datainnovations.com

EP Evaluator Overview

Overview and Getting Started with New experiments

Carol R. Lee

Data Innovations Implementation Consultant

DATA INNOVATIONS
Simple Ideas, Better Solutions

Session Objectives

- Create new experiments

- Enter data 2 of the 10 ways
  1. Manual entry
  2. Paste data into an experiment

- Print Reports

- Describe the STAT modules in EE 11.0
  - 30 for the standard version
  - 10 for the CLIA and COFRAC versions
  - We will review AMC, 2IC, MIC, QMC, LIN, SP

Copyright 2016 Data Innovations LLC

EE Documentation

- the EE manual,
- Lab Stats Manual.
- the QuickStart Guide.
  - Download free to Subscription users or
  - PDFs in the physical disk set.
- Context sensitive HELP is part of the program.

EP Evaluator Features

- **Clinical Laboratory Compliance Toolkit**
  - Meets all CLIA ’88 and CAP requirements for validating and evaluating methods. www.cms.hhs.gov/clia
  - New Method Validation / Verification
  - Ongoing Quality Assurance, Performance Verification, Harmonization
- 30 Statistical Modules including 9 CLSI documents
- 4 Lab Management Modules
- **Vendor Tools**
  - FDA submissions
  - Reagent Quality Control
  - Customer Installations with instrument interfaces

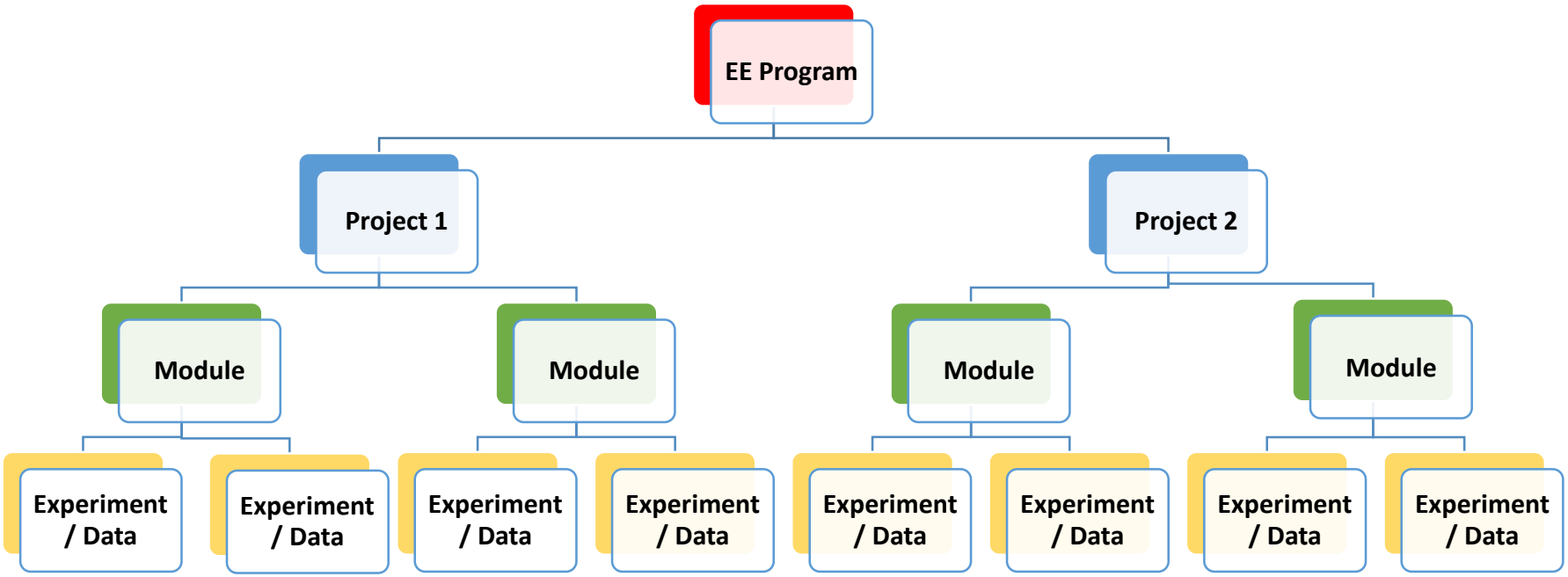
Copyright 2016 Data Innovations LLC

EP Evaluator Concepts

- **Statistical Module** – Does calculations and reports for a specific type of experiment - Like method comparison.
- **Project** – – a database folder containing a collection of Experiments from one or more Statistical Modules
- **Experiment** – one set of data collected for a specific purpose for one analyte
- **Instrument** = method (think outside the box!)
- (**RRE) Rapid Results Entry** – mechanisms to efficiently enter data into EE
- **"Policies" = Policy Definitions –** A MASTER template of parameters used in RRE. Policy definitions in a project autofill the key parameters needed to define the experiment.

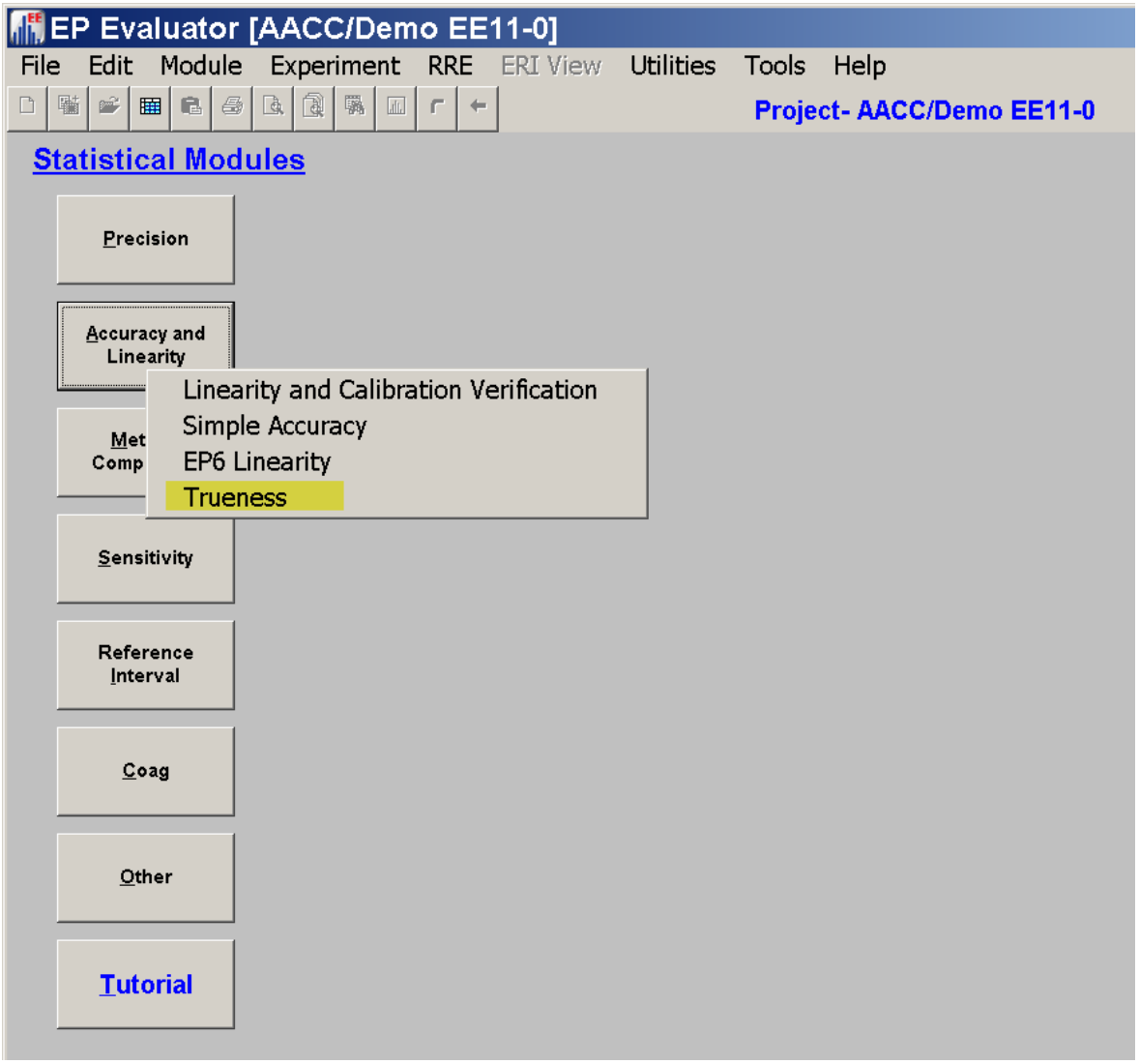
Copyright 2016 Data Innovations LLC

EE Hierarchy



Statistical Module Screen

- Main screen
- 34 modules (10 in CLIA and COFRAC versions)
- Tutorial - a very basic overview –



30 Statistical Modules

- Precision (2)
- Accuracy and Linearity (4)
- Method Comparison (7)
- Sensitivity (2)
- Reference Intervals, ROC (3)
- COAG (4)
- Carryover
- Interference
- Stability
- Other (6)

Copyright 2016 Data Innovations LLC

EP Evaluator Pass / Fail criteria

- **Some modules grade the results as Pass/Fail**
- **Allowable error as pass/fail criteria**
  - Relates observed data quality to the lab's performance limits (allowable error specification)
  - TEA = 3*Random Err (Rea) + bias (SEa)
  - The +/- 3 SD model is used by CLIA, CAP, NYS and means that 99.7% of the data is within the TEA limit
    - (error rate of 3 in 1000)
    - A 3 sigma process

Copyright 2016 Data Innovations LLC

Performance limits

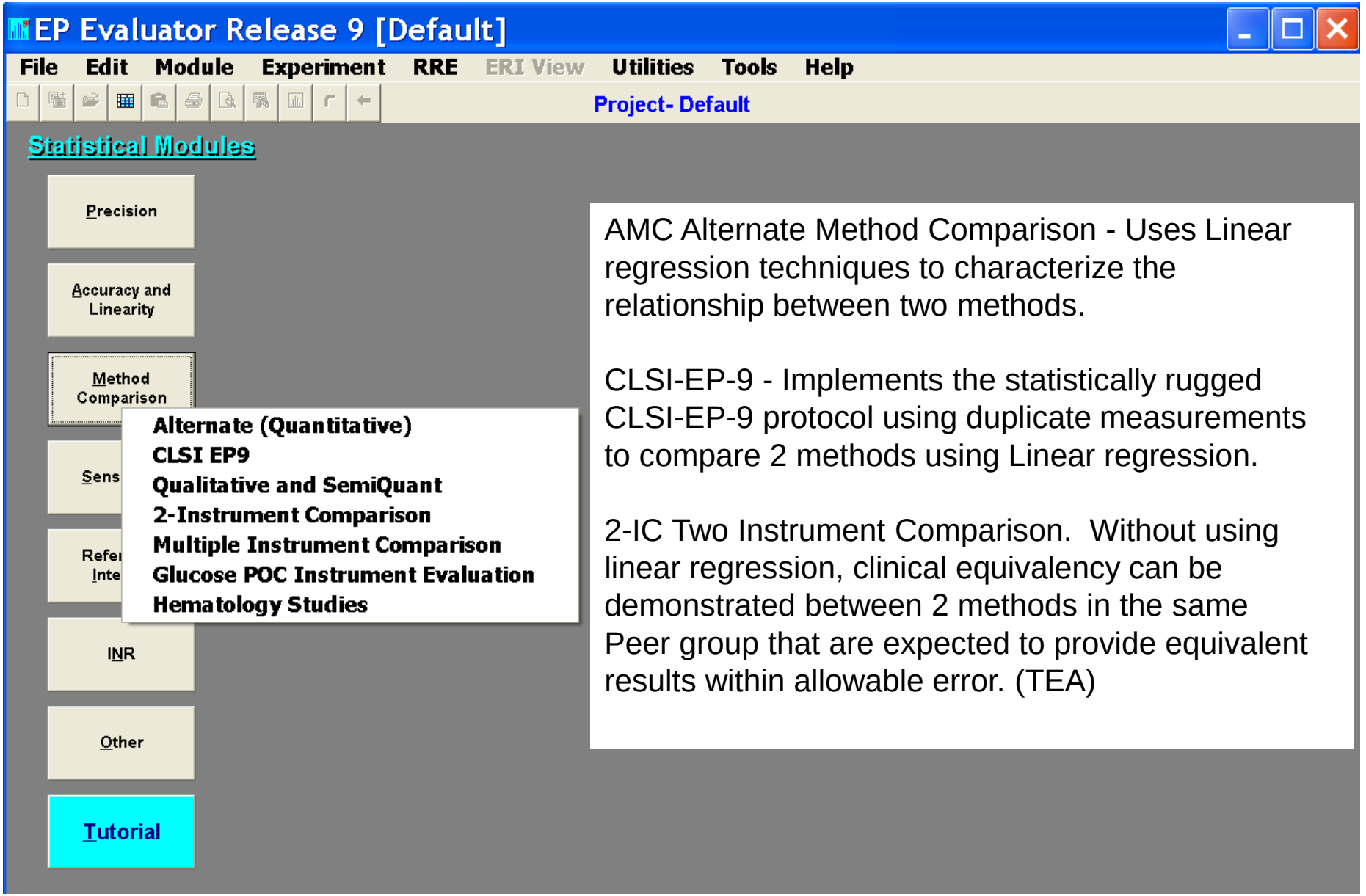
- Per CLIA, your laboratory is responsible for defining a policy or *specification* for the amount of ***Total Allowable Error* (TEa)** medically or administratively acceptable for your methods
- Allowable error examples can be found:
  - **Official CLIA limits table** from the EE Tools menu
  - **"Rhoads Suggested Performance Standards.pdf"** in EE\Resources
  - **Allowable Total Error Tables** on our DI website http://www.datainnovations.com/products/ep-evaluator/allowable-total-error-table

Copyright 2016 Data Innovations LLC

What module to use - 1

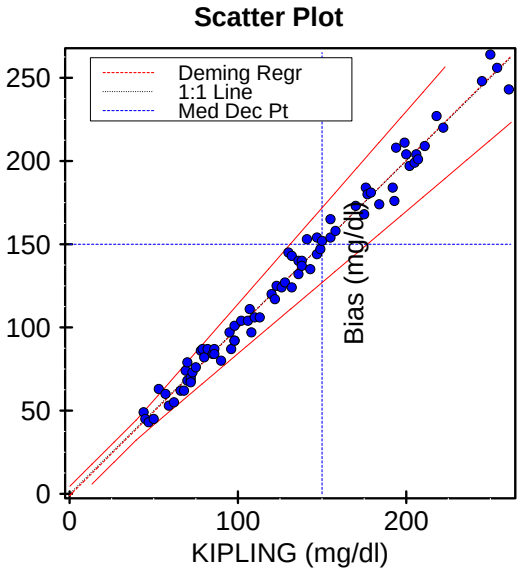
- New method Validation Verification V/V
  - AMC: Alternate Method Comparison AMC
    - Accuracy vs older method
    - Verify agreement at Medical Decision points – verify old reference intervals can be used for new method
  - 2IC
    - Harmonization of “equivalent” methods
    - Lot to lot verification
  - Simple Precision (SP)
    - Repeatability within run
  - * Complex Precision (CLSI EP05 and EP15) *Not in EE CLIA version
    - Reproducibility within Instrument / between run / between day
  - LIN: Calibration Verification LIN - CalVer
    - Calibration Verification (accuracy and Reportable range compared to a set of at least 3 true value standards)
    - Linearity of related materials

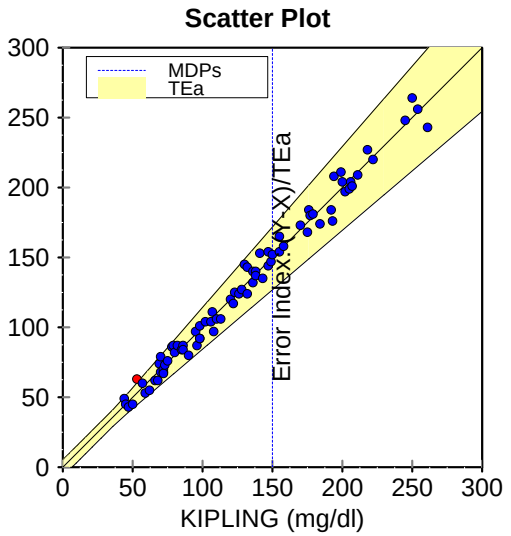
Copyright 2016 Data Innovations LLC


EP Evaluator Release 9 [Default]
File
Edit
Module
Experiment
RRE
ERI View
Utilities
Tools
Help
Project- Default
Statistical Modules
Precision
Accuracy and Linearity
Method Comparison
Alternate (Quantitative)
CLSI EP9
Qualitative and SemiQuant
2-Instrument Comparison
Multiple Instrument Comparison
Glucose POC Instrument Evaluation
Hematology Studies
Sens
Refer
Inte
INR
Other
Tutorial
AMC Alternate Method Comparison - Uses Linear regression techniques to characterize the relationship between two methods.
CLSI-EP-9 - Implements the statistically rugged CLSI-EP-9 protocol using duplicate measurements to compare 2 methods using Linear regression.
2-IC Two Instrument Comparison. Without using linear regression, clinical equivalency can be demonstrated between 2 methods in the same Peer group that are expected to provide equivalent results within allowable error. (TEA)

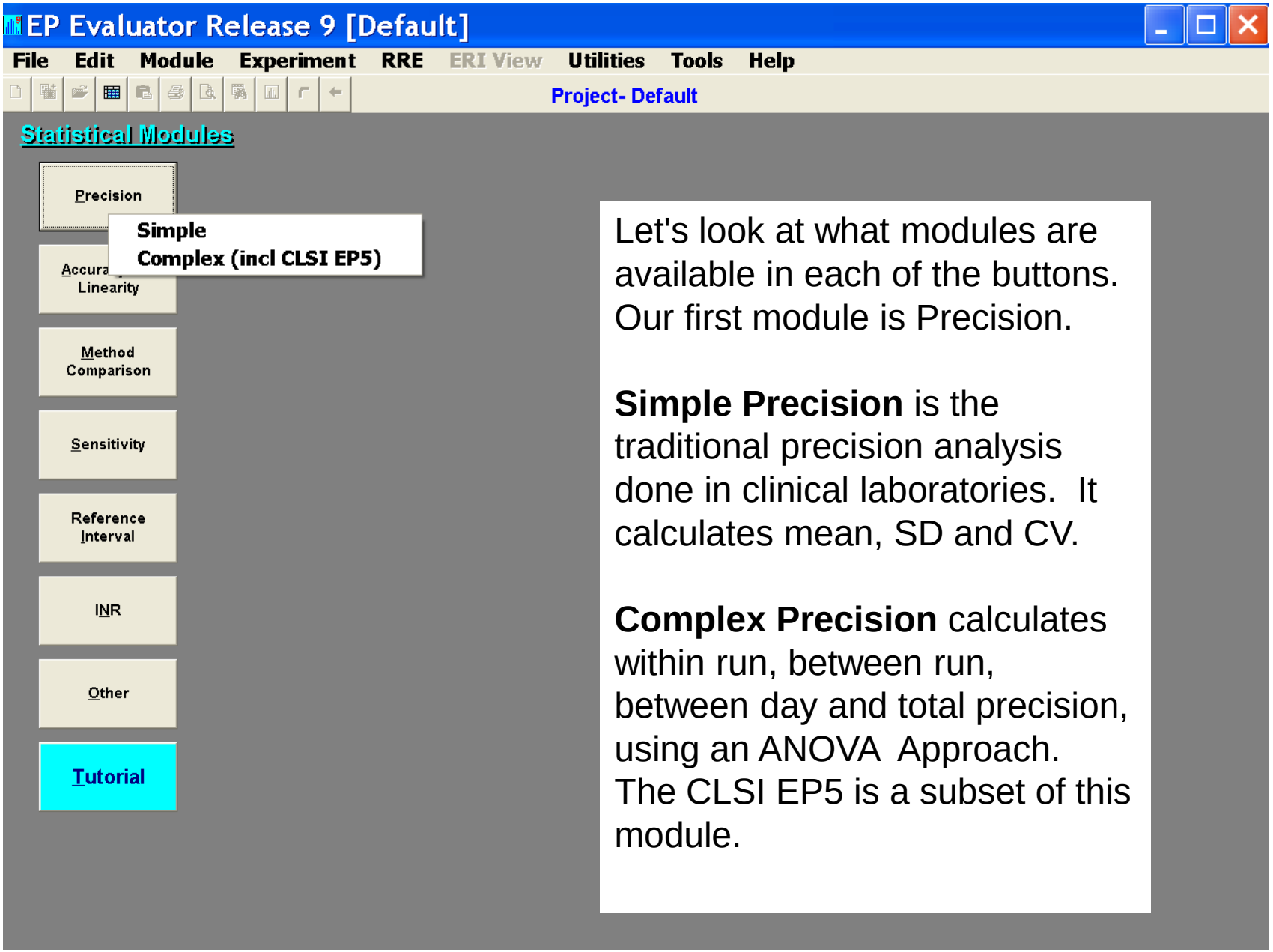
Method Comparison
Validation vs Harmonization

