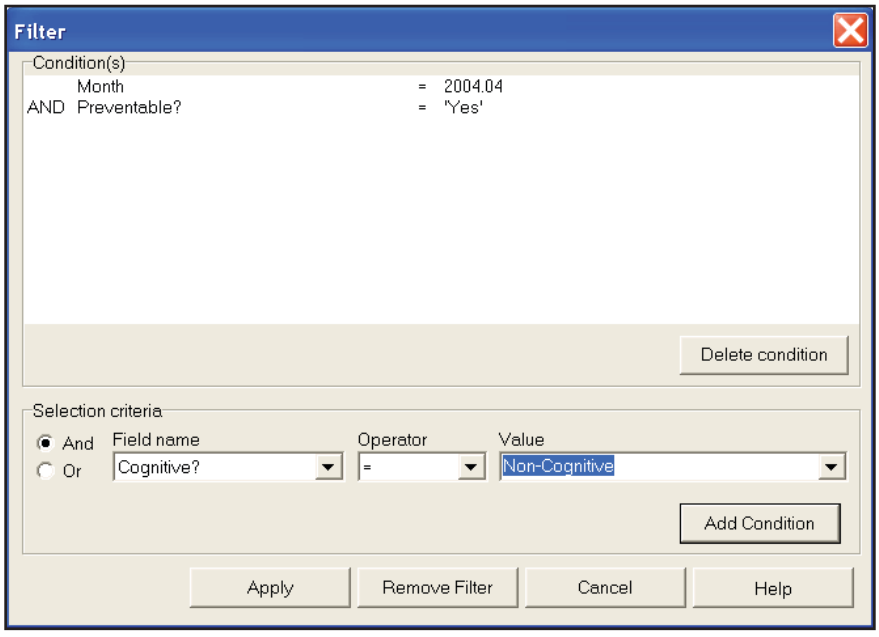
Click the **Columns** button on the Incident Browser to select the which columns are visible on the Browse screen. Perhaps you have many fields, but you are only interested in the Patient ID, Date, Problem, and Preventability. You can hide the other fields, so all the fields you want to see fit on the screen without left/right scrolling.

Check the box for each column you want to show; leave it unchecked to hide the column.



Defining a Filter

A filter limits what incidents are displayed in the Browse screen or the Breakdown report. For example: show only incidents that occurred in March 2004, were preventable, and had cognitive causes.



A filter consists of one or more logical conditions, combined with AND or OR.

The conditions are displayed at the top of the Filter dialog.

- To add a condition, pick a **Field name**, **Operator**, and **Value**, then click **Add Condition**.
- To remove a condition, highlight it in the condition list, then click **Delete Condition**.
- When the condition list is complete, click **Apply** to apply the filter.
- To show all incidents, click **Remove Filter** to remove the filter.

Operators

The operators < (less than), <= (less than or equal to), > (greater than), >= (greater than or equal to), = (equal), and <> (not equal) should be familiar. The others are less familiar:

IS NULL means the field doesn't have a value. Example: select Date Closed IS NULL to show only incidents that don't have a close date (i.e., open incidents).

IS NOT NULL means the field does have a value. Example: select Comment IS NOT NULL to show all incidents for which a comment has been entered.

LIKE is a wild card match, with % as the wild card character. Example: Reporter LIKE %ri% would show incidents reported by Ch**ri**s and **Ri**ta. Reporter LIKE sa% would show incidents reported by **Sa**m and **Sa**lly, but not those reported by Tessa.

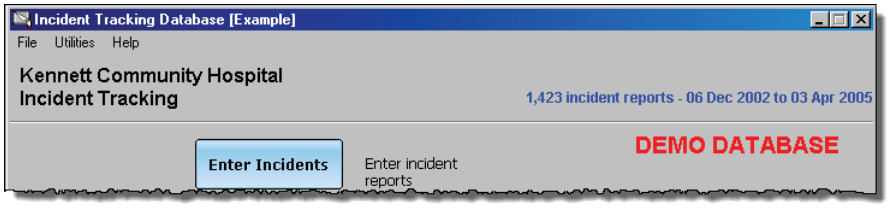
Special Fields

Closed (yes/no) indicates whether a close date has been entered.

Peer Excluded (yes/no) is Yes for Administrative incidents (like "rude to co-worker or client") and incidents that have not yet been classified to a test phase. These incidents are not included in the Big Picture report unless you check the box in **Preferences** to include all classified incidents.

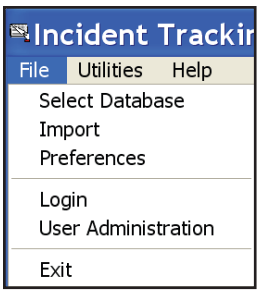
Horizontal Menu Functions

The three entries (**File**, **Utilities** and **Help**) on the horizontal menu provide tremendous flexibility to the user. The File and Utility items will be discussed in separate sections.



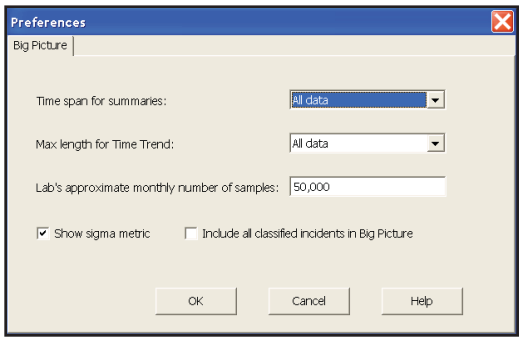
File

Select Database. Once you have created your live database, it is automatically loaded each time the program starts. Use the **Select Database** function if you want to open the Demo/Example database, another live database, or an Archive.



Import. Import information in appropriately formatted text files. See Data Innovations Support for details.

Preferences: Control which incidents are included in the Big Picture report.



Utility Functions

Backup and Restore Items

Backups of the Incident Database are very important. If you accidentally destroy data for a standard statistical module like Simple Precision or Linearity, we might be able to reconstruct it for you. If you accidentally destroy the Incident Database, WE CANNOT RECOVER IT. Hence the importance of having a backup.

Backups made with normal program commands are kept on the same computer and in the same folder with the database. They are intended to protect more against human error and less against computer malfunctions like a hard drive crash. It is a good idea to make periodic backups of the EE11\IRDatabases folder to a different computer.

Automatic Backup: The database is automatically backed up when you exit the program. These automatic backups are also automatically "aged." The program keeps the latest 5 automatic backups for the current day, plus the last daily backup for the last 5 days on which the program was used.

You can exit without making a backup, by using the **Exit without backup** command in the **Utilities** menu. However, we recommend that you don't use this command unless you know the active database is in some way defective.

Manual Backup: In addition to the automatic backups, you can make manual backups with the **Utilities/Backup** and **Restore/Create a Backup File**. For example, you might want to make a manual backup just before you change the database setup. Manual backups are not automatically aged – they remain available until you delete them.

Restoring a Backup: Use **Utilities/Backup** and **Restore/Restore to an Earlier Time** to restore a backup file. Note that, if you are using the software in a network environment, you can't restore a backup if other users are using the database.

Undo Last Restore: Immediately after restoring, you can undo the restore.

Other Utility Items

Deleting a Backup File: Use Utilities/Backup and Restore/Delete Backup File(s) to remove backups you no longer need.

Utilities/Database Repair Fix corrupted database indexes.

Utilities/Restore Original Demo Data Restore the sample databases to factory default.

Archiving Incident Reports If you keep years of obsolete incident reports in your active database, program operation may become sluggish—particularly if you are operating over a network. You can improve performance by archiving old data.

- Select **Utilities/Delete Incident Reports/Archive Incidents prior to ...** from the menu.

- The program will ask for an archive date. Your live database will be split into two parts. Incidents dated on or before the archive date will be deleted from the live database and moved to a separate, archive database.

The old reports are not gone—if you need to see them later, you can open the Archive in the same way that you can open the Demo/Example database.

Help

Help/Show tips when starting Setup. When the program is first installed, it shows a Tips window every time you enter Setup. There is a check box at the top where you can turn the tips off. If you turn them off, then decide you want to see them again, select the **Show tips** item in the **Help** menu.

Help/About. Shows the program version.

Incident Tracking Glossary

Archive. Process of removing incidents prior to a cutoff date from the live database and placing them in a separate history (archive) database.

Big Picture. A report that summarizes important characteristics of the database. (See the example of the Big Picture Report in this chapter.)

Breakdown Report. A report that shows the distribution of incidents by a user-selectable classifier.

Code Sheet. A report that shows the number-codes of pick list values (used in designing an import file).

Cognitive. Cognitive errors are mistakes that involve misinterpretation of results or faulty decision making on the part of the technologist. Examples:

- Failure to properly interpret a common instrument flag.
- Mistaking yeasts for host cells on a Gram stain.
- Calling in a critical value to a voice mailbox, despite knowing that the policy is that the care provider must accept the value directly.

In contrast, non-cognitive errors are slips due to a lapse in attention while performing routine or repetitive tasks. Examples:

- Failure to enter information from a requisition into the LIS.
- Data entry errors.
- Mislabeling.
- Math errors.

Database Repair. See Repair

Demo Database. See Live Database

Filter. A set of conditions to limit what incidents are displayed. Example: show incident reports that:

- Occurred during March, 2004, and
- Occurred in the Pre-analytic phase, and
- Resulted in serious harm to the patient

Incident. Also known as Error, Problem, Mistake, Event, Adverse Event.

Live Database. The database where real incidents in your lab are recorded. There can be more than one live database. One Demo/Example database is provided when the software is installed to help you become familiar with the program's capabilities. When you are using a demo database, the word DEMO is printed on many of the screens in large red letters, so you won't accidentally enter a real incident in the wrong place.

Pick List. The list of possible values for an incident classifier. Example:
Field: Laboratory Function
Pick List: Phlebotomy, Processing, Chemistry, etc.

Repair. The process of rebuilding the database indices if mysterious problems – like incorrect sort orders – begin to occur.

Setup. The process of defining what fields will appear on the input form and possible values for them. You cannot enter incident reports until the Setup process is complete.

Severity. A numeric rank ranging from 1 to 3 that indicates how serious a patient outcome is: 1-No effect, 2-Minor, 3-Serious.

Examples of *Minor* impact:

- Redraw or recollection of specimen
- Additional unnecessary laboratory tests performed
- Delay in diagnosis or treatment
- Effect on medical management without change in outcome (change in drug dose, IV fluids, etc.)

Examples of *Serious* impact:

- Effect on medical management possibly contributing to adverse outcome.
- Unnecessary transfusion given.
- Non-indicated invasive procedure performed.
- Indicated invasive procedure delayed or cancelled.
- Patient death associated with incident.

Template. A Template contains boiler-plate text to guide the operator in entering the free-form text description of an incident. When a new incident report is created, its Description field is initialized from the template. The operator can then type over "instruction" text, replacing it with the appropriate content.

Unassigned. The default value assigned to a pick list field when it is first created. In a yes/no field, Unassigned is not the same as No; it is more like "I don't know" or "not entered yet." If you add a new pick list field to your input form after you have already entered Incident reports, its value for previously-entered incidents is set to Unassigned.

Acknowledgements

Our thanks to several individuals at University Hospitals of Cleveland. Their input was critical to the design of this module. These individuals are: Linda M. Sandhaus, M.S., M.D., Patt Sullivan, MT (ASCP), and Elizabeth Lavallo, MT (ASCP). Linda Sandhaus is an Associate Editor of "*Laboratory Errors and Patient Safety.*" Patt Sullivan and Elizabeth Lavallo are responsible for many of the QA and QC processes in their laboratories.

We also would like to recognize Michael Astion, M.D. of the University of Washington and his associates for their efforts in promoting patient safety.

A primary reference for developing this program was Astion et al (2003).

The Big Picture Report Example (Page1)

EP Evaluator DEMO DATABASE

Users Manual -- Data Innovations

NOTE: This report excludes Administrative incidents, and incidents that have not yet been classified to a test phase.

For 1,233 incidents reported between 06 Dec 2002 and 03 Apr 2005:

1,550 samples were affected, an average of 1.26 samples per incident

Error Rate: Number of errors per 1000 samples = 1.11, assuming a typical volume of 50,000 samples/month x 27.95 months = 1,397,260 samples
This error rate is equivalent to a Sigma Metric of 4.6σ

Patient Safety: Patient safety impact was evaluated for 984 (80%) of incidents.
For these incidents, the average severity of patient outcome was 1.31 (1=No Effect, 2=Minor, 3=Severe)

1,149 (93%) of incidents were potentially serious adverse events (near misses)

489 (40%) caused specimen to be redrawn

1,052 (85%) caused a delay in reporting results

360 (29%) caused incorrect results to be reported

Lab was responsible for 693 (56%) of incidents

500 (72%) of incidents for which lab was responsible were preventable

211 (30%) of incidents for which lab was responsible were cognitive (mistakes that involve misinterpretation of results, or faulty decision-making by the technologist)

The top 3 problems were:
1. Primary specimen or aliquot mislabeled or unlabeled - 576 (47%)
2. Requisition incorrect - 189 (15%)
3. Wrong patient ordered or drawn - 98 (8%)

Distribution of Incidents by Test Phase
06 Dec 2002 to 03 Apr 2005

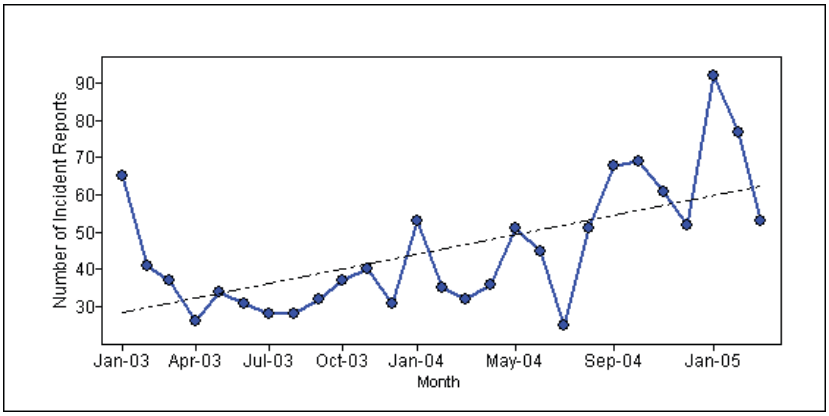
Test Phase	Count	Percent
Pre-analytic	1,093	88.6%
Analytic	133	10.8%
Post-analytic	7	0.6%
Total	**1,233**	**100.0%**

The Big Picture Report Example (Page 2)

Distribution of Incidents for which Lab was Responsible by Laboratory function
06 Dec 2002 to 03 Apr 2005

Lab function	Count	Percent
Processing	293	42.3%
Microbiology	184	26.6%
Phlebotomy	113	16.3%
Hematology	48	6.9%
Chemistry	44	6.3%
LIS	11	1.6%
Total	**693**	**100.0%**

Time Trend
01 Jan 2003 to 01 Apr 2005



FICTICIOUS SAMPLE DATA

Chapter

35

Competency Assessment

Overview

The primary purpose of the Competency Assessment (CAT) module is to administer random quizzes to employees ("students") and track their performance. Your perspective on CAT will depend on your Role in the competency process:

Student Role

A student can only select a quiz and answer its questions. Because the questions are chosen at random from a pool, the specific questions the students sees are different each time. The student can take the quiz for practice or for credit:

- If s/he takes a practice quiz, s/he gets feedback when he answers a question incorrectly. Thus the process can be used for training as well as for assessment. Scores on practice quizzes are not recorded.

- If s/he takes the quiz for credit s/he does not get feedback, and his/her final score is recorded in the training record. If s/he passes, s/he can print a certificate indicating that s/he successfully completed the quiz.

Non-Student Roles

There are three non-student roles: Administrator, Author, and Manager. Managers can only view status reports showing who has completed quizzes. Authors can only write questions. Administrators can view reports and write questions, plus:

- Perform database functions, such as creating a new database, back up, restore, etc.

- Add users, and assign their roles.

- Define Quizzes; enroll students in Quizzes.
- Review question performance (what percent of students answering a specific question answered it correctly).

Getting Started

Quick Start for Administrators

- Create a database
- Add Users
- Add Subject Categories
- Write Questions
- Define Quizzes
- Assign Questions to Quizzes
- Publish the Quizzes
- Enroll Employees in Quizzes

Stock Questions

In the documentation you may see references to "Stock" questions. What are stock questions? They are questions bundled with EP Evaluator®. You can use these questions in your quizzes, but you cannot edit or delete them. The initial release of the software does not include any stock questions.

Questions, Categories, and Quizzes

A Question is a multiple choice question with one correct answer. The program identifies questions by number, not by content. When you add a question, the program assigns it a Question ID number. If you add exactly the same text again, the program assigns a second Question ID, and treats the copy as a completely separate question. If you export a question from database A, then import that question into database B, it will have a different question ID in database B than it had in database A.

Each question is assigned to a Category. Categories group the questions by subject. A category is not necessarily the same as a competency. A competency might require knowledge from more than one category. Also, you might use categories to separate questions by source. Suppose John and Mary both write questions on Lab Safety. In addition, there may be some stock questions about Lab Safety. The stock category (which you can't change) is "_Safety." In addition, you might have categories "John_Safety" and "Mary_Safety."

A Quiz contains a pool of questions from one or more categories. In defining a quiz, the administrator selects questions from various categories to make up the pool. He also specifies how many questions will be shown to each student. The number of questions in the pool is greater than the number of questions shown.

How should you organize quizzes in relation to competencies?

The fundamental problem is that you have many employees who need to demonstrate competence in many areas by taking a quiz. Using a paper system, you might write 20 questions for each competency. Every employee would see the same 20 questions every time. With CAT, the idea is to write more than 20 questions, so the employee will see different questions each time he takes the quiz. Ideally, the number of questions assigned to a quiz should be 3 to 5 times the number presented to the student. Questions and Quizzes are independent entities. Questions are first written, then assigned to Quizzes. A question may be assigned to one quiz, or to many quizzes. Or a question may not be assigned to any quiz at all.

Suppose you have 20 bench techs who must demonstrate competence in 1) Lab Safety, 2) Eximer 500 instrument, and 3) Microsoft Excel, and 5 QA analysts who must demonstrate competence in 1) Lab Safety and 2) CLIA regs. How many quizzes do you need?

- Strategy #1 - have two quizzes, one for each job function. The Med Tech quiz would include questions from three subject categories, and the QA analyst quiz would include questions from two categories. Each employee would be required to complete one quiz specific to his job function.

- Strategy #2 - have four quizzes, one for each competency (Safety, Eximer 500, Excel, and CLIA Regs). A Med Tech would need to complete three quizzes, and a QA analyst would need to complete two.

Regardless of which strategy you choose:

- Define one of the user demographic fields to represent job function. This allows you to select all of the bench techs and enroll them in a quiz in one operation. Otherwise you will have to find them by name and enroll them one at a time.

- Define four subject categories for questions: Safety, Eximer 500, Excel, and CLIA Regs. Designate an author to write questions for each category. Print the questions and circulate them for approval prior to publishing them as live questions. Once a question is published, you can't change it.

  There are two strategies for handling authors. Perhaps the best is to give each author a private database with Admin rights. Then the author can both write questions and practice taking quizzes based on his questions, all without affecting the production system. The author can also allow others to take quizzes and comment on clarity and relevance of the questions. Once the questions are approved, the author exports them, and the production system Admin imports them to the production system. The potential problem here is that the author might export a question more than once, resulting in two copies of the same question in the production database.

The other approach is to grant the Author rights on the production system. The author then writes questions directly in the production database. He can only write questions; he can't assign them to quizzes. The disadvantage of this approach is that the author can also modify and delete any (nonpublished) question on any subject, even questions written by other authors.

If you opt for Strategy #1 (one quiz for each job function)

- Define a quiz id MT001 for Med Techs. Specify that the quiz is to display 20 questions to the student, and that it is to repeat annually. (In other words, the student is automatically re-enrolled in the quiz after he completes it. Due date for the new quiz is one year after completion.)

- Assign all questions in the Lab Safety, Eximer 500, and Excel categories to the quiz. The total number of questions in these three categories must be at least 20, or you can't achieve a quiz with 20 questions. If the total number of questions is 100 (5X the size of the quiz), a student who takes the quiz twice might see 4 repeated questions. Distribution of questions in a given random quiz is approximately proportional to the total number of questions in the category.

- If you prefer, you can go through the questions one-by-one and assign only selected questions to the quiz.

- Publish the quiz. Once the quiz is published, you can't delete or modify any of its questions. The quiz appears in the All Quizzes page of the student opening screen, so anybody can take it.

- Go to the Employee Roster, select all the Med Techs, and enroll them in quiz MT001. The quiz now shows up on the My Quizzes page for each Med Tech.

- Define a quiz id QA001 for QA analysts. Select questions for this quiz from the Safety and CLIA categories. Enroll the QA analysts in this quiz.

If you opt for Strategy #2 (one quiz for each competency), create four quizzes for the four competencies. The main differences with this approach are that each employee must take more than one quiz, and you may need to write more questions in each category to minimize the chance of repeated questions.

Managing Questions

One of the more challenging aspects of managing questions is that a question does not have a short unique identifier. Question IDs are auto-assigned by the program and are unique within a database, but these IDs are just sequential numbers. They do not encapsulate the content of the question. Some examples of issues to keep in mind.

- You have two questions with pictures. The question text for both questions is "What kind of error does this picture illustrate?" The pictures are different. The answers are different, but the two questions look exactly alike on the question overview screen except, of course, that they have different numeric IDs...

- Mary is a question author. She doesn't write questions directly in the production database. Instead she has a separate database that she uses to develop and test questions. She writes 10 questions on Lab Safety. In her private database the question numbers are 1-10. After getting her questions approved, she creates an export file and gives it to the Admin of the production database. The production database already has 50 questions in it, numbered 1-50. The Admin can't preserve Mary's original question IDs without over-writing existing questions, so Mary's questions become 51-60 instead of 1-10.

- Suppose Mary now writes 10 additional questions. The new questions have IDs 11-21 in her database. She creates an export file for the Admin, and forgets that she has already sent the first 10 questions. She exports all 20 questions. When the Admin imports Mary's file, there is no indication that the first 10 are duplicates. All 20 go in as 20 new questions. Even worse, Mary might have modified the first 10 questions to correct spelling. Now the production database contains old and new versions of what are essentially the same questions.

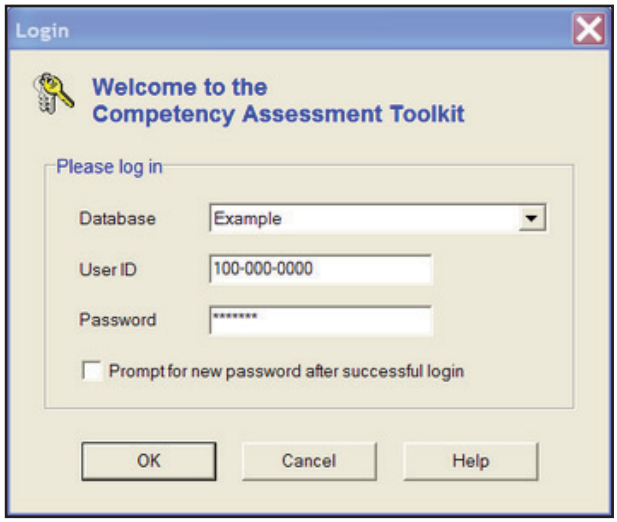
Taking Quizzes

Login

You must log in to use the software. Fields on the login screen are:

Database

Use the down arrow button to see what is available. We recommend that you have only one production database, though you may wish to create others for practice, or for authors to use during question development. The Example database is always available – it is installed with the software to demonstrate program features.



The program remembers your database choice between sessions.

User ID / Password

These are assigned by an Administrator and both are CASE-SENSITIVE. Also, they may vary depending on your choice of database. Your User ID establishes your role within the database (student, manager, author, or administrator).

You can log into the Example database using:

- ID admin, Password admin
- ID manager, Password manager
- ID author, Password author
- ID student, Password student

Prompt for new password

Check this box if you want to change your password. After a successful login you will be prompted to enter a new password. This box is not available if you are using a generic user id ("admin", "manager", "author", or "student").

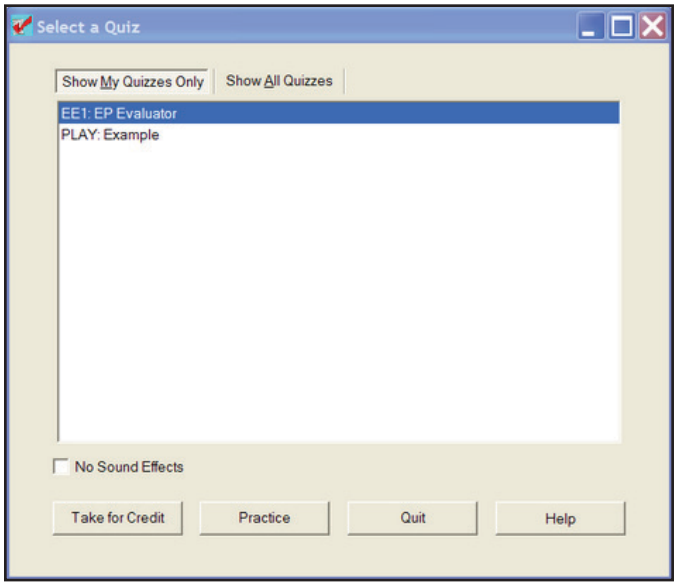
If you forget your password ...

- If you are not an Administrator, contact your Administrator

- If you are an Administrator, you have two options. If there is another Administrator on the database, ask him/her to look up your password. If you are the only Administrator, press Control-Alt-U. You will be asked for an authorization code. Upon successful entry of the code, you will be logged in to an administrator account, where you can look up your own password. To obtain an authorization code, you must contact Data Innovations. The code is valid for one day only.

Selecting a Quiz

Upon successful login to a student account, the student selects a quiz. The Show My Quizzes Only page lists quizzes you are specifically enrolled for. For example, all new employees may be required to take the Example quiz. The administrator identifies you as a new employee and enrolls you in the quiz. The quiz remains on your My Quizzes page until you take it for credit and complete it successfully.

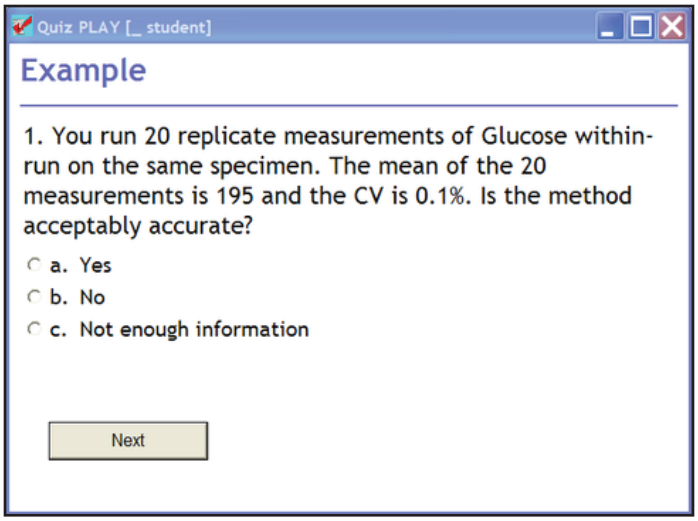


The **Show All Quizzes** page lists all published quizzes, whether or not you are enrolled.

You can highlight a quiz on either page, then select **Take for Credit** to have your score recorded, or Practice if you want to use the program as a study aid. In practice mode the program normally plays feedback sounds as you answer questions. Check the **No Sound Effects** box to take the quiz silently.

Taking a Quiz

When you start the quiz, the program presents one multiple choice question per page. Select a radio button to register your answer, then click Next to proceed to the next question. You cannot go backward. Also, if you go forward without making a selection, the question you skipped will register an incorrect answer. You can abandon the quiz early by closing the window with the red X in the upper right corner.



If the question window is too large or too small, you can resize it. The program will remember your preferred window size in future sessions. Ideally, you want the window big enough so you can see the question, all the answers, and the picture all at once, with no scrollbar on the right.

When you take a quiz for practice, the computer does not record the results.

When you take it for credit, your results are recorded. If you pass, you will be unenrolled from the quiz. Also, you will be asked if you want a certificate of completion. The certificate is a PDF file that you can save on your computer or print and submit for inclusion in your training file.

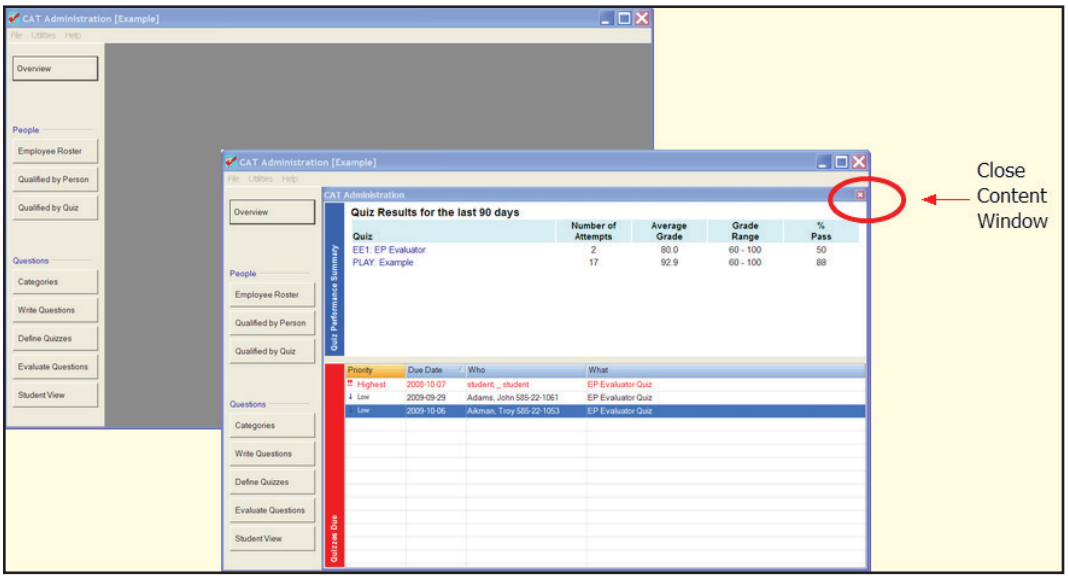
Reviewing Performance

The CAT Administration Screen

Upon successful login to an Administrator, Manager, or Author account, you enter the CAT Administration screen. Clicking one of the large buttons on the left displays content in the dark gray area of the screen. Clicking the small red X at the upper right closes the content window. Clicking the large red X closes the program.

In addition to the buttons on the left, additional functions are available from the menu at the top of the screen.

Some functions may be grayed out depending on your role. For example, a Manager can't write questions or define quizzes. Functions available from this screen include:



Reviewing Performance

Overview - Review average grade by quiz; see who is scheduled to take a quiz but hasn't completed it.

Qualified by Person - Show results of quizzes completed successfully or due within 30 days, grouped by employee.

Qualified by Quiz - Show results of quizzes completed successfully or due within 30 days, grouped by quiz.

Managing Employees

Employee Roster - Add/Delete/Edit employees; enroll or unenroll employees in quizzes.

Utilities / User Fields (Menu Function) - Assign labels to up to 8 user-defined employee demographic fields (e.g., Department, Title, Site). The first two of these fields appear in the Employee Roster listing. Others can be used in filtering.

Questions and Quizzes

Categories - Define question categories
Write Questions - Question text, answers, optional picture, etc. Writing a question makes it available but does not assign it to a quiz.

Define Quizzes - Create a quiz and select which questions go into it.

Evaluate Questions - See percentage of correct answers for each question.

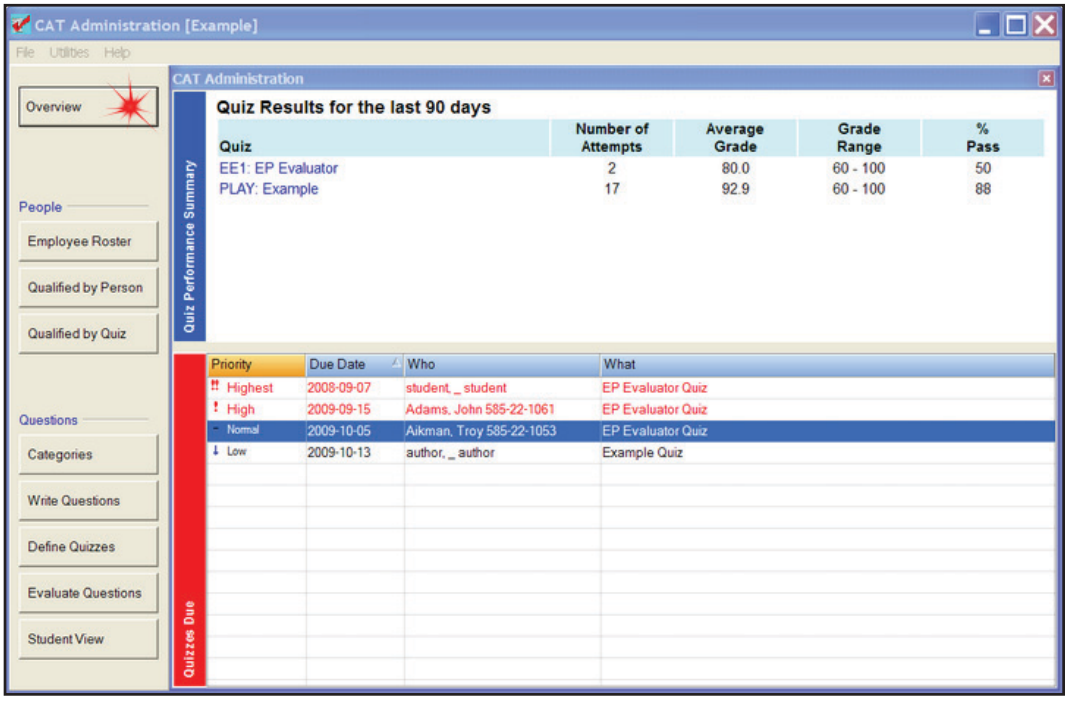
Student View - See a quiz from the student perspective.

Database Management

Utility Functions - Backup / Restore, etc.

Performance Overview

The top panel summarizes results for quizzes completed (for credit) during the last 90 days. Clicking a quiz name brings up a list of people who took the quiz, and shows what their grades were.



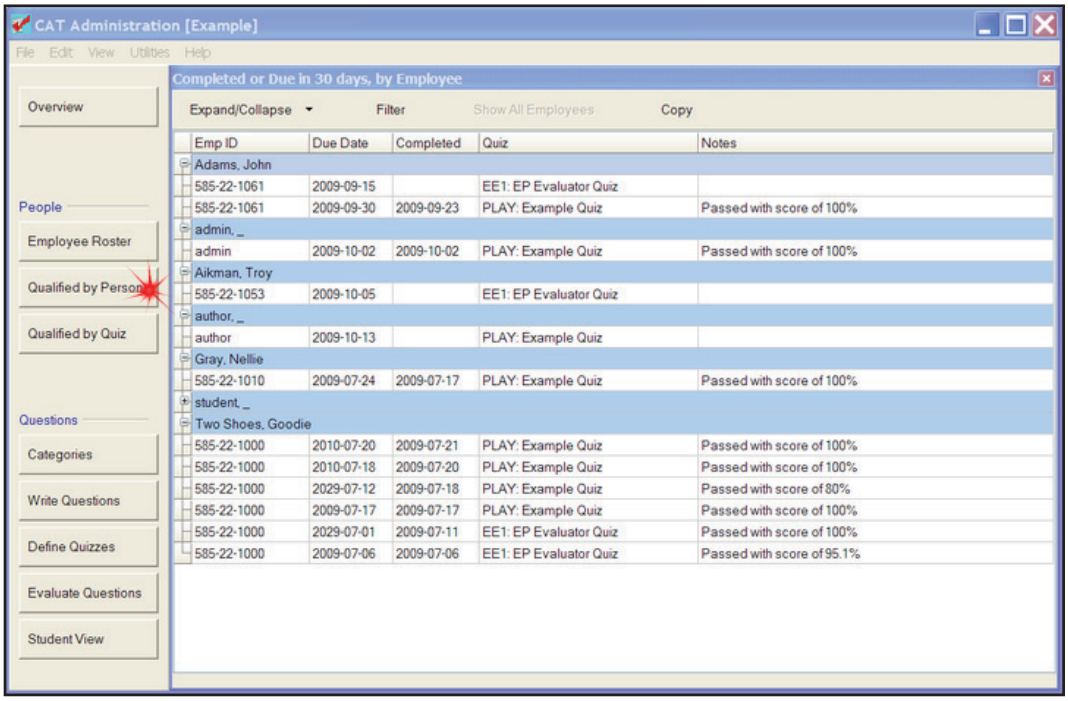
The bottom panel shows quizzes past due or due within the next 7 days, sorted by due date. Items more than 30 days past due have "Highest" priority. Items more than 7 days past due have "High" priority, items 1-7 days past due have "Normal" priority. Items not yet due have "Low" priority. Note: the priority settings might seem off by as much as one day due to rounding.

Clicking the column headings in the bottom panel changes the sort order.

An administrator can right-click a line in the bottom panel and unenroll an employee from a quiz.

Qualified by Person

This screen summarizes results by employee. It includes quizzes successfully completed, plus those due in the next 30 days. It does not show results of failed quizzes or quizzes taken for practice.



The user can:

- Use the +/- buttons in the first column to expand or contract results for a single employee; expand or collapse all employees.
- **Filter** to see selected employees (for example, just employees in the Specimen Processing department).
- **Show All Employees** to remove the active filter.
- **Copy** all results to the clipboard, so they can be pasted into another application.