- Method Validation
  - 2 methods not expected to be statistically identical
  - Relationship defined by regression line slope and intercept
  - Alternate Method Comparison - AMC
- Method Harmonization
  - Methods expected to be clinically identical
  - Relationship defined by agreement within allowable error (TEA)
  - 2 Instrument Comparison 2IC
  - Multiple instrument Comparison module – MIC





Copyright 2016 Data Innovations LLC

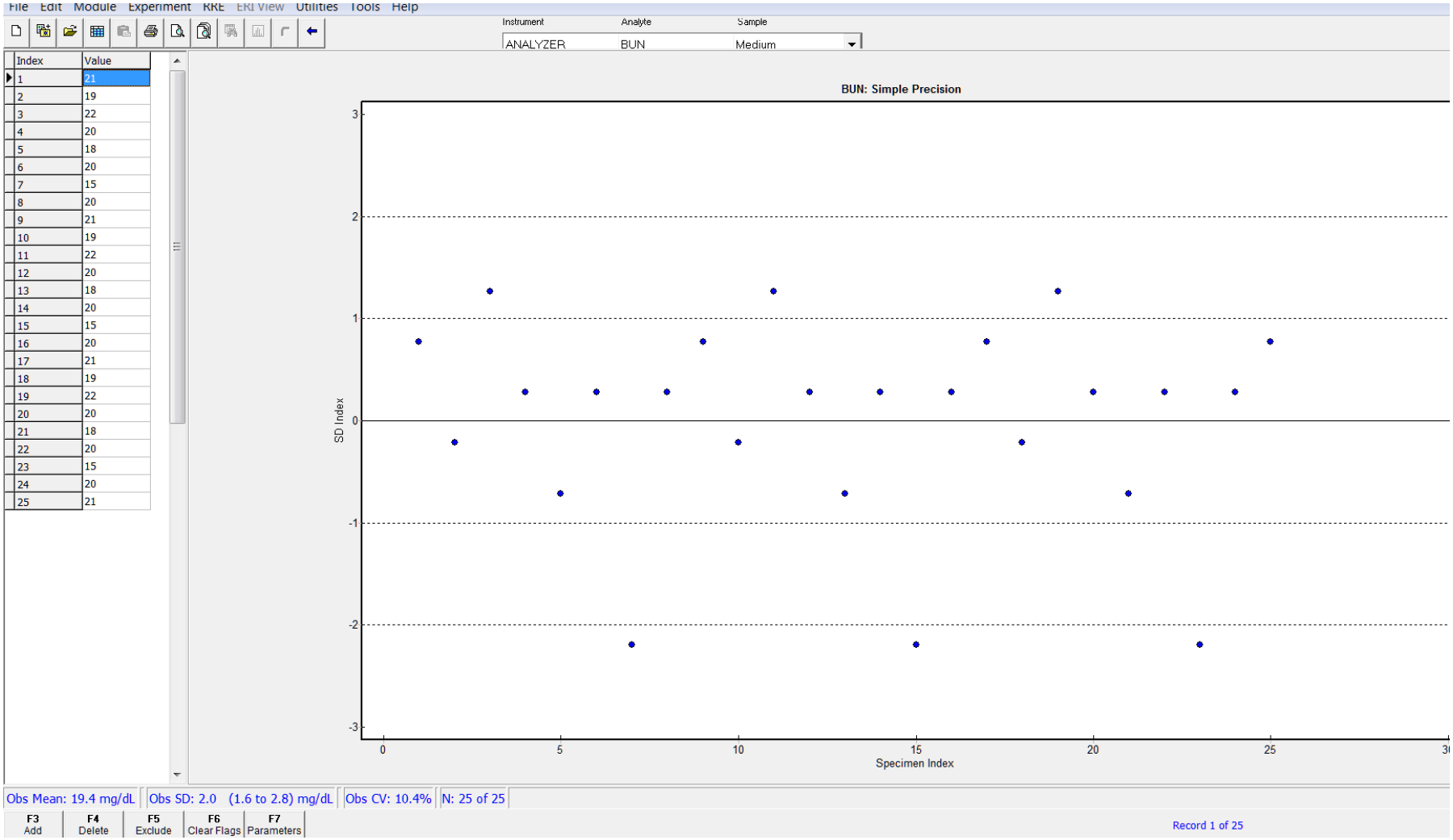


Let's look at what modules are available in each of the buttons. Our first module is Precision.

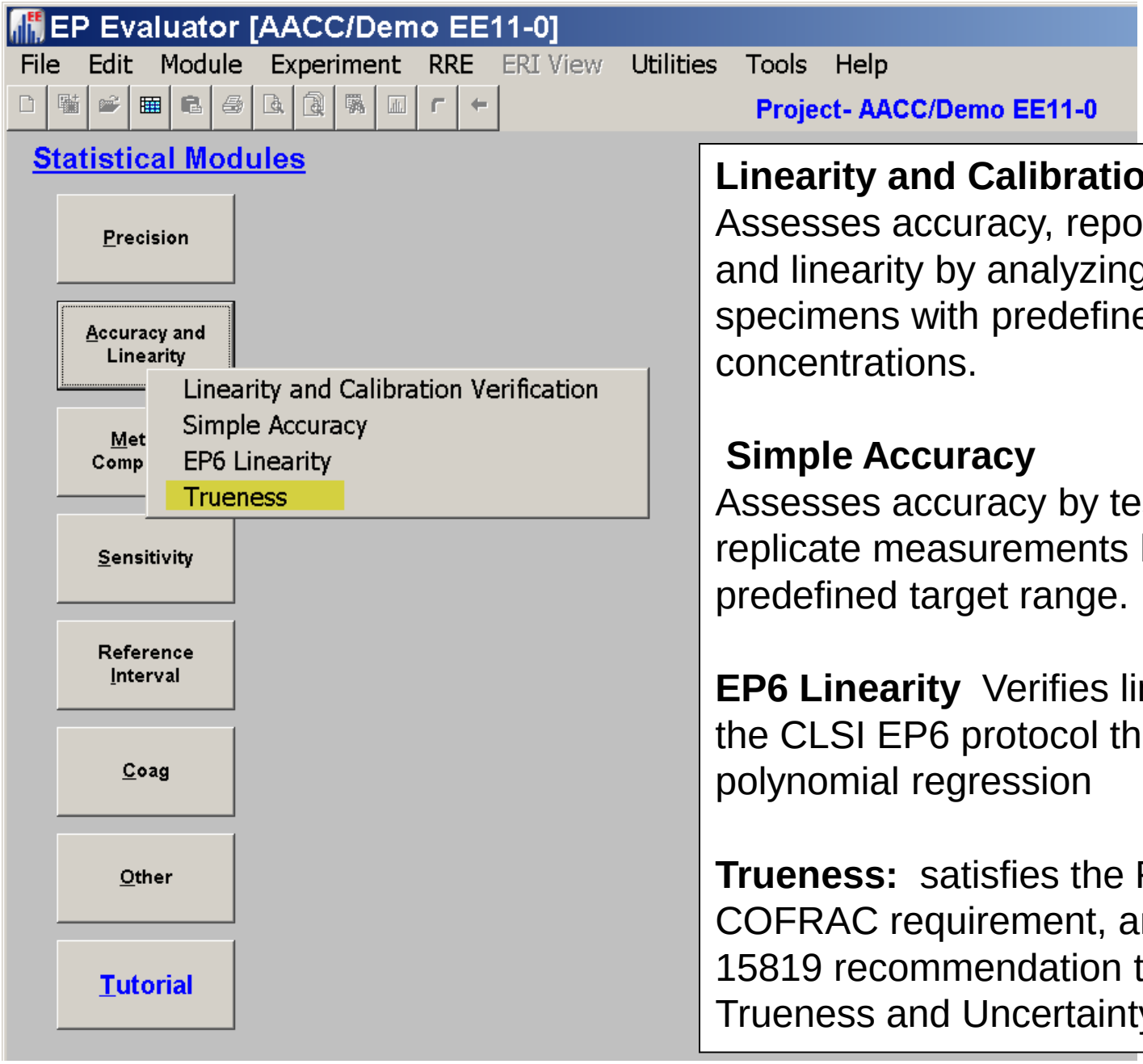
Simple Precision is the traditional precision analysis done in clinical laboratories. It calculates mean, SD and CV.

Complex Precision calculates within run, between run, between day and total precision, using an ANOVA Approach. The CLSI EP5 is a subset of this module.

Simple Precision



Copyright 2016 Data Innovations LLC



Linearity and Calibration Verification
Assesses accuracy, reportable range, and linearity by analyzing more than 3 specimens with predefined concentrations.

Simple Accuracy
Assesses accuracy by testing whether replicate measurements lie within a predefined target range.

EP6 Linearity Verifies linearity using the CLSI EP6 protocol that offers polynomial regression

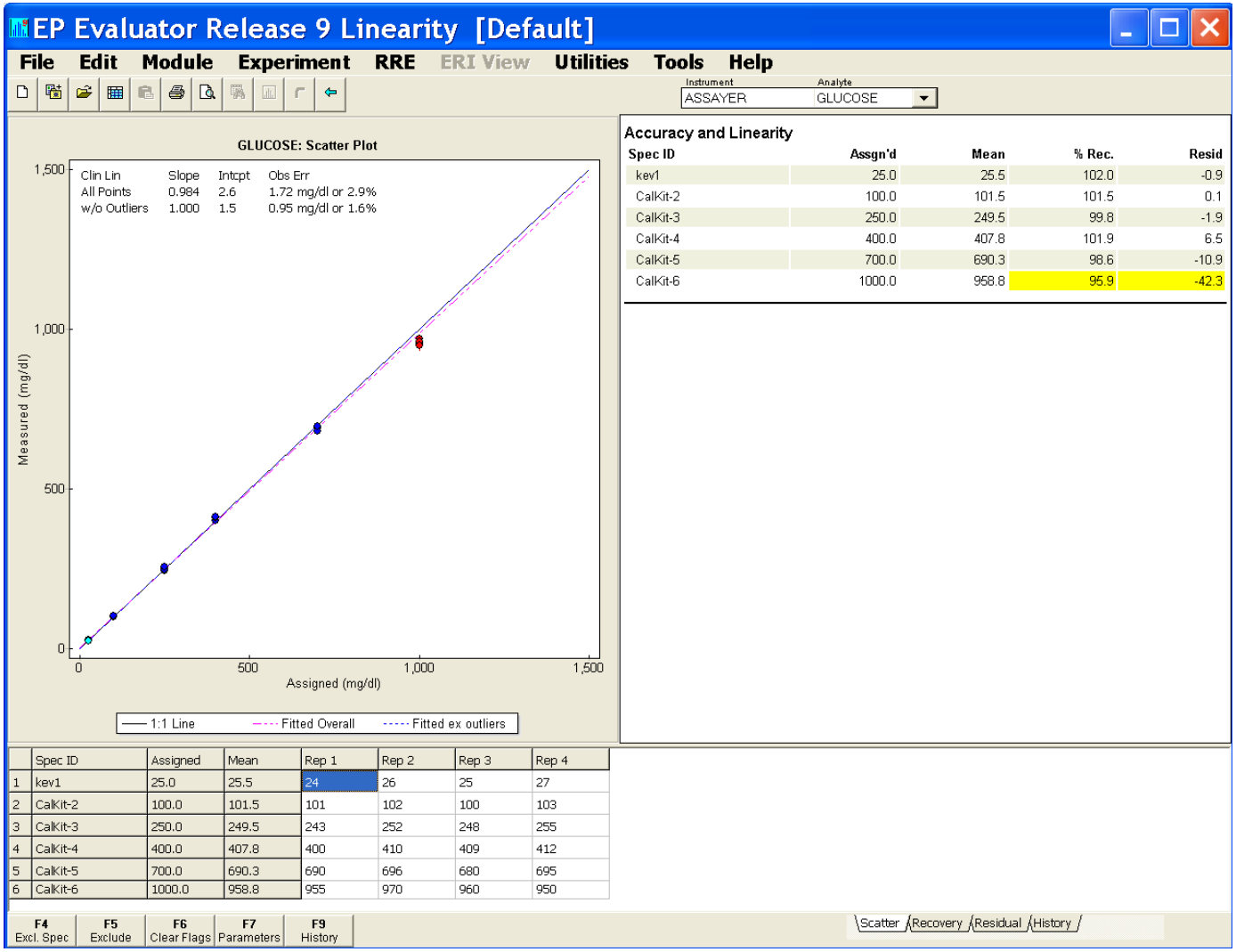
Trueness: satisfies the French COFRAC requirement, and the ISO 15819 recommendation to assess Trueness and Uncertainty

Linearity, Calibration Verification Module

- Satisfies all CLIA requirements –
- Uses Total error (TEA) and SEA (bias) for pass/fail criteria
  - TEA may need a conc component if testing low values
- Report Options
  - Calibration verification.
    - Includes accuracy, reportable range
  - Accuracy
    - Accuracy Passes if all levels (mean value – assigned) less than SEA
  - Clinical Linearity (an EP Evaluator exclusive)
    - Linearity PASSES if: a straight line can be drawn through the SEA error bars around each measured mean value.
  - Reportable range fails if
    - low or high mean recovery fails accuracy test
    - Assigned values not within proximity limits
    - Can choose linearity, accuracy reportable range separately

Copyright 2016 Data Innovations LLC

A typical Linearity Experiment



Simple Accuracy –

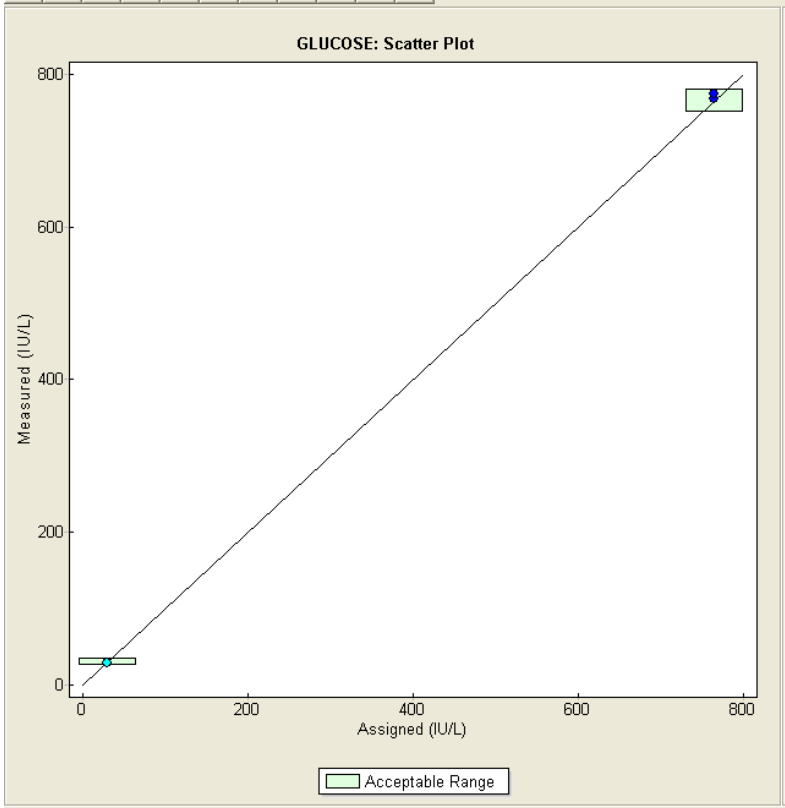
- Good for Coag and POCT departments
- Minimum of 2 controls or standards
- TARGET Ranges provided by Manufacturer define acceptability for accuracy and reportable range.
- Assesses Accuracy and Reportable Range
- PASS or FAIL