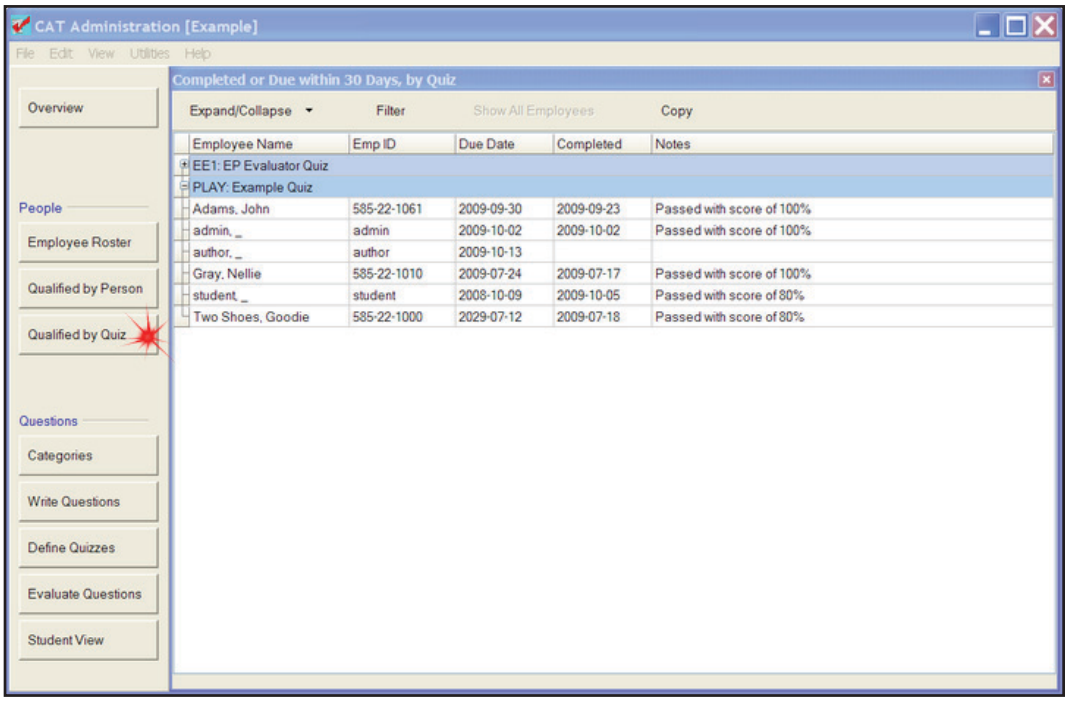
Only visible, expanded rows are copied. For example, in the illustration below, no results for the "student" employee are visible. Results for that employee will not be copied. Similarly, if the list is filtered to show only the Specimen Processing department, only results for Specimen Processing employees will be copied.

Employee header lines are not copied. Instead, the employee name appears in a leading column on each row.

- **File / Print** to create a report showing exactly what is on the screen.

Qualified by Quiz

This screen summarizes results by quiz. It includes quizzes successfully completed, plus those due in the next 30 days. It does not show results of failed quizzes or quizzes taken for practice.



You can:

- Use the +/- buttons in the first column to expand or contract results for a single quiz; expand or collapse all quizzes.

- **Filter** to see selected employees (for example, just employees in the Specimen Processing department).

- **Show All Employees** to remove the active filter.

- **Copy** all results to the clipboard so they can be pasted into another application.
  Only visible, expanded rows are copied. For example, in the illustration above

the EE1 quiz is contracted. Results for that quiz will not be copied. Similarly, if the list is filtered to show only the Specimen Processing department, only Specimen Processing employees will be copied.

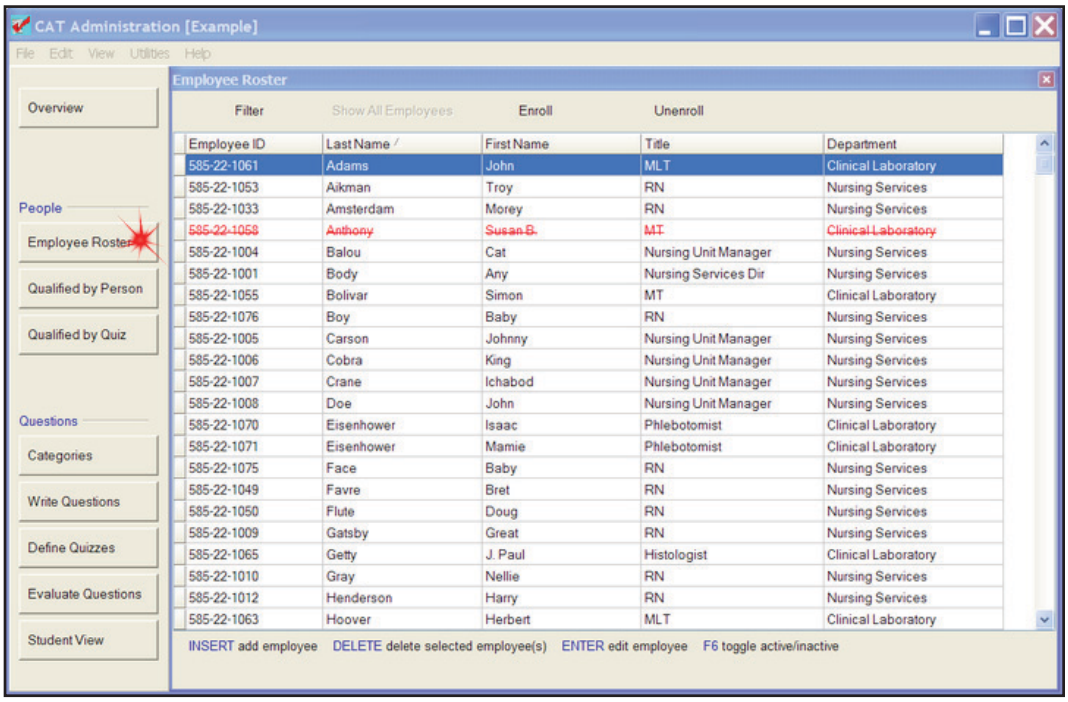
Quiz header lines are not copied. Instead, the Quiz name appears in a leading column on each row.

- **File / Print** to create a report showing exactly what is on the screen.

Managing Employees

Managing Employees

This is the main screen for managing employees. Here you can add, edit, delete, and deactivate employees, and enroll and unenroll them in quizzes. You can also copy employees to the clipboard, edit them in Excel, then paste them back into CAT.



Adding or editing single employees

Insert - add a new employee.

Enter or F2 - edits the highlighted employee. In addition to fields shown on the overview screen, you can change the employee's password, email address, and user-defined fields.

F6 - toggles the employee between Active and Inactive. Inactive employees are shown in a red, strikeout font on the overview screen. Inactive cannot log in, but their quiz results remain in the system. In contrast, if you delete the employee, his quiz results are also deleted.

Delete - deletes the highlighted employee or, if multiple employees are selected, deletes all selected employees.

Sorting, Selecting, Finding, Filtering, and Printing

Range Select - Use shift/click and control/click to select multiple employees. For example, in the screen shown above, click Cat Balou, then shift-click Baby Boy to select the four consecutive employees between Cat Balou and Johnny Carson. If you then control/click Great Gatsby, you have selected five employees.

Edit / Select All (from the menu) selects all visible employees. Edit / Unselect All removes the selection.

Edit / Find searches for text, starting from the top. Then F3 finds the next occurrence.

Sorting - click a column header to sort the grid by that field.

Filter - use employee demographics to limit which employees appear in the grid. For example, show only employees in the Clinical Laboratory department. When the data is filtered you can edit or delete employees, but you can't add new ones.

Example: Suppose you want to enroll all Nursing Services employees in the Laboratory Safety quiz. Use Filter to show only Nursing Services employees. Do Edit / Select All to select all of them, then Enroll to enroll them in the quiz.

Show All Employees - removes the filter.

File / Print - prints a report of everything that appears on the summary screen. Only the fields shown on the summary screen appear in the report. If you have a filter active, only the visible employees are shown.

Actions on Selected Employees

Enroll - enroll an employee in a quiz. The quiz must be published. The due date is 7 days from the date of enrollment. If an employee is already enrolled, he will not be enrolled a second time.

Unenroll - remove an employee from a quiz.

Delete - delete an employee.

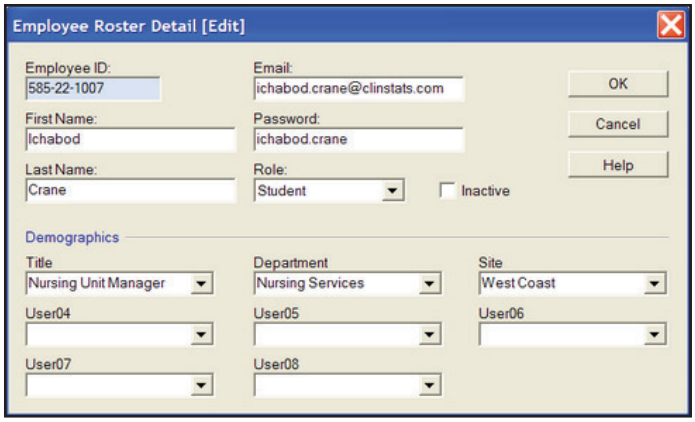
Edit / Copy - copy an employee to the clipboard.

Copy / Paste

If you have an employee list in Excel, you can paste that list into CAT. Before doing the paste, set up your user-defined fields in CAT. Then enter a model employee in CAT. Select that employee, copy to the clipboard, then paste into Excel. This gives you the column headings to use in preparing your input file. Note that the column headings for the user-defined fields are the labels you entered via Utilities / User Fields. When you Edit / Paste data from Excel to CAT, CAT recognize the column headers. A column called EmpID is required. This is the unique employee ID. If a record in the database matches the ID in the paste file, the data fields for that employee will be replaced. If no matching ID is found, the employee will be added.

Add Employee

Employee ID - unique identifier for the employee. The employee uses this ID to log into the system. For login purposes the employee ID is case-sensitive. However you can't have two employees in the system with IDs that are identical except for case. For example, suppose John Doe has an employee id of JDoe. You can't have a different employee with id jDoe. John must login as JDoe. If he enters jdoe, his login will be rejected.



First Name - employee first name

Last Name - employee last name

Email - employee email address

Password - employee login password. When you add a new employee, the program suggests a random password. You are free to change it. Also, the employee may change his own password later.

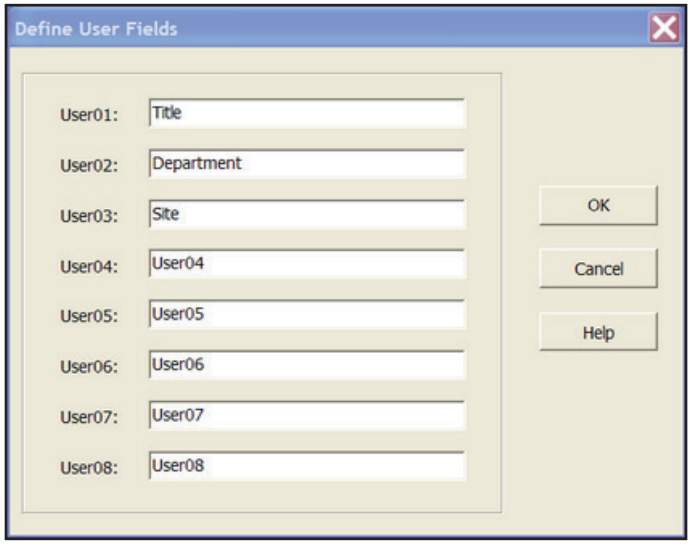
Role - student, author, manager, or admin. Student can only take quizzes. Author can only write questions. Manager can only review results. Admin can perform all functions.

Inactive - If this box is checked, the employee cannot log in. However his quiz results remain in the system. In contrast, if you delete the employee, his quiz results are also deleted.

Demographics - There are eight user-defined fields (32-character text fields). You define the labels and meaning of these fields via Utilities / User Fields. The first two fields appear on the main Employee Roster screen. In the example above, the label for User01 is "Title." User02 is "Department." User03 is "Site." No meaning has been assigned to the other five fields.

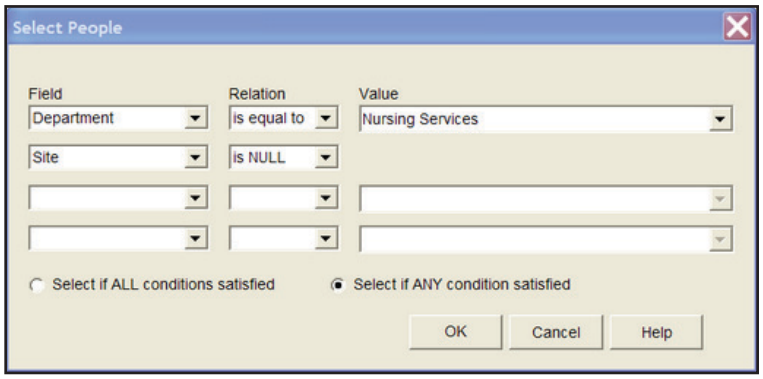
User-defined Fields

This screen defines 20-character labels for the eight user-defined fields. Any field that has a label can be used for filtering employees. Fields with blank labels or with labels like "User 05" will be ignored.



Filtering

This screen lets you define an employee filter based on the user-defined fields. You may define up to four conditions.



Field - one of the user-defined demographic fields (see *Add Employee*).

Relation - is equal to, is not equal to, is NULL, is not NULL, or <none>. NULL means the field is empty.

<none> removes the condition from the filter.

Value - the dropdown shows what values exist in the database. Select one of them.

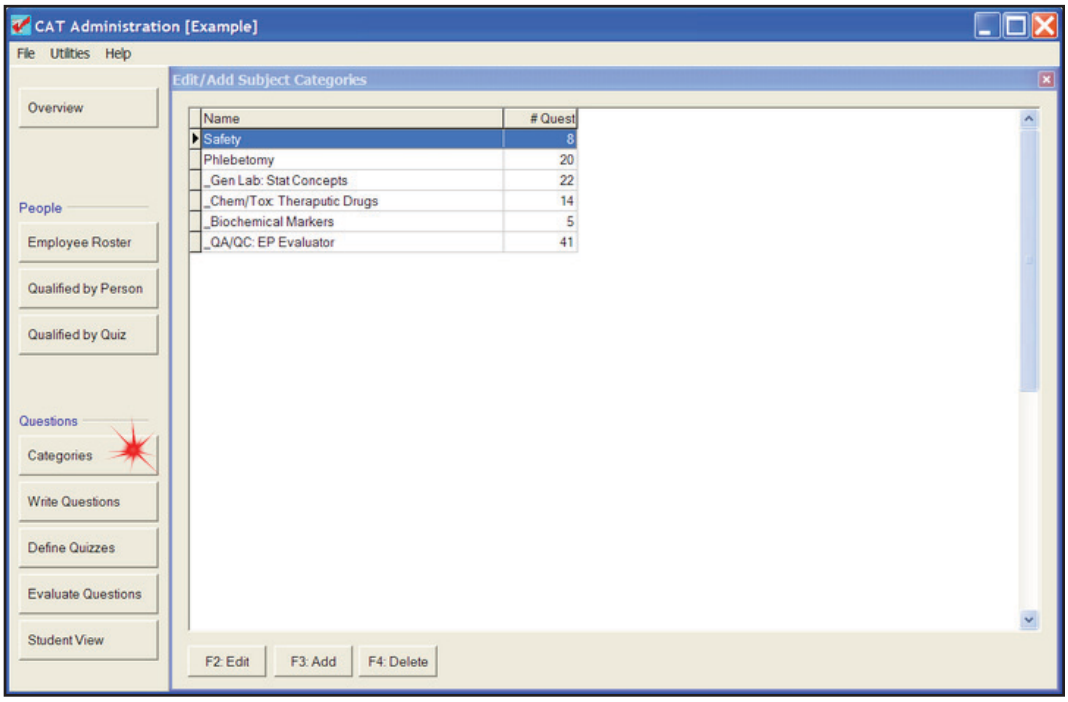
The example above selects all employees in the Nursing Services department, plus all employees for which the Site is undefined.

Writing Questions

Categories

This screen defines subject categories for questions. The summary screen shows currently defined category names, plus the number of questions in each category.

Category names beginning with underscore are reserved for "stock" questions supplied with CAT. You cannot edit or delete these categories. Also, you cannot add a category name beginning with underscore.



F2: Edit - change the name of a category.

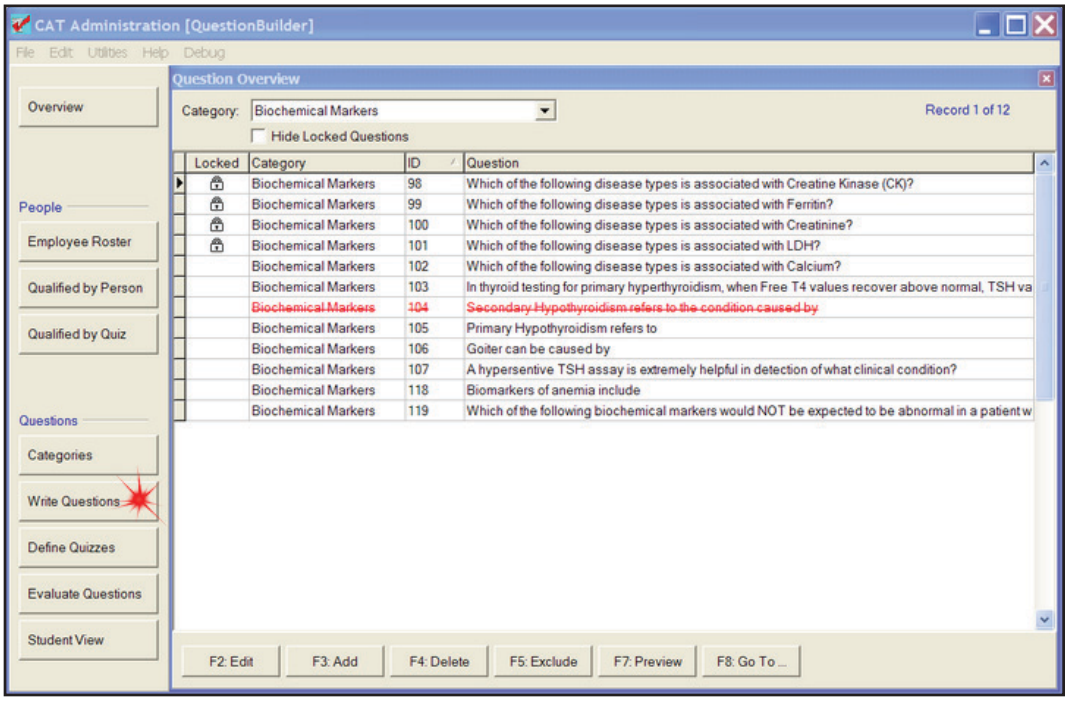
F3: Add - add a new category

F4: Delete - delete the highlighted category.

Also, menu commands **Edit / Copy** copies the category list to the clipboard, and **Edit / Paste** pastes from the clipboard to the category list.

Question Overview Screen

This screen lists all questions in the database – just question text, not answers, feedback, pictures, etc. The summary table shows the locked status, Category, auto-assigned question ID, and the first 200 characters of the question text. If you want to add questions, remember that you must add the category first (from the Categories screen) before you can add questions to that category.



Locked - a locked question is one you cannot edit. A question is locked if it is assigned to a published quiz or if it is a "Stock" question provided with EP Evaluator®. Check the Hide Locked Questions box to show only unlocked questions.

Category - the subject category of the question. Use the Category selector at the top of the screen to show only a single category.

Sorting - click the column headers to sort by Category, ID, or Question. You cannot sort by lock status.

Multi-select - use Click followed by Shift-Click to select a contiguous range of questions. Use Control+Click to select multiple non-contiguous questions. To select all questions use Control+A or **Edit / Select All**. To unselect all questions, use **Edit / Unselect All** or single click on a line.

F2: Edit - Edit the highlighted question (only one question may be selected). You cannot edit a locked question. Remember that, if the question was previously a published question, it may have an accumulated response history. This response history is used to evaluate the "quality" of the question. If you make a material change to the question, the response history may be misleading. An example:

- You wrote and published the question "What color is an orange?" Answer #1 Orange, Answer #2 Green.
- Ten people answered the question, and 100% of them answered it correctly

You unpublish the quiz, then change the question so the answers are #1 Blue, #2 Orange, #3 Green

You then republish the question. Ten more people answer the question, and all of them choose answer #2.

The question performance report will now show that 50% of the people chose answer #1 and 50% chose example #2, so only 50% answered correctly.

To make a material change to the meaning of a previously published question, it is better to delete or exclude the old question and add a new one, rather than editing the existing question.

F3: Add - Add a new question.

F4: Delete - Delete the selected question(s). You cannot delete a locked question. If multiple questions are selected, CAT will delete only the unlocked questions in the group. When you delete a question, any accumulated response history for that question will be deleted also.

F5: Exclude - Toggle the exclude status of the selected question(s). Excluded questions are shown in red/strikeout font in the summary grid. An excluded question remains in the database, but it cannot be added to a quiz. Some reasons you might want to exclude a question:

- It hasn't yet been reviewed and approved.
- The question was once published, you collected some history on what percent of students answered it correctly, and you don't want to lose that history.
- The question is a "stock" question and you can't delete it.

F7: Preview - Show the selected question(s) in a format more similar to what the quiz-taker will see. If only one question is selected, the program will ask whether you want to preview just the one selected question or all visible

questions. Use File / Print from the menu to get a printed report instead of an onscreen preview.

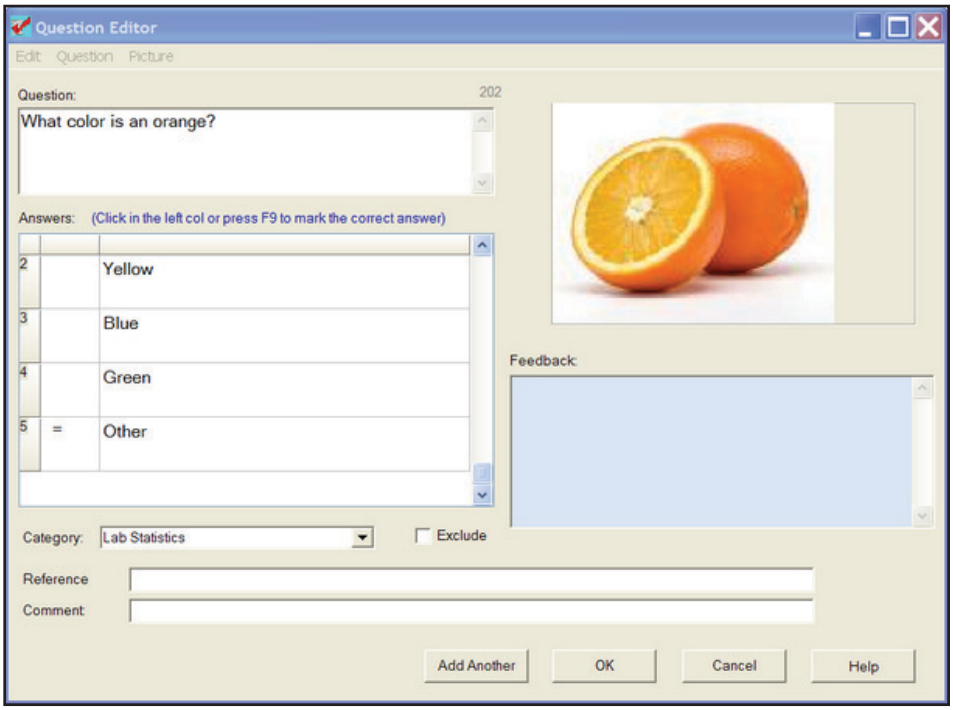
F8: Go To ... - Go to a specific question number.

You can also import and export questions from this screen.

Creating or Editing a Question

This screen is displayed when you ask to add a new question or edit an existing one. Drag the edges of the screen to resize to get more or less space for typing questions and answers. (The program will remember the size between sessions.) If you still don't have enough typing space you can double click on the question, feedback, or any answer to get a larger popup edit box.

The question, possible answers, and subject category are required. All the other fields are optional. Supported question types are multiple choice with a single correct answer and true/false.



- **Question** - A single paragraph of text. Even if you write multiple paragraphs, the program will combine them into one when presenting the question to a student. Also, you can't use special formatting (bold, italic, etc.) or change the font. The number at the top-right of the question field is the auto-assigned question ID number.

- **Answers** - Possible answers for the question, one answer per row. There is no limit on the number of possible answers; however, only one answer is correct. Mark the correct answer by pressing the F9 key or by clicking in the left column.

- **Category** - Subject category to assign the question to. You must create the category first before you can add the question to it. Also, you cannot add questions to a category with a name which begins with underscore.

- **Picture** - Optionally you can provide a jpg or png image relevant to the question – one picture per question. To add a picture, use **Picture / Load** from the menu bar. Use **Picture / Clear** to remove the picture from the question. When you add a picture, that picture is copied into the database – so it is ok if you delete or move the picture's disk file.

The other picture menu command, Picture / Stretch, controls the format of the picture preview on the question edit page. When stretch is checked, the picture is reduced so the whole picture fits in the preview frame. When stretch is unchecked, you see the upper left corner of the picture at full resolution. Size of the preview picture on the edit page is unrelated to what the user sees when he takes the quiz. In the actual quiz setting the program scales the picture to fit on the screen. In most cases you don't need to worry about sizing your picture prior to loading it into CAT.

- To see the question in a format more similar to what the quiz-taker will see, use **Question / Preview** from the menu bar.

- To get a printed copy of the question, use **Question / Print**.

Feedback - Explanatory text a student sees when he answers the question incorrectly. (Feedback is shown only when the quiz is taken for practice.) Feedback is optional. If you omit it, the program simply shows correct answer.

Exclude - If this box is checked, the question remains in the database, but it cannot be added to a quiz. Some reasons you might want to exclude a question:

- It hasn't yet been reviewed and approved.

- The question was once published, you collected some history on what percent of students answered it correctly, and you don't want to lose that history.

- The question is a "stock" question and you can't delete it.

Reference - Supporting data documenting where the question came from.

Comment - Any note you wish to make. For example, you might use this field for the author's name.

Comment and reference are not shown to the student. When you are adding new questions, the Add Another button at the bottom of the screen lets you add more questions without going back to the question summary screen. When you are editing an existing question, this button is not present.

Copying and Pasting Questions

Can I copy/paste questions? Can I import them from a Word/Excel/PDF/PowerPoint file?

You cannot import questions from a file (other than from files created in CAT). There is a very limited ability to copy/paste into the screen where you normally type questions.

If you are willing to paste each field one at a time (i.e., paste the question, paste answer 1, paste answer 2, etc.) you can use Control-V, just as you would in any other application.

If you want to paste everything at once ...

- You must paste one question at a time.
- You can only paste the question and answer text. You can't paste picture, category, feedback, reference, etc.
- The question must be a single paragraph; each answer must be a single paragraph.
- You cannot include question or answer numbers unless they are auto-generated by Word style tags or separated from the text by a single tab.
- You must be able to select and copy the question and answers in text format from the source application in a single operation, without any extraneous text. For example, you can do this in Microsoft Word if the questions have a simple structure. You can't do it in PowerPoint if the question is the slide title and the answers are in the slide body.

To paste question and answers, select **Edit / Paste Question** from the menu. If you already have text in the question or answer fields, that text will be replaced.

To paste single snippets of text into an edit control, put your cursor where you want to insert the snippet, then press **Control+V**.

Note that Control+V is not a synonym for **Edit / Paste Question**. The two commands perform different functions.

Edit / Paste Question Examples

Example 1. You can copy a question formatted in outline style when the question is the first level of the outline, answers are second level, and each question and answer is one paragraph. If the first character of an answer is '=', that is the correct answer. You can also omit the '=', then mark the correct answer after pasting. Outline numbering will not be preserved, so don't refer to the answers as "choice a" or "choice b" in the body of the question.

1. In thyroid testing for primary hyperthyroidism, when Free T4 values recover above normal, TSH values are expected to recover
    a. In the normal range
    b. = Below normal
    c. Above normal
    d. No Free T4 is expected to be found.

Example 2. You can also paste if the question and answers are typed in flat (non-outline) format. The question and answers may be in a different font. The font will not be preserved, but the text will paste correctly.

In thyroid testing for primary hyperthyroidism, when Free T4 values recover above normal, TSH values are expected to recover
In the normal range
= Below normal
Above normal
No Free T4 is expected to be found.

Example 3. This example DOES NOT WORK, even though it looks exactly like Example 2 if display of paragraph symbols is turned off. The problem is that the author used a paragraph mark to force a line break in the question.

In·thyroid·testing·for·primary·hyperthyroidism,·when·Free·T4·values·recover·above¶
normal,·TSH·values·are·expected·to·recover·¶
In·the·normal·range¶
=·Below·normal·¶
Above·normal¶
No·Free·T4·is·expected·to·be·found.¶

Example 4. Here is an example where a blank paragraph is inserted between question and answers for readability. This WILL paste correctly. The blank paragraph is ignored.

In thyroid testing for primary hyperthyroidism, when Free T4 values recover above normal, TSH values are expected to recover

In the normal range
= Below normal
Above normal
No Free T4 is expected to be found.

Example 5. Another example that DOES NOT WORK, even though on the surface it looks exactly like Example 1. The problem is that the a), b), c) answer labels are typed as text, rather than generated automatically by Word as part of the outline numbering. You may not explicitly include answer numbers (because the program will generate them). It's OK to use outline format; there the importer can recognize and skip the answer numbers. You could also type a tab between the answer number and the answer text.

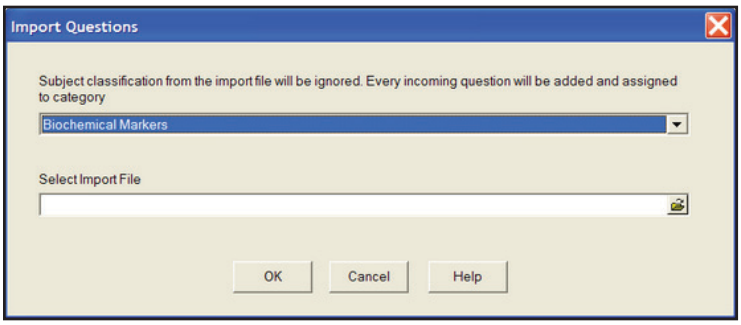
1. In thyroid testing for primary hyperthyroidism, when Free T4 values recover above normal, TSH values are expected to recover

a) In the normal range
b) = Below normal
c) Above normal
d) No Free T4 is expected to be found.

Exporting and Importing Questions

Menu commands to import and export questions are **File / Import** and **File / Export**. These menu functions are available from the Question Overview screen.

The most important thing to remember about importing and exporting is that the category is not exported with the question – because there is no reason to assume that the category will be present in the database the file is imported to.



- When you import a question file, you select a category. That category must already exist in the database. Every question in the import file will be added and assigned to the selected category. The program cannot identify duplicate questions, so every question in the import file will be added as a new question.

- From the Question Overview screen you can multi-select questions, including questions from different categories, then select File / Export to export the selected questions to a text file. If you select questions from different categories the program will warn you, but you may ignore the warning and proceed with the export.

Import/Export Examples

- Mary is a question author, writing questions about Lab Safety in a private database. When she has reviewed and approved a set of questions, she goes to

her question editor, selects the questions, and requests **File / Export**. She then gives her export file to the Admin of the production database. The Admin uses **File / Import** to import Mary's questions to the production database.

- An Example database is distributed with the software. In order to incorporate some of the Example questions into your production database, you open the Example database, select the questions you want to use, then do File / Export. Do a separate export for each category; or you can select questions from several of our categories targeted for one category of your own. Open your production database and do **File / Import** to add each export file to a category.

Managing Quizzes

Define Quizzes

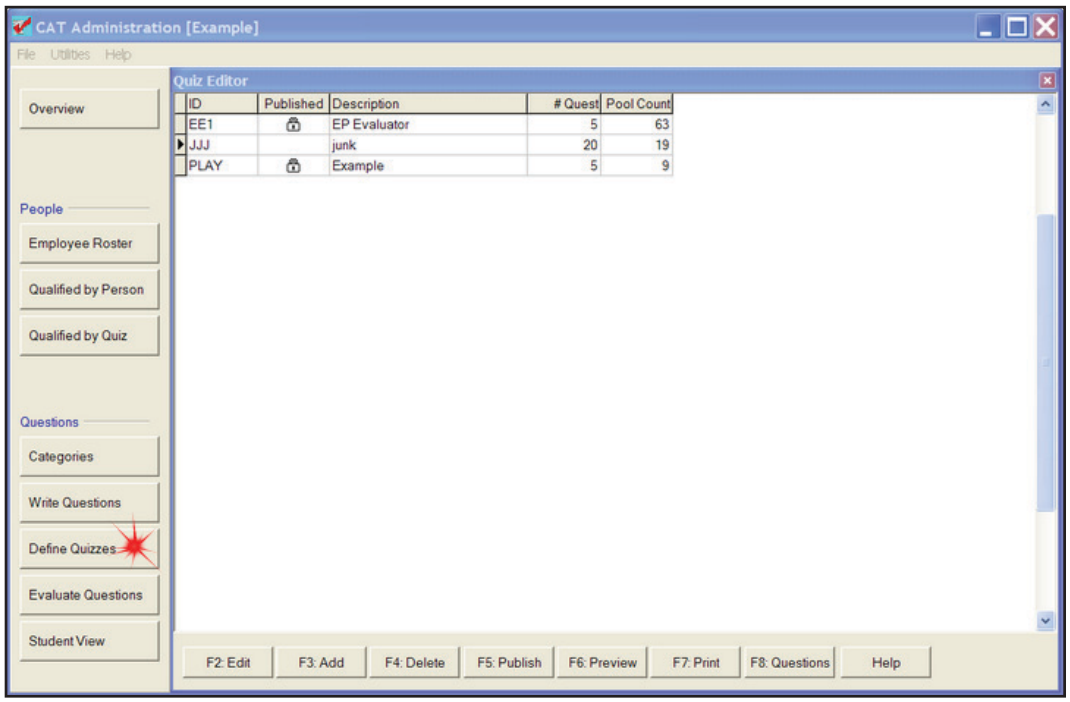
Use this screen to define or edit quizzes. **# Quest** is the number of questions presented to the student. **Pool Count** is the number of questions assigned to the quiz. For example, suppose you have created a pool of 100 questions on safety, and you want the student to see 20 questions chosen at random from the pool. In this example, # Quest is 20, and Pool Count is 100.

F2: Edit - Change the quiz id, description, number of questions, etc.

F3: Add - Add a new quiz.

F4: Delete - Deletes a quiz. Note that deleting a quiz also deletes all records on those who have completed the quiz. To make the quiz unavailable without deleting its underlying records, make the quiz unpublished.

F5: Publish - Toggles the published status for the quiz.



- If a quiz is published, students can see and take the quiz. You cannot edit the quiz or add questions to it. Also, you cannot edit any question associated with that quiz.
- If a quiz is not published, you can edit the quiz and the questions, but students can't see the quiz.
- If you need to modify a published quiz, first toggle it to unpublished, then edit it, then toggle it back to published.
- You cannot publish the quiz if # Quest is greater than Pool Count.

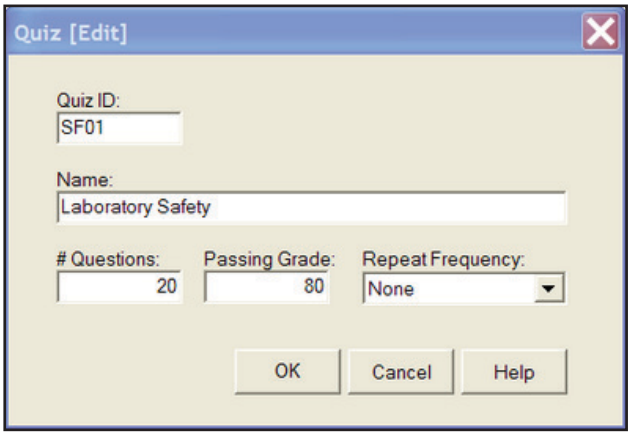
F6: Preview - See the quiz in a format similar to what students will see.

F7: Print - Print all questions in a quiz (perhaps to distribute to others for review).

F8: Questions - Add or remove questions from the quiz.

Adding a Quiz

Quiz ID - unique identifier for the quiz.



Name - quiz title or description.

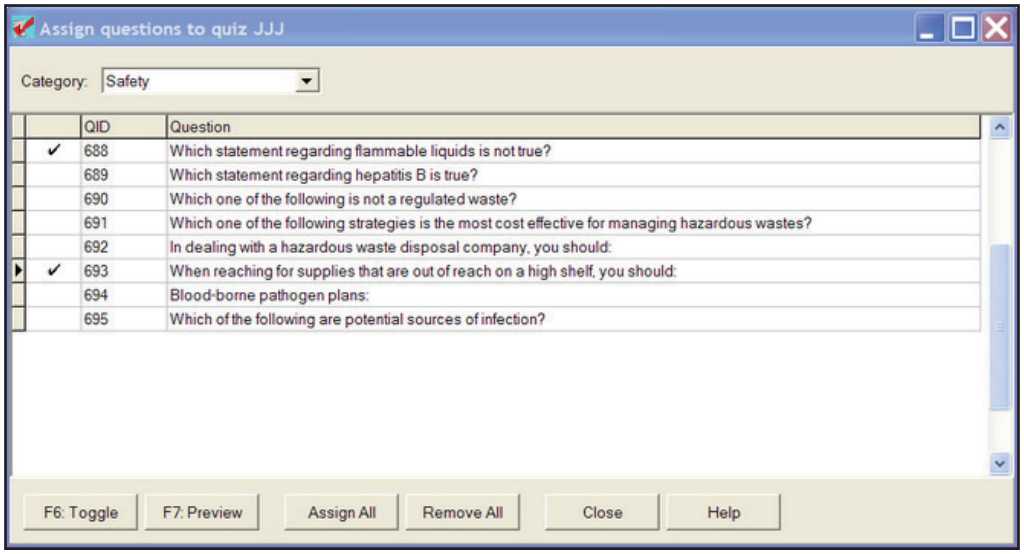
 # Questions - number of questions presented to the student.

Passing Grade - percent of questions that must be answered correctly to pass.

Repeat Frequency - None, Bi-Annual, Annual, Semi-Annual. If you select Bi-Annual, Annual, or Semi-Annual, the employee will be automatically scheduled to repeat the quiz when he completes it successfully.

Assigning Questions to a Quiz

This screen presents a list of available questions and allows you to choose which ones to assign to a quiz. A check mark in the first column means the question is currently assigned to the quiz. The title bar of the window shows which quiz is being assigned ("JJJ" in the example shown).



You can move and resize the window to your viewing preferences; the program will remember your settings between sessions.

Category: Filter the selection list to show only a single subject category.

F6: Toggle - toggles whether the question is assigned to the quiz. In the example above, quiz JJJ contains two questions from the Safety Category.

F7: Preview - The summary screen shows only the question text. Use F7: Preview to see the full question in a format similar to what the employee will see when taking the quiz.

Assign All - Assign all questions to the quiz (selected category only). For example, if you are creating a quiz on safety, you might use the Category selector to show questions in the Safety category, then use Assign All to add them to the quiz.

Remove All - Remove all questions from the quiz (selected category only).

Evaluating Questions

This screen shows the percent of correct answers for the questions, across all students who have answered the question in a For-Credit Quiz. Use the Category selector at the top of the screen to select the question category.

 # Attempts - Number of times the question has been presented to a student.

% Correct - Percent of attempts for which the answer was correct.