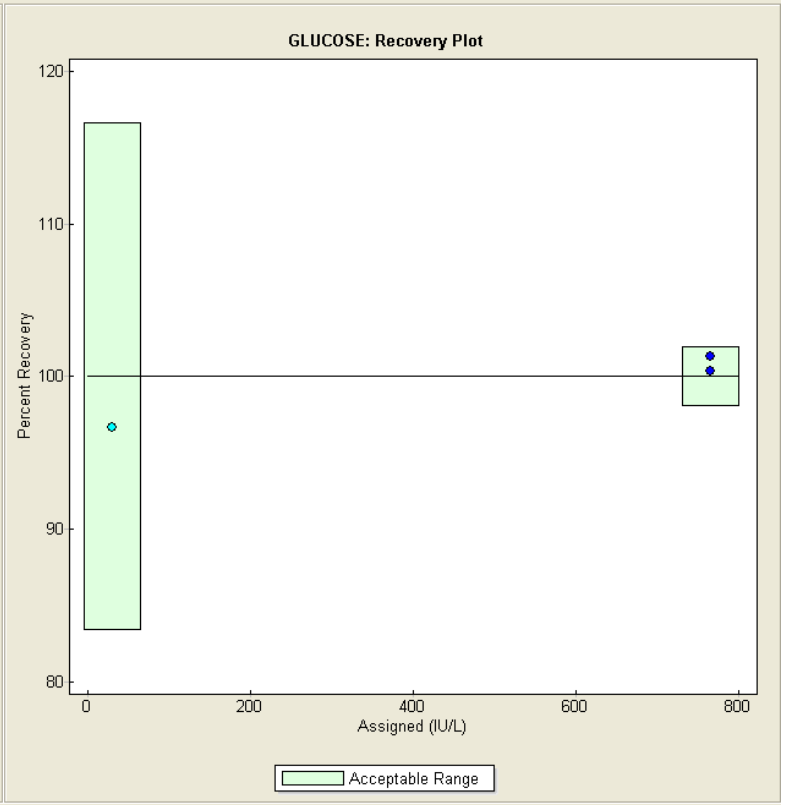
Copyright 2016 Data Innovations LLC

Simple Accuracy

File Edit Module Experiment RRE ERI View Utilities Tools Help

Instrument: Meter 1 Analyte: GLUCOSE

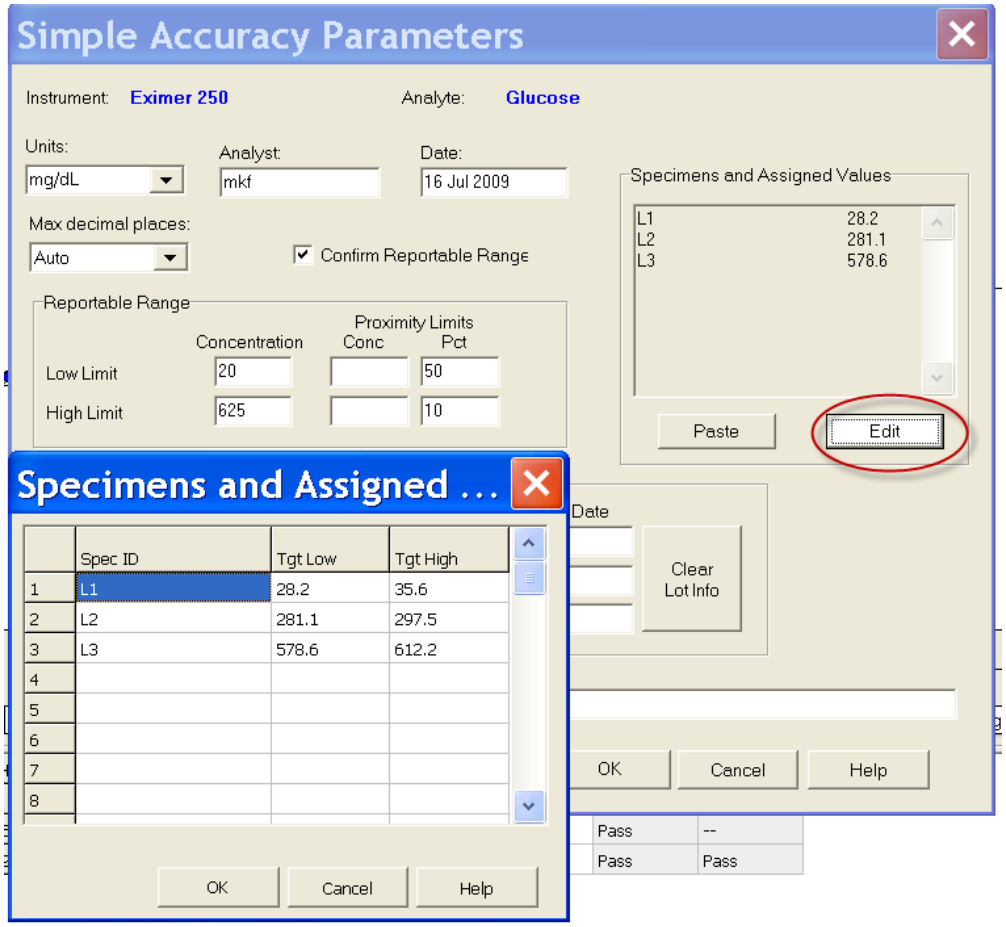




	Spec ID	Tgt Low	Tgt High	Rep 1	Rep 2	Rep 3	Rep 4	Rep 5	Accuracy?	RR?
1	G31	25	35	29	29	29	29		Pass	--
2	G34	750	780	768	775	768	775		Pass	--

Copyright 2016 Data Innovations LLC

Set up Target ranges.



Copyright 2016 Data Innovations LLC

What module to use - 2

- New method Validation Verification V/V
  - QMC
    - Method comparison of qualitative / semi quant methods
    - Repeatability of Qualitative methods
  - * MIC – Multiple Instrument Comparison
    - Harmonization of up to 30 methods, e.g. POCT devices
- Reference intervals or cutoff points
  - VRI – Verify that new method ref interval is statistically the same as old
  - * ERI - When VRI fails, Establish Ref Interval for analyte
  - * ROC – establish clinical cutoff points
  - INR Geo mean & VRI verify new lots of PT reagent

    - * Not in EE CLIA version

Copyright 2016 Data Innovations LLC

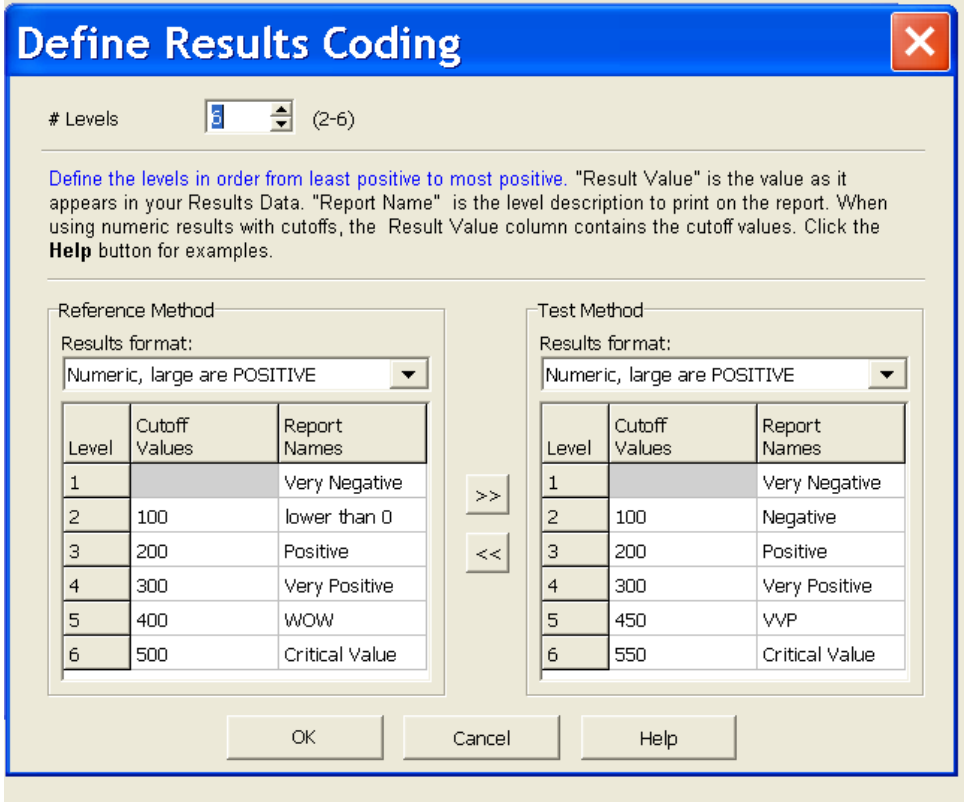
Data Entry – Gold Standard

Experimental Design
Semi-Quantitative

Custom Results Codes

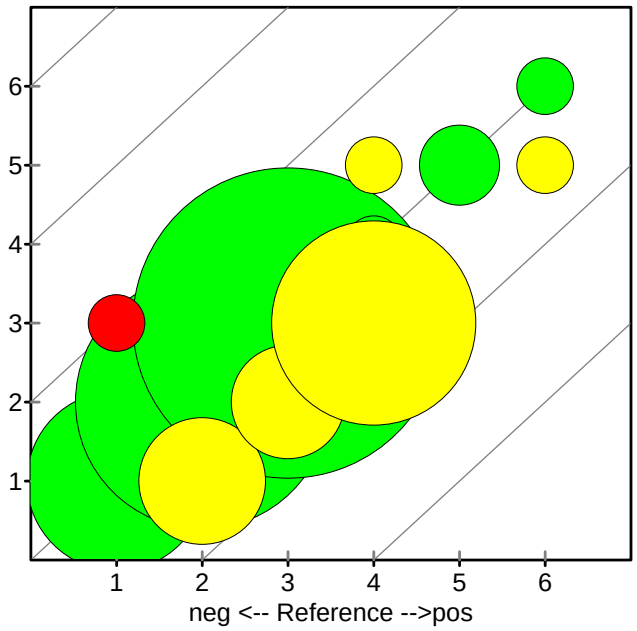
- Up to 6 User defined ‘states”
  - Alphanumeric i.e., Equivocal, gray zone
  - Numeric cutoff values
- User defined Labels

	Reference	Test
1	<=100	<=100
2	101 to 200	101 to 200
3	201 to 300	201 to 300
4	301 to 400	301 to 450
5	401 to 500	451 to 550
6	>500	>550



Allow 1 step difference to accommodate “gray zones” *

Ref. Method: Chem Assay **Test Method: Analyzer**



Statistical Analysis
(Comparison of two Laboratory Methods)

Agreement	71.9% (61.8 to 80.2%)
Agreement within two	98.9% (93.9 to 99.8%)

95% confidence intervals calculated by the "Score" method.

McNemar Test for Symmetry:

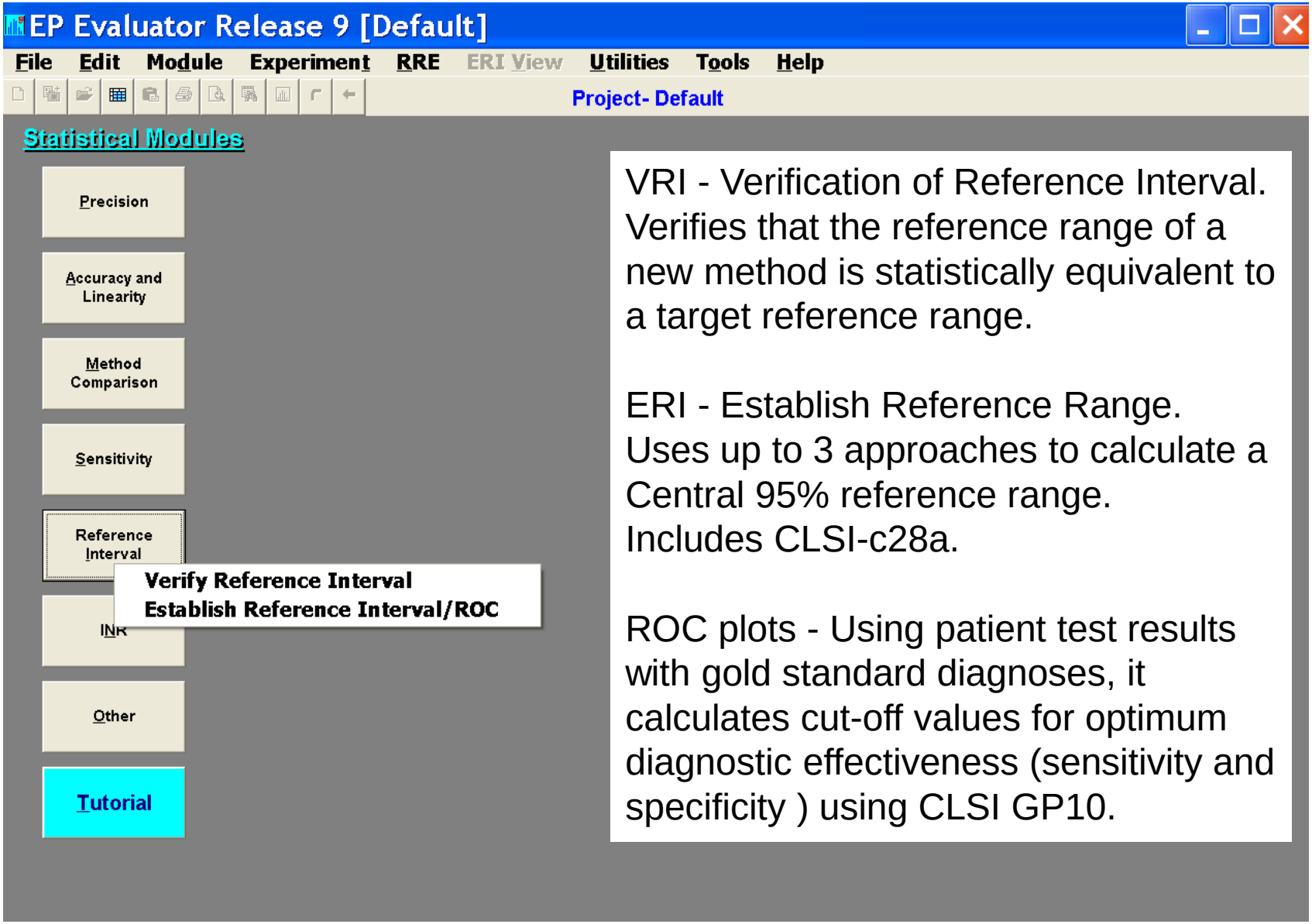
Test < Reference	23 (25.8%)
Test > Reference	2 (2.2%)
Symmetry test FAILS	p < 0.001 (ChiSq=17.640, 1 df)

A value of p<0.05 suggests that one method is consistently "larger".

Cohen's Kappa	60.5% (47.4 to 73.6%)

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.

* Enabled in preferences

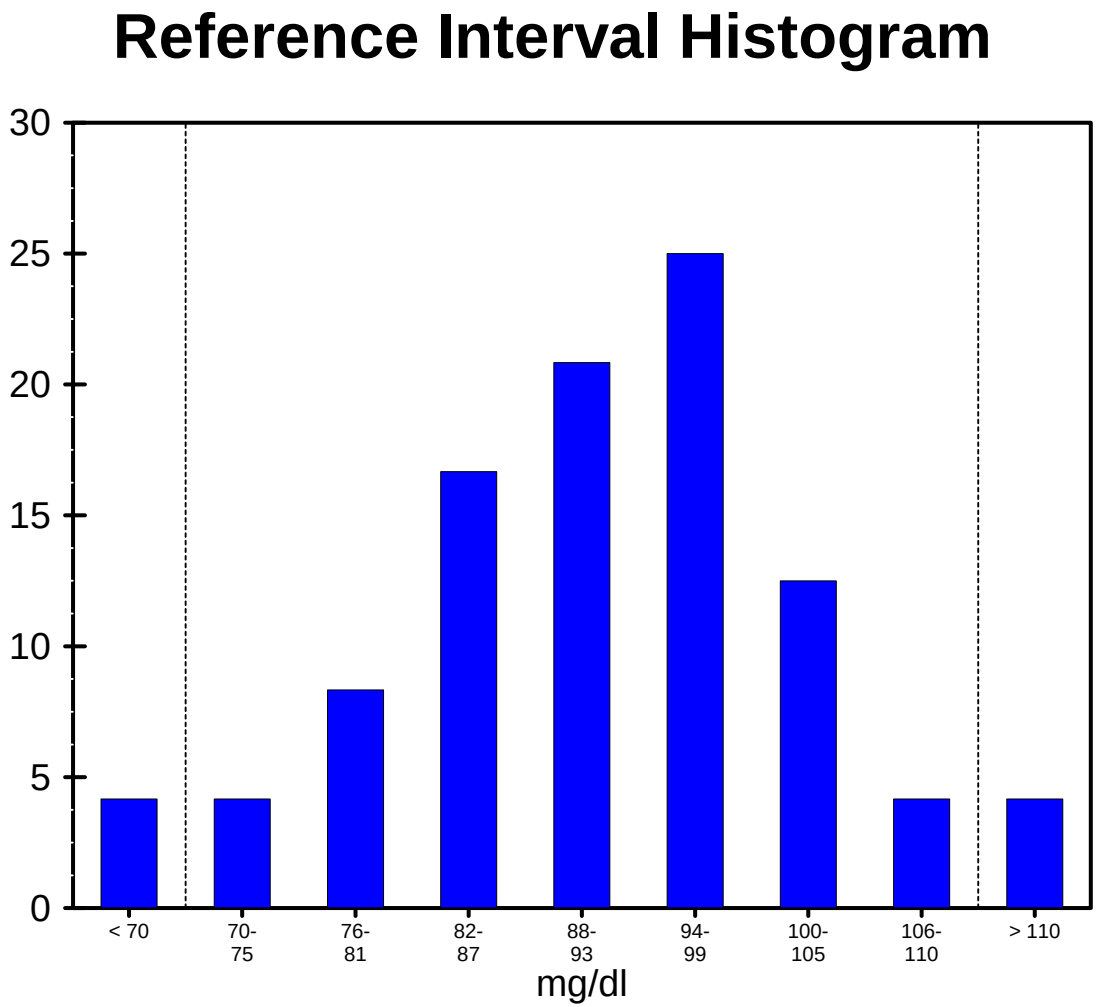


VRI - Verification of Reference Interval. Verifies that the reference range of a new method is statistically equivalent to a target reference range.

ERI - Establish Reference Range. Uses up to 3 approaches to calculate a Central 95% reference range. Includes CLSI-c28a.

ROC plots - Using patient test results with gold standard diagnoses, it calculates cut-off values for optimum diagnostic effectiveness (sensitivity and specificity) using CLSI GP10.

Verify Reference intervals



Copyright 2016 Data Innovations LLC

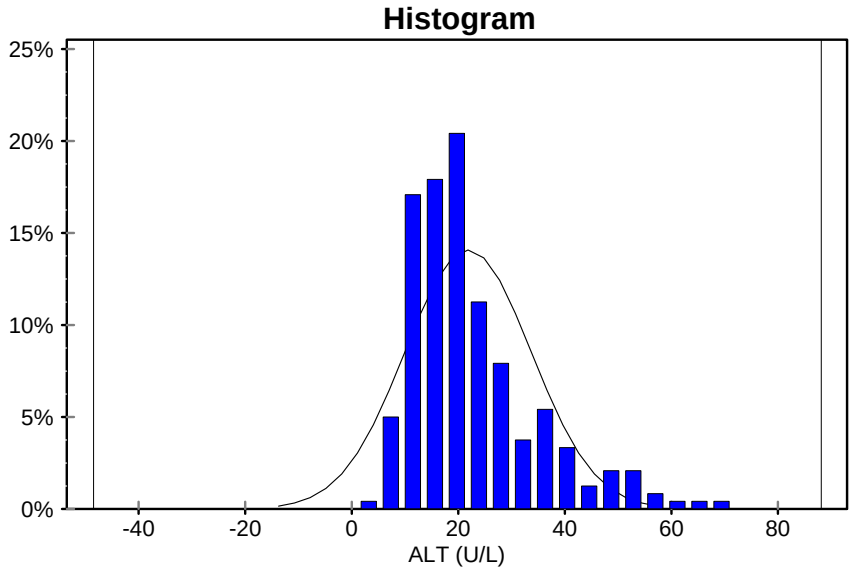
Establish Reference Intervals - ERI

Reference Interval Estimation: Combined

Central 95% Interval
(N = 240)

	Lower		*Upper*		*Confidence*
	Value	*90% CI*	*Value*	*90% CI*	*Ratio*
Nonparametric (CLSI C28-A)	**8**	**6 to 9**	**54**	**49 to 65**	**0.21**
Alternatives:					
Transformed Parametric	8	7 to 8	52	48 to 57	0.12
Parametric	-1	-3 to 1	46	44 to 48	0.09

Confidence Limits for Nonparametric CLSI C-28A method computed from C28-A Table 8.