Kappa - Percent correct, adjusted for chance. If a multiple choice question has only two possible answers, someone answering that question could get it right 50% of the time by just guessing. If the question has four answers, he has a 25% chance of getting it right by guessing. In this example, most of the questions had four answers. The question responses were created with a random number generator. The average percent correct was about 25%. The average kappa was about 0%. Kappa adjusts percent correct to allow for the probability of getting the right answer by guessing. Questions with negative kappa may be confusing to readers. Questions with very high kappa may be too obvious.

The chart on the right shows a distribution of question kappa.

- The white box represents the central 50%. In the illustration above there are 12 questions. The top of the white box is a kappa of about 10%. 3 of 12 questions, or 25% have kappa > 10. Another 3 have kappa below the bottom of the white box.
- The dashed line in the center of the white box is the median.
- The solid blue line moves as you select different questions to show where the selected question falls in relation to other questions in the category.

Double-click on the question to see it in a form similar to what the student sees.

Clear Response History removes the response history for all questions in the selected category.

Utility Functions

Creating a New Database

Use the menu command File / New Database to create a new database. This database will contain:

- A complete list of users for the database, including Students, Authors, Managers, and Admins. When you create the database, one user is added by default, with a user ID of admin and password of admin. The first thing you should do is go to the employee roster, add yourself as an Admin, and deactivate the default admin. Why not simply delete admin or change the user name? It's easier to recover a lost admin password if the default admin account is present but disabled.

- Questions covering all subjects you will use for competency assessment.

- Tickler system showing who needs to take what quiz by what date; record of completed quizzes and grades.

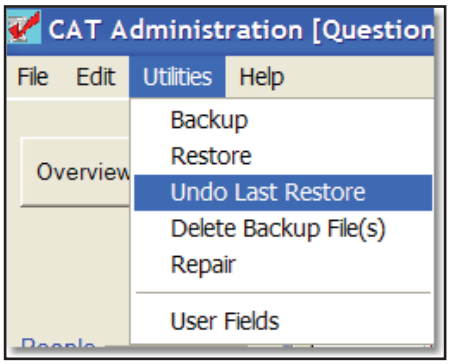
At issue is number of production databases. We recommend that you have only one production database rather than many of them. The problem is that each data-

base stores not only the questions, but also the users, their demographics and their passwords. If you have multiple databases, then you will have to copy all changes to employees to all the others. The only occasion to have multiple production databases is if there is NO overlap of questions or employees between them.

However, it is useful to have a separate database for each author to use for question development. This allows the author to practice and get feedback on his questions without affecting the production database.

Back up and Restore

Functions in the Utilities menu are available only to Administrators. These include:



Backup - Create a backup of the database. The program will prompt you for a description of the backup file. You can either provide a specific name or choose the default "<auto>."

Auto backups are named based on the backup date, and they are automatically pruned by the program to keep the most recent five backups for the current date, and one backup per day for earlier dates. The latest five historic backups will be kept. For example, suppose you make ten auto-named backups every day from January 1 through January 10 for a total of 100. As of the last backup on January 10, you will have 5 backups for January 10, and one each for January 9, 8, 7, 6, and 5.

Specifically named backups are kept until you delete them.

Restore - Restore a backup file. Remember that when you do this, you will lose all test scores for students who completed quizzes between the date the backup was made and the current date. In a network environment, you cannot restore a backup while others are using the software.

Undo Last Restore - Reverse the effect of the most recent restore.

Delete Backup File(s) - Remove backups you no longer need.

Repair - Repair a damaged database.

User Fields - This function defines labels for employee demographic fields. See User-defined Fields.

Sending a Bug Report

Use this form to email a bug report to the developer.

As this program runs it collects information about your computer configuration and error messages you receive. When you send a bug report, the program collects that information into an e-mail file attachment.

In the message text, please provide as much detail as possible:
1. What went wrong? Describe the problem as fully as possible.
2. What were you trying to do when the error occurred?
3. Is the problem repeatable?

The automatic e-mail may not work for you, depending on your computer's e-mail setup. If the mail does not work, the program will still create the attachment file. You can send it to us from another computer, or on disk by postal mail.

Chapter

36

Introduction to Rapid Results Entry (RRE)

What is Rapid Results Entry? The meaning of the term has evolved over time. Today, it means any of a number of ways to get input into EE rapidly—either without typing at all or, if you have to type, using the most convenient format possible.

This chapter describes several different types of RRE. Some of them are very easy and obvious "tricks" that are immediately useful to anybody. Others require some work to set up, namely by defining parameters or Policies, but they offer huge productivity gains in return—particularly if you routinely repeat the same calculations for the same instruments and analytes. (For example: doing the same calibration verifications every six months.) .

NOTE: This chapter does not apply to Hematology Studies, ERI/ROC, Average of Normals, or the lab management modules. Data acquisition for those modules is described in their own chapters.

Understanding your Options

RRE is not hard to do, once you figure out where to start

Table 36.1 shows an overview of the RRE methods listed by the EE menu commands used to initiate them. Approaches marked with a ★ are our favorites. Here's how they are classified:

- Ease with which the process can be understood
- Type of data which is entered rapidly: results, parameters or both.
- Manages data for one or more than one experiment.
- Whether the method used Policy Definitions.

- EE Version support.
  - Methods 1, 2, and 4. All versions.
  - Methods 3, 5, 7, and 9. All versions but CLIA and COFRAC.
  - Methods 6 and 8. All versions but CLIA, COFRAC, and Standard.

An EE experiment requires two types of input: experimental results and parameters. Experimental results are often available in spreadsheets.

Parameters — like units and allowable error — are a different story. Even if you "rapidly" enter the results, you have to edit each experiment to enter units and other evaluation criteria. *Policy Definition* is a way of putting all this information into a database so that when EE recognizes the analyte names, it will automatically supply most, if not all, of the needed parameters when it creates the experiment. The process for defining policies is described in Chapter 37, *Policy Definition*.

RRE Example Spreadsheets

In the years we have spent working with EP Evaluator, we have seen many spreadsheets from customers. Most of them are columns of experimental results with analyte names as column headings. Several of the RRE methods represent ways to get those columns of numbers into EE simply by copying them to the clipboard and then pasting them into EE.

The software that is installed on your PC includes example spreadsheets. There are specific spreadsheets for each RRE method that uses copy/paste from Excel. The spreadsheets contain specific examples for each applicable statistical module, with instructions. Not all spreadsheets support copy/paste for every module. You will find these spreadsheets in the C:\EE11\Resources folder (assuming you installed the program to C:\EE11).

NOTE: The spreadsheets are write-protected. If you want to revise them for your own use, please don't change the originals. Instead, make a copy. Then remove protection from your copy. Each tab page ("sheet" in Excel language) is protected separately. To remove protection, select the tab page, then select **Tools/Protection/Unprotect Sheet** from the Excel menu.

The sections in this chapter will explain those two methods (1 and 7) which do not use Policies. Chapter 38, *Rapid Results Entry (RRE) With Policies* will explain the rest, all of which do use Policies. There are slight variations in the procedure depending on the statistical module. Our examples in these chapters only illustrate the AMC module. The spreadsheets in the Resources folder cover all the modules individually.

Date Formats during RRE in non-English Languages

Dates can sometimes be the source of problems when using RRE. If you see messages warning you that dates were ignored, or if you look at your data and notice that the days, months, or years have been interchanged, the problem is most likely that the date format you are using in Excel does not match the date format you have asked the operating system to use.

In Excel, select the cells that contain dates, and use the Format Cells menu entry to alter the visible format of the cells. The preferred format will have the day, month, and year fields in the same order as specified in your operating system date setting.

To view or set the operating system date format, go into the Control Panel, Regional and Language Options, and click on the Customize button in the Regional Options tab. Then click on the Date tab, and select a Short Date format that has an asterisk, preferably one that is purely numeric.

Table 36.1. Comparison of the RRE Methods

Menu command and how it works	"Rapid" entry of what?	Multi or Single Expt?	Needs Policies?	Notes
1 Edit/Paste (at Experiment Detail Screen) Create an experiment as usual, right up to the point where you would type the results. Then paste the results instead of typing them. Use the PasteExptDetail.xls.	Results	Single	No	1
2 Edit/Paste (at Module Overview Screen, results & parameters) The spreadsheet to be pasted into EE, contains both results and parameters, in a special "RRE format". Use the PasteParmsInSS.xls.	Results and Parameters	Multi	No	
3 Experiment/New from Policies Exactly like the normal Experiment/New command, except you pick the instrument and analyte from a list, and the parameters screen is filled automatically from Policies. No spreadsheets or pasting involved. You must still add the results. No spreadsheet required, but PasteExptDetail.xls can be used.	Parameters	Single	Yes	2
4 Edit/Paste with Policies/Table Format Spreadsheet contains data in columns, with analyte names as column headings. Paste the spreadsheet into the Module Overview Screen to create an experiment for each analyte. If Policies are defined, Parameters are populated from Policies so no manual editing is necessary. Use the PasteWithPoliciesTable.xls.	Results and Parameter	Multi	No	2
5 Edit/Paste with Policies/List Format Identical to method 4 except for the format of the spreadsheet. List format contains only one result per line. Use the PasteWithPoliciesList.xls.	Results and Parameter	Multi	Yes	2
6 RRE/Create Experiments (with Instrument Interface) PC is connected to the instrument with a serial cable, and results are transmitted directly from the instrument into EE. EE creates a "Worksheet" containing both the captured data and parameters obtained from Policies. The worksheet may be edited if necessary. When editing is complete, individual experiments are created from it. Also, the file is saved to disk in "RRE Format". This file can be opened and edited later in Excel.	Results and Parameter	Multi	Yes	2, 3
7 RRE/Create Experiments (keyboard entry of results) You select instrument and analytes from a list. EE creates a Worksheet with parameters filled in, and blank cells where you type the results. After typing the results, individual experiments are created from the worksheet.	Parameters	Multi	Yes	2
8 Data Acquisition via ODBC Provides for capturing all results for an experiment from a source application very simply and quickly. You specify the analytes, specimens and date ranges and the software will automatically load it into the EE experiments.	Results and Parameter	Multi	Yes	2, 4
9 Rapid Results Entry - Trueness **RRE/Create Experiments** in the Trueness Module is designed to accept spreadsheet data where each row has the data for one specimen. The input file is configured from a Trueness RRE Setup screen. This method is only available for the Trueness module. Use the TRU RRE Example.xls.	Results and Parameter	Multi	Yes	1, 2

[1]Only for a limited number of statistical modules
[2] Not available in the CLIA version
[3] Requires Vendor, Standard plus Data Capture, or Professional version with suitable instrument interface program.
[4] Requires Vendor, Standard plus Data Capture or Professional version and ODBC.

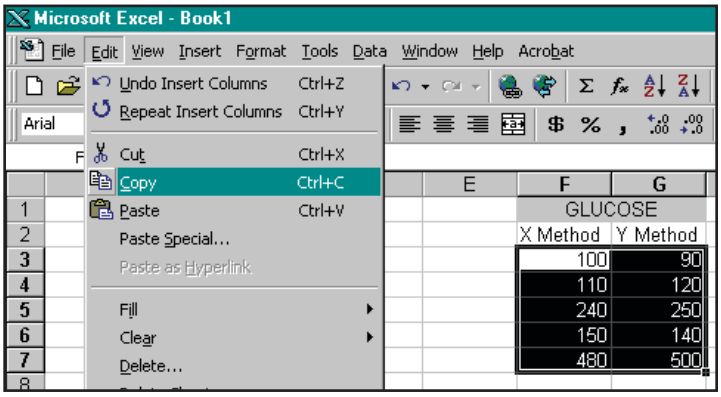
Method 1: Edit/Paste (at Experiment Detail Screen)

This is the easiest (and least powerful) method. It has very few steps, does not require Policies, and is available in all EE11 versions (including the CLIA version).

- Excel and EE must both be running, so you can switch between them by clicking their icons on the Windows task bar.

- Switch to EE. Create the experiment just as you would to type the results into it. Do everything up to the point of actually typing the results. (The example illustrates an AMC experiment.)

- Switch to Excel and open the spreadsheet with the results in it. The spreadsheet columns must be set up just like the EE columns—X and Y methods in adjacent columns, with X on the left. Highlight just the numbers (NOT the column headings), and select Edit/Copy from the Excel menu.



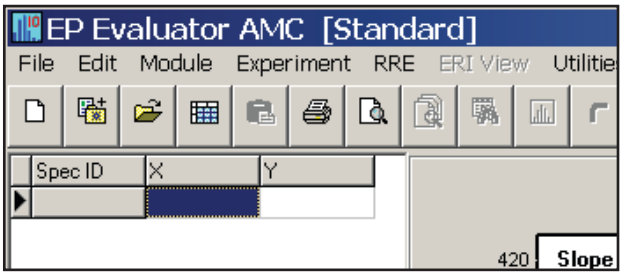
- Switch back to EE. Select Edit/Paste from the EE menu. The results from Excel will drop into the EE grid just as if you had typed them. (You can't paste Spec IDs, just results.)

This approach is particularly convenient for method comparison experiments like AMC. It requires you to set up spreadsheet columns exactly like EE columns, so it doesn't work for modules with complex data layouts. It does work in Simple Precision, all of the method comparison modules, and VRI. Examples for other modules are in C:\EE11\Resources\PasteExptDetail.xls.

Method 2: Edit/Paste at Overview Screen (results & parameters)

Method 2 is one of our older RRE procedures. Others are easier to use and accomplish exactly the same result. The only reasons to use Method 2 are:

- You have the CLIA version of EE. In EE-CLIA, Method 2 is the only way to create multiple experiments with both parameters and results in place.
- Customized automation. For example, one of our customers has created an extensive set of Excel macros that take data from the LIS and re-format it into RRE format, setting up parameters exactly as that particular company wants them.

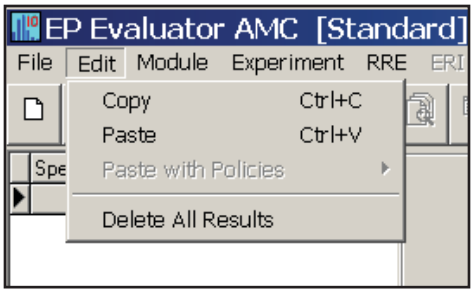


Method 2 requires manually creating a spreadsheet in RRE File Format. Once you have the file, transferring it to EE is very easy. Just highlight the whole page in Excel and do **Edit/Copy**. Then switch to EE, go to the Module Overview Screen, and do **Edit/Paste**. At least, you don't have to edit if you correctly entered all of the parameters in your spreadsheet.

The most difficult part is creating the spreadsheet template. The best way to do it is to start with a model and change it to fit your needs. Consult Data Innovations if you have additional questions.

Remaining methods

All the remaining modules will be discussed in Chapter 38, *Rapid Results Entry (RRE) With Policies* after the discussion of Policy Definitions.



Chapter

37

Policy Definition

Policy Definition establishes standard parameters for a complete set of experiments. Defined policies are combined with experimental results during Rapid Results Entry—either keyboard-based RRE, by selecting **Experiment>New from Policies**, or from an instrument interface. You can then calculate and print reports immediately with no need to click down into each individual experiment to fill in missing parameters. Policy Definition is REQUIRED for the process of capturing data from instruments.

Policy Definition is not available in the CLIA version of EE.

Policy Definitions are separated into two groups: (1) policies for Hematology Method Comparison and (2) everything else (Non-Hematology Policies). This chapter covers Non-Hematology Policies only. Hematology Policies are covered in Chapter 16, *Hematology Studies*.

A model master project has been created for Non-Hematology Policies. It is Example Policies (for both US and SI units respectively). It includes about 20 analytes and is meant to be a starting point for each facilities' effort to create its own Master Project. Each facility will need to personalize its own Master Project.

Defining a Policy

To start the Policy Editor, select the **RRE / Define Policies** command from the menu. The Policy Editor has its own main screen and command buttons. The normal EE menu will be unavailable until you quit the Policy Editor.

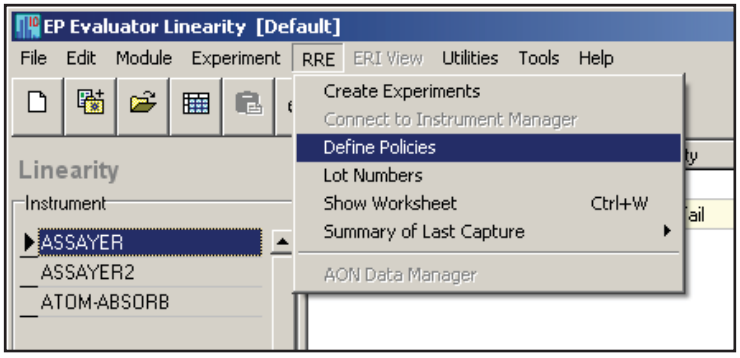


Figure 37.1. RRE Define Policies Menu Fragment

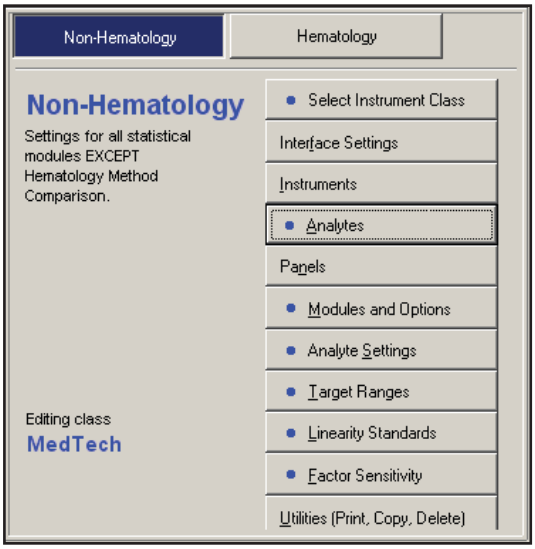
The remainder of this chapter describes the Policy Editor screens. If the policies for your instrument(s) are already established, you can skip this section.

Elements included in policies:

- Instrument classes.
- Individual instruments.
- Communication protocols.
- Analytes and analyte parameters.
- Panels.
- Statistical modules.
- Linearity materials.
- Simple accuracy materials.

Main Policy Editor Screen

This screen is the starting point for Policy Definition. The two buttons at the top of the screen switch between Non-Hematology and Hematology policies. The other buttons represent the major steps in preparing a policy definition.



The items marked with a blue dot represent the major tasks needed to define policies. Follow the steps below to define policies.

Step 1. Select Instrument Class

An Instrument Class is a group of instruments that are exactly alike in terms of what analytes they process, Allowable Error, and other EE experiment parameters. Instruments of the same model can always be placed in the same class. Often different instrument models from the same vendor can also be placed in the same class. One way the policy definition process saves you time—you can define one set of input for the whole instrument class. You don't have to input analysis parameters for each individual instrument.

The first step in defining policies is to select what class they apply to—or to create a new, empty class to build from "scratch". There is no limit on the number of classes you can create.

Step 2. Interface Settings

If you use an IF32 program to capture your data (i.e. the connectivity feature) directly from an instrument or from a file created by your LIS, use the Interface Settings button to define the IF32 program and a few major communications parameters. These items must be the same for all instruments in the specified class.

Step 3. Instruments and Analytes

Step 3 is to list the Instruments in the class and define what Analytes they process.

Step 4. Panels

Step 4 is to define panels which are ordered lists of analytes arranged in a convenient order for keyboard entry. Panels are also used to define the analytes for which data will be captured from an instrument.

Step 5. Modules and Options

Step 5 is to specify which EE modules you will run and global options for them. For example: Do you want Linearity studies? Alternate Method Comparison? Do you want to verify linearity, accuracy, and reportable range? Options selected in this step apply to all analytes. Another time saver: you define these settings just once for the entire instrument class. You don't have to enter them for every instrument and analyte.

Step 6. Analyte Settings

In Step 6 you define analyte-specific parameters such as allowable total error, reportable range and reference interval. The columns in this step depend on which Module/Analysis Options were selected in Step 5. For example, if the only statistical module you will run is VRI, you will be asked for only two numbers per analyte.

Step 7. Target Ranges

Step 7 is to provide target ranges for linearity materials used in the Simple Accuracy module. Otherwise they are not required.

Step 8. Linearity Standards

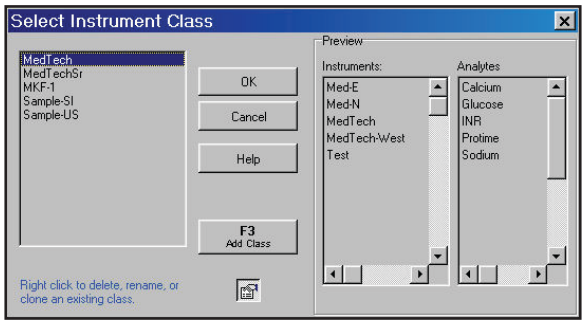
Step 8 is to provide assigned values for linearity materials used in two modules: CLSI EP6 and Linearity and Accuracy. Otherwise they are not required.

Step 9. Utilities (Print, Copy, Delete)

The remaining steps (copy, print and delete policy definitions) in this process are administrative only. They are not required to setup a new instrument from "scratch." They are required to share the Policy Definitions with others.

Instrument Class

Select the instrument class to edit: Highlight it and click **OK**, or double-click it.



Cancel: Closes the form without changing the current selection.

The Preview Panel: shows what instruments and analytes are assigned to the highlighted instrument class.

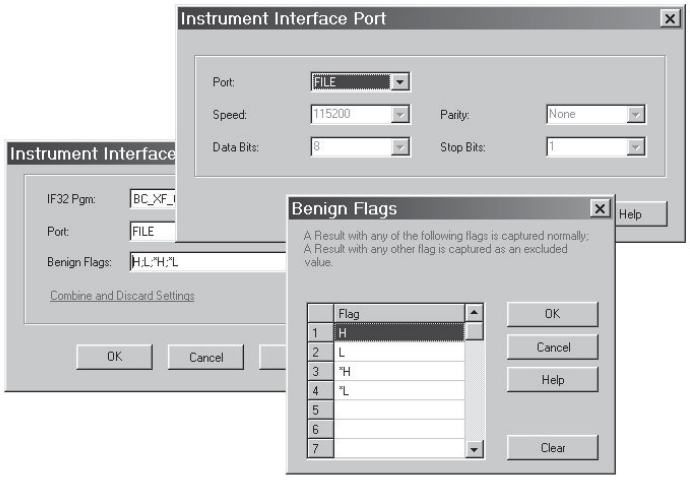
The **Show/Hide Preview** button: toggles whether the preview panel is visible.

To **rename** or **delete** a class: right-click it.

To **add a new class**: click the **Add Class** button (or press F3).

Instrument Interface Settings

This screen defines the instrument interface program and the instrument communication settings. You don't need to enter anything on this screen if you don't have an instrument interface.



IF32 Pgm: The name of the instrument interface program. You must install an interface program on your computer before you can select it here (see *Installing an Instrument Interface Program*). Click the down arrow at the right to pick from a list of installed programs.

Port: The I/O port the instrument is connected to. You can't edit this field directly. Click the button at the right for a secondary form (screen B in the example above) where you input the port name which may be FILE or one of the COM

ports. For a COM port, also enter the baud rate, parity, number of data bits, and number of stop bits.

Benign Flags: EE captures all results—whether or not they have flags. If a result is flagged, generally it will be excluded. However if a flag is "benign," the result will not be excluded. As with the port, you cannot edit this field directly. Click the button at the right for a secondary form (screen C) where you enter the benign flags — one per line. Flags may have one or more characters. Flags are case-sensitive.

Benign flags occur when the instrument analyzes the specimen without detecting errors in the analytical process. They may indicate that a result is above or below normal or in a critical range. Examples of the alternative are for an analytical process flag which would indicate some sort of analytical issue such as insufficient specimen volume or a failing lamp.

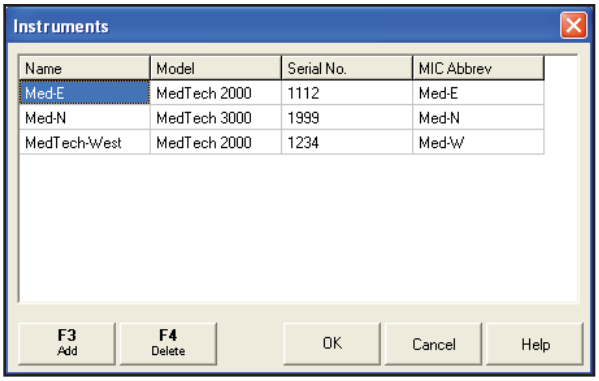
Combine and Discard is a special feature designed to deal with complex cases of specimen and test identity which include the following:

- Test codes that come through the instrument that are never needed in EP Evaluator®. For example codes that represent instrument diagnostics rather than analytes.
- Specimen IDs that are never needed. Examples: BACKGROUND, WASH SOLUTION
- Multiple test codes that are to be combined into a single code in EP Evaluator®. Example: tests that are auto-reflexed, where the auto-reflex test reports a separate test code.
- Equivalent test codes with slightly different spellings.
- Equivalent Spec IDs, useful for creating IDs compatible with the EE linearity module when specimens can't be renamed on the instrument.

This feature is described in detail in the associated help screen.

Instruments in the Class

Lists the instruments in the class. Click **Delete** (or press **F4**) to delete the highlighted instrument. Click **Add** (or press **F3**) to scroll to the end of the list and add a blank line. You can also move to the last line and press the down arrow key. You can edit any of the fields by typing over the value. Click **OK** when done to save your changes and return to the main Policy Editor screen. If you click **Cancel** instead of **OK**, changes are not saved



Name: 16-character instrument name to appear on most EE reports.

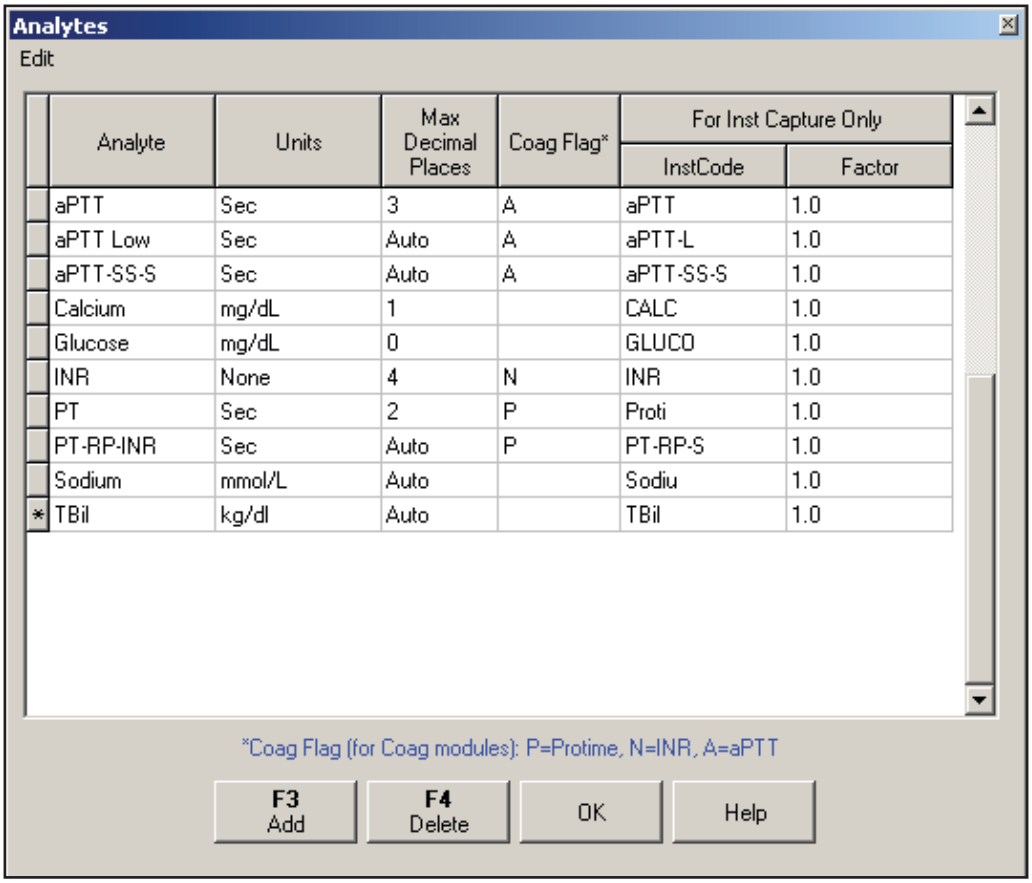
Model: Instrument model.

Serial No.: Instrument serial number. This value is particularly important when using an instrument interface program that captures results from multiple instruments (as you might see in a POC setting). In this situation, EE identifies captured results by comparing the serial number transmitted by the instrument with the one in the EE Policy Definition.

MIC Abbrev: A shorter (10-character) form of the instrument name. This short form is used on Multiple Instrument Comparison reports where the 16-character name is too long to fit.

Analytes

Lists the analytes in the instrument class. Click **Delete** (or press **F4**) to delete the highlighted analyte. Click **Add** (or press **F3**) to scroll to the end of the list and add a blank line. You can also move to the last line and press the down arrow key. You can edit any of the fields by typing over the value. Click **OK** when done to return to the main Policy Editor screen.



Analyte: Analyte name as it is to appear on EE reports.

Units: Measurement units. If the analyte has no units (like a qualitative test or ratio), don't leave the units column blank. Enter the word None.

Max Decimal Places: This field can contain "Auto", 0, 1, 2, 3, or 4. Auto means the number of decimal places is determined from the data. 0-4 means results will be reported with no more than the specified maximum number of decimal places. This setting affects only how results are reported; calculations are done at full precision.

INR Flag is used only if the analyte is used in the INR modules. Mark the analyte with a "P" if the analyte is Protime and with an "N" if the analyte is INR.

The last two columns are used only when results are captured from an instrument interface:

InstCode: If the instrument returns an analyte name different from the one to appear on your EE reports, enter the instrument's name here. The default entry is the entry previously made under Analyte above.

Factor: Provides for units conversion—results from the instrument are multiplied by the conversion factor prior to entry into EE.

Copying from Excel

- To copy the analyte list from EE to Excel, select Edit/Copy from the menu just above the table. Then switch to Excel and do Edit/Paste.
- To paste from Excel to EE, prepare data in Excel with the column headings Analyte, Units, NDec, InstCode, and Factor. Then enter data under the column headings. Enter -1 in the Max Decimal Places column to indicate Auto.

Highlight the data in Excel and do Edit/Copy. Then switch to EE and do Edit/Paste. If you paste an analyte name that is already in the table, its values will be replaced. If you paste a new analyte name, the analyte will be added.

Factor Sensitivity Analytes

One often defines more than one Analyte when evaluating PT or aPTT. Factor Sensitivity (FS) presumes that the Combine/Discard features of RRE will be used so that all of these Analytes are merged into one of two Analytes, which we will call PT and aPTT. The actual Analytes used are indicated by flagging them in the Analytes entry form under RRE, Define Policies. Set the Coag Flag to "P" for the PT Analyte, and set the Coag Flag to "A" for the aPTT Analyte. Note that you may find it useful to name the Instrument Analyte the same as the Reagent name, since the Analyte will not appear in the Factor Sensitivity Report.

Factor Sensitivity Policies Form

FS data is entered into Policies using the Factor Sensitivity button. Five kinds of FS data can be entered:

- Reagents
- Reference Plasmas for PT
- Reference Plasmas for aPTT
- Factor Deficient Plasmas
- Factor Sensitivity Controls

Reagents: Enter Source, Lot Number, and Expiration Date, as for any other Material; in addition, specify the Upper Limit of the Normal Range as established by your Normal Range study and specify the Assay (PT or aPTT).

Reference Plasma for PT: Enter Source, Lot Number, and Expiration Date, as for any other Material; in addition, enter the Reference Factor Concentrations for Factors II, V, VII, and X.

Reference Plasma for aPTT: Enter Source, Lot Number, and Expiration Date, as for any other Material; in addition, enter the Reference Factor Concentrations for Factors VII, IX, XI, and XII.

Factor Deficient Plasmas: Enter Source, Lot Number, and Expiration Date, as for any other Material; in addition, specify the Factor in which the plasma is deficient.

Factor Sensitivity Controls: Enter Source, Lot Number, and Expiration Date, as for any other Materials.

Panels

When you first enter the Panels page, it is in read-only mode. You can look at the definition of any panel, but you can't change it. The defined panel names are displayed on the left. When you highlight a panel name, its analyte list shows on the right. From this screen, you can select:

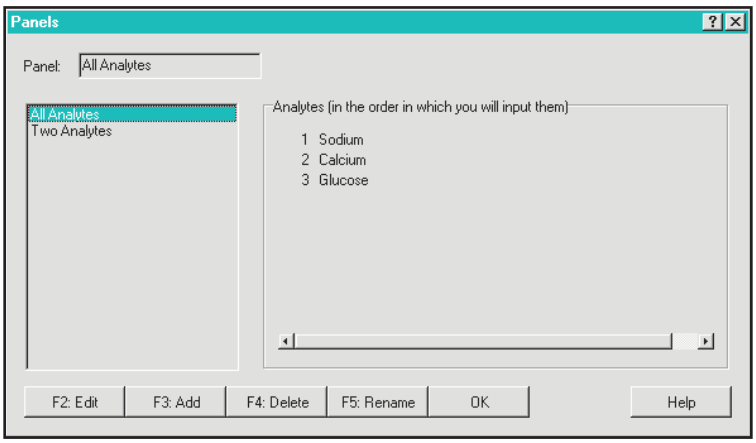
F2: Edit to edit the analyte list for the highlighted panel.

F3: Add to define a new panel.

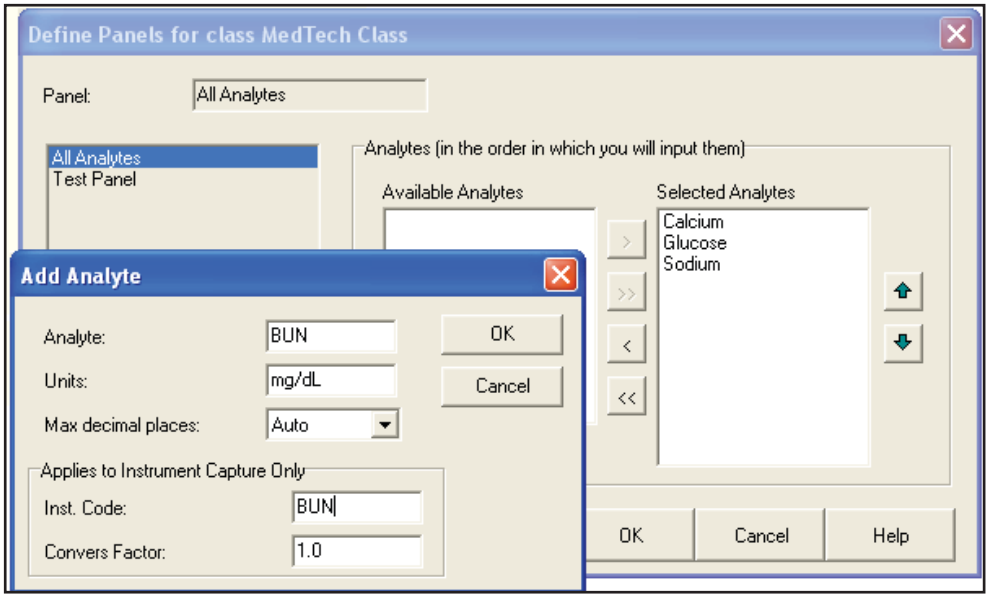
F4: Delete to delete the highlighted panel.

F5: Rename to rename the highlighted panel.

Click **OK**: to return to the main Policy Editor Screen.



When you select **Add** or **Edit**, the analyte list area shows the familiar 2-pane analyte list, with available analytes on the left and selected analytes on the right. Selected analytes are the ones in the panel. Available analytes are in the instrument's analyte list but are not in the panel.



New Analyte: If you forgot an analyte when you set up the instrument's analyte list, click the **New Analyte** button to add it.

Arrow buttons between the analyte lists: move analytes between the two lists. The >> and << buttons move all analytes. The < and > buttons move only the highlighted analyte.

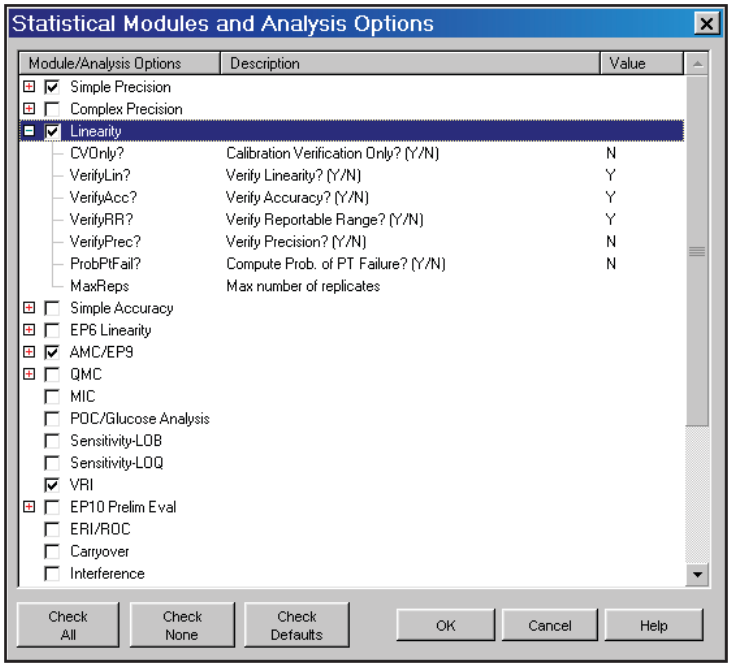
Up/Down Arrows at the right: move the highlighted analyte up or down in the list of selected analytes. (The object is to list the analytes in the order of your instrument reports for convenient keyboard entry.)

OK: saves your changes.

Cancel: returns to browse mode without saving.

Modules and Analysis Options

This screen provides for specification of the statistical modules and the options within those modules appropriate for the user's application.



Checkboxes: Check the box if you intend to use that statistical module. Otherwise leave it unchecked. Reason—so the program won't ask for unnecessary analyte parameters.

Plus/Minus signs left of the check box: Some modules provide a number of different options, such as selection of Report Options for the Linearity module shown in the example in which the user may choose to verify accuracy, precision, etc. Click a plus sign to expand the display to show the supplemental question or minus to contract it.

Answering a supplemental question: Highlight the line and type the appropriate response. Press Enter or just start typing and if necessary, the input editor will open automatically. Press Enter again to finish the entry.

Check All: Check all module checkboxes.

Check None: Uncheck all module checkboxes.

OK: Save your changes.

Cancel: Close the form without saving.

Analyte Parameters

The Analyte Parameters Form adapts to reflect the choices you made on the Analysis Options page, so you won't be asked for unneeded input. At the bottom left there are several tabs to select different tab pages. Most of these tabs correspond to statistical modules. You will not see any tabs for modules you didn't check in the Analysis Options screen. For example, you won't see the SP tab if you didn't check the Simple Precision module

.