Selection Criteria:

Bounds	None
Filter	None

Statistics:

Mean	22.5 U/L
SD	11.9
Median	19.5
Range	5 to 69
N	240 of 240
Distinct values	50
Zeroes	0
Central 95% Index	6.0 to 235.0

Analyst	mkf
Expt. Date	13 Apr 2000

Copyright 2016 Data Innovations LLC

EP Evaluator Features : Clinical Chemistry concepts not in generic SW packages

- Beyond p, “t”, Chi2 and R2
- Allowable error (TEA)
  - Clinical linearity
  - Accuracy, reportable range
- Method comparisons
  - Error boundaries TEA, conf limits, binomial
  - OLS, Passing Bablok or Deming regressions
  - Bias and Bland Altman Plots
- Trueness and Uncertainty
- Sensitivity / specificity
  - LOQ Functional sensitivity
  - LOB Analytical sensitivity
  - Truth tables in HMC and QMC
- Carryover
- Reference Intervals and ROC plots

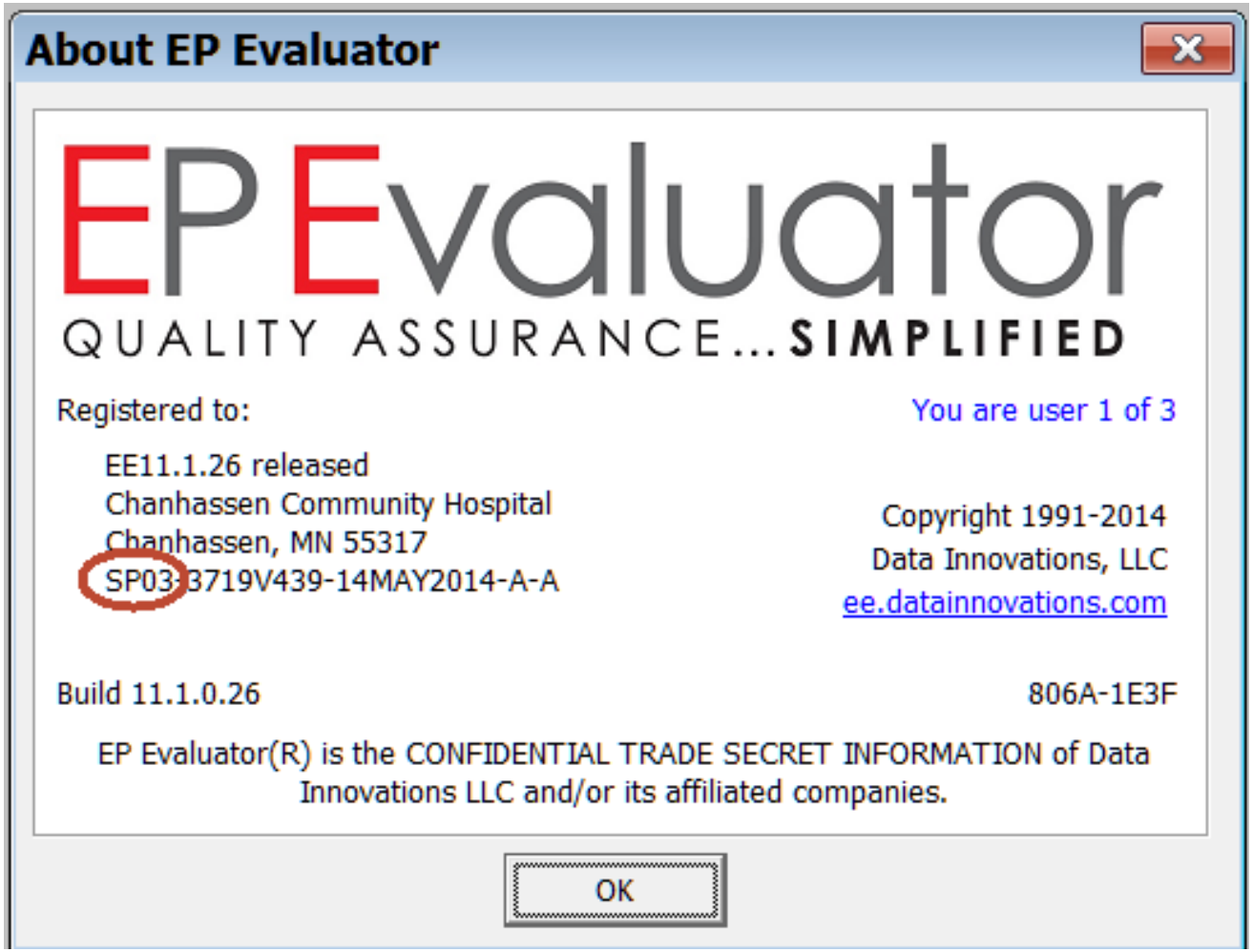
- CLSI protocols and algorithms - 9
  - EP5 A2 Precision
  - EP6 Linearity
  - EP7 Interference (partial)
  - EP9 A2 Method Comparison
  - EP10 Preliminary Evaluation of Methods
  - EP12 Qualitative Method Comparison
  - C28a Establishment of Reference Intervals
  - GP10 ROC Curves
  - EP26 Lot-to-Lot Verification

datainnovations.com

Starting EP Evaluator

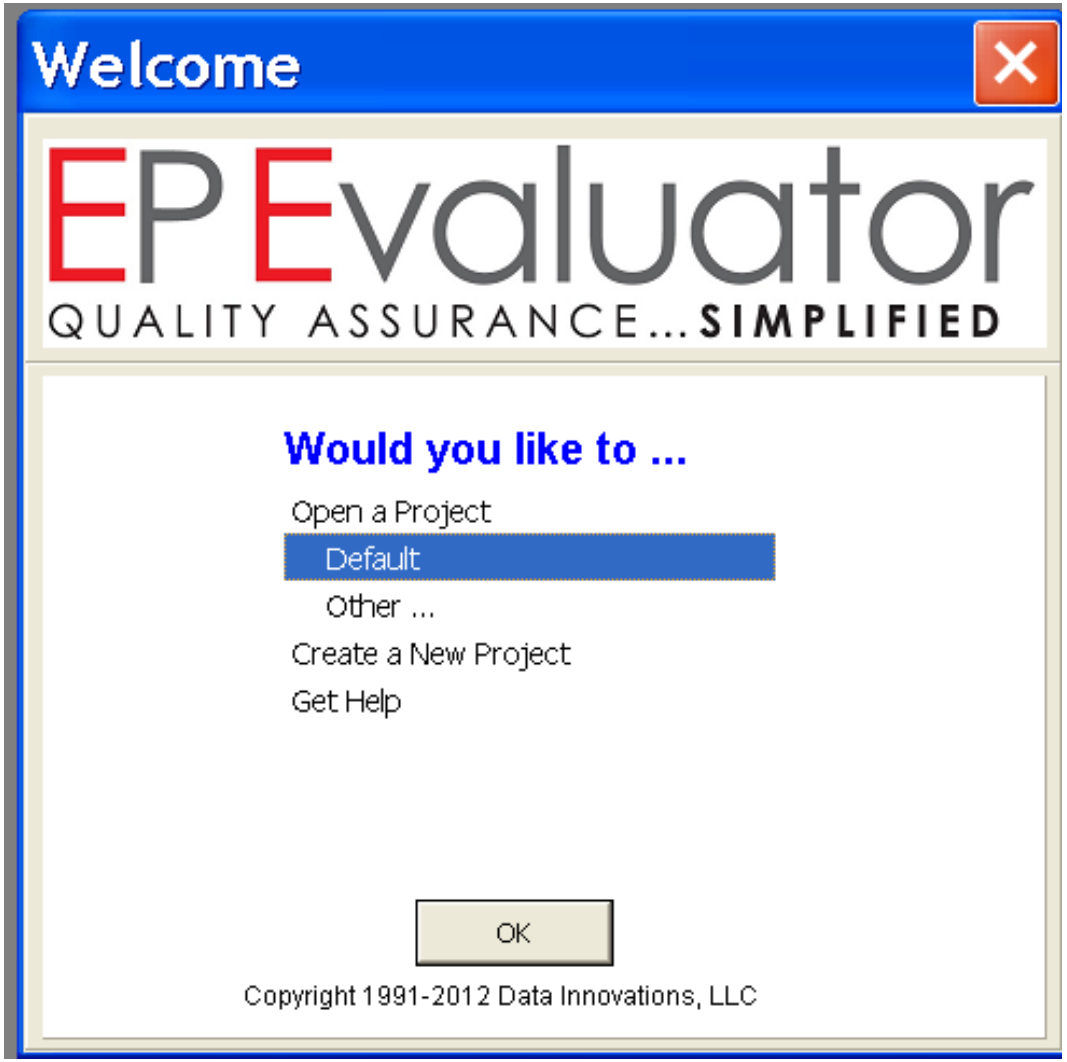
DATA INNOVATIONS
Simple Ideas, Better Solutions

The About screen

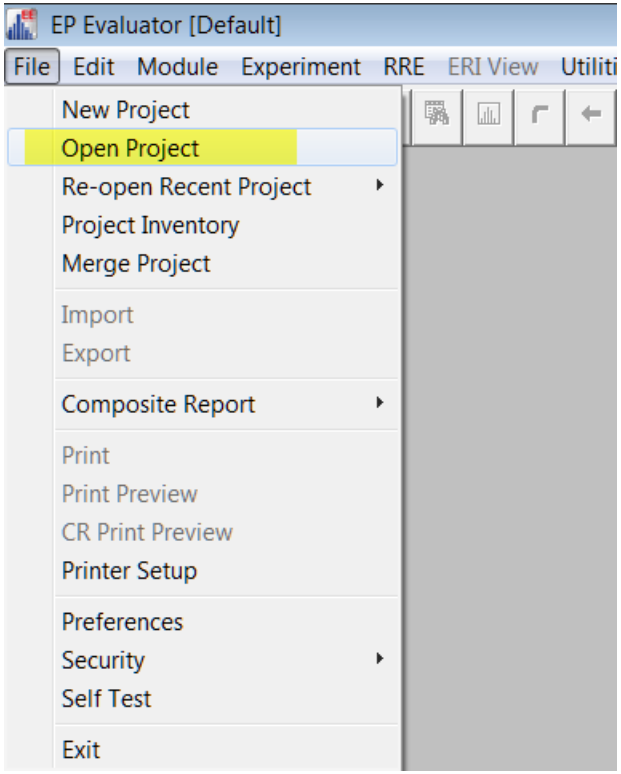


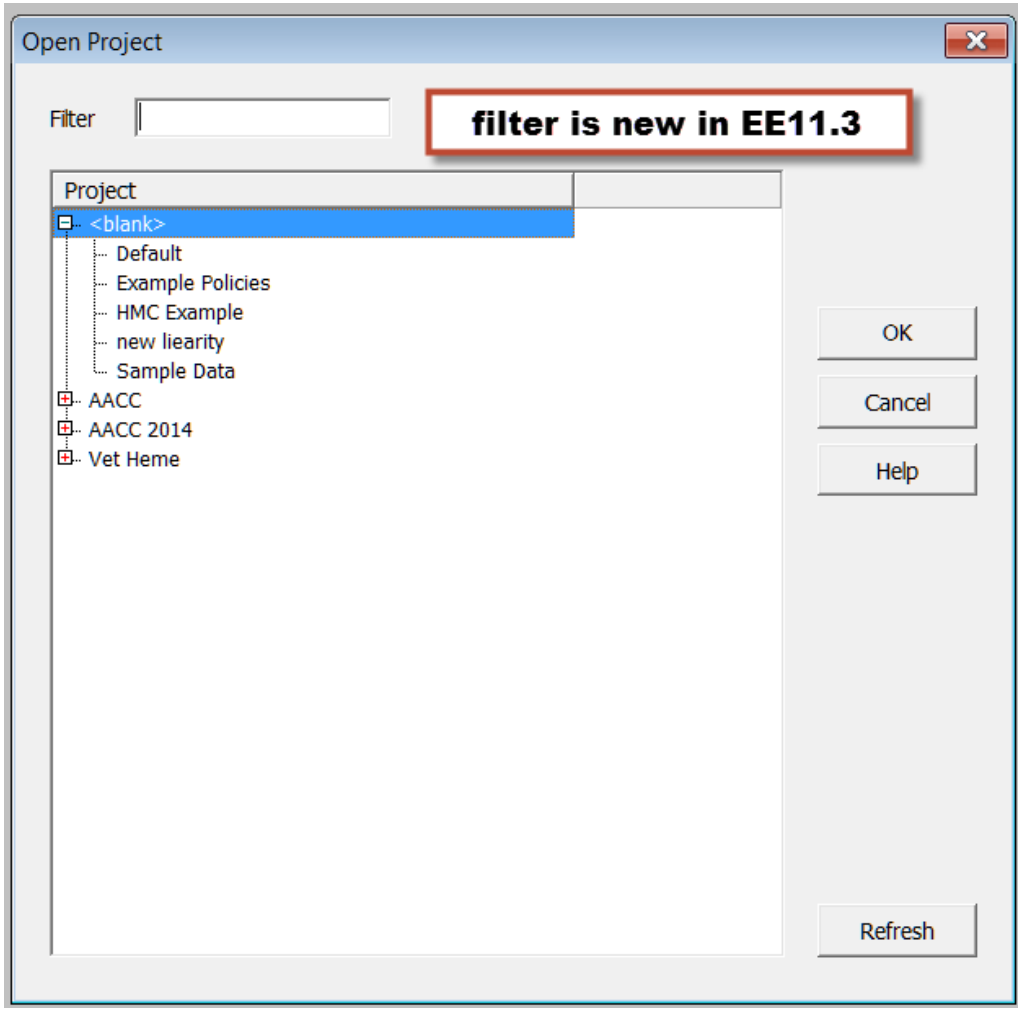
Go to HELP\About to get back to this screen at any time

The Welcome Screen



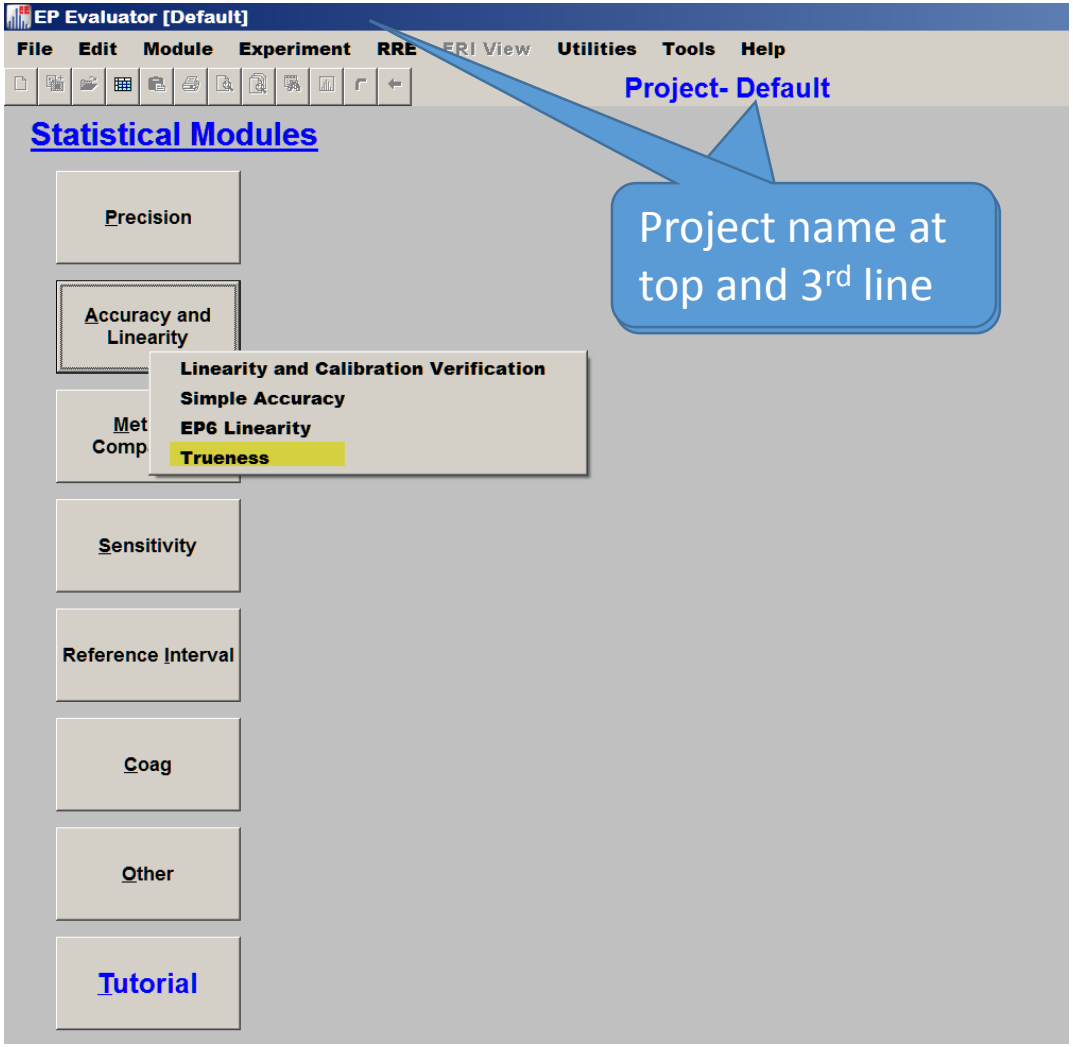
Open a Project



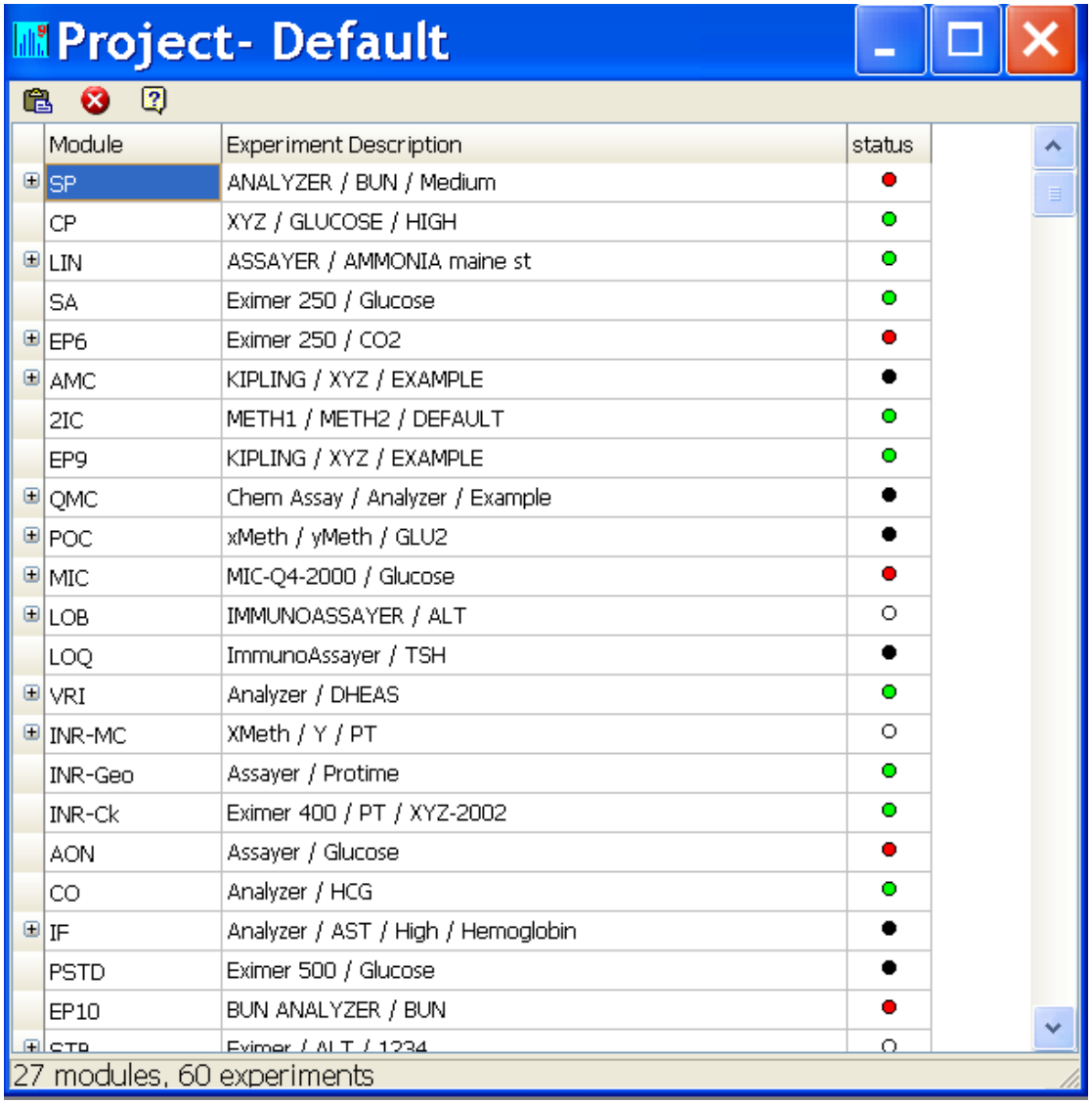


What Project Are You In?