You can't edit the Analyte column—it lists all analytes assigned to the instrument class. If you forgot to list an analyte, click the **F3: Add Analyte** button to add it.

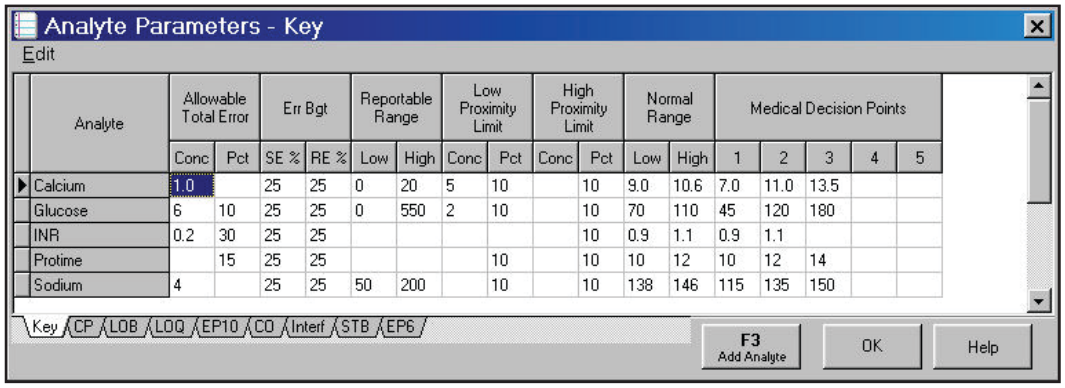
You don't have to enter every single number for every analyte if you know the input won't be used. For example, you may do Interference studies on only a few analytes. You can leave the other analyte lines blank on the Interference tab page.

There is nothing new on these tab pages—you are supplying exactly the same input that you would if you defined the experiments one at a time. If you need further description of a column, refer to the description of the module's parameter screen.

Click **OK** to close the form when done with all tab pages.

Key Parameters

This page defines several important parameters. Some of them—like Allowable Total Error and Error Budget—are used in more than one statistical module. Some are used in only one module, and some are not required. However, looking at them together on a single form helps define them consistently.



Analyte	Allowable Total Error		Err Bgt		Reportable Range		Low Proximity Limit		High Proximity Limit		Normal Range		Medical Decision Points				
	Conc	Pct	SE %	RE %	Low	High	Conc	Pct	Conc	Pct	Low	High	1	2	3	4	5
Calcium	1.0		25	25	0	20	5	10		10	9.0	10.6	7.0	11.0	13.5		
Glucose	6	10	25	25	0	550	2	10		10	70	110	45	120	180		
INR	0.2	30	25	25						10	0.9	1.1	0.9	1.1			
Protime		15	25	25				10		10	10	12	10	12	14		
Sodium	4		25	25	50	200		10		10	138	146	115	135	150		

These items are discussed in great detail in the Rhoads (2012) *Laboratory Statistics* manual.

The illustration here shows all possible columns. You won't see the ones you don't need (based on your Analysis Options). For example, if you didn't select the VRI module, you won't see the Reportable Range columns.

Allowable Total Error (synonym Medically Allowable Error): is a central concept throughout EE as a specification for Pass or Fail. It is used in twelve of the statistical modules and is required in seven of them.

Error Budget: defines Allowable Systematic Error (SE) and Allowable Random Error (RE) as percents of Allowable Total Error. Values for SE budget should be in the range of 25-50%. Values for the RE budget should be in the range of 17 to 25%.

Reportable Range (synonym Analytical Range): is the range of values the instrument can measure without diluting the specimen, often specified in the package insert.

Proximity Limits: define how close the lowest or highest specimen must be to the respective reportable range limit to pass the reportable range test. (See Chapter 4, *Linearity and Calibration Verification* for details). Proximity Limits are used in two modules: Linearity and Simple Accuracy.

Normal Range (Central 95% Interval, Reference Interval): is the range of results for the central 95% of a healthy population. This is used to Verify Reference Intervals.

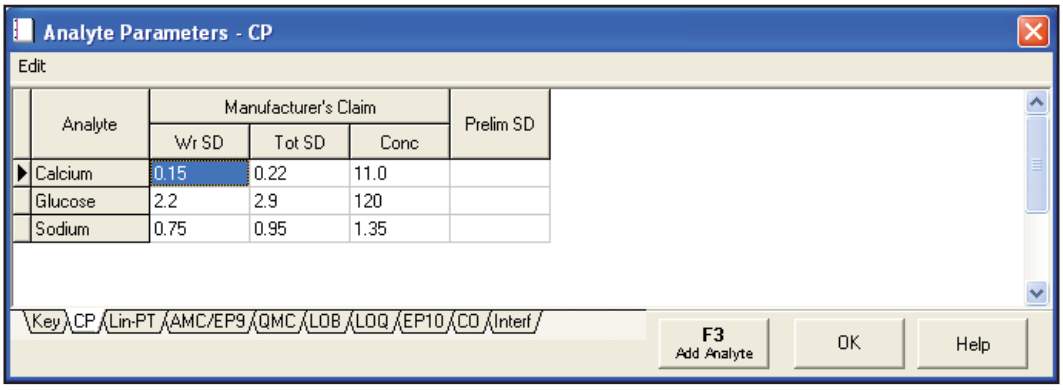
Medical Decision Points (MDPs): are values at which medical decisions change. These include normal and therapeutic ranges. These values are used in AMC, EP9 Method Comparison, 2IC, and Hematology Method Comparison.

Module-Specific Policy Parameter Screens

There is an extensive series of screens for the input of module-specific parameters. The first example is shown below for Complex Precision. The remaining ones are similar in nature.

Complex Precision (CP) Parameters

Note that there is only one set of inputs for each analyte—you cannot use the Policy Definition to set up vendor claims that vary by sample.



Manufacturer's Claim: Within-run SD, Total SD, and Concentration at which the claim is made; all in units.

Preliminary SD: This column appears only if you choose to input the SD for outlier rejection rather than computing it from a preliminary run.

Simple Precision (SP) Parameters

This screen defines the parameters for using the vendor's claim as the Pass/Fail specification. You can define parameters for within run SD, concentration at the SD goal, and a target mean. Note that there is only one set of inputs for each analyte.

Probability of PT Failure (Lin-PT) Parameters

This screen defines parameters used to estimate the probability of PT failure. For details, see the section *Probability of Proficiency Testing Tab*.

AMC/EP9 Parameters

This screen collects input for some of the less common parameters for Alternate and EP9 Method Comparison. You will see this screen if:

- You requested a Results Range Analysis;
- You want to enter specific representative SDs for Deming regression; or
- You want scatter plot bounds based on differential cell counts.

For discussion of these fields, see items on Scatter Plot Bounds and Results Distribution (*Experimental Parameters* in Chapter 10 and *Parameters Screen* in Chapter 11.)

QMC Parameters

This screen defines input for Qualitative Method Comparison when using custom results codes.

Custom Lvls? - Enter N for standard results codes (P=Positive, N=Negative). Enter Y if there are more than two levels, or if the results codes are non-standard. For analytes with standard results codes, leave the remaining columns blank.

Results Type - Set type to "0" if results are alphanumeric, "1" if they are numeric with large numbers representing Positive, and "2" if results are numeric with smaller numbers representing Positive.

Level Name and Value - Name is what prints on the report; Value can be either an instrument result or an alphanumeric level designation. For example, in usual case *Positive* is the Name, *P* is the Value. (This is just an example of the difference between the Name and the Value. If the values are P and N you don't have to enter the names and values at all.) Alphanumeric level designations appear in a dropdown list when results are entered in the Experiment Detail Screen.

- Enter a Name for each test level. Enter them left to right, with the cutoff that defines Negative entered first.
- For Results Type alphanumeric (0), enter a Value for each defined level.
- For Results Type 1 or 2, the Values are cutoffs. The number of Values is one less than the number of levels.
- The cutoff values define the result levels as follows:

  Results with values less than or equal (<=) to the first cutoff go into the first level, results with values less than or equal (<=) to the next cutoff go into the 2nd level, etc. Results with values greater than (>) the last cutoff go into the last defined level. For example, for Type 1 results:

Level Name	Cutoff Value	Includes Result values
Lvl 1	(blank)	<=100
Lvl 2	100	101 - 200
Lvl 3	200	201-300
Lvl 4	300	>300

- Leave the left-most value column blank for Type 1 results. Leave the value column for the last level blank for Type 2 results.

Sensitivity-LOB (LOB) Parameters

This screen defines input for Sensitivity-Limit of Blank. The two fields to be entered are Lowest Non-Zero Concentration and Manufacturer's Sensitivity Claim. (For more explanation, see Chapter 17.)

Sensitivity-LOQ (LOQ) Parameters

This screen defines target CVs for Sensitivity by Limits of Quantitation. For more details see Chapter 18.

EP10 Parameters

This screen appears only when running EP10 Preliminary Evaluation of Methods. High and Low concentrations and the six allowable error columns are described in more detail in *Parameter Screen* in Chapter 24. The six allowable error columns don't appear unless you specify on the Module and Options screen that you want to input the allowable error values as defined concentrations.

Carryover (CO) Parameters

This screen defines the concentration of the low and high specimens for the Carryover module. See *Parameter Screen* on Chapter 26 for details.

Interference (Interf) Parameters

This screen defines parameters for the Interference module, specifically the several interferent and analyte parameters. See *Parameter Screen* in Chapter 29 for details.

Stability (STB) Parameters

This screen defines parameters for the Stability module, specifically time units, the stability budget and whether the calculation should use a logarithmic fitting process. See *Parameter Screen* in Chapter 30 for details.

EP6 Parameters

This screen defines parameters for the CLSI EP6 Linearity module, specifically the Non-Linearity Error Budget. See *Parameter Screen* in Chapter 6 for details.

Trueness

This screen allows you to pre-define the parameters that used for creating experiments using the following options:

- **Experiment>New from Policies**
- **RRE>Create Experiments**

These parameters include the Group Eval Mode (Peer or All Methods), the Analytical Goal (AG)Mode, specific values for any or all of the AG modes, and IQC values for up to three levels. See the *Experimental Parameters* section in Chapter 7, *Trueness,* for more information.

When you import data using **Rapid Results Entry (RRE)>Create Experiment**s, you can pre-define up to 3 level names and 2 level cutoffs for each calculation mode. The IQC values for each level apply to both EQC and EQA level definitions.

The cutoff values assign the incoming result values into as many as 3 experiments per calculation mode. You can define up to three levels with 2 numeric cutoff values. For example, given two cutoff values (100 and 200) and 3 levels (Low, Medium, and High), incoming values <100 go into the Low level experiment, values >=100 and <200 go into the Medium level experiment, and values >=200 go into the High level experiment. When defining three levels, the first cutoff value ***must*** be lower than the second cutoff value.

Level Name	Cutoff Value	Includes Result values
Low	100	<100
Medium	200	100 - 199
High		>=200

Copying from Excel

You can copy these settings to/from the clipboard to exchange data with Excel:

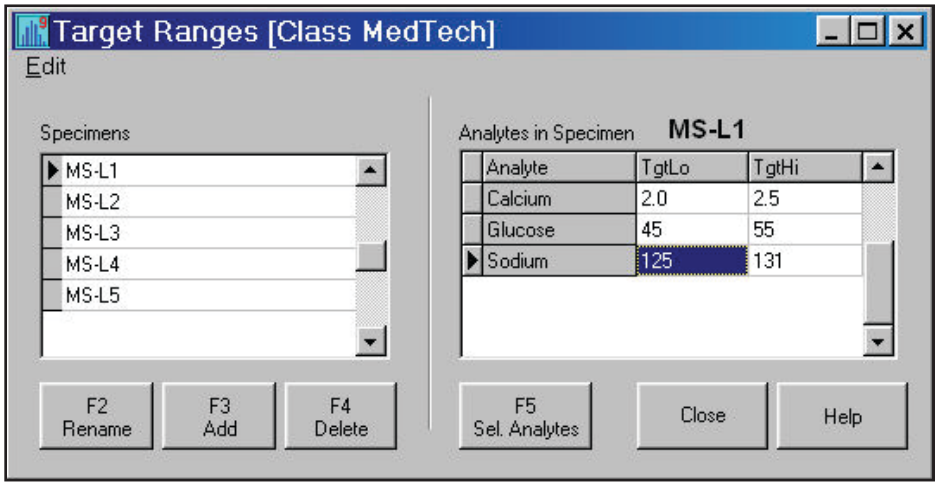
- To copy from EE to Excel, **select Edit/Copy All** or **Edit/Copy Visible Page** from the menu just above the table. Then switch to Excel and do **Edit/Paste**. Here "All" means all the tab sheets, and "Visible Page" means only the tab sheet you are looking at.
- To paste from Excel to EE, you must prepare the spreadsheet with the column headings EE expects. The easiest way to do this is to copy something from EE to Excel to establish the column headings.

- Highlight the data in Excel and do **Edit/Copy**. Then switch to EE and do **Edit/Paste**. If you paste an analyte name that is already in the table, its values will be replaced. If you paste a new analyte name, the analyte will be added.

You need not supply every single column. However, if you omit a column, do not include a column heading for it. Including a column heading but leaving the values blank tells EE to erase the value in its database. In contrast, omitting the column means don't change the current value.

Target Ranges

This section allows you to enter the target ranges for Simple Accuracy specimens. The screen is a model of simplicity.

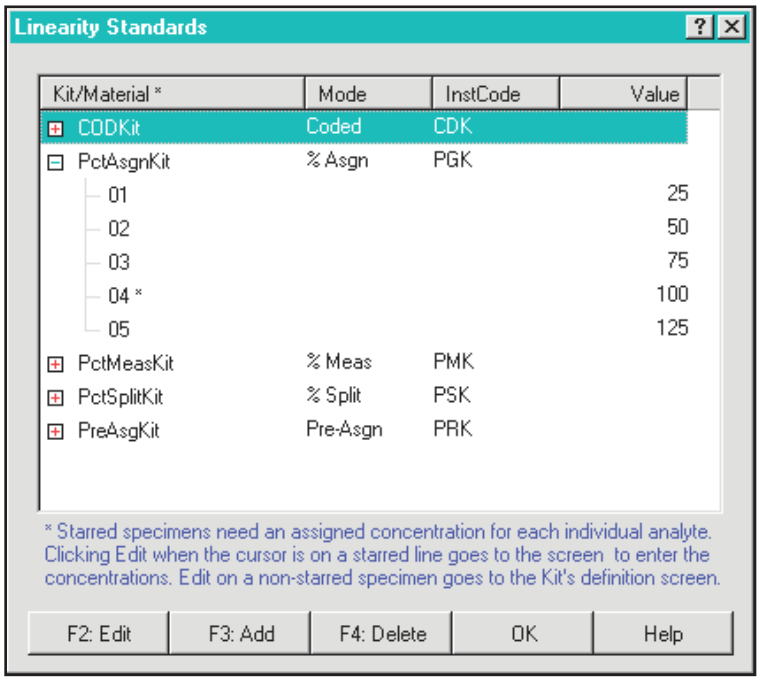


To enter a series of specimens, simply click on F3-Add and enter the specimen name. To add the target ranges, select your specimen, then click on F5-Select Analytes. After you've selected your analytes, enter the lower and upper ranges for each specimen.

You may also copy data to and from a spreadsheet using the Edit button in the top left corner of the form.

Linearity Standards

EE shows this form when you click the **Linearity Standards** button on the main Policy Editor screen. It shows a list of defined linearity kits. If you haven't defined any kits yet, the list is empty. The first thing to do is click the **F3: Add** button at the bottom of the screen to define a new kit.



A linearity kit may contain up to 11 specimens. When you click the plus mark just to the left of the kit name, the list expands to show the specimens in it.

The columns in the table summarize the values for a kit:

Kit/Material: On a kit line, the name of the kit is shown as it will print on reports. On a specimen line, the level number is shown. It will range from 1 to the number of specimens in the kit.

Mode: Value mode indicating how assigned values are determined: Pre-assigned, Coded, Percent Assigned, Percent Measured, or Percent Split.

Inst Code: Prefix for specimen names as returned by the instrument. See discussion below for Add/Edit Linearity Kit.

Value: This item appears only on a specimen line. It defines the percent value a given specimen is of the 100% specimen. It applies to all analytes in the kit. It is used only when the Defined Value Mode is Percent Assigned, Percent Measured or Percent Split.

Asterisk following the level number: Indicates that the specimen needs a concentration input for each analyte.

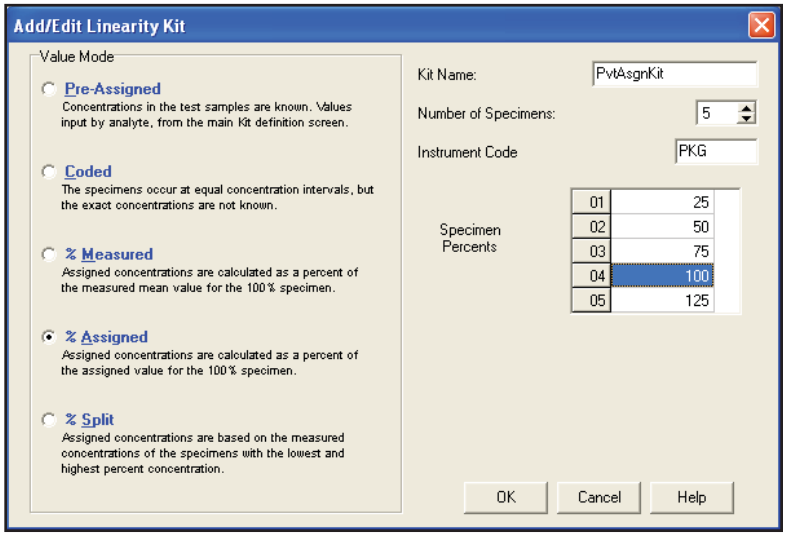
Buttons at the bottom of the screen:

- **F2: Edit**: Edit the highlighted kit or specimen. If highlighted line is a specimen with an asterisk (i.e. "01*"), you may edit assigned values on an analyte-by-analyte basis. If the highlighted line is a kit name, or a specimen without

an asterisk, pressing this key will allow you to edit the kit definition. You can also select the item to edit by double-clicking the line.

- **F3**: Add: Add a new linearity kit.
- **F4**: Delete: Delete the highlighted kit. You can only delete the whole kit. You cannot delete an individual specimen within it.
- **OK**: Close the form and return to the main Policy Editor screen.

Add/Edit Linearity Kit



Value Mode: determines how assigned values are specified—either as percents that apply to all analytes in the kit, or as analyte-specific concentrations.

Kit Name: Prefix of the name of the specimens in the kit as used in the printed reports. See discussion below on the relationship of Kit Name and Instrument Code. If you enter the data manually, you will be entering the Kit Name, not the Instrument Code to identify the specimens. Hence a short name is preferred.

Number of Specimens: Number of levels in the kit (3-11).

Instrument Code: Prefix for specimen names as returned by the instrument. This code is used to link the experimental results received from an instrument interface with the assigned values specified in your policy data. Using the example shown in the figure, suppose you analyze PctAsgnKit. When you order tests on the instrument, name your specimens PKG-01, PKG-02, PKG-03, PKG-04, and PKG-05. These spec IDs are required by EE to determine the correct assigned values. The data from PKG-01 will be associated with the specimen ID of PctAsgnKit-01 for the calculations and report.

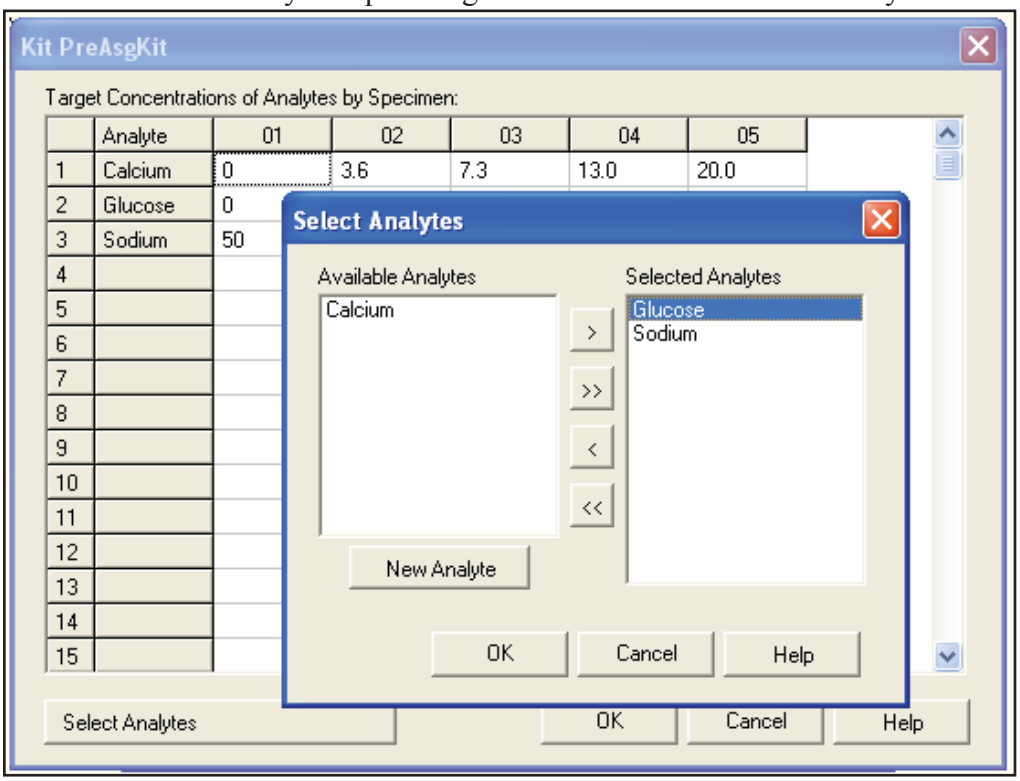
Specimen Percents: Percents for the kit levels. This appears only when the Value Mode is % Measured, % Assigned or % Split.

OK: Save your changes.

Cancel: Close the form without saving.

Assigned Values by Analyte

This is the screen where you input assigned concentrations for a linearity kit.



Columns of the table define specimens. The illustration shows a pre-assigned kit with five levels (specimens). EE needs an assigned value for each analyte and level. For a percent assigned kit, EE only needs values by analyte for the 100% specimen, and the table would only have one column. You will not see this screen for a coded, percent measured, percent assigned or percent split kit, since assigned values are not entered for individual specimens.

Rows of the table are analytes. For initial definition of a new kit, no analytes are shown. Click the **Select Analytes** button at the bottom of the screen to pick the applicable analytes. The popup form is the familiar two-panel list, showing available analytes on the left and selected analytes on the right. Use the buttons between the panels to move analytes from one list to the other. Click **OK**, to close the popup form and update the row names on the Targets screen.

You can only assign values to analytes that "belong" to the instrument. For example, the linearity kit may contain AST, but your instrument doesn't test for AST. There is no reason to enter assigned values for it. The other possibility is that you forgot about AST when you entered the instrument's analyte list. In that case, click New Analyte on the Select Analytes screen and add AST to the instrument's analyte list. When you finish defining linearity kits, go back to Analyte Parameters and enter its statistical module parameters.

Linearity Kit Examples

Preassigned Kit Example.
In preassigned mode, percents are not applicable. An assigned value is required for each analyte and level.

		Lvl 1	Lvl 2	Lvl 3	Lvl 4	Lvl 5
Percents	Not applicable in preassigned mode					
Assigned Values by Analyte	Calcium	0	3.6	7.3	13.0	20.0
	Glucose	0	100	200	350	550
	Sodium	50	75	100	150	200

Coded Kit Example.
In coded mode, neither percents nor assigned values are entered.

		Lvl 1	Lvl 2	Lvl 3	Lvl 4	Lvl 5
Percents	Not applicable in coded mode					
Assigned Values by Analyte	Calcium	Not applicable in coded mode				
	Glucose					
	Sodium					

Percent Measured Kit Example.
In Percent Measured mode, the assigned values are percents of the measured mean value for the 100% specimen. The percents apply to all analytes, and one of the percents must be 100%.

		Lvl 1	Lvl 2	Lvl 3	Lvl 4	Lvl 5
Percents		25	50	75	100	125
Assigned Values by Analyte	Calcium	Not applicable in percent measured mode				
	Glucose					
	Sodium					

Percent Assigned Kit Example
In percent assigned mode, the assigned values are percents of the assigned value for the 100% specimen. The percents apply to all analytes, and one of them must be 100%. Assigned values by analyte are required for the 100% specimen only.

		Lvl 1	Lvl 2	Lvl 3	Lvl 4	Lvl 5
Percents	25		50	75	100	125
Assigned Values by Analyte	Calcium				20.0	
	Glucose				550	
	Sodium				200	

Percent Split Kit Example.
In percent split mode, assigned concentrations are based on measured values of the specimens with the lowest and highest concentrations. The percents apply to all analytes in the kit. Assigned values by analyte are not required.

		Lvl 1	Lvl 2	Lvl 3	Lvl 4	Lvl 5
Percents	25		50	75	100	125
Assigned Values by Analyte	Calcium					
	Glucose	Not applicable in percent split mode				
	Sodium					

Policy Administration

Moving policies between projects and/or computers

Policy definitions are distributed across projects and individuals within organizations by use of a special, privileged project called MASTER. The MASTER project contains no experiments, only policy definitions. Furthermore, you can't open, delete, or rename it. There is only ONE Master project.

- Whenever you create a new project, all policy definitions from MASTER are automatically copied into it. In a network environment, any user on the network who creates a new project starts with a copy of the MASTER policies. This allows you to standardize your Policies in your institution!!

- When you invoke the Policy Editor in your project, you modify your current working copy of the MASTER policies. Your changes affect only the project you are working in. They do not affect MASTER or any other project.

- After making changes, you can copy these changes back to MASTER, making them the default for your system when you create new projects at a later time. In EE Professional with User ID/Password logon in effect, copying policies to MASTER requires EE System Administrator rights.

- If someone changes MASTER after you have created a project, you can manually copy current settings from MASTER to your project.

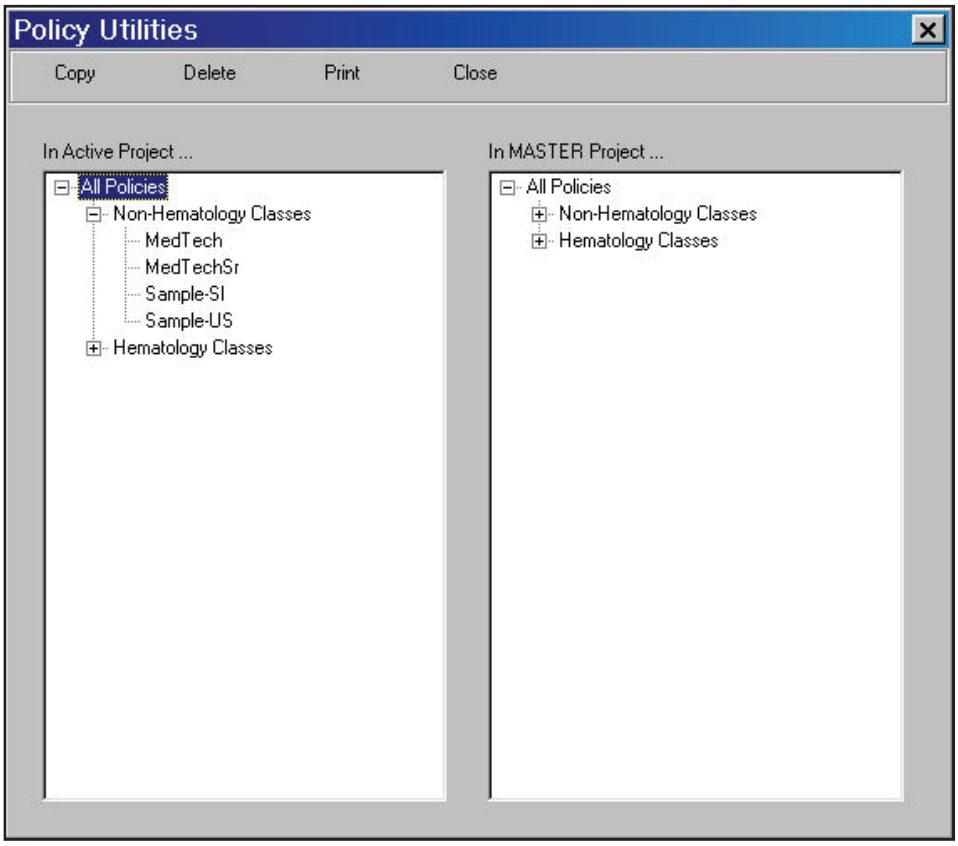
- You can copy policies directly from one project to another only by going through MASTER.

While copying through MASTER allows sharing of policies among users running on a single, network version of EE, it does not provide for sharing policies across computer systems. To move policies from one computer to another, use **File Manager** to make a backup of the Master project on the source computer. Then move that backup file to the destination computer and use **File Manager** to restore the backup.

NOTE: Restoring a backup of MASTER completely replaces the original version. For safety, we suggest that you make a backup copy before you replace the original.

Utilities

Use the Utilities button to deal with issues of managing policies which includes the tasks of copying, printing and deleting policy definitions.



These operations have become very easy to understand and do. Simply highlight the object on which the operation is to be done, then click on the Operation button at the top.

To copy something from the Source Project to the Destination Project, highlight the object in the Source Project and click on Copy. For example, to copy All Policies from the Active Project to the Master Project, highlight “All Policies in the Active Project, then click on Copy.

Similarly for Delete and Print, just highlight the object and click on the button to accomplish your task.

Sample Policy Files

A sample project (ExamplePolicies) containing examples for both Hematology and Non-Hematology is available in the EE Backups folder.

- Go to File Manager and restore the backup (ExamplePolicies).
- Close File Manager.
- Open the ExamplePolicies project.
- Click on RRE, then Policy Definitions. The data present is for the fictitious Sample-US instrument. Click on Select Instrument Class. Then right-click on the Sample-US instrument. Select the “Clone” option and enter the name of your desired instrument class (i.e. Beckman DXc or Roche Modular). Select the new instrument class. Then add or edit the policy definition data as necessary. The existing data is set up to be approximately correct for many common analytes. **You will need to edit reportable ranges, reference intervals and medical decision points because they are lab-specific.**
- Copy policies from ChemistryMaster-US to the Master project. When you create a new project, your new policies will be inherited into that project.

Chapter

38

Rapid Results Entry (RRE) With Policies

This chapter describes the process by which results are brought into EP Evaluator using RRE with Policy Definitions. An earlier chapter (Chapter 36, *Introduction to Rapid Results Entry (RRE)*) introduced the concepts of RRE and listed the different methods both with and without Policies. The Method numbers below refer to those listed in Table 36.1. The purpose of the following table is that all these methods with some variation, go through a similar sequence of screens. Conceptually, they all utilize the same four general steps: Process initiation, data source specification, data acquisition and data integration.

Note that the following Statistical Modules do not support Rapid Results Entry:

- Average of Normals
- Cost Per Test
- Performance Standards
- Stability
- Six Sigma

Order of Screens / Menus for RRE Policy Data Entry Methods					
Screen/Menu	**PP-Tbl (4)**	**PP-List (5)**	**Inst IF (6)**	**Kbd Ent (7)**	**DAq (8)**
Process Initiation					
Method specific	Y	Y	Y	Y	Y
Data Source Specification					
Instrument Selection	Y	Y	Y	Y	D
Communications Proto	-	-	Y	-	-
Data Acquisition					
Start Data Capture	-	-	Y	-	D
Panel Selection	-	-	-	Y	D
Transfer and Integration					
Mod Specific Items	Y	Y	Y	Y	Y
Lot number entry	Y	Y	Y	Y	Y
Finish	Y	Y	Y	Y	Y
Grid (optional)	Y	Y	Y	Y	Y
Parameters	Y	Y	Y	Y	Y
Activity Log	Y	Y	Y	Y	Y
Process Complete	Y	Y	Y	Y	Y
PP=Paste w/ Policies. Kbd Ent = Keyboard Entry. DAq = Data Acquisition. Inst IF = Instrument Interface. D = DAq specific					

All four sets of steps are required to move data from the external source into EE. The differences are all based on the immediate source of the data (spreadsheet, instrument or written page) and the statistical module into which the data is transferred.

RRE (Policies) Data Entry Process - Overview

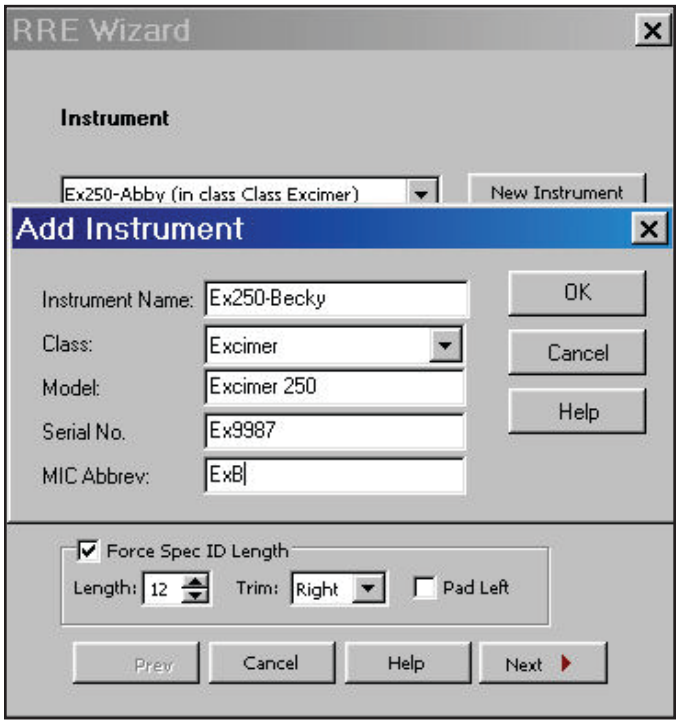
This section is an overview of the steps common to all of the four RRE methods which utilize Policies. The method specific steps will be discussed later in this chapter. While all these steps occur in each of these methods, there can be significant variation between them because of the timing and nature of the data acquisition process.

Process Initiation

Several steps specific to each method are required to initiate the process.

Data Source Items

Select / Add Instrument



This screen has two major roles. The first defines the instrument for which the data is to be captured. The second defines how the specimen ID is handled. If the instrument is not in the drop-down menu, it can be easily added by clicking on the New Instrument button. At that point, the Add Instrument form appears as shown at right.
The non-obvious fields are used as follows:

- Instrument Name: The name used for the instrument on the report.
- Class: Defines which set of policies are to be used.
- MIC Abbrev: The identifier for the instrument in the captured data. Note that this identifier may be different than the name used in the reports.
- Below the Add Instrument form is a check box labeled “Force Spec. ID Length.” This allows the user to control specimen IDs. The problem is that sometimes specIDs are longer than is allowed by EE (maximum length: 12 characters). The issue then is how to truncate the specID. The facility allows you to trim characters from the left or the right end so you get to a specified length. It also allows you to pad the specID (on the left with zeroes).

Data Acquisition

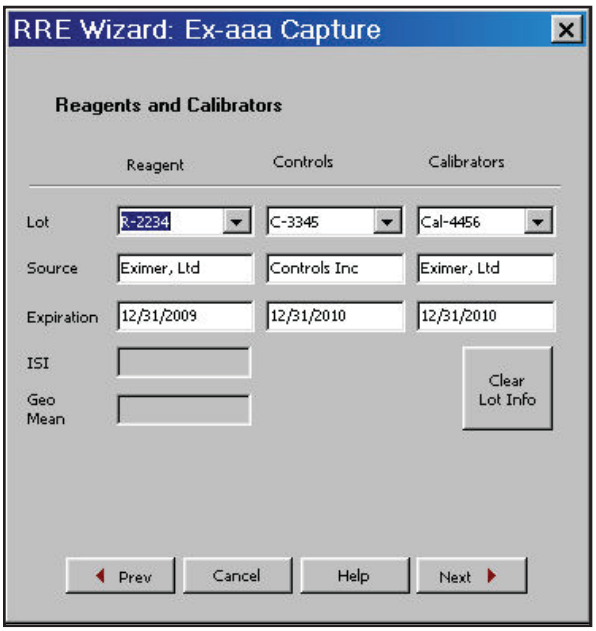
These steps actually acquire the data from the source specified earlier. The data sources are the data in the clipboard from the spreadsheets (Methods 4 and 5), the instrument (Method 6) and raw reports (Method 7). In fact, this phase uses no additional screens when the data source is the clipboard since the data was there before the process began.

Module Specific Data

For all methods, certain data specific to each module are required. One example is for the Simple Precision module in which a screen is provided to convert the incoming specimen IDs to the name to be used on the report. Similar screens are provided for many other statistical modules.

Lot Numbers

Lot numbers for reagents, controls and calibrators are entered in the following screen.



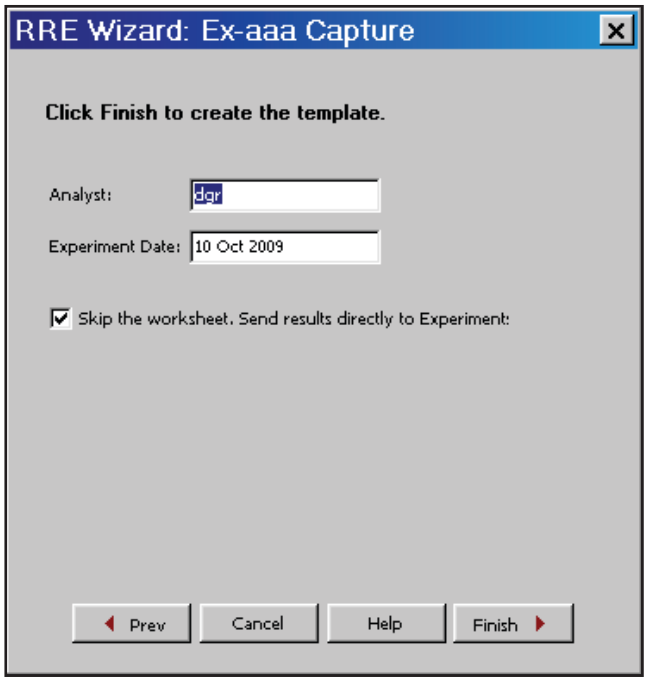
Fields are provided for entry of Reagents, Controls and Calibrators. To select a lot number (and associated source and expiration date), you may see a pull-down list for each. Alternatively, you may enter lot numbers in this screen. Note that whatever lot you select will be applied across all analytes.

It is far more efficient to enter the lot numbers for all the lots in advance and then select them at this screen. This may be done using the RRE/Lot Number screen. (See the *Lot Numbers* section in Chapter 3, *Common Operations*.)