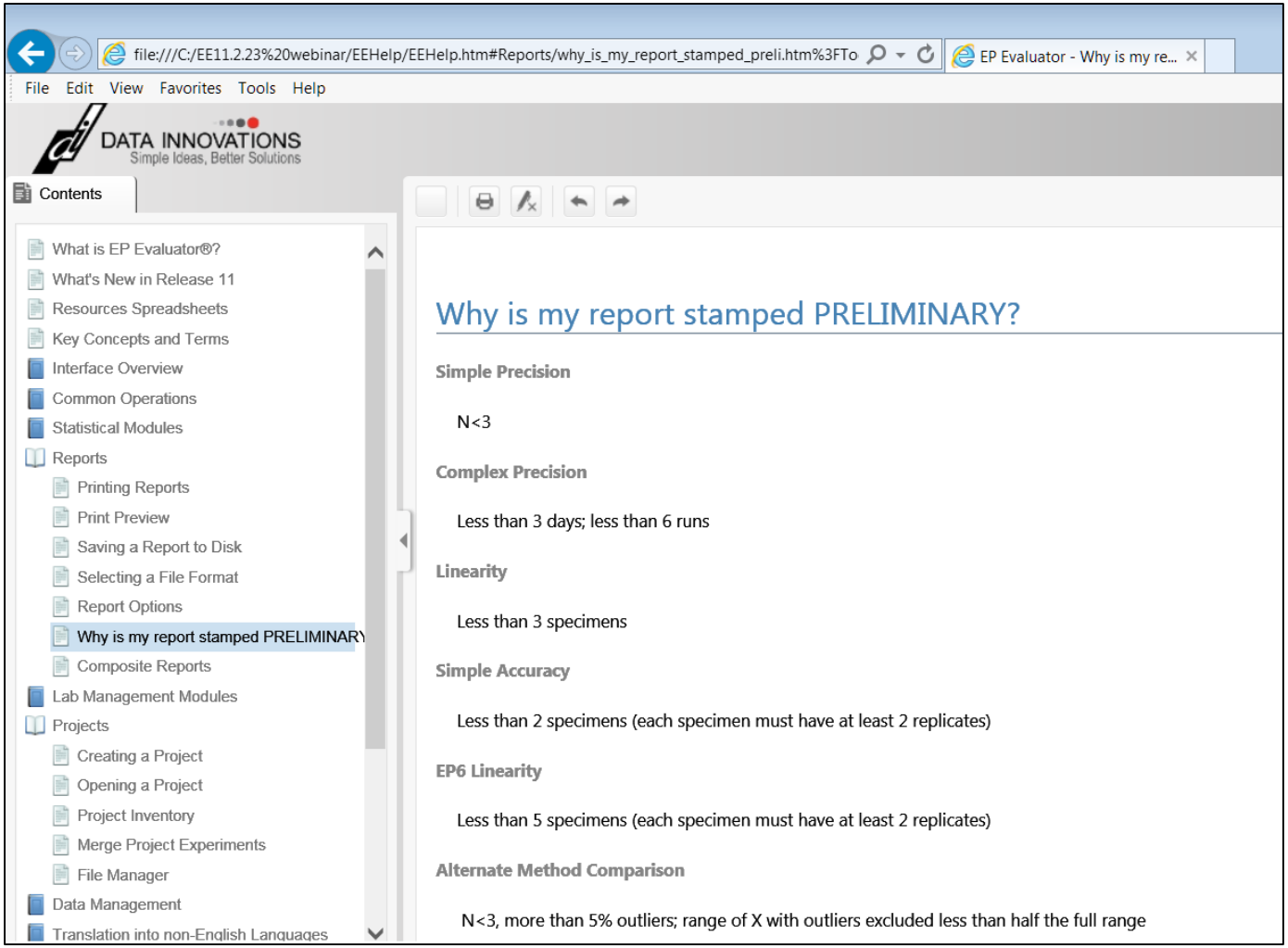
- Main screen
- Project name on 1st and 3rd lines



Inventory


Project- Default
Module
Experiment Description
status
SP
ANALYZER / BUN / Medium
CP
XYZ / GLUCOSE / HIGH
LIN
ASSAYER / AMMONIA maine st
SA
Eximer 250 / Glucose
EP6
Eximer 250 / CO2
AMC
KIPLING / XYZ / EXAMPLE
2IC
METH1 / METH2 / DEFAULT
EP9
KIPLING / XYZ / EXAMPLE
QMC
Chem Assay / Analyzer / Example
POC
xMeth / yMeth / GLU2
MIC
MIC-Q4-2000 / Glucose
LOB
IMMUNOASSAYER / ALT
LOQ
ImmunoAssayer / TSH
VRI
Analyzer / DHEAS
INR-MC
XMeth / Y / PT
INR-Geo
Assayer / Protime
INR-Ck
Eximer 400 / PT / XYZ-2002
AON
Assayer / Glucose
CO
Analyzer / HCG
IF
Analyzer / AST / High / Hemoglobin
PSTD
Eximer 500 / Glucose
EP10
BUN ANALYZER / BUN
27 modules, 60 experiments

HELP!



Copyright 2016 Data Innovations LLC

datainnovations.com

Creating New Experiments

Starting with Alternate Method Comparison - AMC

DATA INNOVATIONS
Simple Ideas, Better Solutions

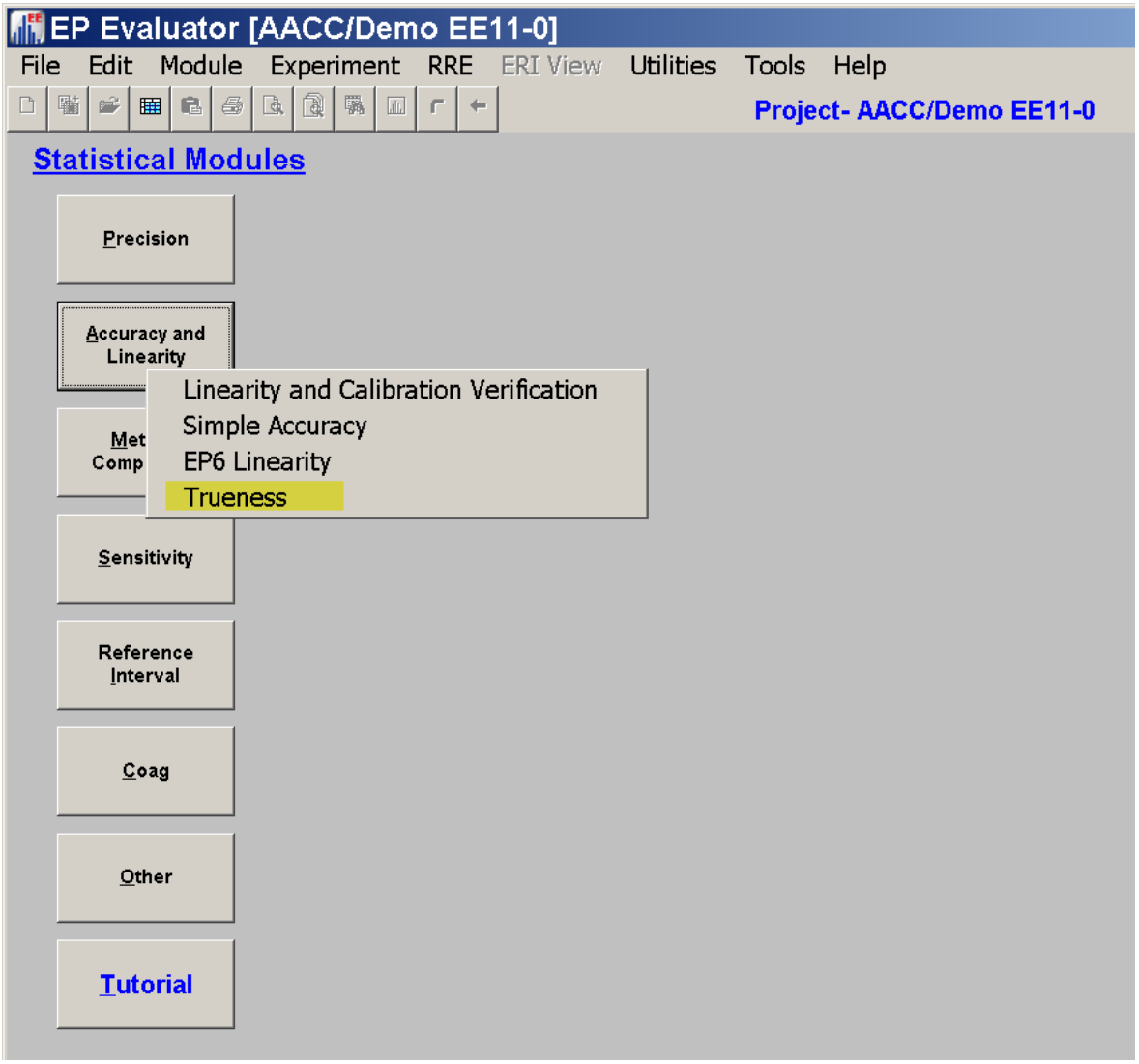
Key Screens

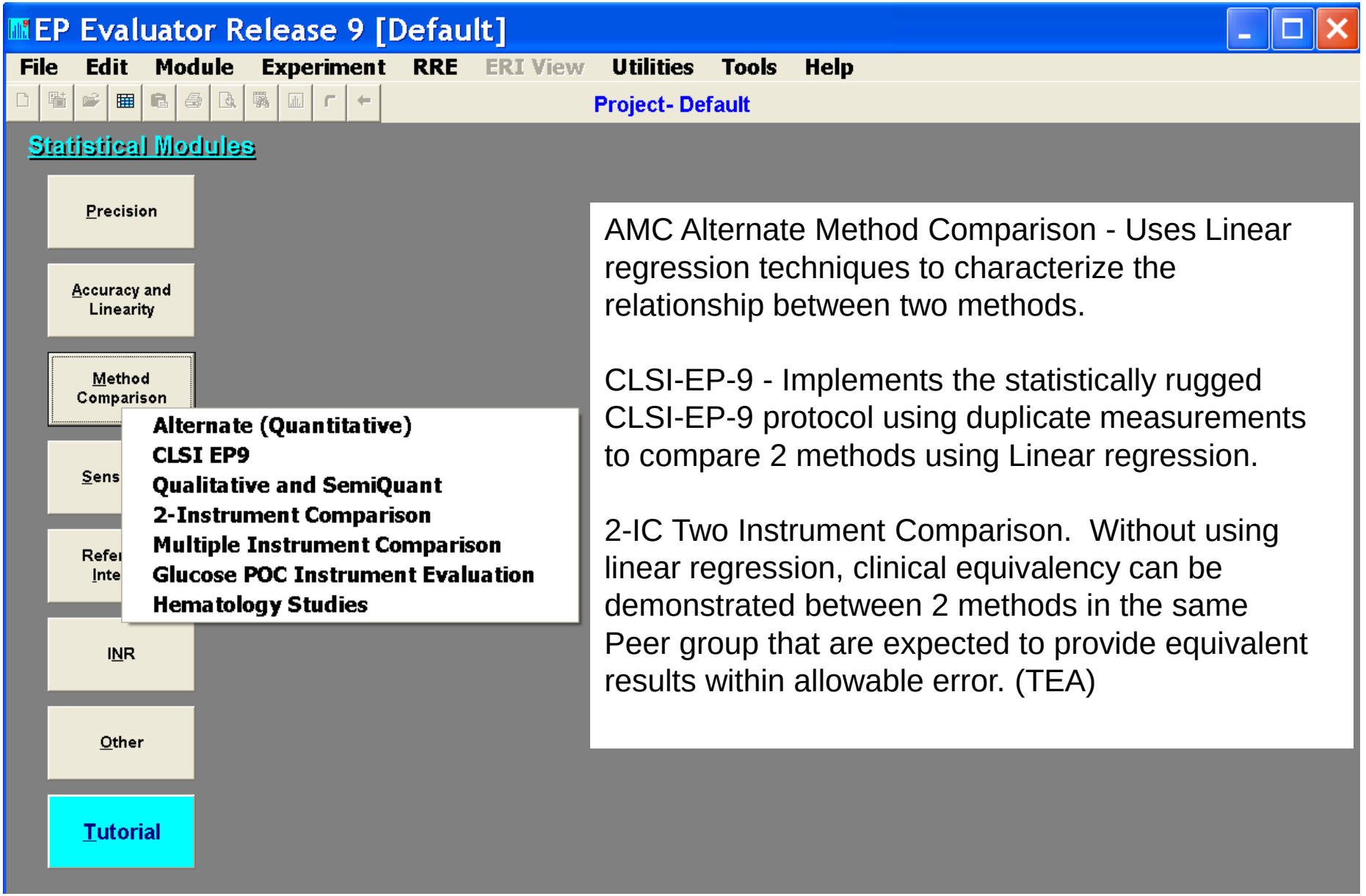
- **Statistical Module screen** main screen
- **Module Overview Screen** – the main entry screen for each module- summary of all current experiments in a project
- **Parameter screen** – customizes the options for each experiment, when creating the experiment initially or modifying later.
- **Experiment Detail screen** – data entry and experiment statistics.

Copyright 2016 Data Innovations LLC

Statistical Module Screen

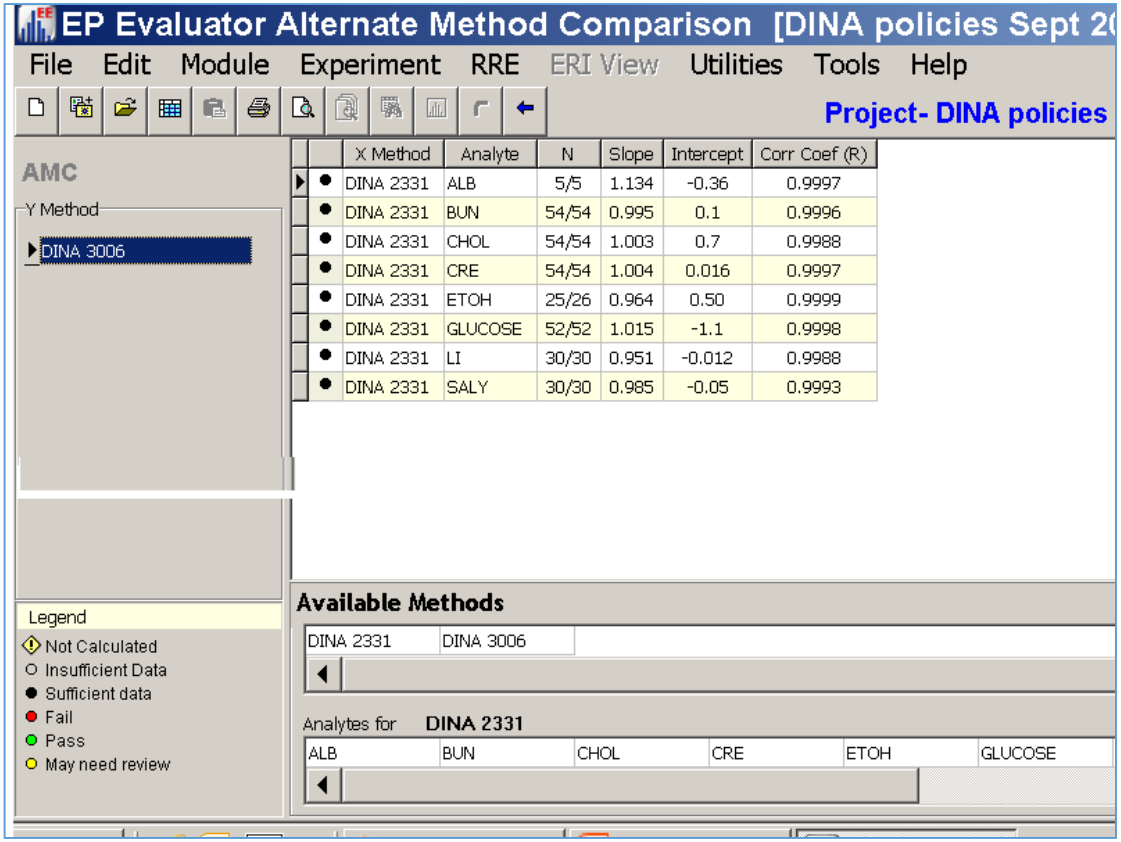
- Main screen
- 34 modules (10 in CLIA and COFRAC versions)
- Tutorial - a very basic overview –




EP Evaluator Release 9 [Default]
File
Edit
Module
Experiment
RRE
ERI View
Utilities
Tools
Help
Project- Default
Statistical Modules
Precision
Accuracy and Linearity
Method Comparison
Alternate (Quantitative)
CLSI EP9
Qualitative and SemiQuant
2-Instrument Comparison
Multiple Instrument Comparison
Glucose POC Instrument Evaluation
Hematology Studies
Sens
Refer
Inte
INR
Other
Tutorial
AMC Alternate Method Comparison - Uses Linear regression techniques to characterize the relationship between two methods.
CLSI-EP-9 - Implements the statistically rugged CLSI-EP-9 protocol using duplicate measurements to compare 2 methods using Linear regression.
2-IC Two Instrument Comparison. Without using linear regression, clinical equivalency can be demonstrated between 2 methods in the same Peer group that are expected to provide equivalent results within allowable error. (TEA)

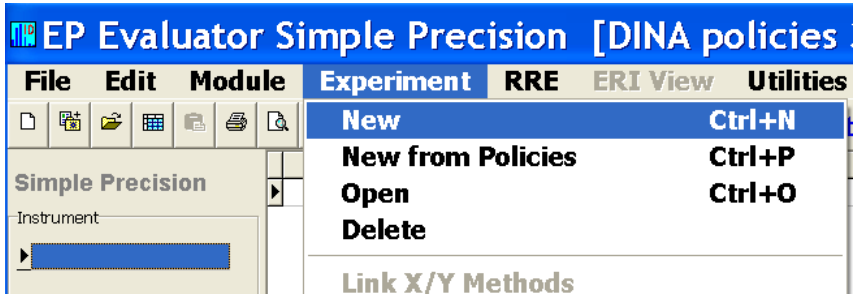
Module Overview Screen

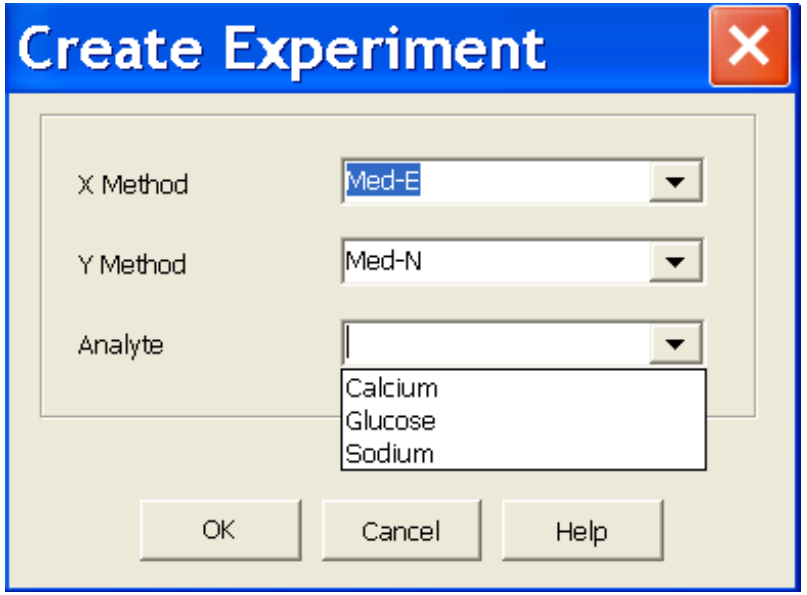
- Gray Table of contents
  - Module name
  - All instruments with experiments
- White grid:
  - For each instrument Lists all experiments with basic stats. their status: pass, fail, not calculated, etc.
- Experiment: one analyte
- Double click experiment to open it



Creating a new experiment

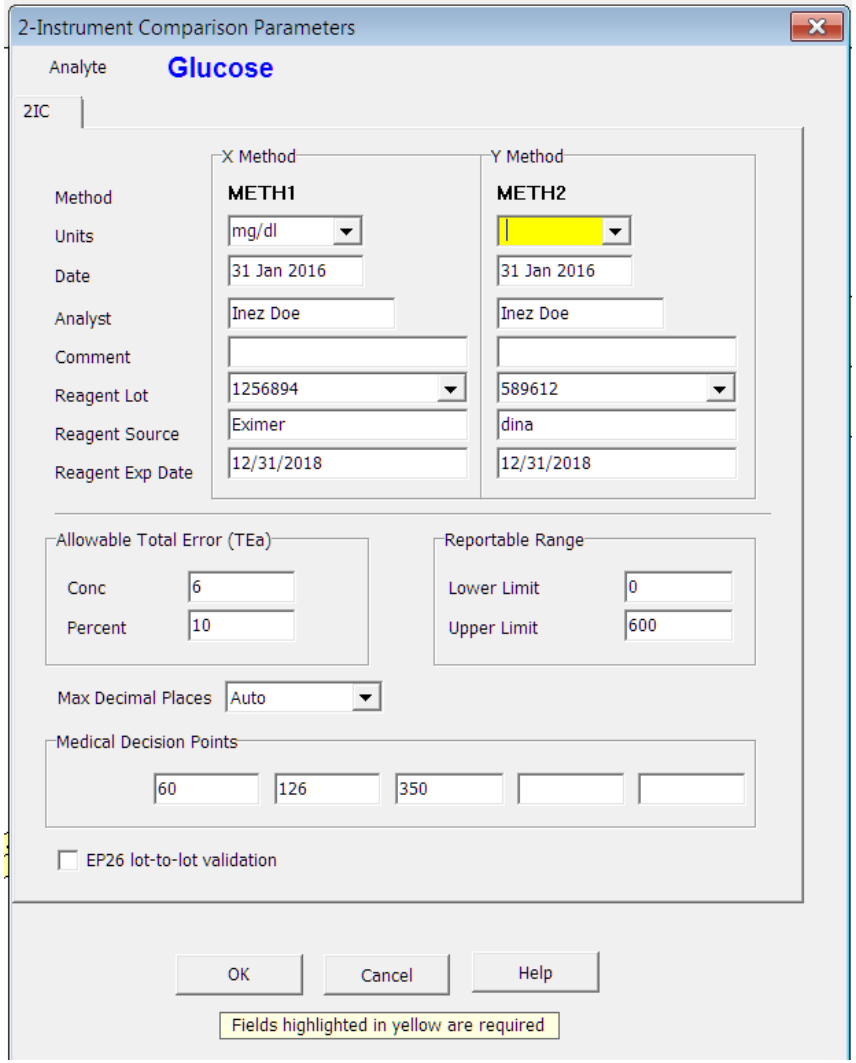
- Click the New Experiment icon , or choose Experiment / New from the Experiment Menu.
- Name the new experiment
  - Method or instrument name
  - Analyte name
  - For precision experiments enter the Sample Name
  - Method comparison experiments need two instrument or method names
    - Method X (reference)
    - Method Y (test)
  - Names entered previously appear in the drop-down items
  - Click OK to go to the Parameters screen





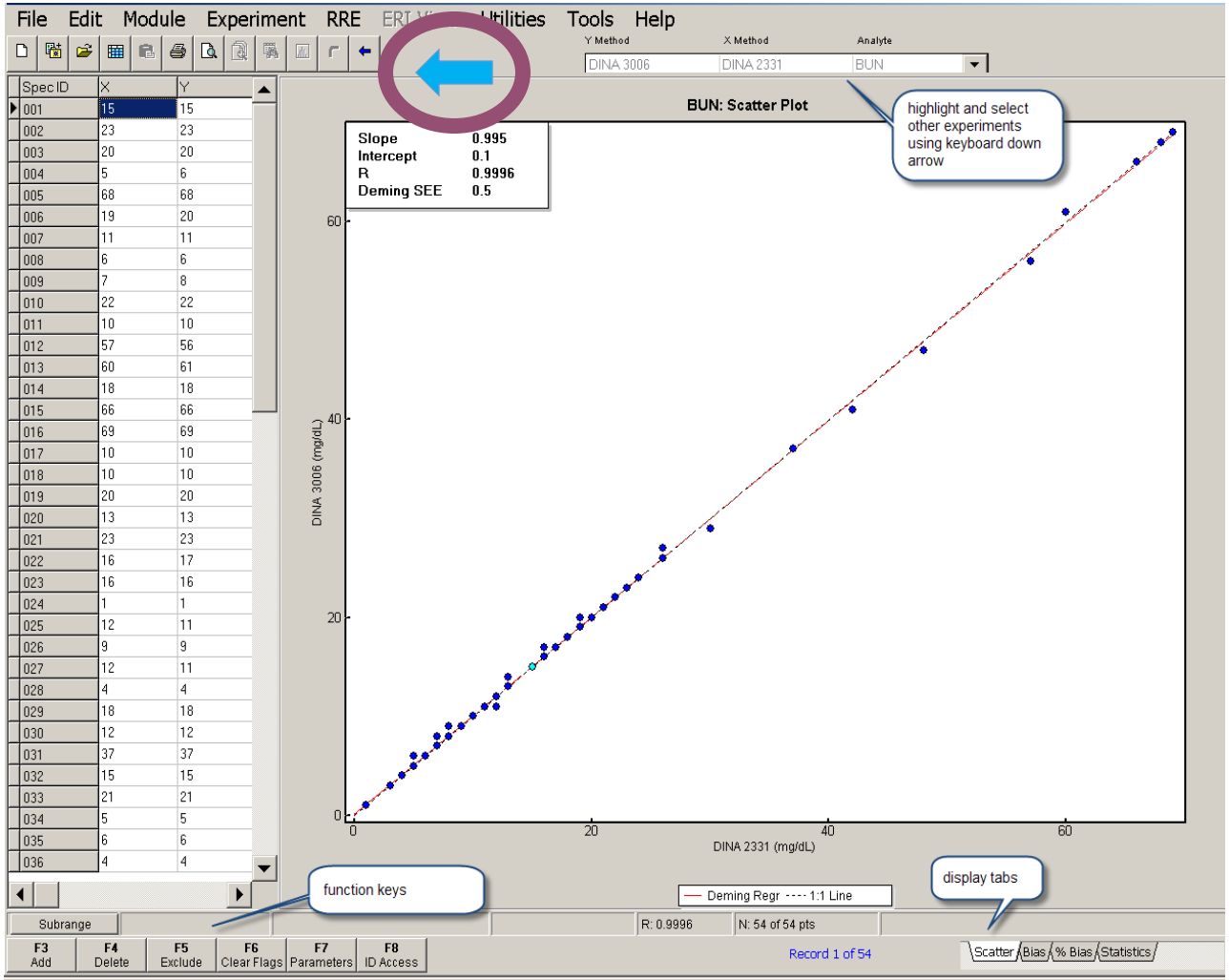
The Parameters Screen

- The parameters screen is where you customize your experiment.
- Define Evaluation criteria like Allowable Error.
- Enter units, analyst name, decimal places, lot numbers, etc.



Experiment Detail Screen

- One analyte
- Data Entry
  - Manual or
  - paste from Excel
- Blue Back arrow
- Function keys
- Observed statistics

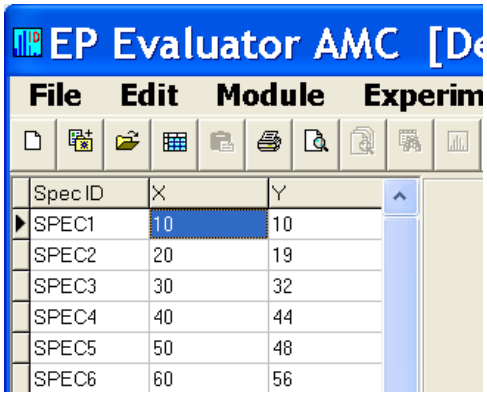


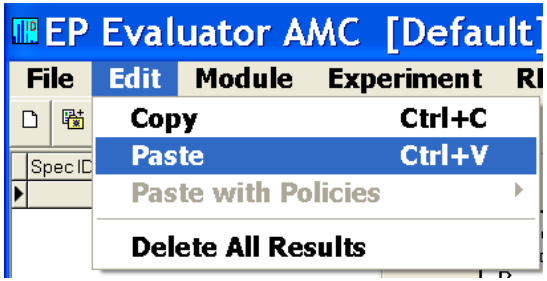
Copyright 2016 Data Innovations LLC

Entering Data

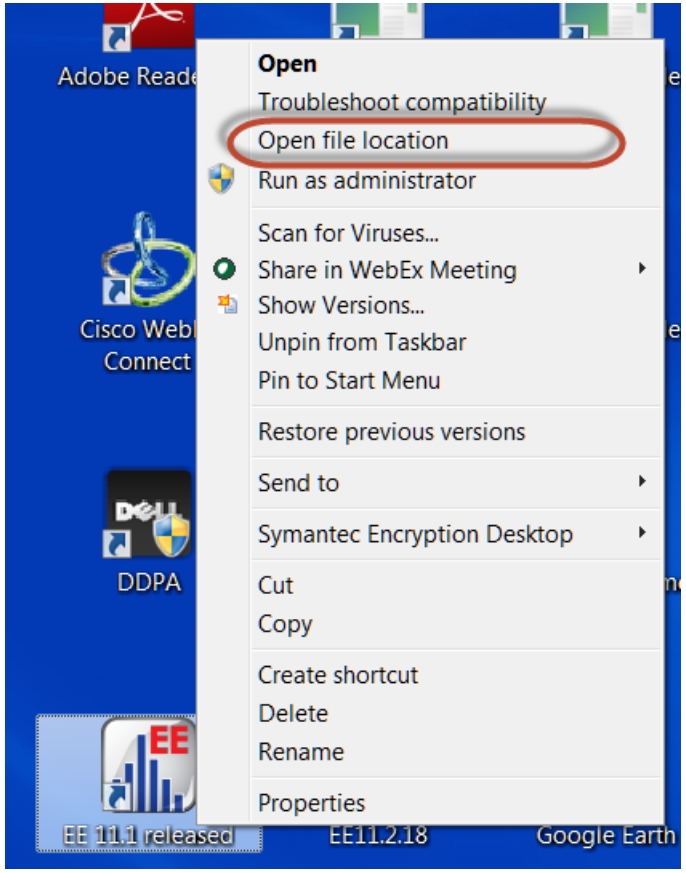
Here are 2 ways to enter data into the Experimental Detail Screen.

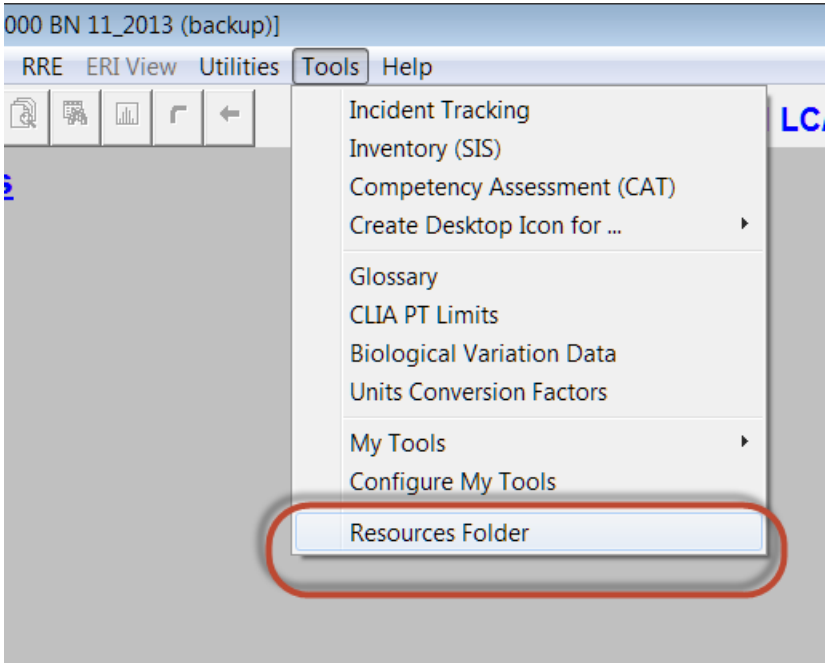
1. Type it into the highlighted cell.
2. You can paste data from a Microsoft® Excel spreadsheet.
   - The EE program folder on your computer or network contains a spreadsheet with examples of correct formats to paste data into the experimental detail screen for most modules. i.e., "**C:\EE11\Resources\PasteExptDetail.xls**"
   - Simply COPY the data from the spreadsheet and PASTE it into EE using the PASTE command in the EDIT menu.





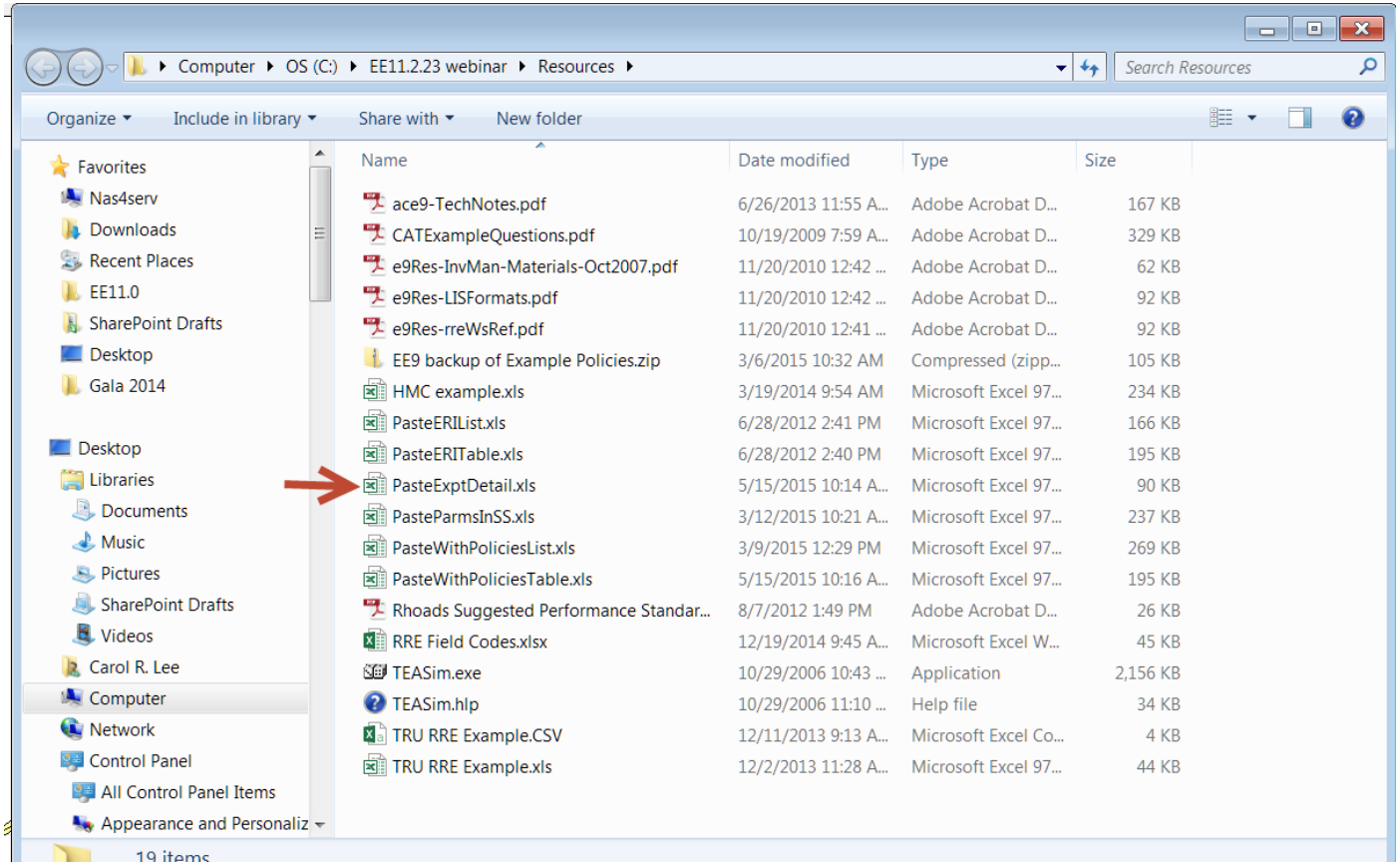
Find your Resource folder





EE Resources Folder

Annotated examples for RRE techniques are available in your EE\Resources folder. Use with the project ExamplePolicies



Paste into Experiment Detail Screen

- Create an experiment as if you were going to type the results …
  - Experiment – New
  - Experiment – New from Policies
- Then paste the results instead of typing them
- Paste just the numbers – not column headings or Sample IDs.

- Note: This technique doesn't work for all statistical modules

Copyright 2016 Data Innovations LLC

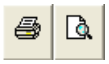
Specimen IDs

- Header = SPECID
- Method Comparison SPECID used to link the data pairs
- Linearity SPEC IDS convention for each level of “standards” Lin-01, Lin-02, Lin-03, etc. The dash is configurable in Preferences.
- SpecID is alphanumeric
- SPECID sort is alphanumeric, not numeric. 1, 10, 2, 20, 3, 30, …..
- Default SPECIDs for EE follow the format S00001

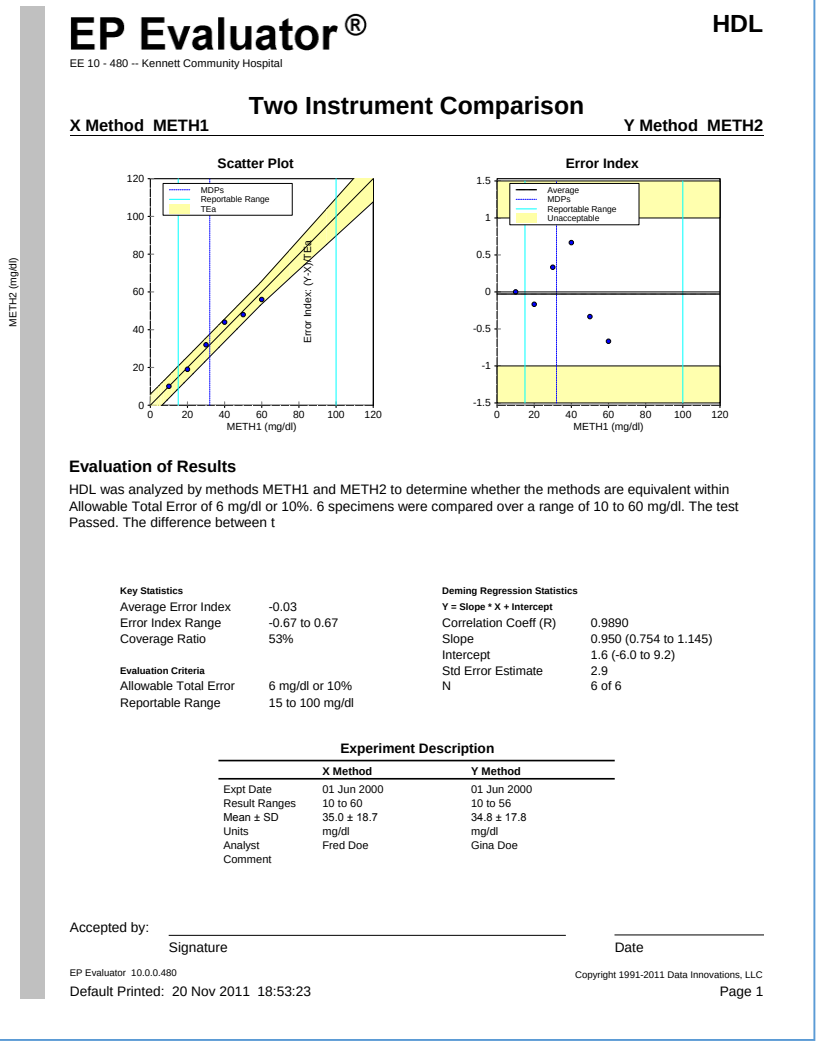
Copyright 2016 Data Innovations LLC

Printing a Report

- **Single Experiment Report.** To Print or Preview a single report from the Experimental detail screen, select Print (or Print Preview) from The FILE Menu. Or click the appropriate icon.