An alternative to connect the lot numbers with the experiments uses the Batch Edit Lot Number facility available from the Module menu.

Finish

This screen signals to the operator that all the data needed for the Worksheet is complete.
Note the checkbox which allows you to skip the worksheet. This is acceptable if everything is working well. However if there are issues, it can be very useful to see the data in the Worksheet as that can identify the source(s) of the problems.

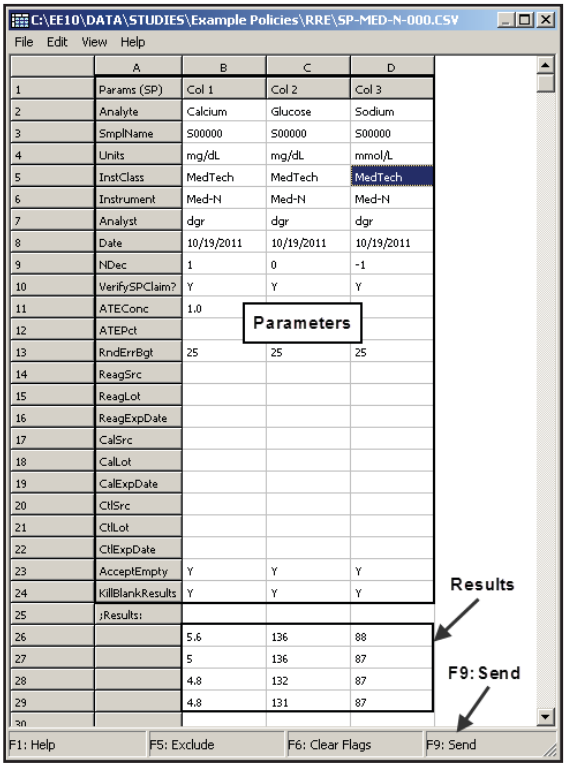


Worksheet

The Worksheet contains all the data to be imported into EP Evaluator. It contains the data to be imported into two major sections.
All items in this worksheet in columns B and higher are editable. The contents of column A are not editable.

Parameters: The upper section starting with row 1 down in this case to the row labeled ";Results" in this case row 24.

Parameter Names. These are the names of fields on the Parameter Screen. Some of the names, like Analyst and Units, are obvious. Some are less so. For example, "ATEConc" stands for Allowable Total Error-Concentration. Parameter names are created by the Wizard. You can't edit them.



	A	B	C	D
1	Params (SP)	Col 1	Col 2	Col 3
2	Analyte	Calcium	Glucose	Sodium
3	SmplName	S00000	S00000	S00000
4	Units	mg/dL	mg/dL	mmol/L
5	InstClass	MedTech	MedTech	MedTech
6	Instrument	Med-N	Med-N	Med-N
7	Analyst	dgr	dgr	dgr
8	Date	10/19/2011	10/19/2011	10/19/2011
9	NDec	1	0	-1
10	VerifySPClaim?	Y	Y	Y
11	ATEConc	1.0		
12	ATEPct			
13	RndErrBgt	25	25	25
14	ReagSrc			
15	ReagLot			
16	ReagExpDate			
17	CalSrc			
18	CalLot			
19	CalExpDate			
20	CtlSrc			
21	CtlLot			
22	CtlExpDate			
23	AcceptEmpty	Y	Y	Y
24	KillBlankResults	Y	Y	Y
25	;Results:			
26		5.6	136	88
27		5	136	87
28		4.8	132	87
29		4.8	131	87

Parameter Values. These values go in the Parameters Screen of the created experiments. Pay close attention to this section, particularly if you are testing a new policy definition or process. If a required parameter doesn't have a value, the experiment won't calculate. If a parameter has the wrong value, the experiment may give the wrong answer when calculated. The best place to fix these errors is in Policy Definitions. Then re-capture the data. Second choice—fix them in the worksheet, while all the data is on one screen. If you create experiments without fixing the errors, you will have to edit each individual experiment.

Unique Column Names. You can't edit these cells. Except for cell A1, the exact contents don't matter (at least in the Simple Precision illustration). All that matters is that they are unique. Some of the other modules have columns like "SpecID" or "Date" between columns A and B.

Results. The lower section starting the row below the ";Results" row contains the results. When using keyboard entry, this area is initially blank. This is where you type the results. When capturing from an instrument, the results are already filled in. You can edit them if necessary.

To move the data from the worksheet into the proper part of EE, there are three options: (1) Press the <F9> key; (2) Click on Edit, then Send to <module>; or (3) Click on the pane at the bottom of the worksheet labeled "F9: Send".

Before you send data, click on File at the top and Save your data. The reason is that **the worksheet is not automatically saved after you enter results.** If EE is ended before the worksheet is saved, all changes you to it will be lost.

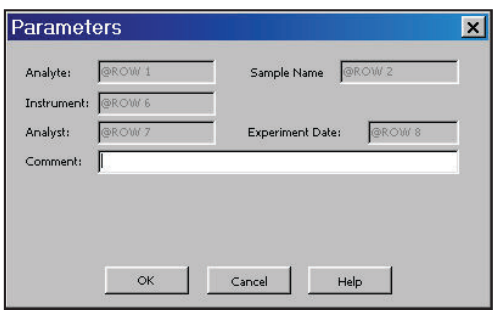
Also utilize the features under the Menu items at the top. Especially useful are those under Edit. Not only may you copy and paste data, but you can also automatically add data after the top item in the column (Fill option). For example, you can highlight a column of numbers and then click on Fill. The options allow you to duplicate that number all the way to the bottom of the highlight or to increment that number by a constant amount all the way to the bottom.

If you return to the Worksheet and the Worksheet is empty, you can access a previous worksheet by clicking on File, Reopen worksheet to display a list of recent worksheets.

Selected elements including the whole worksheet can be copied and pasted into a spreadsheet. The Edit menu contains various options for this process. Likewise data can be copied back into the Worksheet from a spreadsheet. This feature allows tremendous flexibility, albeit at the cost of significant complexity.

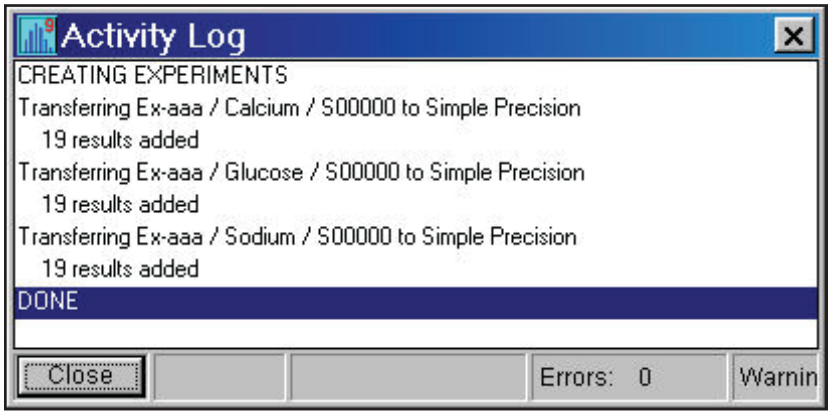
Parameters

This parameter screen is shown so that various elements can be entered if necessary. You will only be able to access a field if the data is not present. Normally, only the Comment field can be entered.



Activity Log and Final Transfer Activities

The Activity Log is generated as the results are transferred (whether you have skipped the worksheet or not) into the EE database. It lists the results of the transfer process.



When the transfer process is complete, click on Close.

At that point, the Module Overview screen will be displayed. To calculate the statistics, select Module and "Recalc All".

Method 3: Experiment/New from Policies

After all the discussion above, this method uses none of those techniques. Its purpose is to provide a simple easy way to do an experiment without the data capture process.

EE enters the Policies, you add the results. The main benefit is not so much rapid entry as standardization of parameters, so evaluation criteria are less likely to change at the whim of a specific operator.

Open the statistical module. At the Module Overview screen, select **Experiment/ New from Policies** from the menu. Select an instrument from the list as shown in the screen shown above. (See the *Select / Add Instrument* section.) If your instrument isn't in the list, click **Add Inst**. to add it. After selecting an instrument, click the **Next** button.

EE will then ask you to pick an analyte from a list. For several statistical modules, you will be asked for supplemental information such as specimen names, lot numbers and the like. When you finish the sequence of screens, EE shows the Parameter Screen, just as it normally does when you create an experiment. Just one difference — the parameters are already filled in. Now you may either enter the results manually or paste them in just as you did for Method 1. Remember all you are pasting in are results – without the column headers.

Methods 4 and 5: Edit/Paste with Policies

Paste and calculate, no editing required

These two methods are identical except for the format of the spreadsheet. The difference is that in one case, the data has one result per line (List format) and the other case, the data has multiple results per line (Table format). For examples, see the two XLS files, both in the EE11\Resources folder which comes with every copy of EE11. The two files are PasteWithPoliciesTable.xls and PasteWithPoliciesList.xls. The following tables show the two file formats.

Table 38.1
Format of Paste with Policies - List Format

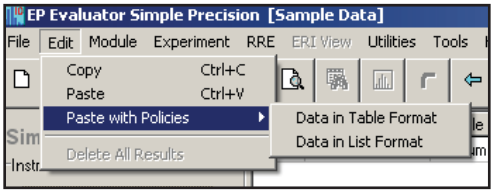
InstSerNo	SpecID	Analyte	TestDate	TestTime	Result
AA-101	XQ123	Calcium	10/1/2009	10:05	7.2
AA-101	XQ123	Glucose	10/1/2009	10:05	72
AA-101	XQ123	Sodium	10/1/2009	10:05	136
AA-101	XQ123	Calcium	10/1/2009	10:05	7.3

Table 38.2
Format of Paste with Policies - Table Format

InstSerNo	SpecID	Calcium	Glucose	Sodium
AA-101	XQ123	7.2	72	135
AA-101	XQ123	7.3	74	136
AA-101	XQ123	7.1	75	137
AA-101	XQ123	7.2	73	134

After that, the process is very simple. Load your data into a suitably formatted Excel spreadsheet. Then copy it into the clipboard. Then in EE, paste the data into the experiment(s). EE fills in the parameters from policies. Calculate and print your report immediately.

Steps



- Prepare the spreadsheet.
- Select the entire worksheet page in your spreadsheet, and do **Edit/Copy**.
- Switch to EE, go to the Module Overview Screen, do **Edit/Paste** with Policies and select either Data in Table Format or Data in List format.
- EE will ask you to select either an instrument from the list If your instrument is not present, you may easily add it.

- You may be asked for some module specific information such as lot numbers, specimen names and the like (page 38-4 et seq.).

- EE shows the Finish Screen (page 38-5), which gives you a choice of editing the data or immediately creating experiments. Usually the thing to do is check the **Skip Worksheet** box and create experiments immediately.

- EE creates the experiments. Use **Module/ReCalculate/ ReCalculate All Experiments** to calculate.

Method 6: Capturing Data via an Instrument Interface

"Capture" results from instrument

Method 6 captures results directly from an instrument, either from a serial port or from a file.

Process Initiation

Click on RRE/Create Experiment. You will then see this RRE Wizard Screen. Select "1. Instrument Interface."

Instrument Serial Numbers: When reading results from an instrument interface, you have three choices for handling instrument serial numbers:

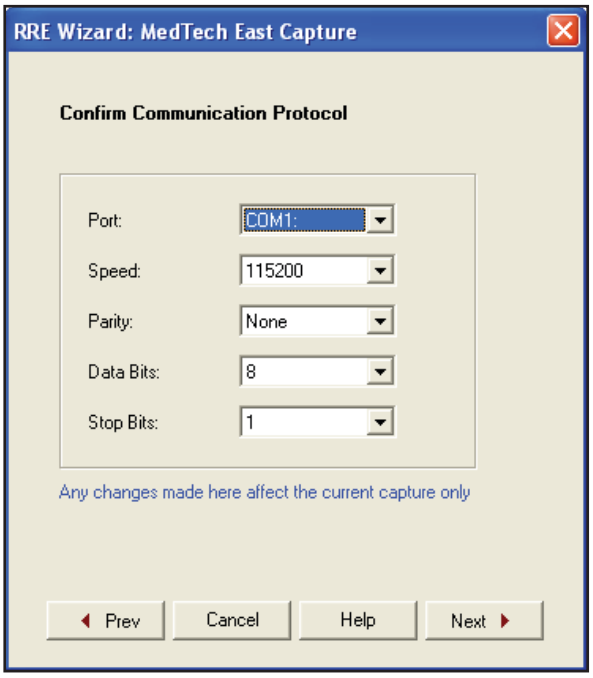
- **Ignore** - Ignore them. Assign all captured results to one, specific, instrument to be chosen on the next screen. This is the usual choice, since most interface programs don't return serial numbers. Don't select the other options unless you are absolutely sure the interface program provides serial numbers.
- **Capture One** - The data stream contains multiple instruments, and you want only one of them—the one whose serial number matches the instrument you will select later.
- **Capture All** - The data stream contains multiple instruments, and you want all of them—in separate experiments. (All of them must belong to the same instrument class.) Select this item if you are doing an MIC experiment and all your data are in the same file.

Re-use results from last download: Check this box to re-process results from your latest instrument capture rather than connecting to the instrument. For example, to repeat a run because you changed the experiment parameters in your policy setup.

Instrument Selection

See discussion in the section *Select / Add Instrument*, earlier in the chapter.

Data Acquisition



The **Define Communications Protocol** screen is the first screen of the Data Acquisition process. Its default content comes from the Instrument Settings screen in Policy Definitions.

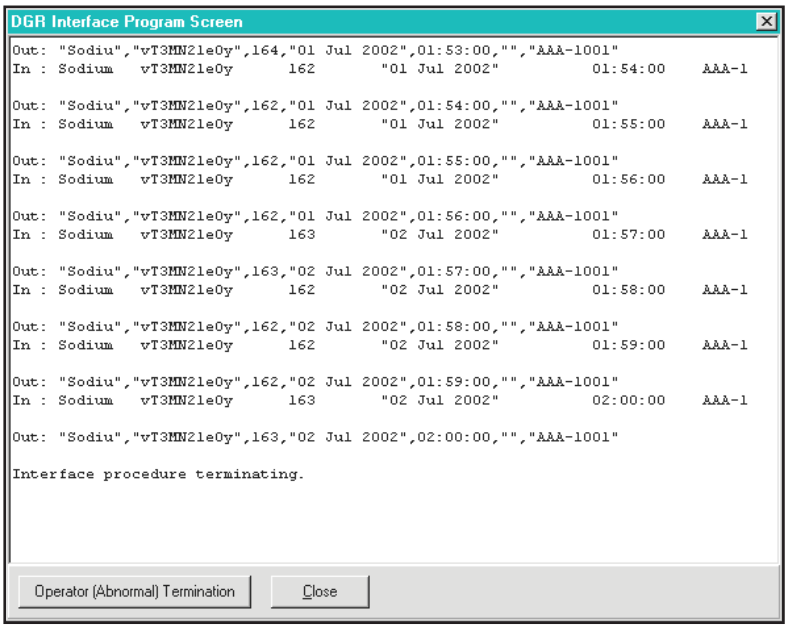
You may specify that the input comes either from a serial port or from a file. If the source is a serial port, EE will ask you to confirm the serial parameters. Settings shown on this screen must match the ones set on the instrument. Otherwise the two ends of the communications chain are speaking different languages.

If the source is a file, the next screen requests the source and location of the file to be input.

Note that the selection made on this screen will ONLY apply to this event. They are not remembered for future events.

If data acquisition is to be from a serial port, the next screen will inform you that the next step is data capture. This allows you time to set up the serial transfer process on the instrument. When you are ready to start the transfer process, click on Next to tell EE to be ready for the serial transfer of results.

The Activity Screen shows all aspects of the communications in real time that occur with the data source whether it is from the serial port or from a file.



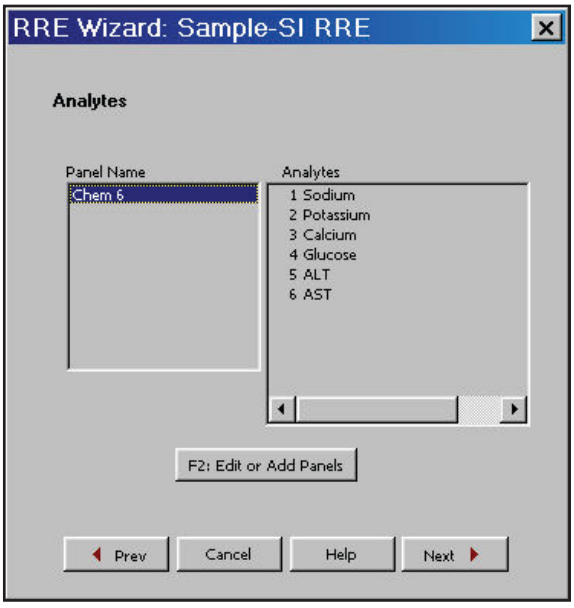
Operator (Abnormal) Termination: Click this button to cancel before the data transfer finishes.

Close: When the transfer is complete, click **Close** to close the transfer screen and continue to the next step in the RRE Wizard.

Escape key works just like the Operator Termination key. In either case, if that action is taken, then the data capture process is aborted and no data is brought into EP Evaluator.

The next screen defines the analytes for which results are to be captured.

If no suitable panel is listed, click the **Edit or Add Panels** button (or press **F2**) to define a new panel.



You need a panel only if:

- You will type (or edit) the results and want to control the order of the analytes on the data entry screen, or
- You don't want to create experiments for all analytes in the capture data stream.

Transfer and Integration

The remainder of this process was described earlier. See the section *Transfer and Integration*.

Method 7: Keyboard Entry of Results

This method is designed so that results may be entered into the Worksheet screen. The process collects the information necessary to create a Worksheet which has all the necessary Policy Information. Then the user enters data into the Worksheet either from the keyboard or a clipboard. After the data has been entered, then it is transferred into EE itself.

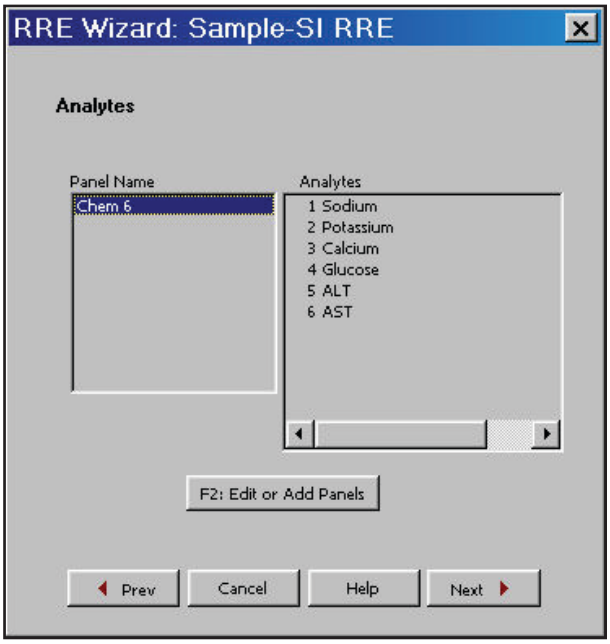
Process Initiation

Keyboard Entry is started exactly the same way as the Instrument Interface Process (Method 6). Click on RRE, then Create Experiment. Then click on Keyboard Entry.

Data Source Specification

Next, select the instrument.

Data Acquisition



This step in this form does not acquire data, but does define the order in which the analytes are going to appear in the Worksheet.

In other words, if the results on the report are in the order of Sodium, Potassium and Calcium, then this screen allows you to specify the order of the analytes on the Worksheet.

There are two places to define panels: (1) In Policy Definitions and (2) in this screen. To add or edit a panel from this screen, click on the button "F2: Edit or Add Panels." Then the process will be identical to that discussed in *Step 4. Panels* in Chapter 37, *Policy Definition*.

Transfer and Integration

After the Lot Number Screen and a Finish screen, the Worksheet appears. On completion of data entry into the Worksheet, be sure to save the Worksheet before you transfer it using the F9 send button.

Follow the prompts for the remainder of the process as the data is transferred into the EP Evaluator database.

Data Entry Details

For each module, the entry of the data into the results section of the worksheet is the same. However, depending on the module, the parameters section has very specific requirements for what needs to be entered in the name rows. The field name rows define the key parameters and options for each experiment. The following paragraphs for each applicable module define what field name rows are required, and what needs to be entered in the corresponding cells.

Complex Precision

The TestDate column is optional. If you omit it, the program will assign dates automatically as consecutive week days, starting from the experiment date. You must enter exactly the right number of replicates and runs for each day, and not omit any.

If you do enter dates, they must be in chronological order, and the date of the first run must be on or after the experiment date.
You must provide a PrelimSDSrc value for each analyte column.

PrelimSDSrc options:

- Option 0 (none): PrelimSDCount must also be 0 (no outlier detection).
- Option 1 (calculated): if PrelimSDCount = N, then the first N results are used to calculate the preliminary SD (for outlier detection).
- Option 2 (input): enter the desired SD value in the PrelimSDCount column(s) for outlier detection.

Simple Accuracy

- The SpecID column is required, and must be filed in for each row of results.
- The ValueMode row is required and must be 0 for each analyte.
- Target Ranges are required. For each SpecID there must be an entry for the low value and an entry in the next line below for the high value.

Linearity and EP6 Linearity

SpecIDs for pre-defined Cal Kits employ a special naming convention to relate the Cal Kits in the Policies to the SpecIDs in the experiments. If you use defined kit values, every specimen ID in the Results section must correspond to a specimen ID in the Assigned Values section. If you do not use a Cal Kit from Policies, you may name your SpecIDs in any way that you wish, but doing so is much more difficult, because the grid that is presented to you will not have most of the experimental parameter rows described below.

You may include an explicit ValueMode line; if you fail to specify a ValueMode, the ValueMode is assumed to be zero (Pre-assigned).

Value mode choices are:
- 0 = Pre-assigned values
- 1 = Coded
- 2 = % Measured
- 3 = % Assigned
- 4 = % Split
- 5 = Delta 1/5
- 6 = Delta 2/3
- 7 = Delta 3/4
- 8 = Delta 1/3
- 9 = Delta 2/4
- 10 = Alternate coded

The **Assigned Values** (or index numbers) for each SpecID/Analyte will be taken from the first row for that SpecID for which the Analyte value is not blank. You may specify the SpecID for each row if you wish, or you may just specify the SpecID for the first row for that level; subsequent rows with blank SpecIDs will use the most recent non-blank SpecID.

You can use "-" as a placeholder for a missing Assigned Value; doing so will force you to enter a numeric value in the experimental Parameters screen.

You also can use "--" as a placeholder for a missing Assigned Value; doing so will cause that level/specimen to be excluded from the experiment.

Sensitivity-LOB

In RRE policy definitions, if LOB module Analyte settings were entered, then the required fields will already be filled in. If not, then they can be entered at this point.
The key field names that must be filled in are:

- ZeroSpec: Enter the zero SpecID
- NZSpec: Enter the non-zero SpecID
- NZConc: Enter the non-zero concentration value

Spec IDs are required.

- In the Spec ID Column for the zero concentration, use the entry from ZeroSpec
- In the Spec ID Column for the non-zero concentration, use the entry from NZSpec.

Manufacturer's Claim (ManufClaim) is optional. Enter the concentration of the manufacturer's LOB claim.

The minimum number of results for each SpecID is

- ZeroSpec: at least 10 raw instrument results
- NZSpec: at least 5 raw instrument results

Sensitivity-LOQ

SpecIDs for pre-defined Cal Kits employ a special naming convention to relate the Cal Kits in the Policies to the SpecIDs in the experiments. If you use defined kit values, every specimen ID in the Results section must correspond to a specimen ID in the Assigned Values section.. If you do not use a Cal Kit from Policies, you may name your SpecIDs in any way that you wish, but doing so is much

more difficult, because the grid that is presented to you will not have most of the rows described in the Parameters discussion, below.

If LOQ module Analyte settings for target CV were entered in policies, then the target CV fields will already be filled in. If not, then they can be entered at this point.

Parameters section

TargetCV: Enter the desired target CV

- TestDate: Enter the date of testing. Results must be entered in chronological order.
- S000x: The SpecID for each level of the linearity kit is filled in from policies, or you can enter them manually
- C000x: The assigned concentration for each SpecID of your "linearity kit" or test solutions is filled in from policies, or you can enter them manually. If this field is blank or contains the placeholders "-" or "—", the values can be filled in at the experiment level in the Parameters screen after sending the data (F9) to the experiment(s).
- nSpecs: The number of specimens in the kit

Results Section

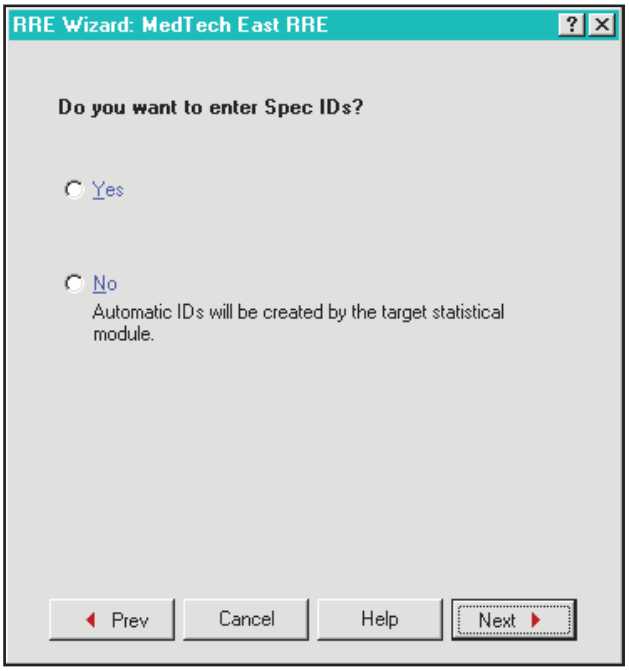
- The SpecID column is required in the results section. SpecIDs for a Linearity Kit defined in your Policies can be the text used for either "linearity Kit", or "Instrument Code"; if you entered the SpecIDs manually, you can copy them from S000x. For example, if "PRK" is the "Kit Name" for a specific linearity kit. PRK-01 is level 1 (S0001) in that kit, PRK-02 (S0002) is level 2, etc.
- The TestDate column is also required, and dates must be in chronological order.
- The TestTime column is optional. It may contain a word (like "morning run") instead of an actual time, or it may be blank
- Results: There can be only one result for each SpecID for each Analyte and for each testDate / testTime. The minimum number of results for each SpecID is:
  - at least 10 days of results
  - at least 3 specimens that do not have a mean of zero.

Module Specific Screens

The next several screens request required information that is not defined in your policies—things such as assignment of dates and IDs for specimens, sources of materials and the like. If you don't understand what input is needed, click the Help button for an explanation. It is important that you enter a value in every field. These screens are present only because the experiments won't calculate if the fields are left blank.

Modules requiring Specimen IDs

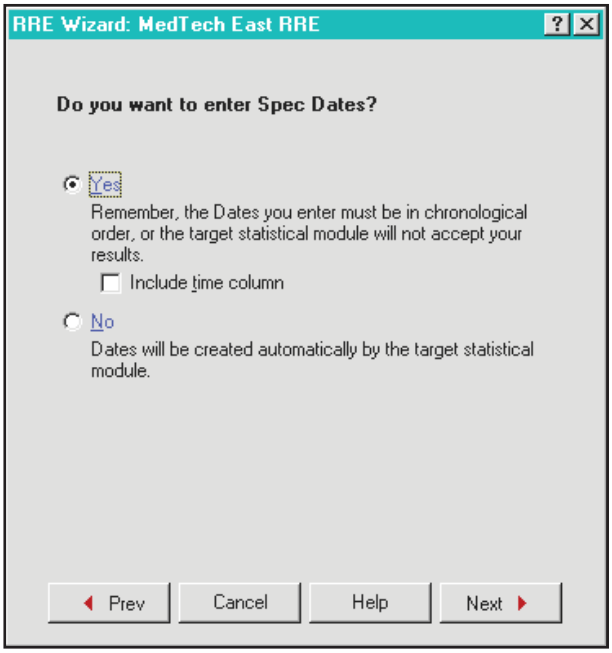
Many modules require the presence of specimen IDs. In some cases, particularly the method comparison modules, the IDs can be generated by EE. This screen deals with that option.



Enter Specimen IDs?: When entering results from the keyboard, you may choose not to enter Spec IDs, and let EE assign automatic IDs.

Caution—when using automatic Spec ID assignment with method comparison experiments, it is very important that specimens be entered in exactly the same order for all instruments being compared.

Modules Requiring Specimen Dates

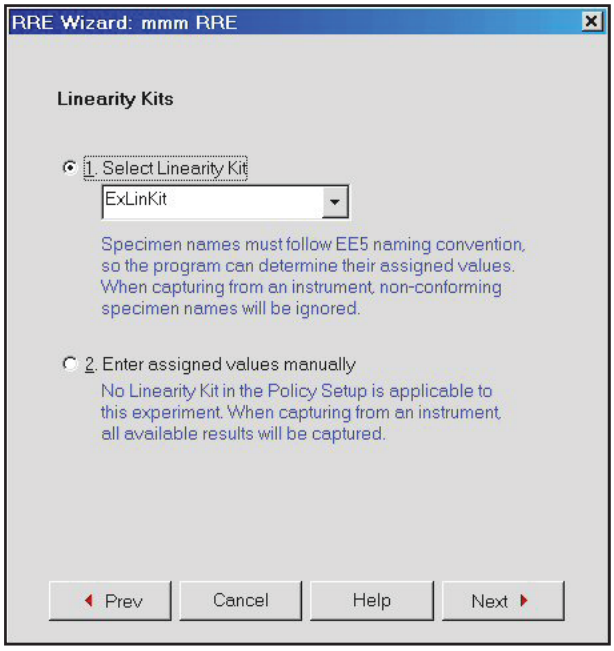


A few statistical modules require that dates be associated with their results. These are Complex Precision, CLSI EP10, and Sensitivity (LOQ).

Enter Specimen Dates?: When entering results from the keyboard, you may choose not to enter Spec dates and let EE assign them automatically.

Caution—when using automatic dating, it is very important that specimens be entered in chronological order, with exactly the expected number of replicates per day. The date of the first result is the Experiment Date. The result date increments by one business day after reading the appropriate number of replicates.

Specimen Selection - Linearity and Sensitivity (LOQ) Modules



The screen where you assign specimen IDs for these two modules warrants special attention.

If you see this page when capturing linearity results from an instrument, it usually means something is wrong.

If the **Select Linearity Kit** radio button is grayed out, the Spec IDs in your capture stream don't match anything in your policy definition. You may have entered Spec IDs incorrectly. They must be of the form KKK-nn, where KKK is the kit instrument code and nn is a 2-digit level number, 01 to 11.

If the **Select Linearity Kit** radio button is available, the Spec IDs in your capture stream are for more than one linearity kit. This may be correct, but you can only capture one kit at a time. Select one kit from the pick list and finish the Wizard to

create experiments for that kit. Then repeat the Wizard for each separate linearity kit, checking the **Re-use results from last capture** checkbox on the initial page of the Wizard.

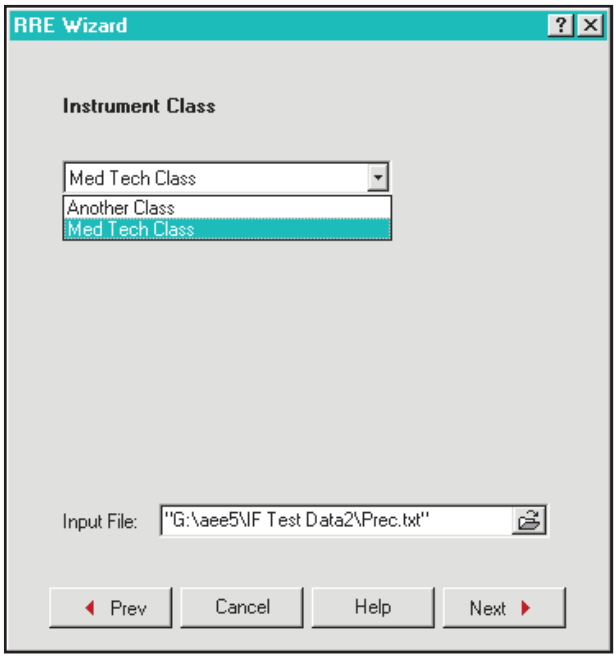
When capturing data for a Sensitivity-LOQ experiment with more than 11 levels, you must choose the **Enter assigned values manually** radio button. You cannot use a Linearity Kit, since kits have a maximum of 11 levels.

If you are using keyboard entry, this screen does not indicate a problem. It is simply asking which kit you want to enter results for.

- Choose the **Select Linearity Kit** radio button. Pick a defined kit from the dropdown list.
- If the **Select Linearity Kit** button is grayed out, you have not defined any linearity kits. Usually the best thing to do is cancel the Wizard, go to Policy Definition, and define the linearity kit.
- When capturing data for a Sensitivity-LOQ experiment with more than 11 levels, you must then choose **Enter assigned values manually** radio button. You cannot use a Linearity Kit, since kits have a maximum of 11 levels.

Select Instrument Class (Multiple Instrument Capture)

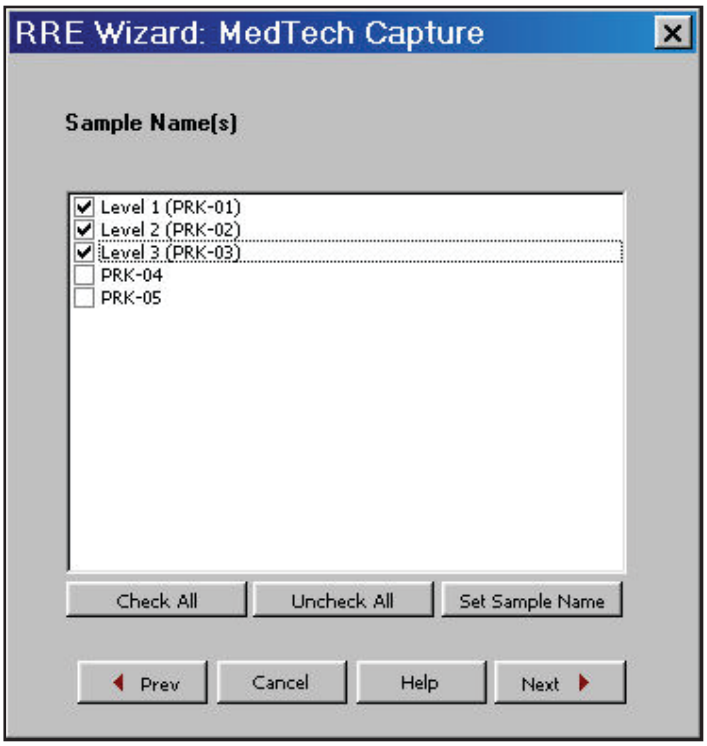
When capturing multiple instruments, all must belong to the same class. Select the class here. EE will determine the instrument names by matching the instrument serial numbers in the capture steam to those in your Policy Definition. (If it doesn't recognize a serial number it will still capture the data, but will put the serial number in the instrument name field.)



Precision

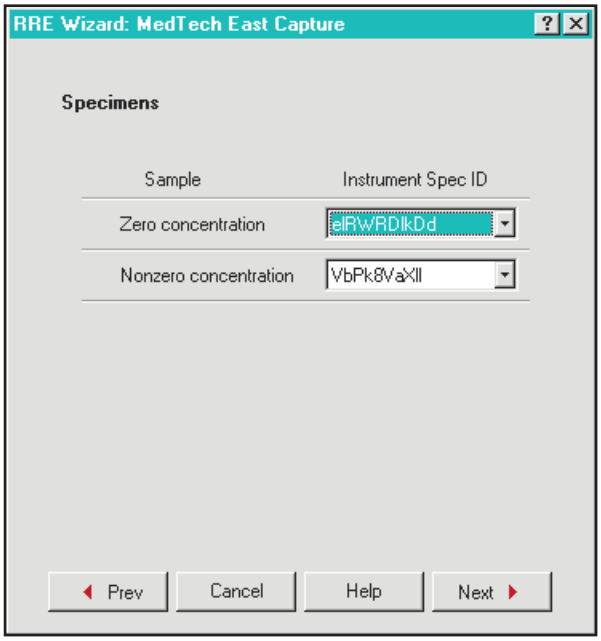
This screen is shown for precision modules. If you are capturing from an instrument, it associates specimen names for the report with Spec IDs reported by the instrument. If you are entering results from the keyboard, the Instrument Spec ID fields are grayed. You can only enter Sample Names to appear on the report.

The software sets no limit on the number of precision samples per session.



Sensitivity-LOD

When capturing instrument responses for Sensitivity-Limits of Detection, indicate which specimen represents the zero concentration and which is the non-zero concentration.



Method 8: Data Acquisition through ODBC

Data Acquisition using ODBC is a very powerful tool for rapidly acquiring results from another application, such as Instrument Manager (IM) or LPM. Essentially, users have the ability to access instrument results using EE's ODBC Data Acquisition (ODA) program.

EP Evaluator® requirements

- EP Evaluator Release 9.0 or above,
- Vendor, Standard with Data Capture, or Professional versions

Requirements

If acquiring data from Instrument Manager or from Laboratory Production Manager, required items are:

- Instrument Manager version 8.10 and higher, with the Specimen Management (SM) Package and an ODBC license **or** Laboratory Production Manager version 5.6.2 and higher.
- A valid IM user with appropriate ODBC privileges.
- An ODBC data source for the EP Evaluator® computer. (In lay terms, this describes the mechanism used so EE can talk with IM's ODBC.)

ODBC connections are licensed on a concurrent user basis. ODBC's connection with EE is active only during the brief period during which you are acquiring data. Thus one ODBC connection can support many EE users as long as only one user is connected at one time.

Query Files Provided for ODA

Each data source has an associated file that contains the ODBC database queries that are appropriate for that database. For IM, when using Test Instrument IDs to identify instruments, the query file is entitled "ODBC-Queries-For-IM-TestInst.txt". The files contain many comments (i.e., lines starting with a ";"). For the most part, you should not edit this text file, but there are three sections that you may wish to or need to edit:

- **ERI/ROC Fields**: You may wish to enable or disable some of the ERI/ROC fields. To disable a field, insert a ";" at the start of the line; to enable a field, remove any leading ";"

- **ODBC Timeout**: You may wish to modify this if you are having problems with queries taking too long to execute. In extreme cases, you may wish to call Support for assistance. Note that you can disable timeouts entirely when you set up your ODBC DSN.

- **User Filters**: You may wish to add new data filters to allow you to use data subsets easily. Adding such a filter query requires detailed understanding of the underlying database structures, so you may need assistance from the database provider.

Note that attempting to acquire huge amounts of data (all dates, many instruments, many test codes, many specimens) can result in huge delays if you are using a large database. Do your best to limit the data you acquire by filtering it as precisely as possible by date, instrument, test code, and specimen.