- **Reports with Multiple Experiments.** To print reports and a Summary page for multiple experiments, you must be in the OVERVIEW screen. Again, select Print or Print Preview from the File Menu, or click the appropriate icon.



EP Evaluator® HDL

EE 10 - 480 -- Kennett Community Hospital

Two Instrument Comparison

X Method METH1 **Y Method METH2**

Scatter Plot

Error Index

Evaluation of Results

HDL was analyzed by methods METH1 and METH2 to determine whether the methods are equivalent within Allowable Total Error of 6 mg/dl or 10%. 6 specimens were compared over a range of 10 to 60 mg/dl. The test Passed. The difference between t

Key Statistics	
Average Error Index	-0.03
Error Index Range	-0.67 to 0.67
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)	0.9890
Slope	0.950 (0.754 to 1.145)
Intercept	1.6 (-6.0 to 9.2)
Std Error Estimate	2.9
N	6 of 6

Experiment Description

	X Method	Y Method
Expt Date	01 Jun 2000	01 Jun 2000
Result Ranges	10 to 60	10 to 56
Mean ± SD	35.0 ± 18.7	34.8 ± 17.8
Units	mg/dl	mg/dl
Analyst	Fred Doe	Gina Doe
Comment		

Accepted by: _____ _____

Signature Date

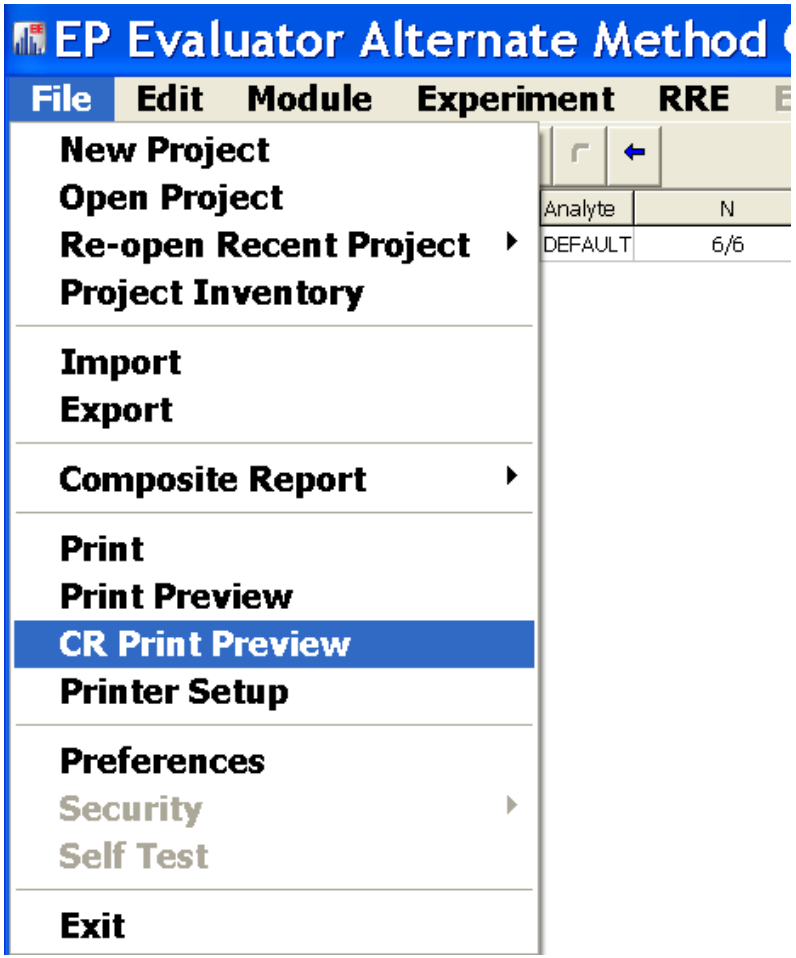
EP Evaluator 10.0.0.480

Copyright 1991-2011 Data Innovations, LLC

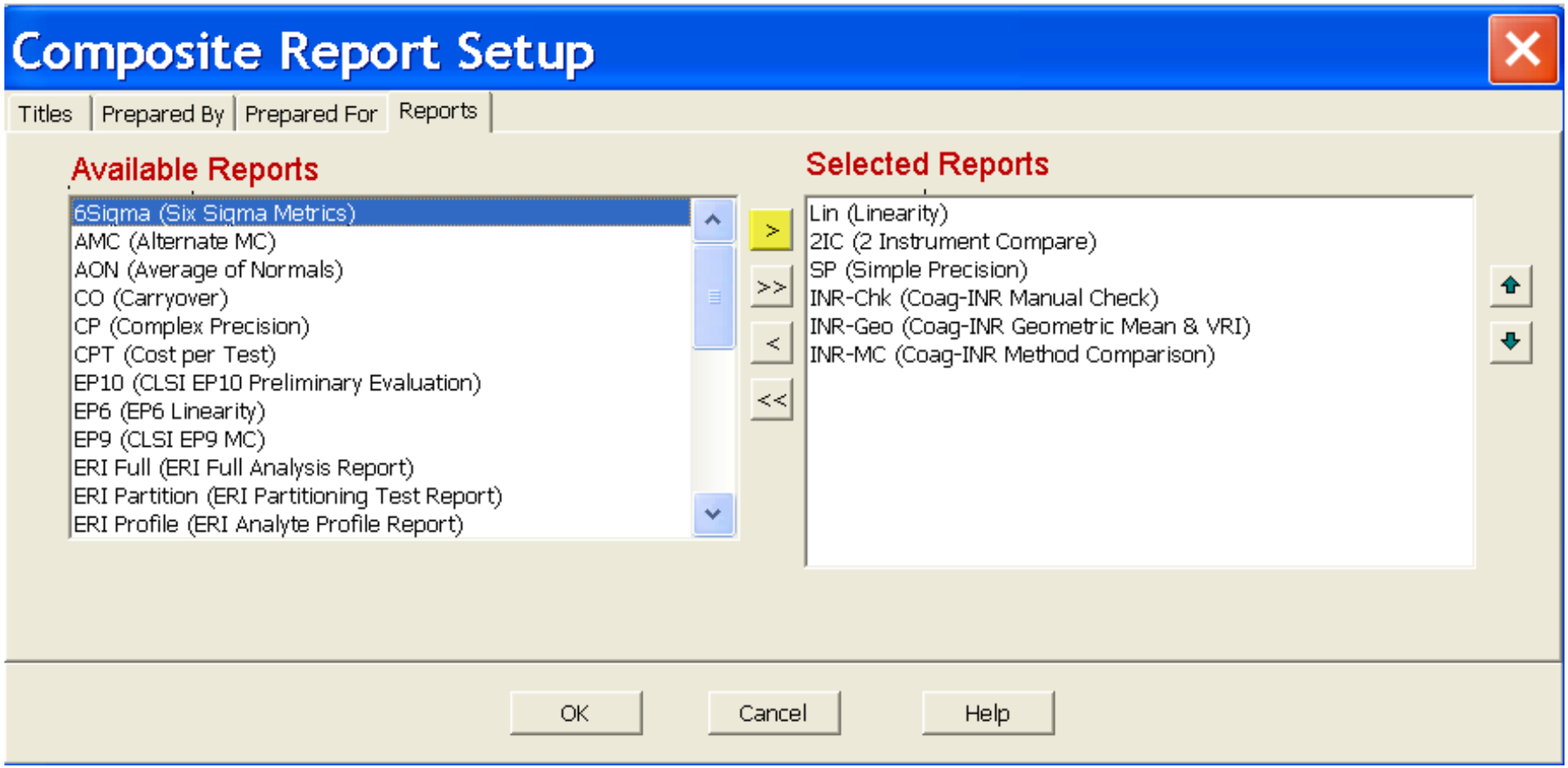
Default Printed: 20 Nov 2011 18:53:23

Composite Reports

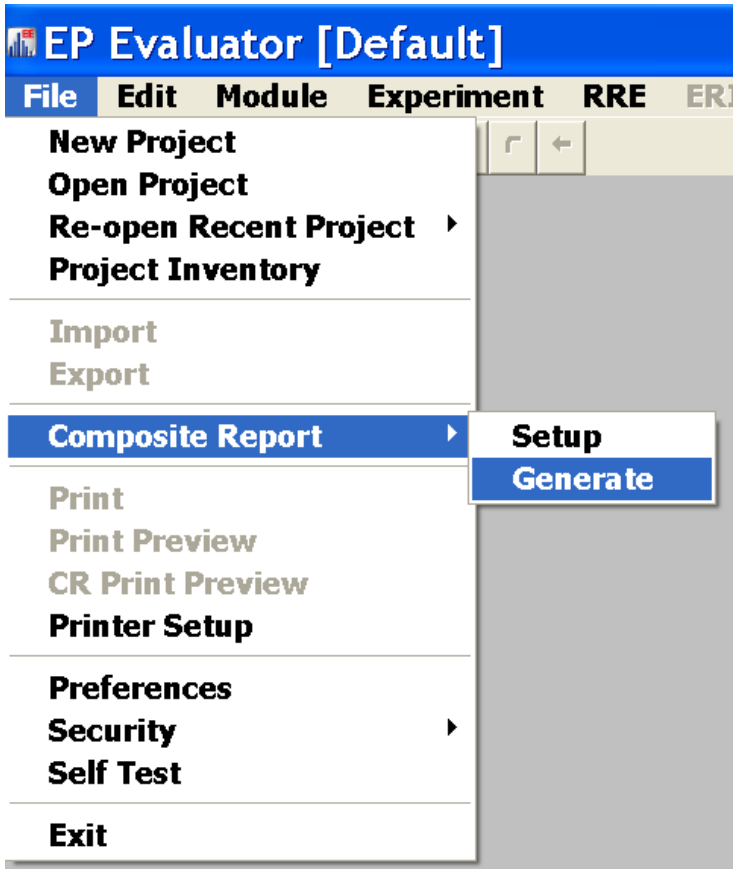
- Create Composite Reports for Multiple Experiments in Multiple Modules.
  - Set up the Composite Report (CR) from the File Menu
  - When an experiment is ready to report, select CR Print Preview (or click the icon) to add the report to the c mposite report list.
  - Generate the Report from the File Menu.

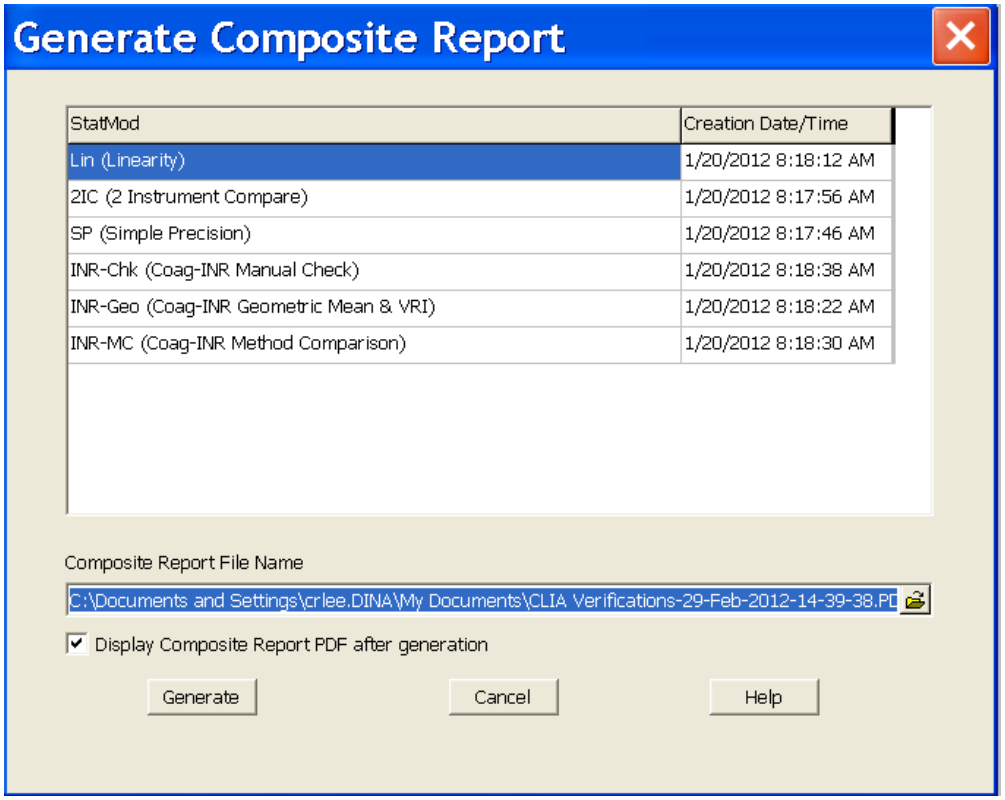


Composite Report Setup



Generate Composite Report





EP Evaluator®

CLIA Verifications

Semi-Annual

2/29/2012

Prepared for

Carl Commissioner
Regularatory Commission
123 Commission Drive
Anytown, XX, 12345

Prepared by

Dr. Mark Mainstay
Clinical Laboratory
Kennett Community Hospital
Kennett Square, PA 19348

Accepted by

Signature

Name / Title

Date

Copyright 1991-2012 Data Innovations, LLC

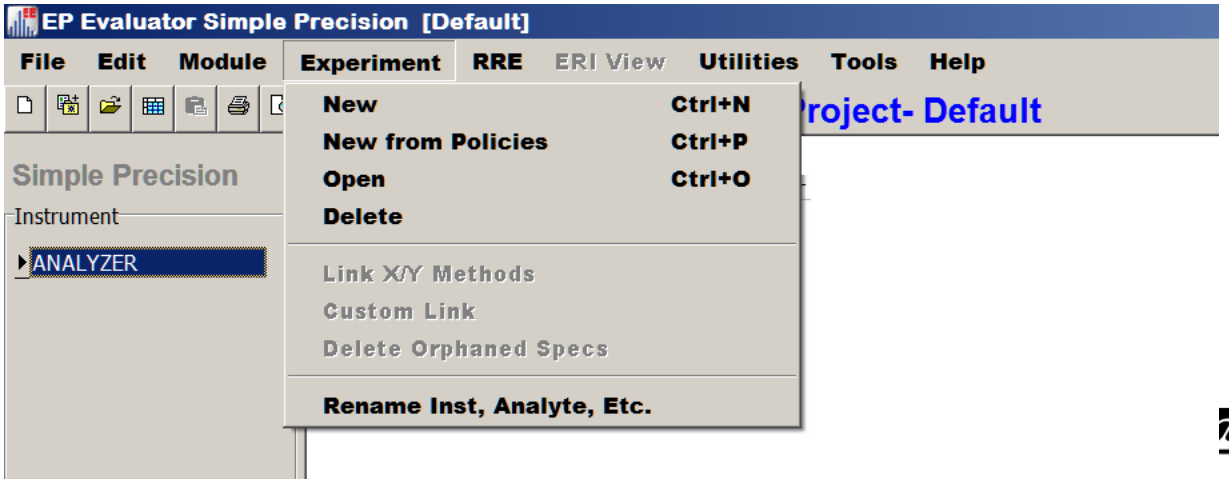
EP Evaluator®

Table of Contents

Module	*Page*
Lin (Linearity)	3
2IC (2 Instrument Compare)	15
SP (Simple Precision)	19
INR-Chk (Coag-INR Manual Check)	22
INR-Geo (Coag-INR Geometric Mean & VRI)	24
INR-MC (Coag-INR Method Comparison)	26

Menu Bar Options

datainnovations.com



DATA INNOVATIONS
Simple Ideas, Better Solutions

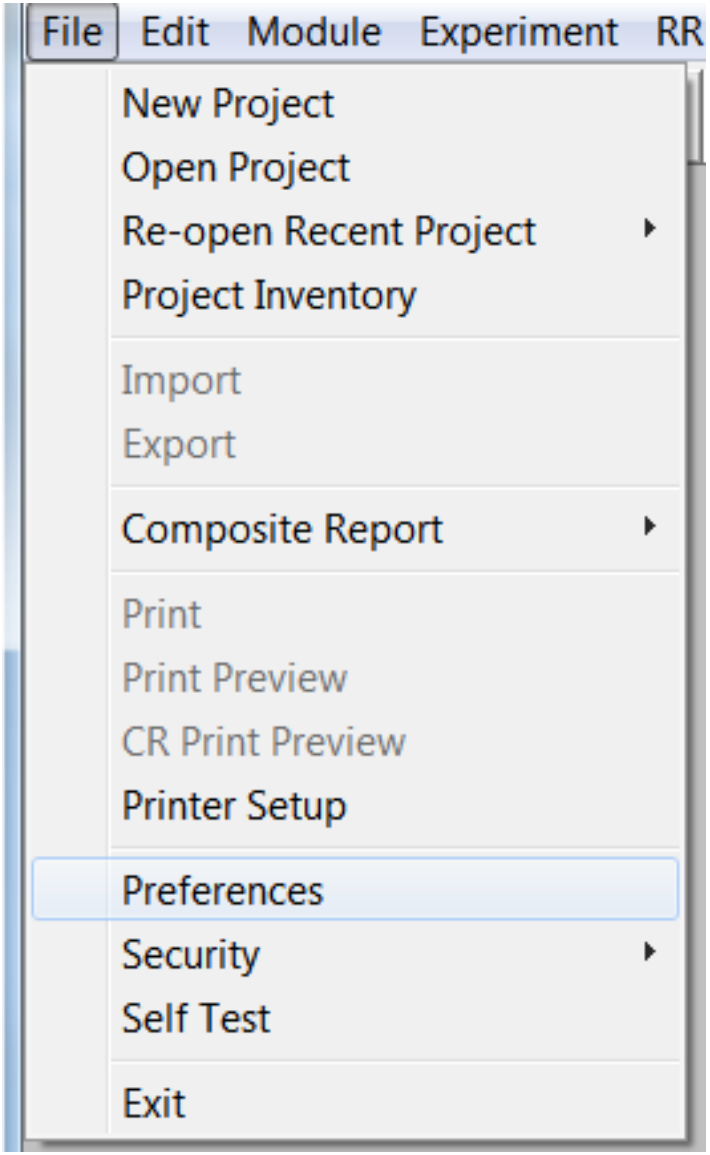
Key Menu Bar options * 1

- **File**
  - New and Open projects
  - Import export: transfer projects and experiments
  - Preferences: set up special options for several modules.
  - Project inventory
  - Print / Print Preview / Print Setup
  - User Security – Professional version
- **Edit:** copy/paste / delete data
- **Module:**
  - shortcuts to the modules from any location.
  - Recalculate statistics. Or Clear Overview statistics
  - Summarize to History for Linearity or MIC modules
  - Batch Edit the lot numbers