Upon upgrade of your EP Evaluator software, the standard query files provided for ODA will be overwritten. If you do edit any of the standard query files, save them with a different file name. The file name must start with the following: ODBC-Queries-For-. (e.g. ODBC-Queries-For-IMAnalyteFilterOn.txt).

Configure Windows with a DSN for ODBC Access

In order to obtain data from the source application, you will have to:

1. Establish a valid user with appropriate ODBC privileges in the program from which you wish to acquire the data.
2. Create a new Data Source (ODBC DSN) on the computer on which you are running EE.
3. Finally, select the correct Data Source Connection in the ODBC Data Acquisition (ODA) main screen.

NOTE: If your computer has a 64-bit Windows Operating System, EE (as a 32-bit application) cannot see or use 64-bit ODBC/DSN connections. The default ODBC Manager on 64-bit systems creates 64-bit ODBC connections, so you will need to ensure you are inspecting, creating, and modifying 32-bit ODBC definition. To do this, use the **DSN** button on the main ODA screen. This button launches the correct ODBC Manager for use with EE.

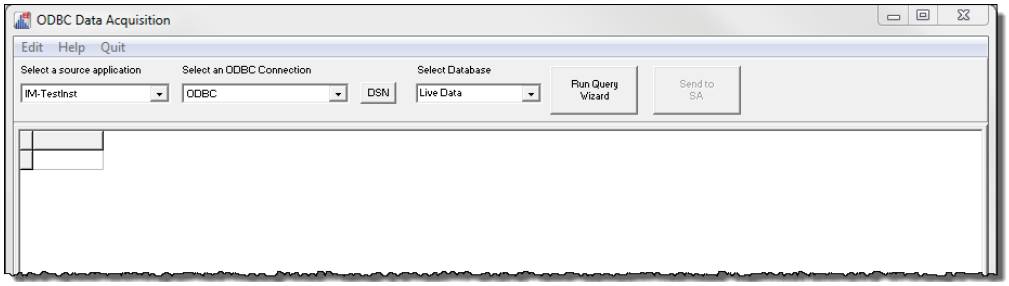
It may take a little fiddling to get the various parts of this linkage to coordinate and synchronize correctly. If at any time you feel that some of the changes that you have made are not being “seen” by ODA, simply quit out of it and re-enter it via the RRE menu in EE. In particular, the ODBC database query files are only loaded when ODA is first run, not each time the program is run.

ODBC Data Acquisition

1. Create an appropriate Policy Definition.

2. To acquire ODBC data from a data source, go to the Module Overview screen of the statistical module for which you are acquiring data and select **ODBC Data Acquisition** from the **RRE** menu.

3. Select the source application that you wish to use from the appropriate drop down.



NOTE: EE is pre-configured to work with both IM and LPM, but can be configured to work with other data sources. Two IM configurations are provided, one which identifies instruments by Test Instrument ID (IM-TestInst), and one which identifies instruments by connection name (IM-Connection). If the instrument communicating with IM does not provide an Instrument ID or the instrument only provides one identifier (ie., Vitros 250) choose the IM-Connection source application. If the instrument provides an Instrument ID or, Instrument Manager is communicating with a Data Manager that connects to multiple instruments (e.g. Data Fusion), choose the IM-TestInst source application. LPM provides only one instrument field for instrument identification.

4. Select your ODBC connection from the dropdown box. If you wish to define a new ODBC connection (DSN) click on the DSN button to bring up the ODBC Manager.

5. Select the database from the **Select Database** dropdown.

   Some data sources have multiple databases. For IM, you can either use the live IM data, or you can use your archived IM data, if you have any. The choice between the two is made by selecting the database from the dropdown. There is only one database for LPM.

6. Click **Run Query Wizard.**

   After confirming your connection settings, click the **Run Query Wizard** button to acquire data. The Query Wizard connects to the data source and leads you through a series of screens to select data for your EE experiment. See the section ***ODBC Data Acquisition Query Wizard Interface*** for more information on these screens.

7. After the data has been acquired, you will disconnect from the data source by clicking the “Send to” button.

8. Open the statistical module and go to its Module Overview Screen to view the data.

ODBC Data Acquisition Query Wizard Interface

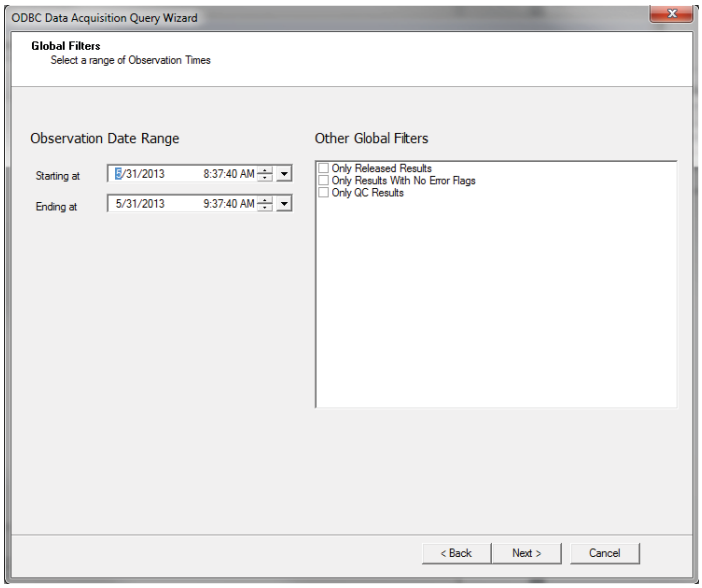
Query Wizard, Filtration and Selection

Follow the ODBC Query Wizard to filter out the results you don’t want EE to acquire. For example, suppose you are doing a linearity experiment with five specimens. You want only results for those five specimens, not all reportable patient results recently run.

The more restrictive you can make your filtration or selection criteria, the faster you will get your results. There are separate pages of the wizard for filtering on dates, instruments, analytes, and specimens.

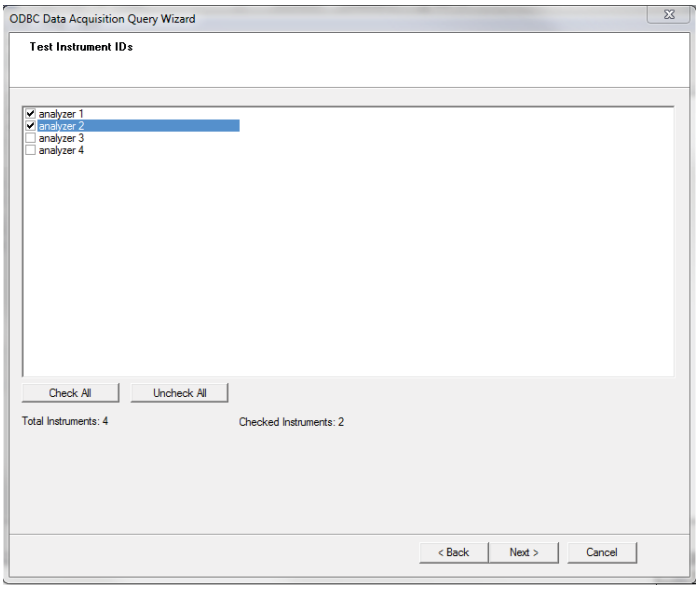
Global Filters

On this screen, select the observation date range and other filters.



Test Instrument IDs

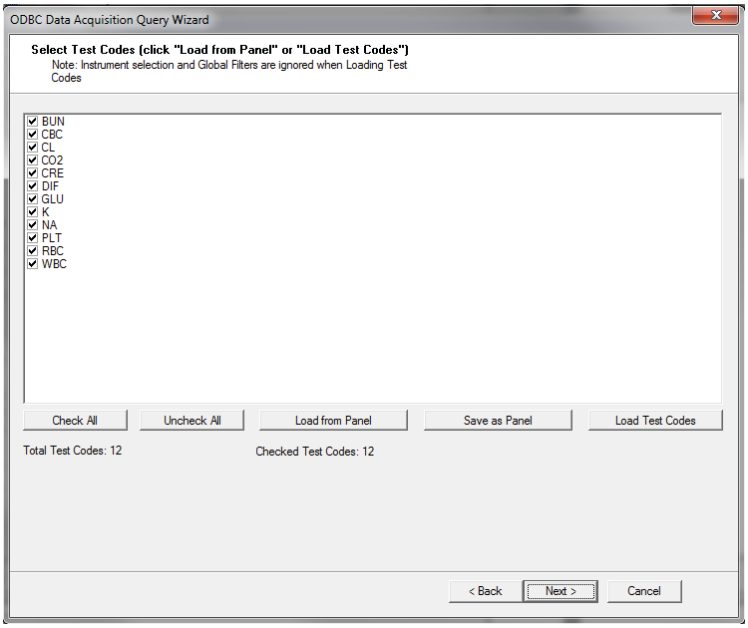
The Test Instrument IDs window loads all test instruments, irrespective of the date range and other global filters defined on the Global Filters window.



Select Test Codes

You can either load a panel of test codes (**Load from Panel**), or you can click on the **Load Test Codes** button to display a list of all of the test codes for the instruments you selected. Clicking on **Load Test Codes** can be very time consuming when you are using a large database. In that case, you may find it quicker and easier to click on **Load from Panel**.

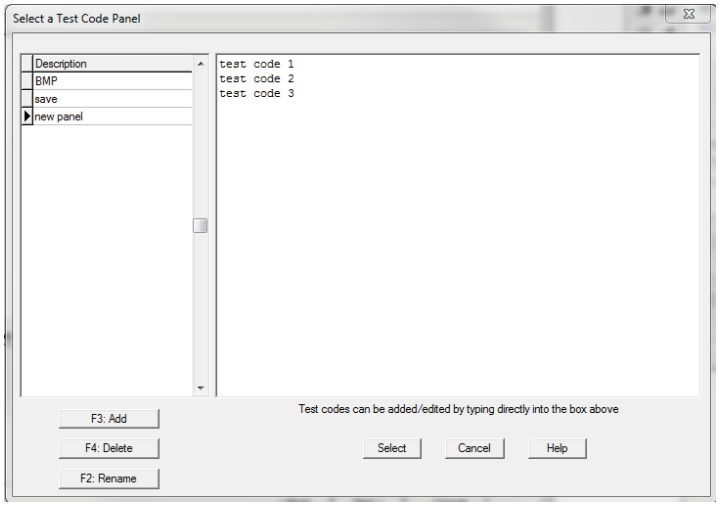
From the **Load Test Codes** screen, you can select all or a subset of the available test codes and click **Save as Panel**. This panel will be available in the Query Wizard by clicking **Load from Panel**. If you set up your Panels correctly when you first start using ODA, you will never need to press the **Load Test Codes** button again.



Panels

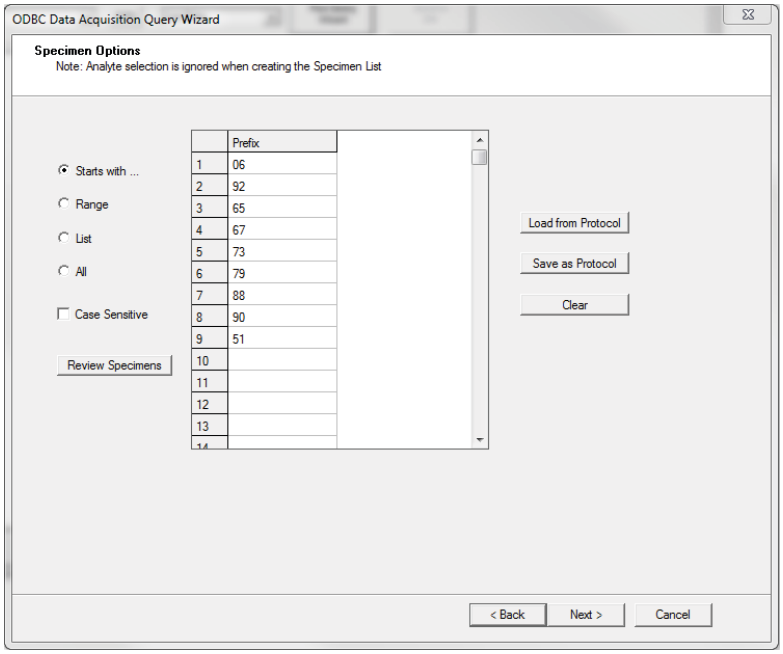
Load from Panel opens the **Select a Test Code Panel** window. Click on the panel description on the left and click the **Select** button to load the panel.

From the **Select a Test Code Panel** window, you can delete or rename an existing panel. Additionally, you can edit an existing panel by selecting it and editing the list in the text box on the right. You can create a new panel by clicking **Add** and typing your test codes in the text box. Press **Enter** after every test code you enter and exit the screen when finished.



Specimen Options

Use this screen to create a filter to pinpoint those specimen IDs that you want EE to acquire. Choose a radio button on the left to specify how specimen IDs are identified for acquisition. Clicking **Next** from this screen takes you to the final screen of the wizard.



Starts with allows you to define prefixes to identify all the specimen IDs that should be pulled into EE. You can enter more than one prefix.

Range allows you to define ranges of specimen IDs. You can enter more than one range.

List allows you to define a list of specific specimen IDs.

Show All will generate a list of those specimens applicable to the instrument, global filters, and date criteria (but not test code selection). Because this option may cause the retrieval of thousands of specimens, **Show All** queries may be slower than any other option.

Specify whether the filter is case sensitive using the **Case Sensitive** checkbox.

Once you've defined Specimen Options, you can click the **Next** button to honor the specified option. To view a list of specimens slated for acquisition, click the **Review Specimens** button. You must select specimens before you can leave this screen and continue through the query wizard.

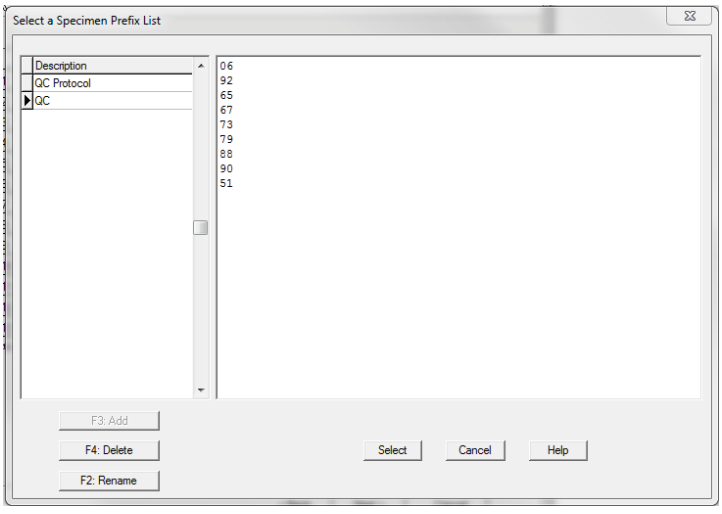
NOTE: It is possible to check individual specimen IDs from the **Review Specimens** screen. However, if you do not check all specimens, the query may take longer to acquire that subset than it would have taken to acquire all the data specified by the filter defined on the Specimen Options screen.

Protocol

You can define a Prefix Protocol, a Range Protocol, or a List Protocol by configuring your specimen options and clicking **Save as Protocol**. This specimen ID protocol will be available in the Query Wizard by clicking **Load from Protocol**.

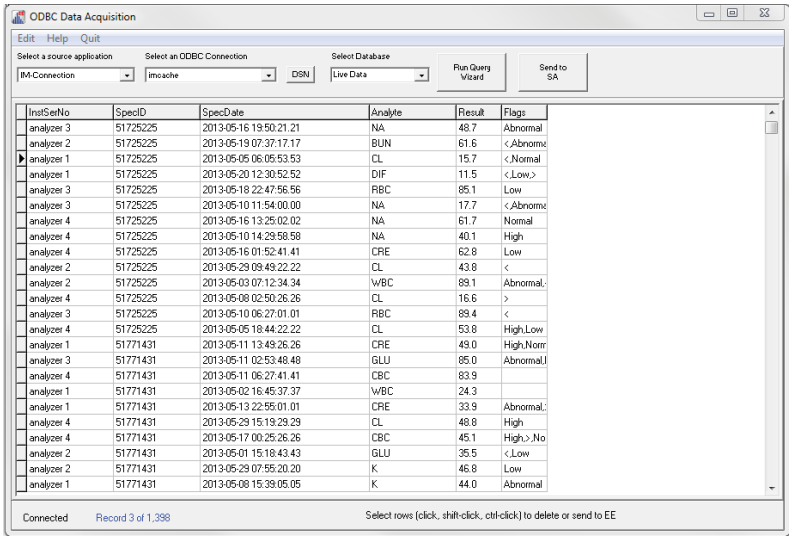
Load from Protocol opens the **Select a Specimen List** window. You can click on the Protocol description on the left and click the **Select** button to load the protocol.

From this window, you can delete or rename an existing protocol. Note that you cannot type in the text box on the right.



Send to Module

After completing the Query Wizard, the results you selected are shown in a grid You can delete results from this grid before sending the data to the EE module.



- Highlight a line and press the **Delete** key to delete a single result.
- Use click followed by (Shift+Click) to select contiguous rows. Use (Control+Click) to select non-contiguous rows.
- Press the **Delete** key to delete all selected rows.
- Click the column headings to sort on the selected column.

Click **Send to <module>** to transfer data into the EE module. If no rows are selected, all rows are sent. If multiple rows are selected, the program will ask whether you want to send all rows or only the selected rows. Upon completion of Send, the ODBC connection to the source application is closed.

Note that while source application data fields may have an arbitrary length, EE data fields have limited, fixed lengths. If any of the source application data exceeds the width of the EE data fields, you will see an error message, warning you that truncation is about to occur. This rarely happens in the analyte, date, result, or flag fields, but sometimes can occur in the Specimen ID and instrument serial number fields. If you see this message, you will have to modify the data in the source application to accommodate the field length requirements in EE.

If the data needs extensive clean-up, use **Edit / Copy** to copy the data to the clipboard. Then paste the data into Excel, edit it as needed, and send it to the EE module using **Edit / Paste with Policies / Data in List Format**.

EE: Transfer and Integration

At this point, the data obtained from the source application goes through the Transfer and Integration steps as described earlier in this chapter.

If the data needs extensive clean-up, use **Edit / Copy** to copy the data to the clipboard. Then paste the data into Excel, edit it as needed, and send it to the EE module using **Edit >Paste with Policies> Data in List Format**.

- Select the desired list in the left panel, then click **Select**.

Acquiring ERI/ROC Data using ODBC

ERI/ROC is unlike any other statistical module in that:

- Rapid Results Entry (RRE) Policies do not need to be defined in order to acquire data from ODBC

- ERI/ROC can use ODBC patient demographic data that other statistical modules cannot use.

In order to provide flexibility, the ODBC patient demographic fields that can be used are stored in text files provided in the EE installation folder. The text file names use the following convention:“ODBC-Queries-For-(applicaiton).txt”. There are two text files for Instrument Manager, one for Test Instrument IDs and one for Connection Name. The file starts with extensive comments about its structure, and then provides the field definitions.

The Query files will contain lines like the following:

```
Specimen->Patient->Sex~L_Sex
Specimen->Patient->DOB~D_DOB
```

The “~” character represents a tab. The part to the left of the tab specifies the field in the database that you wish to use. The part to the right of the tab specifies how that data will be recognized in EE.

The text file for LPM queries for the same information, but the data to the left of the tab provides a different field name.

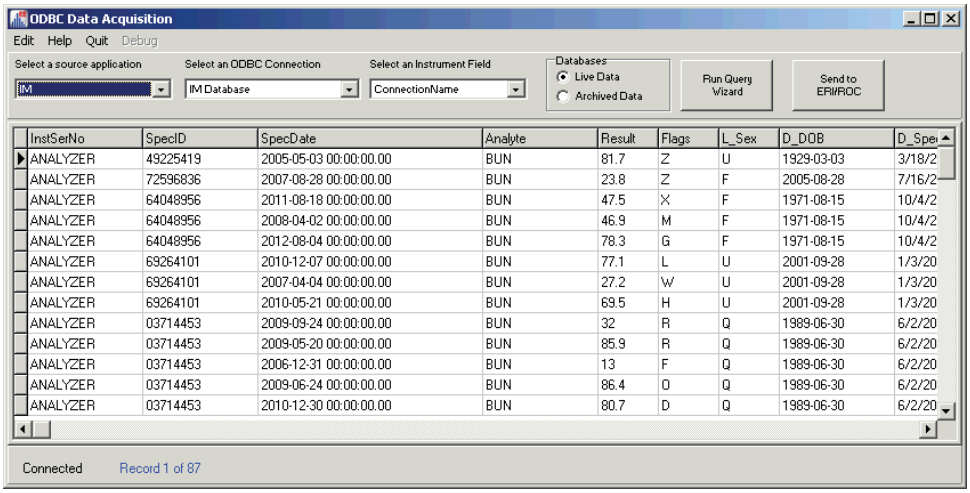
```
(SELECT NVL(SHORTNAME,STANDARDNAME) FROM SEXDEF WHERE
ID=SUBJECT.SEX)~L_Sex
SUBJECT.DATEOFBIRTH~D_DOB
```

NOTE: The EE names always have “L_” or “D_” as a prefix, so that EE and ERI/ROC knows how to process the data. See Chapter 20, *Establishing Reference Intervals*, for a description of the L and D data types.

Using L_Sex data is simple, because there are a small number of values in the data, and the values are compiled automatically by ERI/ROC.

In the case of D_DOB (patient date of birth), EE converts the data from IM into three age variables by computing the difference between the time/date when the specimen was drawn and the DOB. The three variables are: age in weeks, age in months, and age in years. See Chapter 20, *Establishing Reference Intervals*, for information on defining a Computed Demographic to convert these ages into the age categories you wish for your ERI/ROC study.

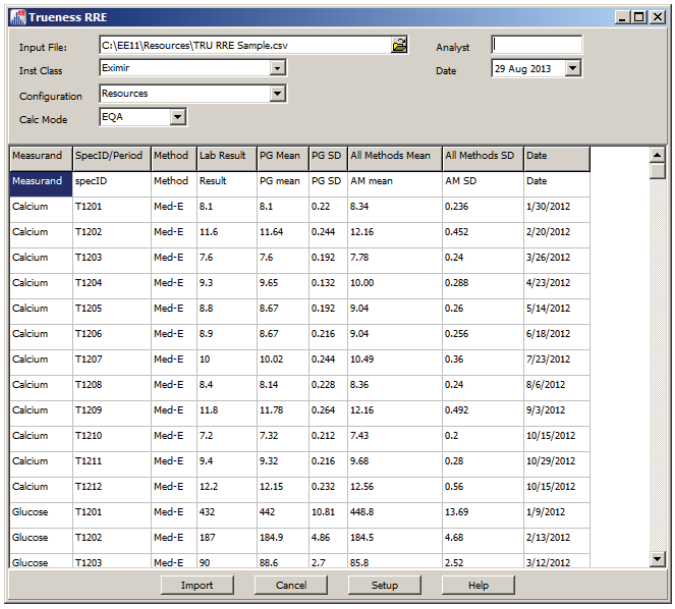
Here is an example of how ERI/ROC data looks as it comes from IM:



InstSerNo	SpecID	SpecDate	Analyte	Result	Flags	L_Sex	D_DOB	D_Spe
ANALYZER	49225419	2005-05-03 00:00:00.00	BUN	81.7	Z	U	1929-03-03	3/18/2
ANALYZER	72596836	2007-08-28 00:00:00.00	BUN	23.8	Z	F	2005-08-28	7/16/2
ANALYZER	64048956	2011-08-18 00:00:00.00	BUN	47.5	X	F	1971-08-15	10/4/2
ANALYZER	64048956	2008-04-02 00:00:00.00	BUN	46.9	M	F	1971-08-15	10/4/2
ANALYZER	64048956	2012-08-04 00:00:00.00	BUN	78.3	G	F	1971-08-15	10/4/2
ANALYZER	69264101	2010-12-07 00:00:00.00	BUN	77.1	L	U	2001-09-28	1/3/20
ANALYZER	69264101	2007-04-04 00:00:00.00	BUN	27.2	W	U	2001-09-28	1/3/20
ANALYZER	69264101	2010-05-21 00:00:00.00	BUN	69.5	H	U	2001-09-28	1/3/20
ANALYZER	03714453	2009-09-24 00:00:00.00	BUN	32	R	Q	1989-06-30	6/2/20
ANALYZER	03714453	2009-05-20 00:00:00.00	BUN	85.9	R	Q	1989-06-30	6/2/20
ANALYZER	03714453	2006-12-31 00:00:00.00	BUN	13	F	Q	1989-06-30	6/2/20
ANALYZER	03714453	2009-06-24 00:00:00.00	BUN	86.4	O	Q	1989-06-30	6/2/20
ANALYZER	03714453	2010-12-30 00:00:00.00	BUN	80.7	D	Q	1989-06-30	6/2/20

Method 9: Rapid Results Entry for Trueness (RRE-T)

Method 9 for RRE applies only to the Trueness module. Trueness rapid results entry is accomplished through an import screen. The import screen allows the user to map their spreadsheet data to the field names that the Trueness module needs. RRE-Trueness is designed to accept spreadsheet data where each row has the data for one specimen. The top line is a header line, which is ignored during RRE.



Measurand	SpecID/Period	Method	Lab Result	PG Mean	PG SD	All Methods Mean	All Methods SD	Date
Measurand	specID	Method	Result	PG mean	PG SD	AM mean	AM SD	Date
Calcium	T1201	Med-E	8.1	8.1	0.22	8.34	0.236	1/30/2012
Calcium	T1202	Med-E	11.6	11.64	0.244	12.16	0.452	2/20/2012
Calcium	T1203	Med-E	7.6	7.6	0.192	7.78	0.24	3/26/2012
Calcium	T1204	Med-E	9.3	9.65	0.132	10.00	0.288	4/23/2012
Calcium	T1205	Med-E	8.8	8.67	0.192	9.04	0.26	5/14/2012
Calcium	T1206	Med-E	8.9	8.67	0.216	9.04	0.256	6/18/2012
Calcium	T1207	Med-E	10	10.02	0.244	10.49	0.36	7/23/2012
Calcium	T1208	Med-E	8.4	8.14	0.228	8.36	0.24	8/6/2012
Calcium	T1209	Med-E	11.8	11.78	0.264	12.16	0.492	9/3/2012
Calcium	T1210	Med-E	7.2	7.32	0.212	7.43	0.2	10/15/2012
Calcium	T1211	Med-E	9.4	9.32	0.216	9.68	0.28	10/29/2012
Calcium	T1212	Med-E	12.2	12.15	0.232	12.56	0.56	10/15/2012
Glucose	T1201	Med-E	432	442	10.81	448.8	13.69	1/9/2012
Glucose	T1202	Med-E	187	184.9	4.86	184.5	4.68	2/13/2012
Glucose	T1203	Med-E	90	88.6	2.7	85.8	2.52	3/12/2012

To perform RRE, select **RRE>Create Experiments** to open the Trueness RRE screen.

You will have to select an input file (either CSV or XLS, but not XLSX), an Instrument Class (from Policies), a Configuration file, and a Calculation Mode.

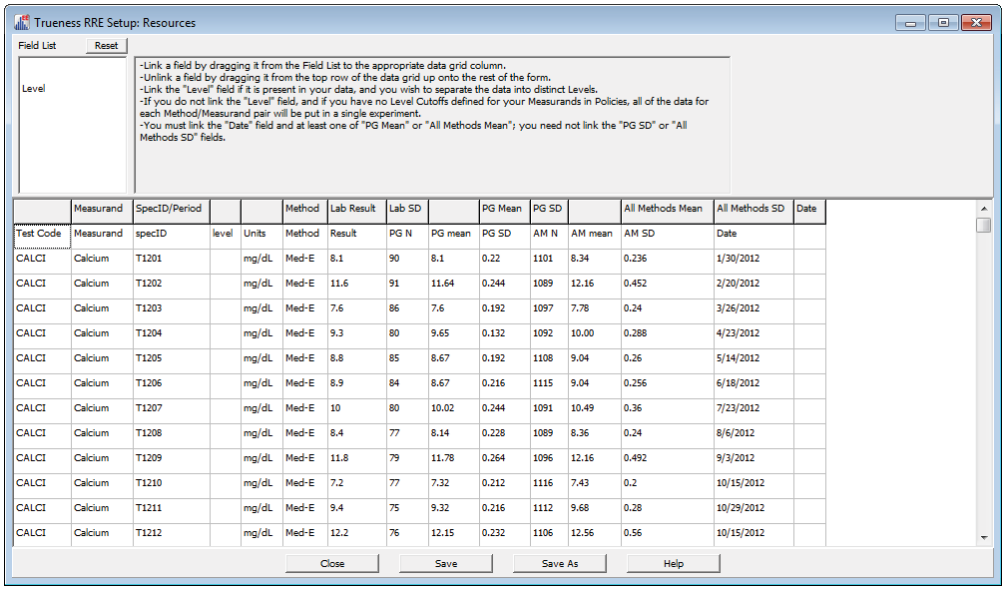
The configuration files contain the correspondence between the columns in your input data file and the fields that Trueness needs in order to perform RRE. Once you have set up one configuration file, you will only need to edit it or create a new file if you are using data with more than one layout/format.

Click **Import** to create Trueness experiments from your data.

Click **Setup** to edit or create configuration files.

RRE-T Configuration File

From the **Trueness RRE** screen, click the **Setup** button to define or modify a configuration file for Trueness RRE.



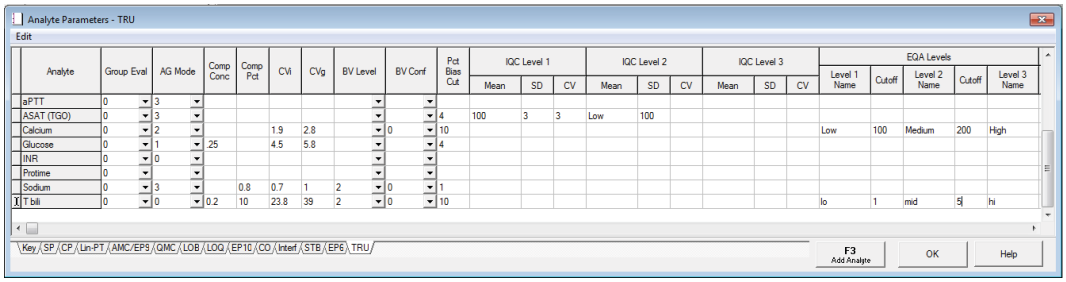
	Measurand	SpecID/Period			Method	Lab Result	Lab SD		PG Mean	PG SD		All Methods Mean	All Methods SD	Date
Test Code	Measurand	specID	level	Units	Method	Result	PG N	PG mean	PG SD	AM N	AM mean	AM SD	Date	
CALCI	Calcium	T1201		mg/dL	Med-E	8.1	90	8.1	0.22	1101	8.34	0.236	1/30/2012	
CALCI	Calcium	T1202		mg/dL	Med-E	11.6	91	11.64	0.244	1089	12.16	0.452	2/20/2012	
CALCI	Calcium	T1203		mg/dL	Med-E	7.6	86	7.6	0.192	1097	7.78	0.24	3/26/2012	
CALCI	Calcium	T1204		mg/dL	Med-E	9.3	80	9.65	0.132	1092	10.00	0.288	4/23/2012	
CALCI	Calcium	T1205		mg/dL	Med-E	8.8	85	8.67	0.192	1108	9.04	0.26	5/14/2012	
CALCI	Calcium	T1206		mg/dL	Med-E	8.9	84	8.67	0.216	1115	9.04	0.256	6/18/2012	
CALCI	Calcium	T1207		mg/dL	Med-E	10	80	10.02	0.244	1091	10.49	0.36	7/23/2012	
CALCI	Calcium	T1208		mg/dL	Med-E	8.4	77	8.14	0.228	1089	8.36	0.24	8/6/2012	
CALCI	Calcium	T1209		mg/dL	Med-E	11.8	79	11.78	0.264	1096	12.16	0.492	9/3/2012	
CALCI	Calcium	T1210		mg/dL	Med-E	7.2	77	7.32	0.212	1116	7.43	0.2	10/15/2012	
CALCI	Calcium	T1211		mg/dL	Med-E	9.4	75	9.32	0.216	1112	9.68	0.28	10/29/2012	
CALCI	Calcium	T1212		mg/dL	Med-E	12.2	76	12.15	0.232	1106	12.56	0.56	10/15/2012	

The Trueness Fields are listed in the Field List box, and the data appears in the white grid. For example, to indicate that a given column should be used for Method, drag the Method down from the Field List and put it in the column header on the grid. If you wish to remove an association, drag the word Method up and out of the grid, and it will return to the Field List. To remove all associations, click **Reset** to return all column headers to the Field List.

When you are finished, click **Save** (to over-write the currently selected Configuration file), or **Save As** (to create a new Configuration file).

Level Cutoffs

For each Measurand and Calculation Mode (EQA or EQC), you can define 1 or 2 Cutoff values which then define 2 or 3 Levels; each of the Levels can have a Level name. In addition, you can define up to 3 sets of IQC data (Mean, SD, and CV), one for each Level; the IQC data is shared between EQA and EQC.



For the T Bili and EQA, in the screenshot above, specimens with Lab values below 1 will be put in an experiment with a Level of "lo"; those with values >= 1 but < 5 will be put in Level "mid"; and those with values >= 5 will be put in an experiment with Level "hi".

Rapid Results Entry for Trueness (RRE-T) creates multiple experiments using Trueness data in spreadsheet form. The data included in the spreadsheet must include columns for:

- Measurand
- Method
- SpecID or Period (depending on the Compute Mode)
- Date/Time
- Lab Result

In addition, it must contain at least one of:

- Peer Group Result, or
- All Methods Result.

It can optionally include:

- Peer Group SD (to allow computation of PG Trueness on a per-specimen basis)
- All methods SD (to allow computation of AM Trueness on a per-specimen basis)
- Level (see discussion below)
- Lab SD (to allow computation of the Lab's Sigma Metric)

RRE-T Modes

RRE-T was designed to function in one of three modes, as follows.

Mode one: If the Level column is available from the RRE-T file.

Policy preparation: For each Measurand and each Level for which the user expects to collect data, the user should define Level names and IQC data in **RRE>Define Policies>Non-Hematology>Analyte Settings>TRU** tab; note that in this mode, the Cutoff values are not required.

- If a RRE-T Level column name is empty, an error message will be inserted in the Activity Log. If you use a Level column in the RRE-T file, there should be non-empty Level data for all of the rows.
- If the RRE-T Level column name is not empty, the specimen is assigned to the experiment with the given Level name.
- If the RRE-T Level column name matches a Level name in Policies, then the IQC data used is that from the corresponding Level in Policies.
- If the RRE-T Level column name cannot be found in the Level names in Policies, then the IQC data will be blank.

Mode two: If the Level column is not available from the RRE-T file, and the user wishes to assign specimens to Levels.

Policy preparation: For each Measurand and each Level for which the user expects to collect data, the user should define the Level names, Cutoff values, and IQC data in **RRE>Define Policies>Non-Hematology>Analyte Settings>TRU** tab.

- The Lab Result for each specimen is compared to the Policy Cutoff values for that Measurand, and the specimen is assigned to a Level based on that comparison. The IQC data used in the experiment is that for the corresponding Level.

Mode three: If the Level column is not available from the RRE-T file, and the user wishes to assign all specimens to a single Level.

Policy preparation: For each Measurand, the user need only define the IQC data for Level 1 in **RRE>Define Policies>Non-Hematology>Analyte Settings>TRU** tab; neither the Cutoff values nor the Level names are required

- All specimens will be assigned to an experiment with Level named “All”.
- All experiments will use the IQC data for level 1 for the Measurand.

The following errors can be encountered during RRE-T:

- You have Levels defined in your RRE-T file, but some of the Level names in that file do not match the Level names you entered into Policies. This will cause your experimental IQC data to be empty.
- You have Levels defined in your RRE-T file, and the Level names in that file match the Level names in Policies, but you failed to enter IQC data for some of those Levels. This will cause your experiment IQC data to be empty.
- You have Levels defined in your RRE-T file, but some of the Level cells are empty. This will cause an error message in the Activity Log.
- You do not have Levels defined in your RRE-T file, and you do have Cutoffs defined in Policies, but you forgot to define Level Names in Policies. This will cause experiments to be created with Level names of "Level 1", "Level 2" or "Level 3".
- You do not have Levels defined in your RRE-T file, and you do have Cutoffs defined in Policies, but you forgot to define IQC data in Policies. This will cause experiments to be created with empty IQC data.
- You do not have Levels defined in your RRE-T file, and you have entered no Policy data. This will cause experiments to be created with the Level name of "All" and with empty IQC data.

Chapter

39

File Operations Including Back up and Import/Export

This chapter deals with two major types of file operations:

- **File Manager (manages projects).**
  - Backing up and Restoring Projects.

    Backup saves a whole project to a single zip archive file. This is very useful for several reasons:

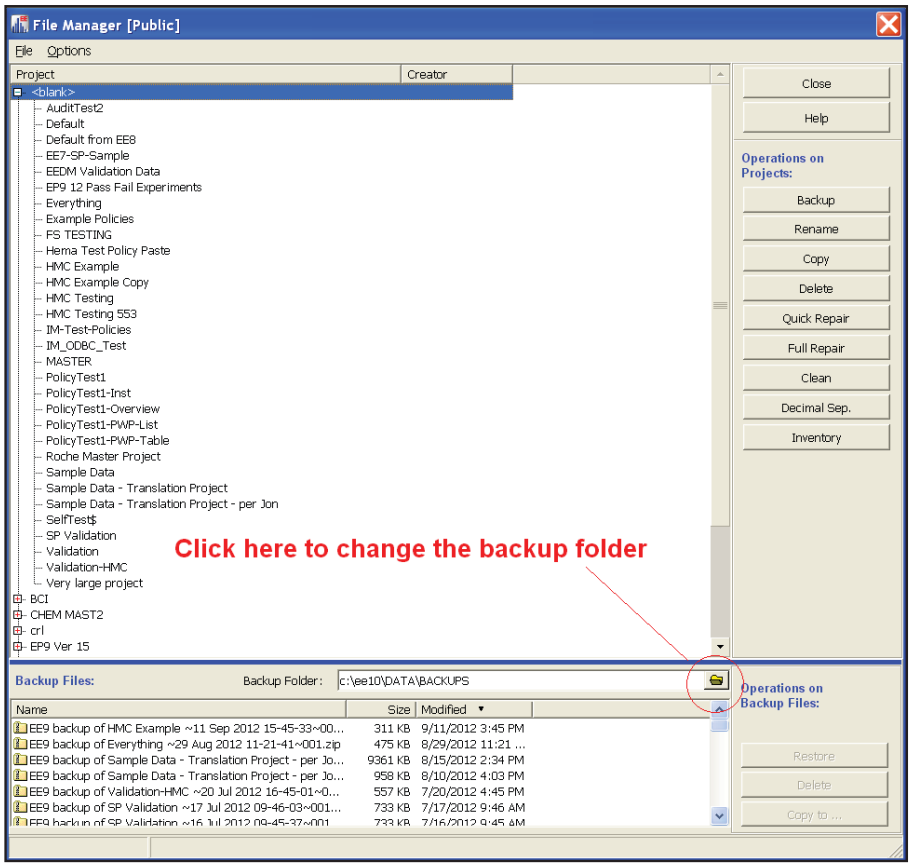
    - The data in the project can be readily transferred to other copies of EE.
    - The data in the project can be saved to external media for future reference.
    - The data in the project can be saved to other media so it can be recovered in case of machine failure.
  - Other project oriented operations which include renaming, repairing and deletions.
  - Conversion of projects created in US into European formats (and vice versa) so they will function properly there.
- **Creating files to transfer existing experiments to other applications**.

  In this case, individual experiments are saved to import/export (text) files on disk. This is useful for several reasons:

  - The content of the files can be transferred to other copies of EP Evaluator including older versions.
  - The content of the files can be imported into spreadsheets for manipulation there.

File Manager

The File Manager screen is organized into two panes. The top pane contains a list of projects. The buttons to the right of it represent operations you can perform on projects. Similarly, the bottom pane contains a list of backup files, and buttons to the right are operations that apply to backup files. Only one set of buttons is active at a time. For example, when you click a backup file in the bottom pane, all the project buttons are disabled.



Project Operations

To perform a project operation, first click the project name in the top pane. Then click the operation button. Note that you can only select an item at the second level of the outline (the individual projects), not parent items.

Backup

A backup file is a zip archive of EVERYTHING in a project – experimental results for all statistical modules and all the contents of that project's IMP-EXP and RRE folders. Once you have a backup you can safely delete the project. If you need to get it back, you can "Restore" it. Restore is one of the Backup File Operations described below.

Backed up projects created by EE4, EE5, EE6, EE7, EE8, EE9 and EE10 may be restored to EE11. Backups created in EE8 can be restored into EE6 and EE7 but

in no earlier releases (i.e., EE4 or EE5). Backups created in EE9 and later cannot be restored in any of the earlier releases.

Important Note The default folder for all backup files is **EE11\DATA\BACKUPS**. Other folders can be selected. Once you create a backup file, DO NOT RENAME IT. If a backup has been renamed incorrectly, EE will not be able to restore it.

Rename
lets you change the project name and client information.

Delete
permanently removes a project. This action is irreversible. If the project contains valuable data, make a backup before deleting it.

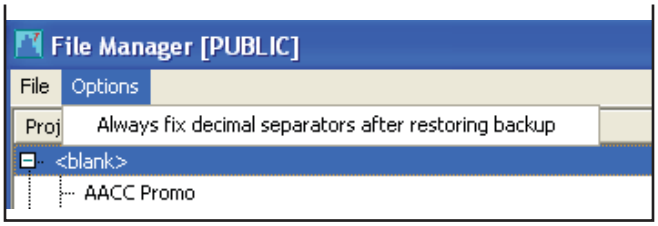
Copy
copies a project. This option allows you to save the copied project under a different project name.

Repair
A project's files may be damaged if you lose power while running EE, if you do not shut down Windows correctly, or if the program malfunctions. The Repair functions try to recover them. There are two kinds of repair: Quick and Full. Quick Repair is substantially faster than Full Repair. Its primary purpose is to make sure the field and table names in the databases are current with the software. Full Repair tries to fix more serious problems. If you get error messages that say "Header Corrupt," you need to do a Full Repair.

Clean
removes empty database files that may have accumulated in a project.

Decimal Sep
EE stores experimental results as strings instead of numbers. This means you see exactly what the instrument produced, even if it contains non-numeric characters. However, it also means that projects are not portable between computers in the US (where the "decimal separator" is a decimal point) and those in Europe (where it is a comma). Projects created on your computer will be built using your native decimal separator, as defined in the Windows control panel. These projects will work fine on your computer. However, if you send a backup file to a colleague in another country, s/he may need to convert it. Symptoms: results with fractional parts are excluded from analysis; if Allowable Error is defined in fractional units, experiments cannot be calculated due to "Missing Parameters."

- If you routinely receive backups from other countries, go to the Options menu item and check **Always fix decimal separators after restoring a backup**. When this item is checked, the conversion procedure will be run automatically each time you restore a backup. (Converting a project that is already consistent with your Windows convention is harmless.)



Inventory
shows you what experiments are in a project—handy if you want to check before deleting it.

Backup File Operations

To perform a backup file operation, first click the backup file in the bottom pane, then click the operation button. If the backup file does not appear in the list, use the Backup Folder selector to browse to the folder where it is located.

Restore
Re-creates a project from its backup file.

Delete
Permanently deletes a backup file.

Copy To
Copies a backup to a different directory (or to a different storage device such as a memory stick or a shared hard drive/server).

Import / Export

Use this facility to move individual experiments between various applications, including other instances and other versions of EP Evaluator and spreadsheets. The program saves Export files in the IMP-EXP folder under your current project. An Export file is an ASCII text file which has been especially formatted to contain most, if not all, of the data that has been entered for an experiment.

Export differs from backup in that:
- Export files are not version dependent.
- Export files for AMC, EP9, and QMC method comparison experiments do not contain linkage information. When you import the files later, you will have to indicate which is the X method and which is the Y method.

- While you can export multiple experiments with a single command, all of them must be from the same statistical module. In other words, you cannot export until you open a module.
- Microsoft Excel (and most other spreadsheets) can read the EE4 export files.

To Export One or More Experiments

- Open a statistical module. To export multiple experiments, you must be at the Module Overview Screen – the one that shows the module name in gray in the upper left corner.

- Select **File / Export / EE4** Format from the menus. If you are going to export your data for import into EECLIA or EE-DOS, then select "EE3 format" instead of "EE4 Format."

- The program will ask whether you want to export all experiments in the module or select by instrument or analyte.

- If you choose all experiments, the export begins immediately. Otherwise you will get a series of screens asking which Instrument, Analyte, and (for precision experiments) Sample to export.

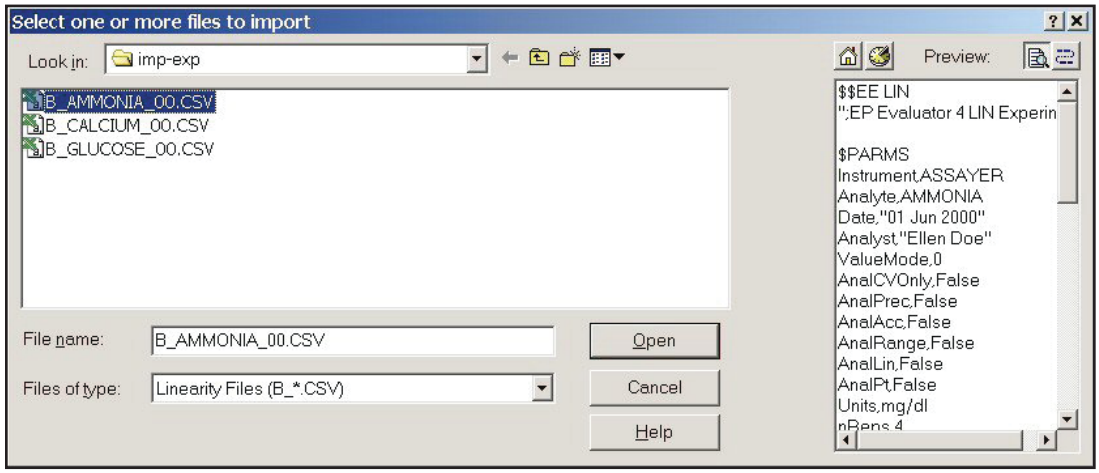
- On each screen, check the cases you want to export and click the **Next** button to continue. You must check at least one box on each screen or there won't be anything to export. If necessary, you can click the **Prev** button to go back and change your selections on the previous screen.

- When your selections are complete, the program asks you to confirm the list of selected experiments. If the list is correct, click "Yes" to create the export files. Otherwise, click "No" to quit without exporting anything.

To Import One or More Experiments

- Select **File / Import / EE4 Format** from the menus.

- The screen below displays the files available for import. If necessary, navigate to the correct folder.



The Preview Panel at the right gives a sneak peak of the file the cursor is on. Initially the dialog displays files in the last folder you used.

To select a consecutive range of files

- Click the first file name.
- While holding down the shift key, click the last file name. This highlights all the names between the first and last.
- Click the **Open** button to complete the operation.

To select non-consecutive files

- While holding down the Ctrl key, click each file name. Clicking highlights (selects) the file. Clicking a file that is already selected will de-select it.
- When you have highlighted the desired files, click the **Open** button to complete the operation.

Chapter

40

Professional Version: Security, User Groups and Audit Trails

This chapter describes the special features of the Professional Version of EE. These features come in three general categories: a) Security - Limiting program access to authorized users; b) Defining subgroups of users who can access specific projects; and c) Audit Trail features so labs can comply with 21 CFR Part 11 regulations.

Features Overview

User ID and password ensure that only authorized users can use the software. When security controls are in effect, EE requires each operator to enter a user ID and password at startup. In addition to allowing access to the software, the user ID controls which projects the operator can access.

- Passwords are case-sensitive and must be at least 6 characters in length.
- No user knows any other user's password. Even a system administrator does not know another user's password. (The initial password the system administrator assigns is temporary; the user must change it the first time s/he uses it.)
- There is no master password. If all system administrators forget their passwords, contact Data Innovations.
- A user is required to change his or her password after every 30 uses of the program.

Each user is assigned to a Group. Users within a group have full access to the group's projects but do not see projects belonging to other groups. (This is different from EE5 and EE6, where projects were owned by an individual user. In subsequent releases, projects are owned by a group.)

There are two classes of operators: system administrators and normal operators. A Normal operator ("user") can only access projects that belong to his or her group. A system administrator can access projects in any group and add or delete users.

Audit trails record the before and after value when an experimental result is changed, along with the operator who made the change, and the transaction date.

- Audit Trails are maintained only for modules that store experimental results. There is no Audit Trail for Performance Standards, or Six Sigma Metrics. Also, there is no audit trail for Average of Normals (AON) or the four Lab Management modules.

- The System Administrator can choose not to keep an audit trail for any project, or s/he can enable auditing for selected projects only. (For example, an audit trail is probably unnecessary for the Sample Data project.)

- Users cannot examine or modify audit trails; there is a separate Audit Viewer program that can be provided to auditors.

Operators

There are two classes of operators: users and system administrators. They have very different sets of privileges. The differences between them are what projects they can access and whether they can add other operators. There may be multiple users and/or system administrators.

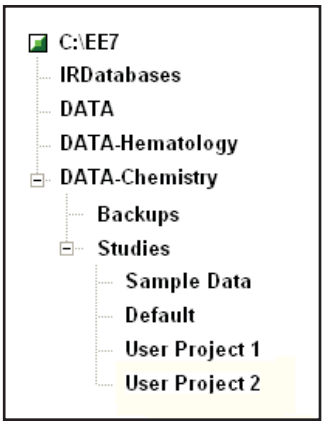
The person who turns on Security becomes the first System Administrator.

Table of Operator Privileges

Tasks	Users	System Administrators
Project Access	Only their own group	Any group
Add operators	No	Yes. Can add both users and operators
Enter results	Yes	Yes
Create projects	Yes, but only in own group	Yes, in any group
Audit Trails	No access	Can enable or disable audit trails in any project.
Modify MASTER project	No	Yes

Data Organization

In the EE Security model, users are divided into **Groups**. Each Group has a completely separate **Data Folder**. A Data Folder contains two sub-folders: Backups and Studies. The Studies folder contains a subfolder for each Project. So, with security in place, the installation folder is organized as shown in this figure.



In this example, the groups are Hematology and Chemistry. When you assign a user to the Chemistry group, that user is automatically pointed at the DATA-Chemistry folder when s/he logs in to EE. The [normal] user has full access to any project in his/her group's folder, including the ability to modify results and create new projects. However, the Chemistry user has no access at all (from within EE) to projects not in their own group. S/he may not even know that other groups exist.

Also, each group has its own MASTER project that holds Policies. These separate MASTER projects may contain different policies. When a Chemistry user creates a new project, that project inherits policies from the Chemistry MASTER. In effect, each Group behaves like a completely separate copy of EE.

The plain vanilla DATA folder is the "public" data folder that everybody sees before security is enabled. Once security is enabled, the DATA folder becomes a Group folder to which only security administrators have access.

If you disable security, all of the group data folders, and any projects within them, become invisible to everybody. Then all users of EE will see only the public DATA folder.

Folder location

The DATA and IRDatabases folders must be subfolders of the EE installation folder. The default location for other group folders is also as a subfolder of the EE folder. It is possible to place the group folders elsewhere on the network. The advantage of doing this is one of performance. Suppose the server is in Philadelphia and the user is in Chicago. If that user's group were also in Chicago, then access to that database could be faster. (This assumes the "fat client" server model. With a "thin client" server model, performance will be best if all the DATA folders are sub-folders of EE.)

However, keep in mind that doing this may require the data to be brought forward manually into future versions of EP Evaluator. To bring data forward, consult with Support at Data Innovations.

How should you assign the groups?

There are two extremes:

- You could put each individual user in his own separate group. That's likely to be a maintenance nightmare due, among other things, to staff turnover. If somebody leaves, you may have to move that person's projects to make them accessible to the replacement.

- At the other extreme, you could put the whole company into one group. Unless it's a small company, this probably allows too many people access to the same projects.

Two possibilities to consider: 1) set up a separate group for each department, like the Chemistry and Hematology groups in the example, or 2) in a geographically dispersed company, set up a separate group for each location (New York, Singapore, London).

System Administrators can access any group's projects

When you first log in to EE, you have access to your group data folder only. If you are a member of the Chemistry group, you have access only to projects that belong to the Chemistry group.

If you are a System Administrator, you can "switch" groups to gain access to projects that belong to a different group. To do this, use the Select Group command in the Security menu. Once switched, you can perform any operation on the group data that a group-member can.

The IRDatabases Folder

In addition to the group folders, every EE user has access to the IRDatabases folder. This folder holds databases for Incident Tracking. There is only one company-wide Incident Tracking database. In other words, Incident Tracking is not specific to either a group or a project.

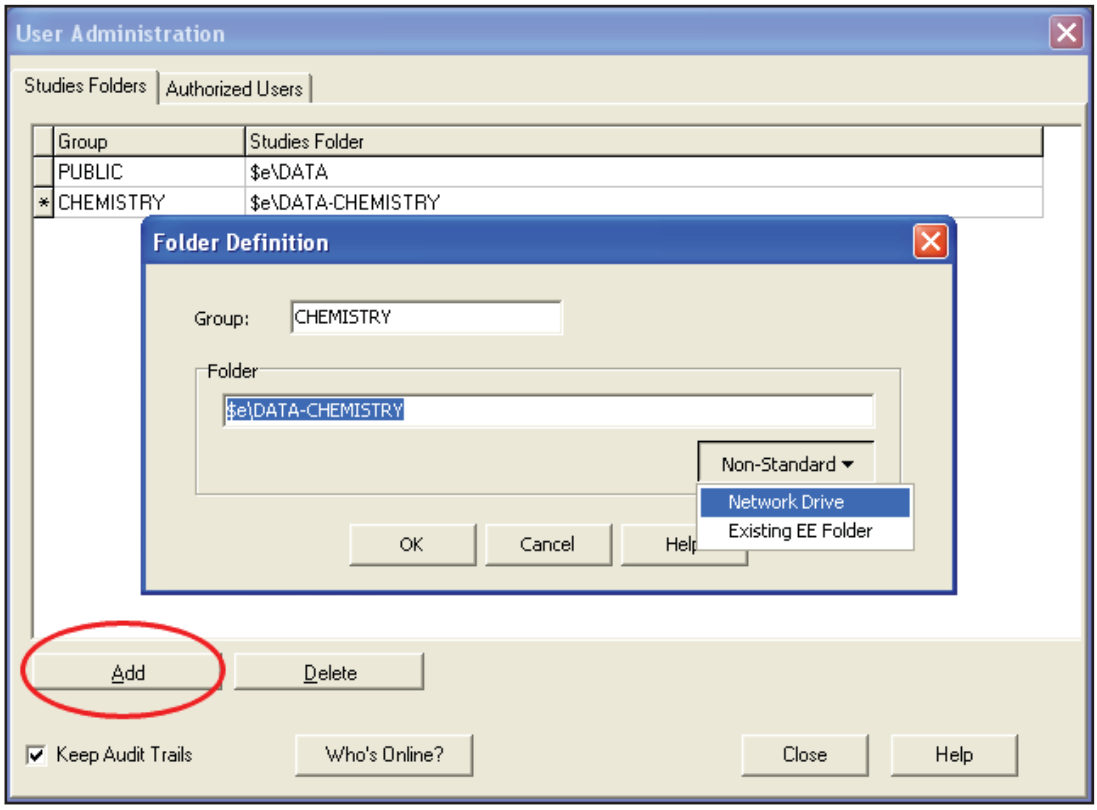
Enabling Security

To enable security, select File/Security/Add Security Controls from the EE menu. You will be asked to choose a name, user ID, and password for yourself. This defines the first System Administrator (i.e. the Primary Administrator) ID discussed in the Operator section above.

Clicking OK takes you to the Folder Administration screen.

Folder Administration

Before you can add users to the system, you must first add group data folders.



Click **Add** and you are prompted for a group name. If you add a group called CHEMISTRY, the default data folder for that group is $e\DATA-CHEMISTRY. $e is a place-holder for the directory where EE is installed.

By default, all data folders are placed under the EE directory. You can, with assistance from your network administrator, locate them elsewhere on the network. The network administrator must create the physical folder and assign appropriate permissions to it. You, as EE System Administrator, need full read/write/delete access to the folder. Also, all users in the group need full read/write/delete access. Click the **Non-Standard** button, and select **Network Drive** from the dropdown menu. Then choose the directory to assign. Make sure to select a directory that is NOT a descendent of the EE directory.

You could also assign the group to an existing EE data folder. This is usually not a good idea. When folders use standard naming convention, it is easier to remember which folder belongs to which group—something multi-group managers need to know to review the group's work.

Delete, which deletes a data folder, is also something to avoid if possible. First you must delete all users in the group. Even then, there is some risk of deleting good data.

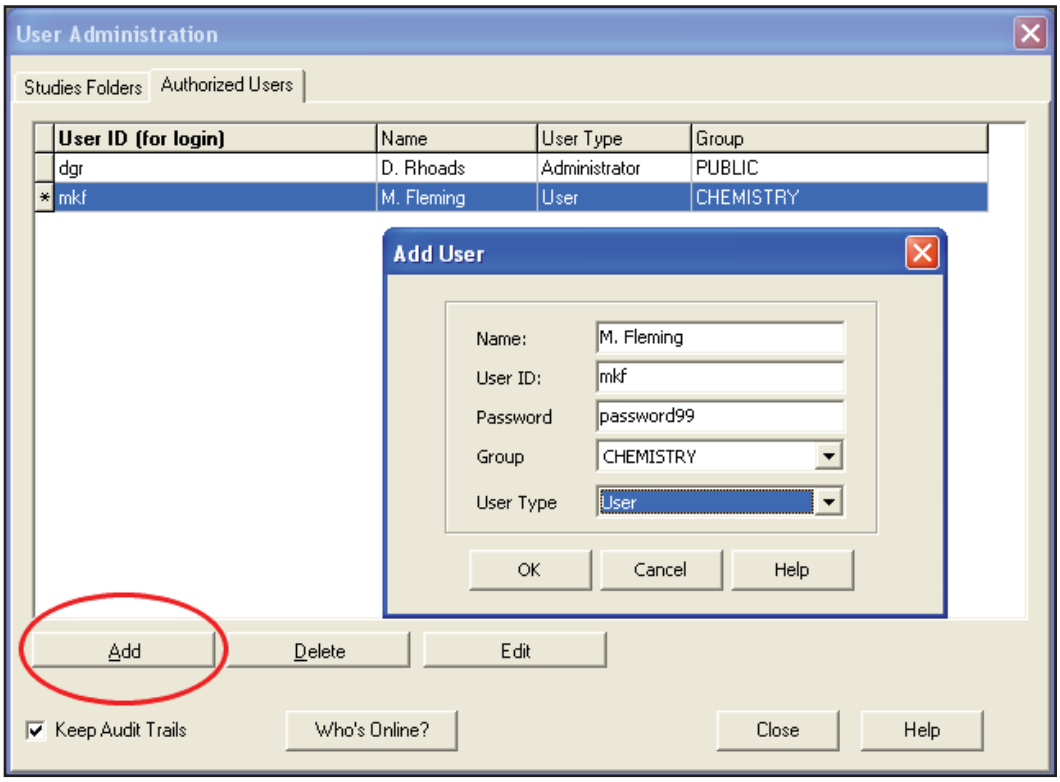
Before making any change that might affect a current user, use **Who's Online?** to see what users are currently using EE.

Check **Keep Audit Trail** checkbox to enable CFR 21 Pt 11 auditing system-wide. If this box is checked, System Administrators can disable auditing for specific projects. However, if the box is not checked, audit trails are totally unavailable.

When you finish adding data folders, the next step is normally to select the Authorized Users tab at the top of the page to add users. If you close the form without adding users, you are the only person who can run EE.

User Administration

The Authorized Users page of the administration screen is where you add, edit, or delete users. Remember that you must add the group folder before you can add a user to that group.



When you Add or Edit, the Add User dialog pops up as shown. Fields are as follows:

Name: User's name, as it will appear in Audit Trails. Names need not be unique. J. Doe could be in the system once as a System Administrator and a second time as a normal user. Maximum size of a Name is 12 characters.

User ID: ID the user enters when s/he logs onto the system. Unlike Names, User IDs must be unique. If J. Doe is in the system twice, he needs two different User IDs – like John1 for his system administrator ID and John2 for his normal user ID. Maximum size of a User ID is in excess of 25 characters.

Password: Preliminary password that will let the user into the software one time only. As soon as s/he logs in with this password, s/he is required to change it. If you assign a password that has been used recently, the program will ask for a different one.

Group: select from the list of assigned groups.

User Type: Select User or System Administrator.

When you **Edit** (as opposed to **Add**) a user, you can't change the Name or User ID. The most likely reason to Edit is to change the System Administrator status. However, you can also use Edit to issue a new preliminary password to a user who forgot his password.

Login Screen

If security controls are in effect, you must enter a User ID and Password to use the software. User IDs are issued by an EE System Administrator – usually the person who instituted the security system. The process works like this.

- The System Administrator assigns you a User ID and a preliminary password. This preliminary password allows you to login to EE just once.
- After you log in successfully, the program will prompt you to choose your own password. Nobody will know this password but you.
- After every 30 logins, EE will ask you to change your password.

Lost Your Password?

- See your EE System Administrator. S/he can assign you a new password.
- If you are the one-and-only System Administrator, contact Data Innovations for instructions. You may be charged a password recovery fee if you have had the software longer than 90 days.

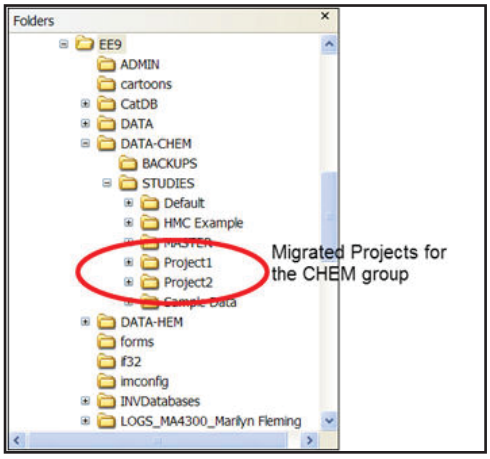
Migrating Data from Prior Versions

The data migration process for Professional Version is almost entirely manual. The two possible cases:

Case 1: Source is not Professional version of EE7, EE8, EE9, or EE10.

Migration source is Release 6 or earlier, or source is not Professional Version.

- Start EE11.
- Add Security Controls. Define User IDs, Passwords, and user Groups. You should have a folder on your hard drive for each group of users. For example
  C:\EE11\DATA folder for the PUBLIC group
  C:\EE11\DATA-CHEM folder for the CHEM group
  C:\EE11\DATA-HEM folder for the HEM group
- Close EE11.
- Examine the list of projects in the STUDIES folder for the EE release you are migrating from. Determine which projects you wish to migrate, who the project owner is, and which group that owner belongs to. Use Windows Explorer to copy each project from the source studies folder to the appropriate destination folder. When done, your EE11 folder should look something the illustration below. In this illustration, Project1 and Project2 are projects copied from the STUDIES folder of the old EE version to the STUDIES folder under DATA-CHEM in EE.

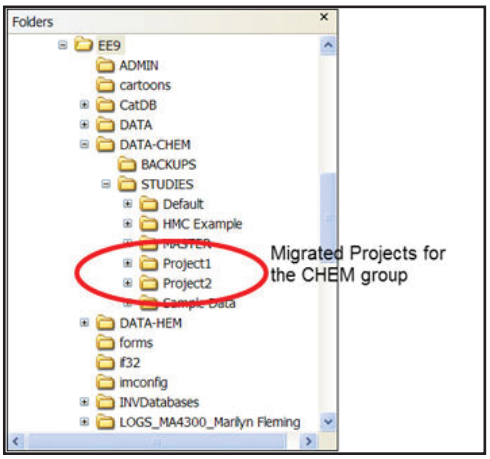


- Use Notepad to create a file called EE11INSTL.MRK in the EE11 directory. Contents of this file don't matter.
- Start EE11. Presence of the EE11EINSTL.MRK file will trigger a restructuring of all project files in the system. This makes the old data you copied compatible with EE11.

Case 2: Source is EE7, EE8, EE9, or EE10 Professional Version

The following text assumes you're bringing data forward from EE9. If you are bringing data forward from EE7, EE8, or EE10 simply substitute the appropriate version for "EE9".

- Install EE11. If you have previously installed security controls on EE11, remove them.
- Make sure EE11 is NOT running.
- Use Windows Explorer to delete the C:\EE11\DATA folder. Then copy the DATA folder and all DATA-groupname folders from C:\EE9 to C:\EE11. When done, the EE11 folder should have a structure similar to that illustrated at right.



- Run the utility program C:\EE11\OtherTools\ProMigrate.exe to copy User IDs from EE9 to EE11.
- If EE9 has any non-standard group data folders located outside the EE data structure, make a backup of those folders. They will be updated in place to EE11, and will then be unreadable by EE9.
- Use Notepad to create a file called EE11INSTL.MRK in the EE11 directory. Contents of this file don't matter.
- Start EE11. You will be asked to enter your User ID/Password from EE9. Presence of the EE11INSTL.MRK file will trigger a restructuring of all project files in the system. This makes the old data you copied compatible with EE11.

Chapter

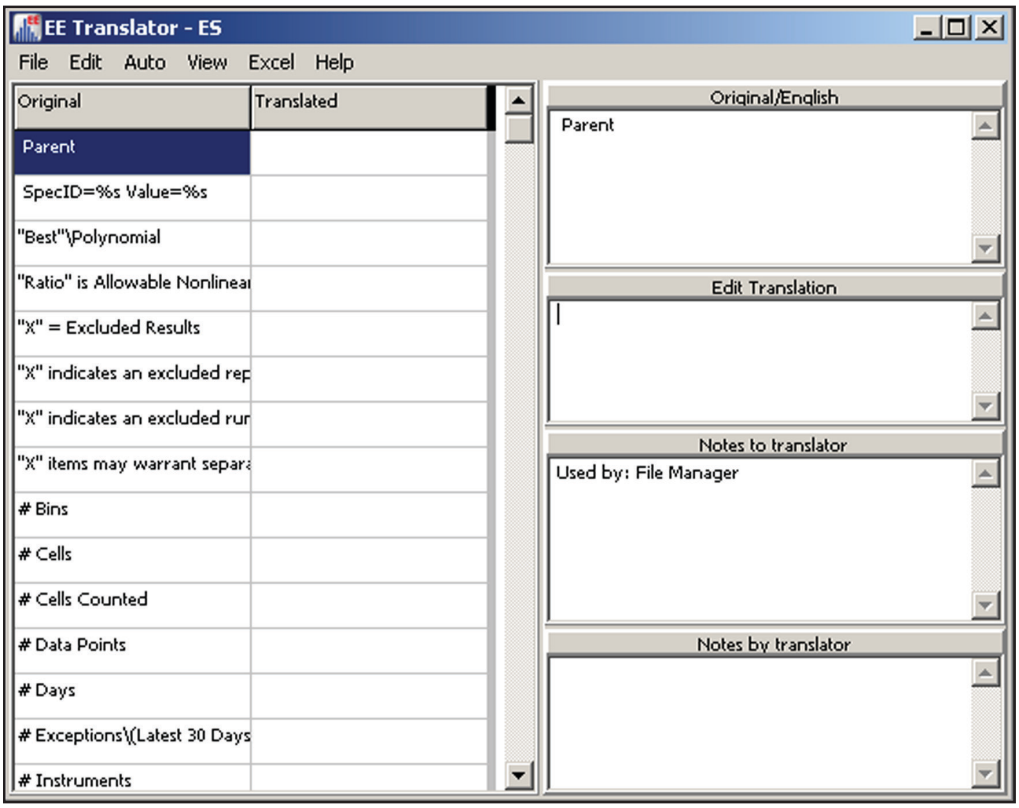
41

Translator

In a non-English locale, EE will attempt to run in the local language by looking for the appropriate language files. The EE software includes language files for French and will automatically run the French language files. For other languages, EE's attempt will fail until translation files are created. To translate the software into another language, EE ships with a program, Translator, which allows users to create the appropriate translation for their locale.

Translator

Translator.exe is the tool that manages translations. It can be found in the C:\EE11 folder, where EE is installed. Open the Translator program to access the **EE Translator window**. Creating new language file prompts Translator to load the this window with all translatable strings. See the section *Creating a New Language File in EE* later in this chapter.



The EE Translator window contains four panels:

- The field on the left displays a list of the original English strings once a new language file is created. Optionally, the translated strings can be displayed.
- The **Original/English** field in the upper right displays the original English string that is selected in the grid, including formatting characters.
- The **Edit Translation** field is where the translation of the original English string selected in the grid will be typed. If the text has already been translated, this field contains the translated text. This field never shows formatting characters.
- The **Notes to translator** field displays hints generated to help the translator understand how to translate the particular phrase.
- The free-text **Notes by translator** field provides a place for translators to add their own notes.

Use the mouse to scroll the grid or select an original English string from the grid. Navigate the grid via **Edit**, **Find**, or via **Edit, Next Untrans**, or move through the grid by use of Control +: <up arrow>, <down arrow>, <left arrow>, <right arrow>, <page up>, <page down>, <home>, and <end>. You can use Alt + C to copy the English text into the Translation Edit box. You can use Control + N to get to the next untranslated string.

EE English Language Files

Translator uses the existing English language files shipped with EE to create the files used for translating EE into another language. These files are reference files for the translation and should not be edited using a text editor.

- **EN.PO** is a text file containing the original English text used in the EE screens. This file contains both static (labels) and dynamic (generated at run-time) text.
- **DRLS-EN.PO** has the same format as the EN.PO, but contains static strings found in the reports.
- **C:\EE11\FORMS\EN** is a folder than contains the report layout files for the English reports.

Each time a new release of EE is distributed, the contents of the EN.PO file, DRLS-EN.PO, and the FORMS\EN may change due to changes in the EE program.

Translation Files

When a new language is to be supported, the following files will be created by the EE Translator. The list below provides an example of the files created by Translator assuming the new language is Spanish and the new language abbreviation is ES.

- **ES.PO** contains the original English text for use in translating EE into a non-English language. Once the translation is complete, this file will also contain the translated Spanish text.

- **ES.MO** is a compressed/binary form of the ES.PO file. This is the file actually used by EE to translate the software.
- **DRLS-ES.PO** contains the original English for the report layout files. Once the translation is complete, this file will also contain the translated Spanish text.
- **C:\EE11\FORMS\ES** is the folder that contains the report layout files, modified and saved to contain the Spanish content from the DRLS-ES.PO file. These are the files that EE uses at run-time to generate the reports when using the Spanish language.

EE Translator Menu Items

File

New creates a new set of language files by copying the English language files, renaming the copied files to reflect the user configured language abbreviation, and also creates a language FORMS folder where the new language files will be placed.

Open allows you to open language files and begin translating text from the EE software in the EE Translator program.

Save will save the current edits in the language files (e.g. ES.PO and DRLS-ES.PO). **Save** will also create the file EE uses to translate the software (e.g. the ES.MO file) and update all files in the FORMS\ES folder.

Save As creates a new set of language files and then saves the current edits there.

Delete will delete all of the files associated with a given language.

Edit

Find allows users to find text in the untranslated, English string of text.

Filter allows users to filter strings based on user-entered text.

Next Untrans moves to the next untranslated English string in the Original/English panel. If new English strings have been added since the last time the file was translated, **Next Untrans** will immediately find the new strings for translation.

Next Size finds the next translated string that appears bigger or smaller than it should be.

Copy Original copies the original/English string to the translation area on the right side of the EE Translator window.

Insert NTS inserts [NTS000] into the translated text. NTS stands for non translatable string. More information about NTSs is provided later in this chapter.

Scan DRLs for "^" scans all DRLs to verify that the "^" command sequences used are legal.

Draw Pictogram Characters will, if checked, cause the characters in the current language to be drawn with strokes when creating a PDF; this is required for some languages, such as Chinese.

Auto

Copy copies the original/English strings to the Translation Edit panel for every string in the grid.

NOTE: The Translator program views the text populated into the Translation Edit panel as a translation. Because **Auto**, **Copy** populates this panel for every original string, it becomes impossible to find the next untranslated string of text once you use this facility.

View

Just Original, when checked, will display only the original English strings in the grid on the left of the EE Translator window.

Original Translated, when checked, will display the original and the translated text, side-by-side, in the grid on the left of the EE Translator window.

Excel

Export creates an ES.XLS file for editing in Excel. The Excel spreadsheet contains the following four columns:

- The original English string
- The original English text in NTS format
- A placeholder for the to-be-translated Spanish string, in NTS format
- Any comments/hints available about the string to help the translator

Import reads an ES.XLS file and creates a new set of strings in EE Translator, used by the EE software.

Help

Translation Help explains how the Translator program works.

User Interface Hints shows a list of key combinations that you can use in the Translator program.

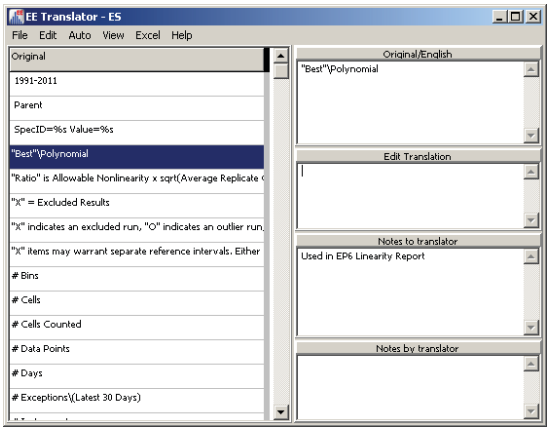
Creating a New Language in EE

Using the EE Translator window

1. Open the Translator.exe program found in the C:\EE11 folder.
2. From the **EE Translator window**, select **File**, **New**.
3. Enter a language name into the New Language Abbreviation dialog and click OK.

NOTE: When naming the language, remember that EE will automatically attempt to correlate the current locale with the existing language files. Name the new language in a way that will make it easy for the software to do this.

4. Click **OK** on the dialog window which appears stating that the language files have been added. The original/English text is loaded into EE Translator.



5. Begin translating text using the **Edit Translation** box once the original/English text strings are loaded into EE Translator. Use Control + <down arrow> to get to the next string.
6. Use **File**, **Save** to save your work.

Using Translator's Excel Feature

1. Use **Excel**, **Export** to create an XLS file for editing in Excel.
2. Translator places the Excel file in the C:\EE11 folder. Browse to the file and open it to perform the translation.
3. Save your work.
4. Use **Excel**, **Import** to import the translation into Translator.

Once imported, the translation is available for use in the EE software.

Limits of Translation

Almost all of the screen contents of EE should be translatable, including form titles, grid column headings, informative messages, etc. Those that cannot be translated include:

- Special strings ("EP Evaluator", "Data Innovations", etc).

- Data from the database. If the user chooses to enter analyte names in a non-English language, that is fine. The names of the standard data projects (Default and Sample Data projects) will continue to remain in English. Someone could take the time to convert the data in the standard data projects into another language, but this would just be another project; it would not be a standard data project. Note that the standard data often uses unrealistic names for instruments, such as "X Meth": in this case, it is correct that "X Meth" is not translated.

- In a few cases, screen data is not translated. For example, RRE, Define Policies, Modules and Options. If you expand the tree, each line consists of three fields: the left text field, a middle descriptive field, and a right user-entered

value field. Of these three, the left one cannot be translated (because it is in fact equivalent to a database field name), the middle one can be translated, and the right one can be translated ("Y/N" can be translated to "O/N" in French, for example).

- The import/export file formats, including the RRE data formats, found in the EE Resources folder, will not be translated, even though there are column and row headings such as "Spec ID" and "Analyte". Translating these would make it difficult to provide support for people who use those file formats in other languages. Any such input file should be processed correctly by EE no matter what the localization might be. Some of the words in this format are in English and EE does not support their translation into other languages.

- The Lab Module names or programs (Simple Inventory, Incident Tracking, Competency Assessment) will not be translated.

- While IM_ODBC has been translated, the other utility programs will not be translated: AuditVu, EEFileChecker, ProMigrate, PTemplate, PUnitsConv, and Zipper.

Non Translatable String (NTS)

Many of the strings used in EE contain portions that should not be translated; they are termed Non Translatable Strings (NTSs). Examples include "format strings" (like "The %s Project contains %n experiments") and report layout strings ("<<Analyte>> passed the Accuracy test"). At run time, "New Instrument" might be substituted for "%s", "18" for "%n", and "Glucose" for "<<Analyte>>". The translator should not modify the "%s", the "%n", and the "<<Analyte>>" values, because doing so will cause the program to malfunction.

To protect against malfunction, these strings are presented to the user for editing in a different format than the original string. Thus, the original string,

"The %s Project contains %n experiments"

is presented to the user for editing as,

"The [NTS000] Project contains [NTS001] experiments".

The translator can modify the non-NTS text, after which the Translator program reconstructs the translated text, substituting "%s" for "[NTS000]" and "%n" for "[NTS001]". In addition, the translator can reorder the NTS:

"[NTS001] experiments were found for Project [NTS000]".