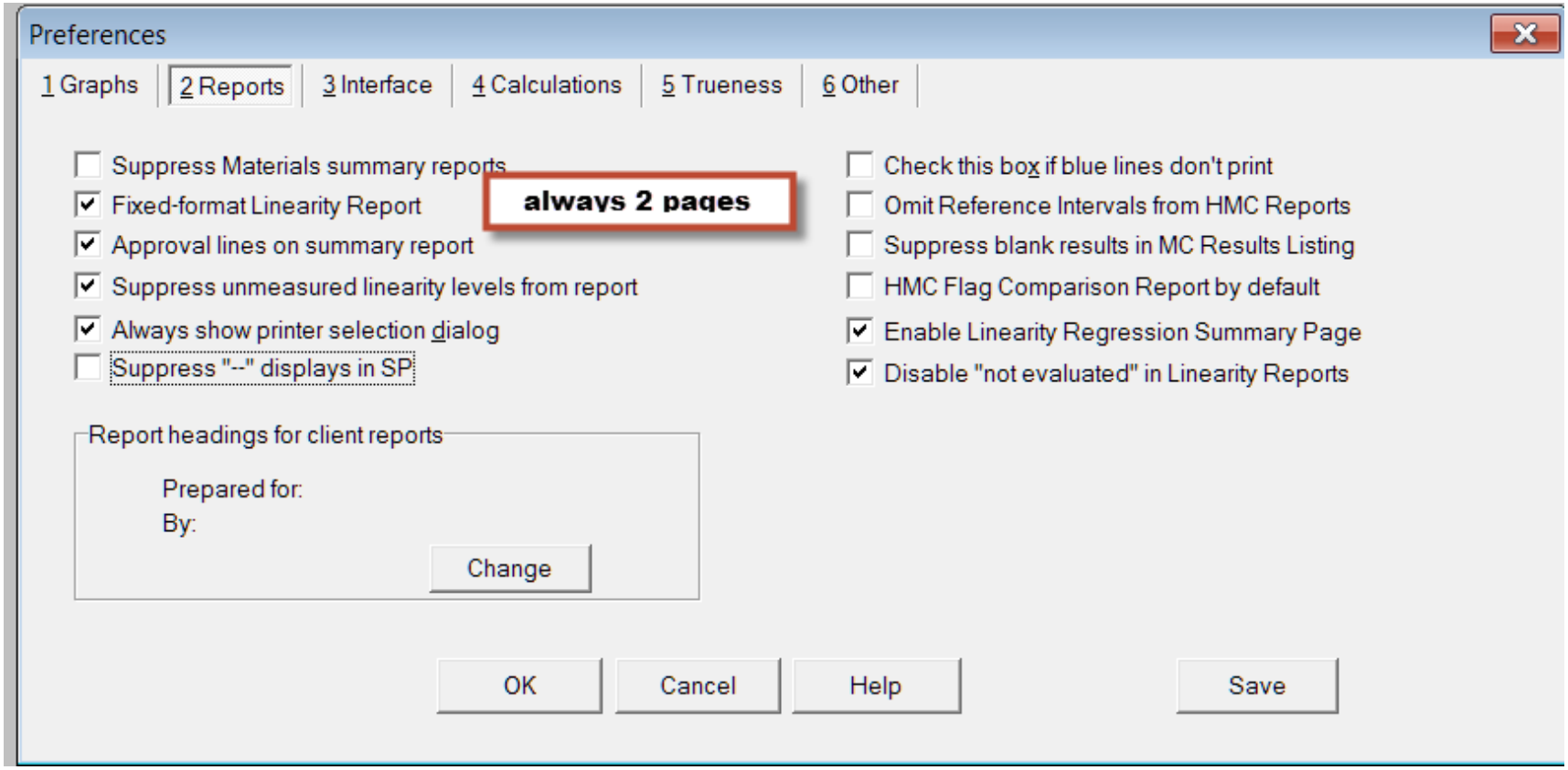
Copyright 2016 Data Innovations LLC

Preferences

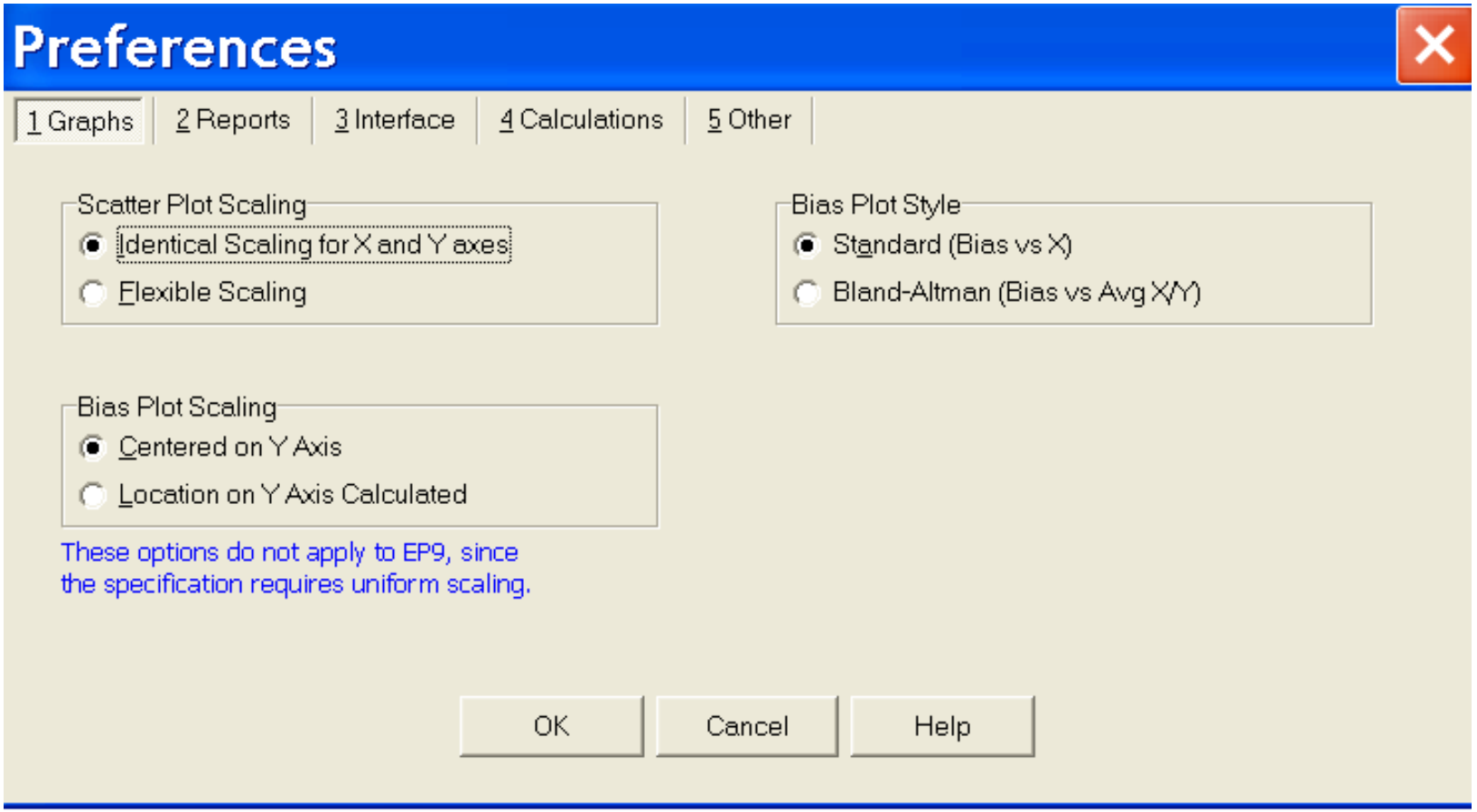
- View Preferences in File \ Preferences
- Within a project, Preferences apply to all existing and future experiments
- Prior to EE11.0, you could change preferences in a project, but when you closed the program and returned, the original preferences came back
- In EE 11.0, you can save preferences as prefernces.ini file that will apply to **all** projects on the local machine.



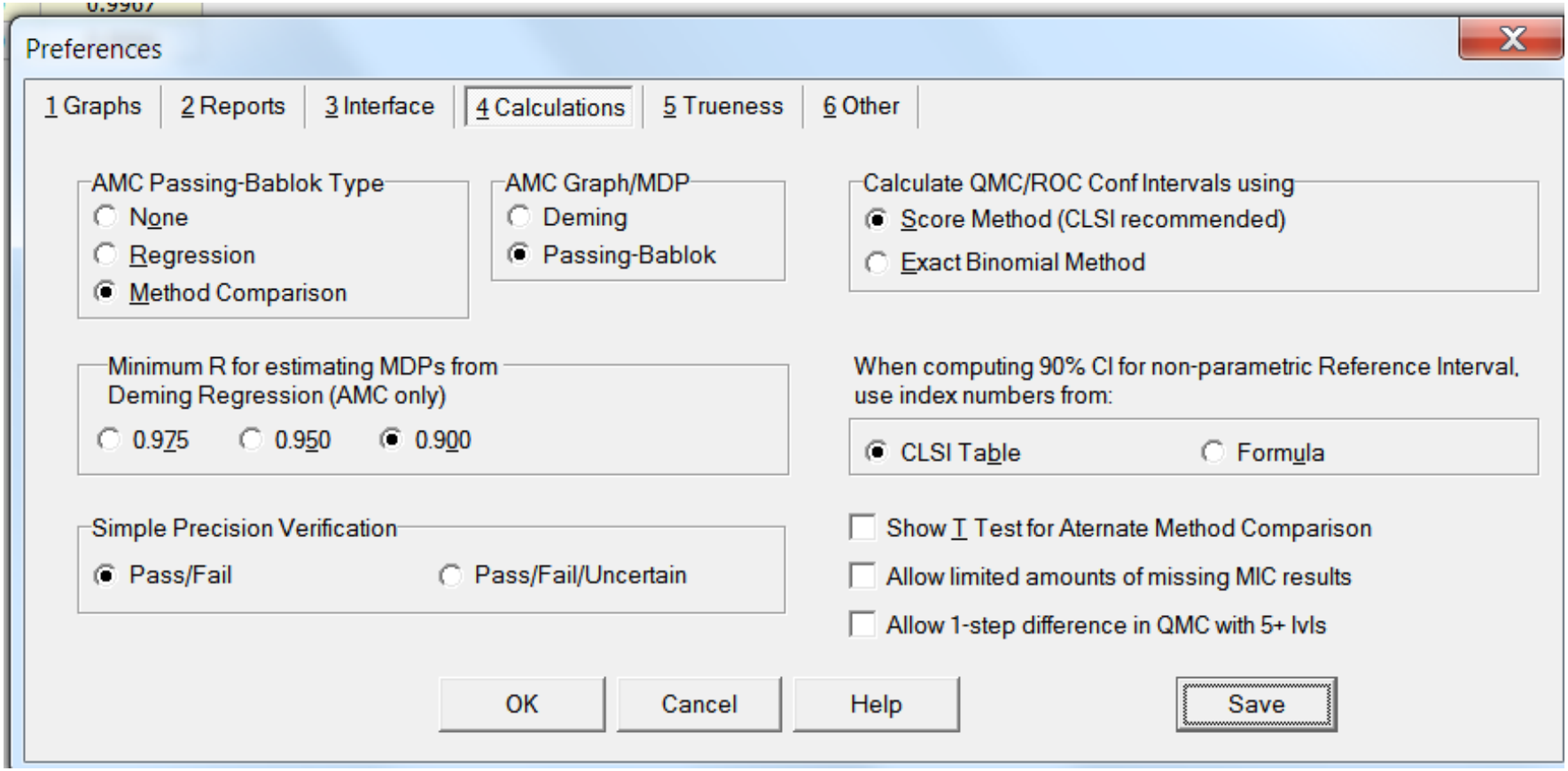
Preferences Affecting Linearity Reports



Preferences for Regression Graphs



Preference Calculations



AMC Statistics Tab

Regression Analysis	Deming	Passing-Bablok	Regular
Slope	1.036 (1.017 to 1.056)	1.000 (1.000 to 1.000)	1.021 (1.002 to 1.041)
Intercept	-3.7 (-5.7 to -1.6)	0.0 (0.0 to 0.0)	-2.2 (-4.2 to -0.1)
Std Err Est	0.9	--	0.9
SMAD	0.6	0.0	0.7

Distribution of Results					
Range	<= 83.3	83.4-116.7	116.8-150.0	150.1-183.3	> 183.3
Percent	2%	98%	0%	0%	0%

Other Statistics	
Points (Plotted/Total)	296/297
Outliers	Not Tested
SubRange Bounds	None
Corr Coef (R)	0.9862
Bias	0.0 (0.0 %)
X Range	79 to 113 (1X)
Y Range	79 to 113 (1X)
X Mean ± SD	102.8 ± 5.0
Y Mean ± SD	102.8 ± 5.1
Rep SD X	1
Rep SD Y	1
SD of differences	0.9
Paired T Test	0.95
T Probability	0.344
Degrees of Freedom	294

Passing Bablock enabled by preferences

Red type indicates ideal slope of 1.0 or intercept of 0.0 is not within the confidence intervals

Confidence intervals calculated per CLSI EP09-A2

Copyright 2016 Data Innovations LLC

Key Menu Bar options - 2

- **Experiment**
  - New experiments from scratch CNTRL N
  - New experiments using policy definitions CNTRL P
  - Open a specific experiment CNTRL O
  - Link X and Y methods
  - Custom Link data with dissimilar names
  - Delete orphaned specs (AMC POC EP9 or 2IC)
  - Rename / delete experiments

Copyright 2016 Data Innovations LLC

Key Menu Bar options - 3

- RRE
  - Create experiments for multiple analytes using
    - instrument capture
    - Keyboard entry from instrument printouts
  - Capture Data from Instrument Manager
  - Define policy definitions to re-use over and over
  - Define global lot numbers
  - Open last or saved RRE worksheets
  - AON Data Manager.

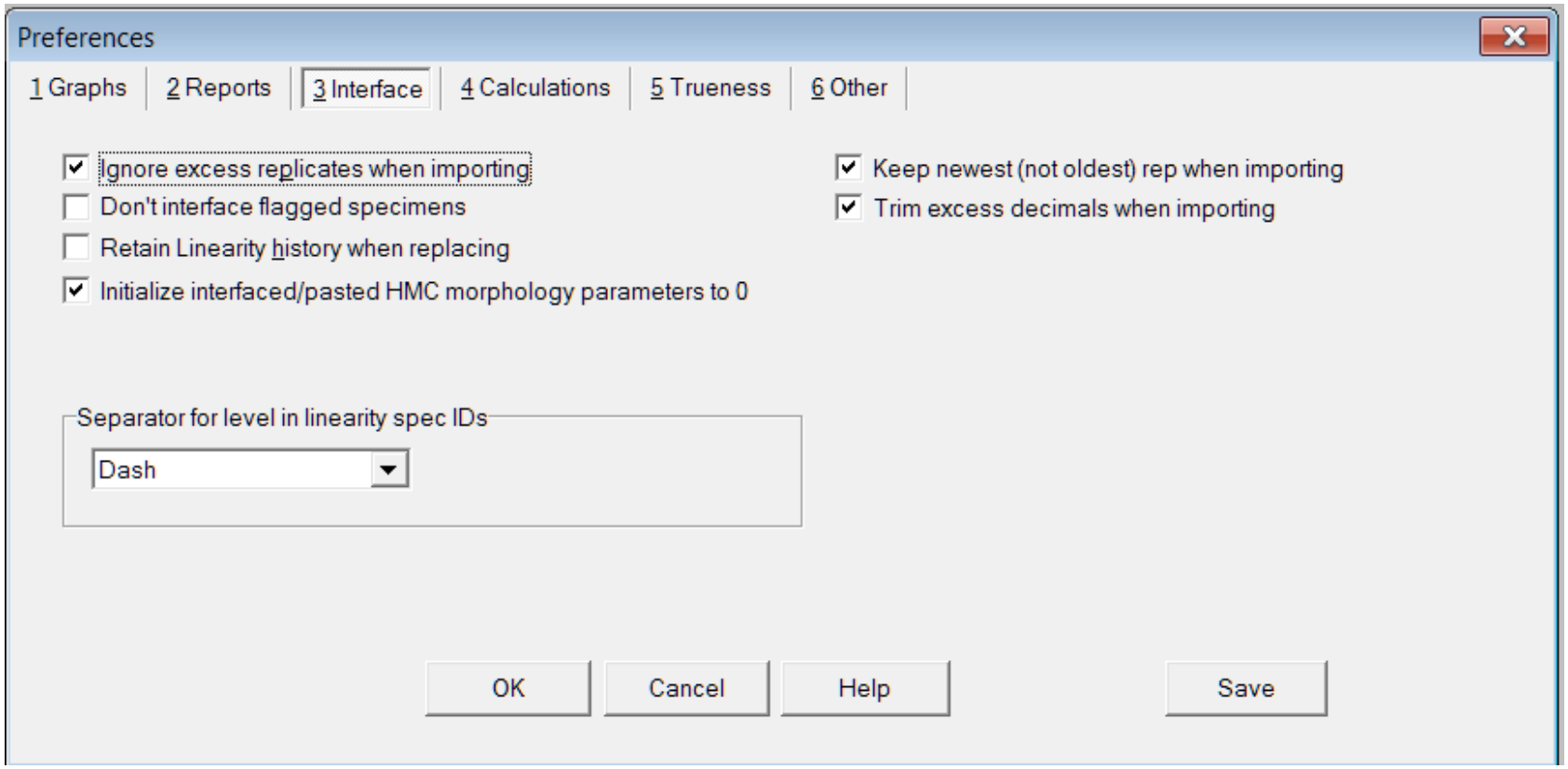
Copyright 2016 Data Innovations LLC

Useful Menu Bar Options – Misc.

- **Utilities**
  - File Manager – manages your projects, backup files, view inventory on all projects
  - Typing Help History Editor – edit items in the dropdowns
  - Update Wizard - brings all active projects into new major version
- **Tools**
  - Open the 3 lab management modules and create their icons
  - CLIA PT limits table
  - Glossary of terms
- **Help**
  - Indexed and Searchable help
  - Send a bug report
  - Check for a newer major or minor version: automatic update as prompted
  - Renew subscription

Copyright 2016 Data Innovations LLC

Preferences affecting Interfacing or copy/paste



For EE Support

- North America Telephone Support (802)-658-1955
  - Northamerica-support@datainnovations.com
- Europe telephone support +32 2 332 24 13
  - Europe-support@datainnovations.com
- Asia Telephone Support 852-2398-3182
  - asia-support@datainnovations.com
- Latin America telephone support 55-11-38013283
  - latinamerica-support@datainnovations.com

Copyright 2016 Data Innovations LLC

Additional Training & Services

- Visit the DI website for information on free training. http://datainnovations.com/services/training/ep-evaluator-training-programs
  - Overview and Getting Started with EP Evaluator
  - Project Management
  - RRE and Policy Definitions
  - Hematology Method Comparison
  - Determining Performance standards
  - Inventory Management
- For more in-depth training or consultation
  - Contact the DI Sales organization for a quote
    - 802-658-2050
    - Northamerica-sales@datainnovations.com

Copyright 2016 Data Innovations LLC

datainnovations.com

Thank You!

DATA INNOVATIONS
Simple Ideas, Better Solutions