Text formatting for reports is supported by a variety of embedded formatting symbols ("^p" to start a new paragraph, "^b" to make text bold, etc). Those symbols are also converted into NTSs for the translator, and those symbols can be re-ordered. The Translator program provides hints in the **Notes** panel about the

meanings of these symbols as each string is edited. Similarly, the exported Excel spreadsheet contains these same hints.

Never add or remove NTSs from format strings. NTSs can be removed from report layout paragraphs, although that should not be necessary.

Newly created languages start out with the translated column empty. You can use **Edit, Copy Original** to copy the original/English text into a particular translated cell or **Auto, Copy** to copy all rows in the grid.

The Translator program views the text populated into the Translation Edit panel as a translation. Because **Auto**, **Copy** populates this panel for every original string, it becomes impossible to find the next untranslated string of text.

The text is presented to the user in this NTS format in the edit box in which they enter their translations, as well as in the file that is exported to Excel. Erroneous translations (NTSs not found, etc.) are refused in the Translator, and cause fatal errors during Excel import. These errors can only be resolved by fixing the import file and re-trying the import. The Translator program protects you by ensuring that each translation is correct as you exit the row.

Translator's Notes

Handling Ampersands

Some strings are used as menu or button captions (e.g., OK, Cancel, Help). Sometimes the ampersand character is used to tell Windows which characters to use as hot keys. For instance, "Save &As" tells Windows to use "A" as the hot key. You can supply an ampersand in your translation, or remove it, as you see fit.

Single and Double Character strings

A number of single and double character strings are used throughout EE. For example, the character "X" is often used as a flag to indicate that a result is excluded. "X" is also used to distinguish between the two methods (instruments) used in a Method Comparison experiment (X vs. Y). While we could translate "X", this translation would take effect for both meanings of "X" (exclusion and the X Method). Because of this, EE does not allow such strings to be translated. These strings are also often described, either on screen or in footnotes in the reports ("X: excluded result"). Though the footnotes should be translated, the double and single character flag values should not be translated.

Below is a list of these flags, their meanings, and a grid detailing the modules where they are found.

- X: Excluded; excessive T value (EP10)
- O: Outlier; exceeds allowable non-linearity (EP6); out of range (POC)
- FP: False Positive (QMC)
- FN: False Negative (QMC)
- F: Value exceeds allowable error; outside proposed reference interval (INR-GEO)

- T: Target Instrument(MIC)
- S: Day does not have full complement of results (CP)
- L: Below limits (AON)
- H: Above limits (AON)
- N: unusual "N" (AON)
- R: out of range flag used generically throughout the MC StatMods

Stat Mod	X	O	FP	FN	F	T	S	L	H	N
2IC	Yes	Yes								
6-Sigma										
AMC	Yes									
AON	Yes							Yes	Yes	Yes
CO										
CP	Yes	Yes					Yes			
CPT										
EP6	Yes	Yes								
EP9	Yes	Yes								
EP10	Yes									
ERI/ ROC	Yes									
FS	Yes									
HIS	Yes									
HMC	Yes		Yes	Yes						
IF	Yes									
INR-CK										
INR-Geo	Yes				Yes					
INR-MC	Yes									
LIN	Yes									
LOD	Yes									
LOQ	Yes									
MIC	Yes				Yes	Yes				
Perf Stds										
POC Glucose	Yes	Yes								
QMC	Yes		Yes	Yes						
SA	Yes									
SP	Yes	Yes								
STB	Yes									
VRI	Yes									

Name Collisions

A number of name collisions occur within EE. For example, “Y”: “Yes” vs. “Y Method”; “N”: “No” vs. “Negative” vs. “INR” vs. “the number of results used in a statistical calculation”; “X”: “Excluded” vs. “X Method”. These are handed in the following manner:

- The “X” string refers to the “X Method”: it cannot be translated.
- The “Y” string refers to the “Y Method”: it cannot be translated.
- “Y” for “Yes” and “N” for “No” are encoded as a single string, “Y/N”, which must remain 3 characters long, with the first character representing “Yes” and the third character representing “No”. So, for example, in German this might be “J/N” and in French, “O/N”.
- “P” for “Positive” and “N” for “Negative” are encoded as a single string, “P/N”, which must remain 3 characters long, with the first character representing “Positive” and the third character representing “Negative”.
- “P” is sometimes used to mean Protime, with “N” used to mean INR. We do NOT allow this to be translated. The string “*Coag Flag (for Coag modules): P=Protime, N=INR, A=aPTT” needs to be translated so that “P” and “N” and “A” are not changed/translated.
- The “N” string refers to the number of results used in a statistical calculation.
- One string (“X;”) is used to convert Boolean values into Exclusions (“X” for TRUE, “” for FALSE). There are quite a few other strings that refer to X and Exclusion. You may not translate “X”.

Glossary

“df” means “degrees of freedom”

“BT” stands for “Billable Test”

“NLa” stands for “non linearity allowed”

“PT” means “Proficiency Testing” in the non-Coag and non-INR parts of EE, while it means “ProTime” in the Coag modules. Because context is important for “PT”, we have not made “PT” and “aPTT” translatable in the Factor Sensitivity module, for fear that any translations relating to Proficiency Testing might cause the Factor Sensitivity values for “PT” and “aPTT” to become incorrect.

“Factor” is a technical jargon when used in the Coag field, but can have the normal English meaning other places. We have not made the various Factor names (Factor II, Factor V, etc.) translatable in Factor Sensitivity.

“Normal” can refer to a “normal Gaussian distribution of data” or it can refer to “test data from a normal [healthy] patient”. The latter meaning is mostly found in VRI, ERI, and ROC.

"Mean" can refer to the statistical concept (average) or have the regular English meaning ("this would mean that the test had to be repeated").

"Sy/x", **"Sy/x"**, **"sy.x"**, **"S.E.E."**, **"SEE"**, **"Std. Err."**, and **"SE"** can be used to mean "standard error of the estimate". "SE" can also be used for "systematic error".

Miscellaneous

- Some of the strings used in report layouts will contain embedded "\" characters (like "# Phases\per BT"): these characters are used to control how a column header is split to make multiple lines in a cell. Do not remove these formatting characters.

- Some of the strings used on forms span multiple lines; you should preserve the width of the lines and the number of lines so as to ensure that the translated string fits correctly on the form.

- In EP10, the user is given a choice between "Calc from total error" and "Assign by conc", (either "C" or "A", respectively). In RRE, Define Policies, Modules and Options, the user is presented with "Allowable Error: C=Calc from error budget; A=input by conc". There is also a translation string of "C/A". All of these must be edited to be consistent.

Selecting Languages in EE

EE tries to use the current local language if it is available. For example, in France, if a FR.MO file can be found, it will be used automatically.

In addition, the user can go into **Files**, **Preferences** to change their default language on the **Other** tab. Thus, a user on a machine with French regional settings could choose to translate EE into Spanish or German through the use of Preferences.

Finally, if a command line parameter is found, it overrides all of the above. Thus, a user could create a shortcut to EE and add the command line parameter "ES" to force EE to run in Spanish whenever that particular shortcut was used, even if in France and even if the preferred language was set to German.

Appendix

A

Published Performance Standards

Two sets of performance standards are listed here. The first set is the proficiency testing (PT) limits were defined for quantitative assays by the CLIA ‘88 regulations published February 28, 1992. Many labs, primarily in the US, are required to abide by these values. The second set are specified by national or governmental organizations.

Semi-quantitative or qualitative analytes are not included. In some jurisdictions, other PT limits may apply. Unless otherwise specified, the lower and upper PT limits are obtained by subtracting and adding the specified quantity to the target value.

We have provided these lists for your information and convenience. While we have checked them for errors, we do not guarantee that the lists are either complete or accurate.

CLIA ‘88 PT Limits

General Immunology

Analyte Name	PT Limit
Alpha-1 antitrypsin	± 3SD
Alpha-fetoprotein (tumor marker)	± 3SD
Complement C3	± 3SD
IgA	± 3SD
IgB	± 3SD
IgG	± 3SD
IgM	± 3SD

Chemistry

Analyte Name	PT Limit
Alanine aminotransferase (ALT/SGPT)	± 20%
Albumin	± 10%
Alkaline phosphatase	± 30%
Amylase	± 30%
Asparate aminotransferase (AST/SGOT)	± 20%
Bilirubin, total	± 0.4 mg/dL or 20% (greater)
Blood gas pO2	± 3 SD
pCO2	± 5 mm Hg or 8% (greater)
pH	± 0.04
Calcium, total	± 1.0 mg/dL
Chloride	± 5%
Cholesterol, total	± 10%
Cholesterol, high density lipoprotein	± 30%
Creatine kinase (CPK)	± 30%
Creatine kinase isoenzymes	MB elevated (presence or absence) or Target value ± 3 SD
Creatinine	± 0.3 mg/dL or 15% (greater)
Glucose (excluding glucose performed on monitoring devices cleared by FDA for home use)	± 6 mg/dL or 10% (greater)
Iron, total	± 20%
Lactate dehyrogenase (LDH)	± 20%
LDH isoenzymes	LDH1/LDH2 (+ or -) or Target value ±30%
Magnesium	± 25%
Potassium	± 0.5 mmol/L
Sodium	± 4 mmol/L
Total protein	± 10%
Triglycerides	± 25%
Urea nitrogen (BUN)	± 2 mg/dL or 9% (greater)
Uric acid	± 17%

Endocrinology

Analyte Name	PT Limit
Cortisol	± 25%
Free Thyroxine	± 3SD
Human Chorionic Gonadotropin (HCG)	± 3SD positive or negative
T3 Uptake	± 3SD
Triiodothyronine	± 3SD
Thyroid-stimulating hormone (TSH)	± 3SD

Thyroxine	± 20% or 1.0 mcg/dL (greater)

Toxicology

Analyte Name	CLIA '88 PT Limit	NYSPT Limits 100% credit	NYSPT Limits 50% credit
Acetaminophen	not stated	± 15%	± 20%
Alcohol, blood	± 25%	± 10%	± 15%
Blood lead	±10% or 4 mcg/dL (greater)	not stated	not stated
Carbamazepine	± 25%	± 15%	± 20%
Digoxin	± 0.2 ng/mL or 20%(greater)	± 0.2 ng/mL or 15% (greater)	± 0.3 ng/mL or 20% (greater)
Ethosuximide	± 20%	± 15%	± 20%
Free phenytoin	not stated	± 20%	± 25%
Gentamicin	± 25%	± 15%	± 20%
Lithium	± 0.3 mmol/L or 20% (greater)	± 0.2 mmol/L or 15% (greater)	± 0.3 mmol/L or 20% (greater)
Phenobarbital	± 20%	± 15%	± 20%
Phenytoin	± 25%	± 15%	± 20%
Primidone	± 25%	± 15%	± 20%
Procainamide / NAPA	± 25%	± 15%	± 20%
Quinidine	± 25%	± 15%	± 20%
Tobramycin	± 25%	± 15%	± 20%
Theophylline	± 25%	± 15%	± 20%
Valproic Acid	± 25%	± 15%	± 20%
Vancomycin	not stated	± 15%	± 20%

New York State has two levels of compliance. They differ in that the PT results inside the tighter one gets 100% credit while results not exceeding the looser one gets only 50% credit. This only affects grades for New York, not for CLIA '88 purposes.

Ref: Wadworth Center TDM Requirements (2009)

Hematology

Analyte Name	PT Limit
White blood cell differential	± 3 SD based on the percentage of different types of white blood cells in the samples.
Erythrocyte count	± 6%
Hematocrit (excluding spun hematocrits)	± 6%
Hemoglobin	± 7%
Leukocyte count	± 15%
Platelet count	± 25%
Fibrinogen	± 20%
Partial thromboplastin	± 15%
Prothrombin time	± 15%

Medical Requirements

The following values were developed by task groups created by the NIH. In all cases, TEa is defined as bias + 2*CV.

From NCEP (NCEP - 1995).

Analyte Name	PT Limit
Cholesterol	9%
HDL Cholesterol	13%
LDL Cholesterol	12%
Triglyceride	15%

From NKEP (Meyers et al - 2006)

Analyte Name	PT Limit
Creatinine	7.6%

From CAP limits as reported by NGSP (2009)

Analyte Name	PT Limit
HbA1c (for 2009B survey)	10%
HbA1c (for 2010 surveys)	8%
HbA1c (for 2011 surveys and beyond)	7%

Appendix

B

EP Evaluator Resources

Many resources are provided for EP Evaluator. In addition to this User's Manual, some can be found on our website (datainnovations.com) and some in the EE Resources folder. These resources (and their locations) are listed below. Note that you can navigate to all the website items from the main page of the website. The EE Resources folder is created when EP Evaluator is installed on a PC and is located under the EE folder at EE11\Resources.

Training

Data Innovations provides training in the use and interpretation of EP Evaluator in addition to the resources listed below. (All training resources are subject to change.)

- **Tutorial**. A short tutorial describing the basic concepts in EP Evaluator. It may be accessed from the Statistical Module screen. Make sure that when you are done with it, you close it because it intercepts all the keystrokes. and EE will appear not to work.

- **Live, interactive, free webinars**. Depending on the subject, these are given on a weekly or monthly basis. You need a PC that can receive data from a website and a telephone. The presence of EE on your PC is not a requirement. Access the Data Innovations' website for details.

- **Live On-site Training workshops.** Live, instructor-led training can be arranged upon request. Contact northamerica-sales@datainnovations.com to request a quote for purchase.

- **EE Help Facility**. Help is available for all modules and functions in EE. You may access it by clicking on the Help button available on many forms, by touching the F1 key, or by clicking on the Help item on the horizontal menu.

Policies Established by Others

Performance Standards (TEa)

- List of CLIA '88 Performance Standards
  - Appendix A - EE User's Manual
  - http://westgard.com/clia.htm
  - From within EE, click on Tools, CLIA PT Limits.
  - When running EE, click on open book in Tray (near your system clock) and a menu similar to that shown under Tools will appear.

- Rilibak Performance Standards from the German Federal Medical Council
  - http://westgard.com/rilibak.htm (listing of values)
  - http://westgard.com/rilibak-2.htm (approach used to establish the values)

- Complete Federal CLIA Guidelines
  - http://www.phppo.cdc.gov/clia/regs/toc.aspx
    - The CLIA '88 PT limits are spelled out in sections 493.927 (General Immunology), 493.931 (Chemistry), 493.933 (Endocrinology), 493.937 (Toxicology), and 493.941 (Hematology including CBC and coagulation).

- Interpretative CLIA Guidelines (instructions for lab inspectors)
  - http://www.cms.hhs.gov/CLIA/downloads/apcsubk1.pdf

- List of Nationally (in USA) established Performance Standards (Appendix A - EE User's Manual)

- Comprehensive list of Performance Standards from eight sources (http://www.datainnovations.com/products/ep-evaluator/allowable-total-error-table).
- Biological Variation Data. (http://www.westgard.com/biodatabase1.htm).

Reference Intervals

- Reference interval data drawn from several sources. (http://www.datainnovations.com/products/ep-evaluator/reference-interval-tables)

Categories of resources here include Master Projects which include examples of Policies both for hematology and non-hematology, and spreadsheets of data which can be imported into EE.

Spreadsheet Examples

Spreadsheets giving direction (and example data) for importing results into EP Evaluator. These files are all in the Resources folder.

- **PasteERIList.xls** (Paste into the ERI screen.)
- **PasteERITable.xls** (Paste into the ERI table.)
- **PasteExptDetail.xls** (Paste into the Experimental Detail Screen)
- **PasteParmsInSS.xls** (Paste into the Module Overview Screen and the policies are included in the spreadsheet).
- **PasteWithPoliciesList.xls** (Paste into the Module Overview Screen, data is in list format. Policy Definitions exist in EE.)
- **PasteWithPoliciesTable.xls** (Paste in the Module Overview Screen. Data is in table format. Policy Definitions exist in EE.)

Master Projects

The comprehensive use of Policy Definitions requires that Master Projects be set up. We have provided a model for a single Master Project. It is named Example Policies. It is available in two locations both as EE backup files, in the EE10\Resources folder and in the default Backups folder (EE11\DATA\Backups).

- Under the Non-Hematology tab, there are proposed policies for about 30 analytes for chemistry, toxicology, immunoassay and respiratory therapy. They are present in both US and SI units.
- Under the Hematology tab is a comprehensive list of policies for HMC.

Hematology Method Comparison (HMC) Tutorial

Defining HMC policies is one of the more complex tasks in EE as Policy Definitions have to be created before HMC can be used. Three files are available:

- HMC Tutorial: A project with data to show how it works.
- HMC Policies: Contains a comprehensive list of HMC policies. (EE9 Backup of ExamplePolicies).
- Spreadsheet of data (HMC Example.xls) which can be easily imported. (EE Resources).

RRE Field Codes

- List of field codes (identifier for a row of data) for import into EE. This is only needed if you are creating the spreadsheet file from scratch. (EE11 Resources folder. File name is: RRE Field Codes.xlsx)

RRE Worksheet Reference

- The RRE Field Codes worksheet documents which database fields are acquired from Policies for each StatMod during RRE. Additionally, this document details the link between the Policies user interface and the database field names and the Paste into Overview field names. (EE Resources folder. File name is: e9Res-rreWsRef.pdf)

LIS Export File Formats

- Description of the formats needed for files to be imported into EP Evaluator for Average of Normals (AON) and Incident Tracking. (EE10 Resources folder. File name is: e9Res-LISFormats.pdf)

Other

Technical Notes for Network Administrators

This item will appear three places:
- EE User's Manual, Appendix C.
- EE QuickStart Guide
- Resources folder. File name is: ace9-TechNotes.pdf

CLSI Documents

Several CLSI (Clinical and Laboratory Standards Institute) documents are referenced by EP Evaluator. These documents may be purchased from CLSI.
Phone: 610-688-0100.
E-mail CLSI at customerservice@clsi.org.

Validation

Two validation resources are presently available. Others may be added later.

- A **Validation Program** compares the report contents of the current release of EE with those of a previous version and reports any significant differences. The purpose of this program is show differences between versions so users who have already validated the calculations in EE will not have to manually review all the reports when they adopt a later release. This program may be purchased from Data Innovations. Data Innovations currently plans to have just one release of this program that may be used not only to compare outputs from EE10 to previous releases (EE4 through EE8), but for later releases as well (EE9 et seq).
- **Self-test**. A facility has been added to EE (click on **Files**, **Self Test**) to check the accuracy of calculations. This facility performs a limited number of calculations for all modules except Incident Tracking, Inventory Management and Competency Assessment, then compares those results to known answers to determine whether those calculations are correct.

Inventory Management Materials

A file describing the Inventory Management materials (i.e. bar code scanner and labels) is present in the EE11 Resources folder. File name is: e8Res-InvMan-Materials-Oct2007.pdf. The Help file for the Inventory Manager module in EP Evaluator also contains information about the availability of materials.

TEa Simulator Program

A TEa Simulator Program is provided in the EE11 Resources folder. It nicely illustrates the effect that varying amounts of bias and imprecision can have on the percent of results that will be outside the TEa limits.

Appendix

C

Technical Notes for Network Administrators

This appendix deals with several issues of interest to Network and Computer administrators.

Specifications

EP Evaluator has very simple requirements. Only one executable is shipped. Consequently, the same program is installed for a single desktop license or on a server supporting 50 concurrent users. The server has the role of a large remote hard drive. Unless a thin client is used, the CPU for the application is the one on the user's machine.

Operating Systems: The following have been tested and are satisfactory.

Windows:
32 bit Windows operating system (XP, Windows 7).
64 bit Windows operating system (Server 2008, Windows 7).

Space Requirements: The hard disk requirements of the program as initially installed is less than 200 MB. If the users generate lots of data (hundreds of projects), the total size may get as large as 1 to 2 GB.

Network Servers: The role of the server is normally that of a large remote hard drive. Consequently the type of server is not important. The server may be Windows, Linux, Unix or Novell. It may also work on other systems.

Database Engine: The database engine (DBISAM) is included in the executable. Consequently there will be no conflict with other database applications on the server.

System Requirements

Hardware and software requirements for EE11 are listed below.

- An IBM compatible PC with a Pentium CPU or above.
- A 32-bit Microsoft Windows operating system (XP, Windows 7).
- A 64-bit Microsoft Windows operating system (Server 2008, Windows 7).
- A minimum of 128 MB of RAM.
- Screen resolution: 1024 x 768 and larger.
- A minimum of 200 MB of space on the hard drive.
- An available printer, either local or networked.

Access Requirements

- The Setup package does not install anything to Windows System folders; it does not register any controls, DLLS, or ODBC connections. If absolutely necessary, you could completely remove EE from the computer by removing the folder it is installed in. (This is not the recommended procedure, since the program would remain in the Add/Remove Programs list, shortcuts would remain on the desktop, and the user's data would be removed along with the program.)

- Once unlocked, EE only "writes" to three places on the computer: 1) the directory is installed in, 2) the user's Application Data folder, and 3) The HKEY_CURRENT_USER area of the registry. (Exception: with the Professional Version, it is possible to move user-data to a location outside the EE folder, but the applicable folders must be specifically enumerated by name within EE.)

- Prior to entry of the unlock code, the user needs System Administrator rights to his/her computer. Once the unlock code has been entered, this is no longer necessary.

- Each EE user needs full read/write/delete access to **both the EE folder and all underlying folders** and to the user's Application Data folder. (Inheritance of full access is not the default behavior on many Windows XP systems.) The first time EE runs, it performs a test to see if it can create and access subfolders. If the test fails, EE reports error messages that indicate which folder it could not access properly.

Temporary Files

EE writes many temporary files as a part of processing results and generating reports. At the time of this writing (Feb, 2012) the temporary files are written to the folder "DGRhoadsTempFiles" which is located in the Application Data folder (strictly speaking "%APPDATA%").
Users must have full read/write/delete access to whichever Temp folder is being used.

The DGRhoadsTempFiles folder can be removed at any time (as long as EE is not running). The program will re-create it when necessary.

Internet Access

Allowing EE direct access (http and ftp) to the Internet qualifies as "nice, but not necessary." Without Internet access, the following features do not work:

- Web activation
- Check for/download the latest EE build
- Send Bug Report (packages relevant files into a zip archive and sends them to the Data Innovations' web site).

Network Installation

- No software is installed on the client machine. Run the setup package to install the software on the server, then place a shortcut to EE.EXE on each client.

- We recommend that the shortcut use the UNC path (\\server\EE.exe) rather than a mapped drive letter (Y:\EE.exe).

- EE does not require, install, or use a server-side database (e.g., Oracle, MS-SQL Server). It does not use MS-Access, or ODBC. The database engine is built into EE (DBISAM) and is fully multi-user capable. For more information, see www.elevatesoft.com.

- EE does not require any installation of service applications; it does not use any special TCP-IP ports.

- When requesting an unlock code, you may notice that the 8-digit system ID is different for each client. This is normal. The first four digits identify the server, and the last four identify the client. For a network license, a workstation is given access as long as the first four digits agree with 8 digit system ID used to generate the unlock code.

Sometimes the first four digits for the server and client will differ. In this case, request an unlock code for what's reported on the client machine, and enter the unlock code at that client. Then EE should work from the clients but not the server.

Thin Client Application

We have users who have installed EP Evaluator in a thin client model using Citrix. Reports are generally favorable about this program environment. The major advantage of this approach is its performance across the network. Users can install EE on a server in once country and access it from a thin client model in another country..

Re-Installation

Within a release, always install a later build on top of an earlier build. The unlock code will not change. No data will be lost. All data is automatically restructured to make it consistent with the later build.

- NEVER install a newer release in the same folder with an older release.
- In other words:
  NEVER install EE11.x.x.x in the same folder as EE10.x.x.x.
  ALWAYS install EE11.x.x.y in the same folder as EE11.x.x.x

Backups

To make a backup of the user's data, you need only backup the EE11\DATA folder. (Or, with the Professional version, all EE11\DATA* folders.)

Anti-virus Software

If you are using virus protection software, note that the DGRhoadsTempFiles directory must be excluded from virus scanning. EE must have access to this directory at all times to store temporary files necessary for the creation of reports and print previews. Because anti-virus software locks each file as it opens them for scanning, EE may temporarily not have access to these files. EE would work properly in general, but fail sporadically when creating reports.

The location of the DGRhoadsTempFiles directory changes based on your Operating System and on the current user. For example:

Windows 7: C:\Documents and Settings\Users\<username>\DGRhoadsTempFiles
Windows XP: C:\Documents and Settings\<user>\Application Data\DGRhoadsTempFiles

Appendix

D

Glossary

Allowable Total Error is often defined from information external to the method. One of several definitions is "the amount of error that can be tolerated without invalidating the medical usefulness of the analytical result" (Carey and Garber - 1989).

Analyte is the substance being measured. Examples of analytes are glucose (chemistry), red blood cells (RBC) (hematology), prothrombin time (PT) (homeostasis), phonating (toxicology), TSH (endocrinology) and Egg (immunology) to mention just a few. Hematological analytes are called "parameters".

Analyte Concentration is the amount of analyte present in whatever units are being measured, whether an actual concentration (mmol/L), an activity (U/L), time (seconds), cell count percentage or some other measurable quantity.

Assigned Concentrations refers to the concentration of a set of specimens as defined (or assigned) by the user. This is in contrast with measured concentrations which are assayed results. This term refers to the assigned concentrations for the linearity and calibration verification protocols. The five approaches used in EP Evaluator® to assign concentrations are:

a) **Pre-assigned**: Concentrations entered by the user which are expressed in units of concentration (such as 4.25 mMol/L);
b) **Coded**: Concentrations known relative to other solutions. In these cases, it is only necessary to know an approximate concentration, sometimes "low" or "high" is all that is known. In preparing a coded set of linearity solutions, Solution C is prepared by diluting 1 part of Solution A (with a low concentration) with 1 part of Solution B (with a high concentration). The three solutions can be assigned values of 1 (solution A), 2 (solution C) and 3 (solution B). Additional combinations of dilutions are usually done. This works out very nicely for the linear regression method as the three solutions will fall at equal concentration intervals along the X axis.
c) **Pct-assigned**: The concentrations are calculated as a percent of the defined concentration of a specimen declared as 100%.
d) **Pct-measured**: The concentrations are calculated as a percent of the

mean of the measured concentrations of the specimen declared as 100%.
e) **Pct-split**: The concentrations are calculated based on the concentrations and percents of the two specimens with the lowest and highest concentrations.

Average Bias refers to the mean difference between the concentration of an analyte as determined by one method and that determined by another. A closely related term, the 95% confidence interval (CI), indicates the range of bias expected for 95% of similar future experiments. This concept is similar to a mean and 2 SD limit, except that the mean applies to the mean difference in results between two methods at a specific concentration, and the confidence interval applies to the dispersion of biases expected in future experiments.

Backup is the process of copying the contents of a disk to some other storage medium. This is usually done to protect from potential disaster in the event of computer failure. See Restore.

Bias is the difference between two related numbers. There are several uses for this term. A common one is (Ymean - Xmean). A second meaning is to indicate the difference between results obtained from two different methods (Yi -Xi). A third meaning is to indicate the difference between a calculated value and an experimental value.

Bins are discussed in Section 3.3 of CLSI:EP9. A suggested list of bins is given in CLSI:EP9 Table I. Bins represent clinical or statistical groups into which results for a given analyte can be distributed. For example, CLSI:EP9 suggests that glucose results be divided into five groups, < 50, 51 to 110, 111 to 150, 151 to 250, and > 250 mg/dl. As the results are entered into the program, the percent in each group are counted and displayed on the data entry screen. The purpose of this concept is to encourage the users to accumulate results from specimens over a fairly wide analytical range.

Carryover occurs if a specimen or reagent used for the assay of one specimen contaminates the mixture used to assay the next specimen. Usually carryover causes the second specimen to have a falsely high value.

Case has to do with whether a name is spelled with “CAPITAL LETTERS LIKE THIS” (upper case), with “little letters like this” (lower case), or with “Both Capital And Little Letters Like This” (mixed case). (In general, you may input data in either upper or lower case. If the program cares about the case, it will make sure that it receives it in the appropriate form.).

Clinical Linearity is an algorithm by which the linearity of a system can be evaluated against user-defined allowable error. See Rhoads (2012) *Laboratory Statistics* manual, for details.

Concentration a generic term which refers to the amount of analyte present in a specimen. It may be expressed in whatever units are appropriate to that analyte.

Confidence Interval The range of values in which results from a large fraction of similar future experiments (usually 95 or 99%) are expected to fall.

Cutoff value: A medical decision point often defined with the use of ROC software. For example, there are two cutoff values for cholesterol of 200 and 240 mg/dL. For some analytes such as drugs of abuse, the cutoff values are established administratively.

Defined concentrations: See Assigned concentrations.

Degrees of freedom is a statistical term for a corrected number of variables used to calculate a number. Generally, a larger number of degrees of freedom provides more reliable statistics.

Deming Regression is a regression calculation made assuming that error exists in the data plotted on the X axis. See Regular Regression.

Drift is the net shift in results over time, either up or down. It is an indicator of the instability of the analytical process. In EP10, it is evaluated in each run.

EE4 Export File is a type of ASCII text file which contains the complete data for a single experiment.

EE10 Resources Folder is a folder under the EE10 folder which contains numerous useful resources. Address: X:\EE10\Resources where X is the drive the system on which EE10 is located. Usually on a single PC, X is the C drive.

Excluded Results When results are excluded, they remain in the data base but are not used in any calculations. To exclude data, hit <F7> with the cursor in the result field. To un-exclude data which is currently excluded, hit <F7> a second time – again with the cursor in the result field. All results entered for a given experiment will always be displayed and printed, regardless of whether they have been excluded or not. The excluded ones will be marked with an “X”.

Executables refers to the various files required to run the program. Not only does it refer to the actual program (EE10.EXE in this case), but to the other files which are required to run the program.

Experiment refers to the process used to evaluate a single analyte by a single method (i.e. instrument). In many instances, experiments are closely related.

File is a named assigned space on a storage device. File folders are the office equivalent of a computer file. Both have names and contain related information. A file name has two parts. The first part, for example the EE in EE.EXE is called the root. The part after the ".", in this case "EXE" is called the extension.

Flags: 1) A specific condition for a single result or set of results. Examples of flags are exclusion ('X') and outlier ('O') flags. This can be set by the EE user. 2) A flag generated by an instrument and associated with a result which is transmitted to EE. There are two general types of these flags: benign and analytical process. These terms reference the quality of the analysis, not the condition of the patient from whom the specimen was obtained. A benign flag could indicate that the result was high, low, critically high, etc. On the other hand, an analytical process flag indicates that the analysis of the specimen was faulty. Conditions contributing to this might be a bad lamp, short sample among others.

Folder is a computer-related construct in which related files can be accessed from one location. For example, the backup files for EP Evaluator are stored in a "backups" folder so it becomes easy to have them all together.

Grid has several definitions. a) The table of experiments shown on the Module Overview Screen; b) The RRE Worksheet into which data is entered prior to moving it into one of the EE10 statistical modules.

IF32 Program is a little program written especially to capture data from either an instrument or a computer file into EE10. This program is specific to the system from which the data is being captured.

Kurtosis refers to the relative steepness of a "bell-shaped" curve as well as the distribution of results in the tails of the curve.

Lab Information System is the computer system which obtains and stores the laboratory results. Also known as an LIS.

Limit of Blank is the lowest concentration of an analyte which is significantly different from zero. See Chapter 17, *Sensitivity (Limits of Blank)* for details.

Limits of Quantitation is the lowest concentration of an analyte which can be measured "accurately." This is one of several types of Sensitivity. See Chapter 18, *Sensitivity (Limits of Quantitation)* for details.

Linearity is a measure of the degree to which the line segments between a series of points approximates a straight line. There are several definitions of linearity presently used in the clinical laboratory. See Rhoads (2012) Laboratory Statistics manual for details.

Linear Regression is a statistical technique which draws a straight line through a population of pairs of data so that it best describes the relationship between the two subsets of data. For a linearity experiment, the two subsets of data are the theoretical (or coded) concentrations and the results obtained from one's instrument.

LIS: See Lab Information System.

Lot Numbers may be used as a synonym for the group of three items consisting of a lot number, an expiration date and a source. These items can be associated with reagents, controls and calibrators.

Matrix Effects is the term for the case in which significantly different results are obtained by two different methods. One classic example occurs with the VITROS thin film chemistries when compared with the more conventional wet chemistries. A typical linearity specimen for one test might give a result of 150 units by the first method vs. a result of 285 for the second. Such differences are normally not seen with fresh serum. The differences occur with linearity materials because they are a highly artificial mixture designed for long-term stability and contain specific concentrations of various analytes.

Medical Decision Point is that value for an analyte which represents the boundary between different therapeutic approaches. This includes the lower and upper limits of the reference interval (i.e. 136 to 144 mmol/L for sodium), critical values both lower and upper, etc.

Method Comparison is a process which statistically compares two methods. The usual purpose of the comparison process is to show the statistical relationship of the methods being compared. The comparison may be either quantitative or qualitative.

NCCLS is the acronym which was derived from the name National Committee for Clinical Laboratory Standards, a voluntary organization which defines standards for the clinical laboratory industry. Since this organization has become international, the full name has been abandoned in favor of the acronym.

Normal range is a range of results between two medical decision points which corresponds to the central 95% of results from a healthy patient population. It is one form of a reference interval.

Panel: A software construct in EP Evaluator which describes a group of tests and the order in which they are listed. A panel can be defined such that a user can rapidly enter data from a report into the program.

Parameter: 1) An item used to describe a property of an analyte such as units, total allowable error, reference interval and the like (also known as Policy Definitions); 2) A hematology analyte.

Passing-Bablok is a robust approach to calculating the best straight line through a series of points in a method comparison study. In EP Evaluator®, it has been implemented in Alternate Method Comparison.

Performance Standards is a synonym for Allowable Error. The advantage of using this term is that it is intuitively seen as a positive term. In contrast, Allowable Error has negative implications.

POC (**P**oint **o**f **C**are) refers to tests which are performed near the patient, as compared to the laboratory which is often at some distance.

Policy Definitions are the descriptors of the data needed to define an experiment. Policy definitions allow a user to quickly create an experiment, enter or capture results and perform calculations. In other words, they are the non-results type data which must be entered for each experiment such as names, units and reference intervals for analytes. Other objects such instruments, panels and serial communication parameters can also be defined.

Precision is a measure of the agreement between replicate measurements of the same specimen.

Prevalence is the frequency with which positives occur in a defined population.

Predictive Value Positive is the probability that a subject with a positive result actually has the disease. It includes prevalence.

Predictive Value Negative is the probability that a subject with a negative result actually does not have the disease.

Project is a folder containing a group of experiments by one or more of EP Evaluator's statistical modules. Ideally all those experiments are related, for example, the linearity, precision and method comparison experiments used to evaluate a specific new instrument.

Proximity Limits are the acceptable limits for the concentration of the specimen used to test the reportable range. If that concentration is within the proximity limits, then the method passes one part of the two part test for meeting the manufacturer's claim for the reportable range.

PT Limits (Proficiency testing limits) are analytical limits specified by regulatory bodies for surveys. The PT limit for glucose is 6 mg/dL or 10% whichever is greater. At a target concentration of 50 mg/dL, the PT limits are 44 to 56. At a target concentration of 200 mg/dL, the PT limits are 180 to 220. For a list of the PT limits specified by CLIA '88, see Appendix A.

Regression Line is the straight line drawn through the results which minimizes the sum of the square of the distances between each point and the line. Think of it as the "best fit" line.

Recovery is the amount of substance present in a sample that can be detected by the analytical system. Usually this term is referred to as percent recovery. A system in which there is 100% recovery is perfectly accurate.

Reference Interval. See Rhoads (2012) Laboratory Statistics manual.

Regular Regression is a regression calculation made assuming that no error exists in the data plotted on the X axis. This is also termed "Ordinary Linear Regression." See Deming Regression.

Residual is usually calculated in a linear regression environment. It refers to the vertical distance between two numbers, one calculated from a best fit line (often a linear regression line) and an experimental result.

Restore is the process of restoring data, which had previously been backed up, to the original disk. See Backup.

RRE (**R**apid **R**esults **E**ntry) references ways to rapidly and efficiently enter data into EP Evaluator. One major way to improve the efficiency of data entry is to use Policy Definitions. See Chapter 36, *Introduction to Rapid Results Entry (RRE)* and Chapter 37, *Policy Definition* for details.

SD Index: also SDI. See Standard Deviation Index.

Sensitivity: a) The probability that a test will be positive in a population in which everyone has the disease. The ideal sensitivity is 100%. b) The lowest concentration that can be reported. See Limits of Detection and Limits of Quantitation.

Specificity is the probability that a test will be negative in a population in which no one has the disease. The ideal specificity is 100%.

Skew refers to the position of the mode (highest point of the curve) of the bell shaped distribution relative to the mean. If the mode and the mean are significantly different, the curve is said to be skewed. See Kurtosis.

SMAD (Scaled Median Absolute Deviation) is a value similar to Standard Error of the Estimate (SEE) in that it describes the scatter around best fit line, but developed with particular relevance to the Passing-Bablok approach as it is insensitive to outliers.

Standard Deviation (SD) describes the degree of dispersion of data around a central value or mean. In a set of normally distributed data, the central 2 SD constitutes about 66% of the results. Similarly the central 4 SD constitutes about 95% of the results.

Standard Deviation Index (SDI) is a measure of the distance of a point to the mean described in standard deviation units. The equation for SDI is:

SDI = (result - mean) / SD

Standard Deviation of the Differences (SDD) comes from comparing the X value with the Y value in a given pair of values. It represents the statistical difference between the values of X - Y pairs. One helpful analogy is that the SDD is an “envelope” around the bias similar to the “envelope” of the SD around the mean in a Levey-Jennings chart. When using the terms of central tendency and dispersion, SDD is the dispersion component. Bias is the corresponding central tendency.

Standard Error of the Estimate Think of this number (SEE) as the "standard deviation" of the differences between the linear regression line and the plotted points. One helpful analogy is that the SEE is an "envelope" around the regression line similar to the "envelope" of the SD around the mean in a Levey-Jennings chart.

String is a line of one or more characters, typically used as a name or descriptor. An example of a string is "GLUCOSE".

Therapeutic Range is a reference interval applied to therapeutic drugs.

Trueness is the closeness of agreement between the average value obtained from a large series of test results and an accepted reference value.

Unsatisfactory Performance is defined by CLIA '88 regulations occurs when the grade during a proficiency event for an analyte is less than 80.

Unsuccessful Performance is defined by CLIA '88 regulations as that occasion when there have been Unsatisfactory Performances for an analyte in two of the last three consecutive PT events.

Worksheet is the RRE table into which data is entered prior to moving it into one of the EE10 statistical modules.

Appendix

E

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