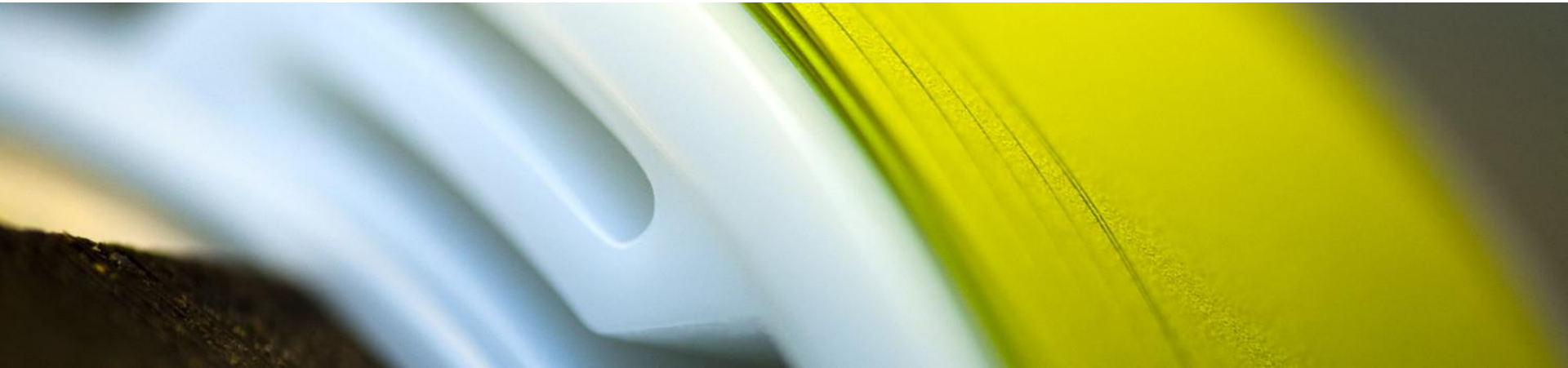
Presented for BASAS at Gilead, Foster City, CA

BASAS

# PrecMod: An Automated SAS® Macro for Estimating Precision via Random Effects Models

*Jesse A. Canchola and Pari Hemyari*

*03-Nov-2016*



# Disclaimer

BASAS Roche

- The views and opinions expressed in this presentation are solely those of the authors and do not necessarily reflect the official policy or position of Roche Molecular Systems, Inc. or its parent company.

# Outline

BASAS Roche

- Typical (Assay) Product Life Cycles
- Introduction to Assays & Performance Metrics Outline
- Precision Definitions
- Motivation
- Theory and Estimation of Precision
- Available tools
- Introducing the PrecMod SAS Macro
- Example

# Outline

BASAS Roche

- Typical (Assay) Product Life Cycles
- Introduction to Assays & Performance Metrics Outline
- Precision Definitions
- Motivation
- Theory and Estimation of Precision
- Available tools
- Introducing the PrecMod SAS Macro
- Example

# Outline

BASAS Roche

- Typical (Assay) Product Life Cycles
- Introduction to Assays & Performance Metrics Outline
- Precision Definitions
- Motivation
- Theory and Estimation of Precision
- Available tools
- Introducing the PrecMod SAS Macro
- Example

# Outline

BASAS Roche

- Typical (Assay) Product Life Cycles
- Introduction to Assays & Performance Metrics Outline
- Precision Definitions
- Motivation
- Theory and Estimation of Precision
- Available tools
- Introducing the PrecMod SAS Macro
- Example

# Outline

BASAS Roche

- Typical (Assay) Product Life Cycles
- Introduction to Assays & Performance Metrics Outline
- Precision Definitions
- Motivation
- Theory and Estimation of Precision
- Available tools
- Introducing the PrecMod SAS Macro
- Example

# Outline

BASAS Roche

- Typical (Assay) Product Life Cycles
- Introduction to Assays & Performance Metrics Outline
- Precision Definitions
- **Motivation**
- Theory and Estimation of Precision
- Available tools
- Introducing the PrecMod SAS Macro
- Example

# Outline

BASAS Roche

- Typical (Assay) Product Life Cycles
- Introduction to Assays & Performance Metrics Outline
- Precision Definitions
- Motivation
- **Theory and Estimation of Precision**
- Available tools
- Introducing the PrecMod SAS Macro
- Example

# Outline

BASAS Roche

- Typical (Assay) Product Life Cycles
- Introduction to Assays & Performance Metrics Outline
- Precision Definitions
- Motivation
- Theory and Estimation of Precision
- Available tools
- Introducing the PrecMod SAS Macro
- Example

# Outline

BASAS Roche

- Typical (Assay) Product Life Cycles
- Introduction to Assays & Performance Metrics Outline
- Precision Definitions
- Motivation
- Theory and Estimation of Precision
- Available tools
- **Introducing the PrecMod SAS Macro**
- Example

# Outline

BASAS Roche

- Typical (Assay) Product Life Cycles
- Introduction to Assays & Performance Metrics Outline
- Precision Definitions
- Motivation
- Theory and Estimation of Precision
- Available tools
- Introducing the PrecMod SAS Macro
- Example

# Outline

BASAS Roche

- Typical (Assay) Product Life Cycles
- Introduction to Assays & Performance Metrics Outline
- Precision Definitions
- Motivation
- Theory and Estimation of Precision
- Available tools
- Introducing the PrecMod SAS Macro
- Example

# Typical Assay Product Life Cycles

# General Product Life Cycles in Diagnostics

BASAS

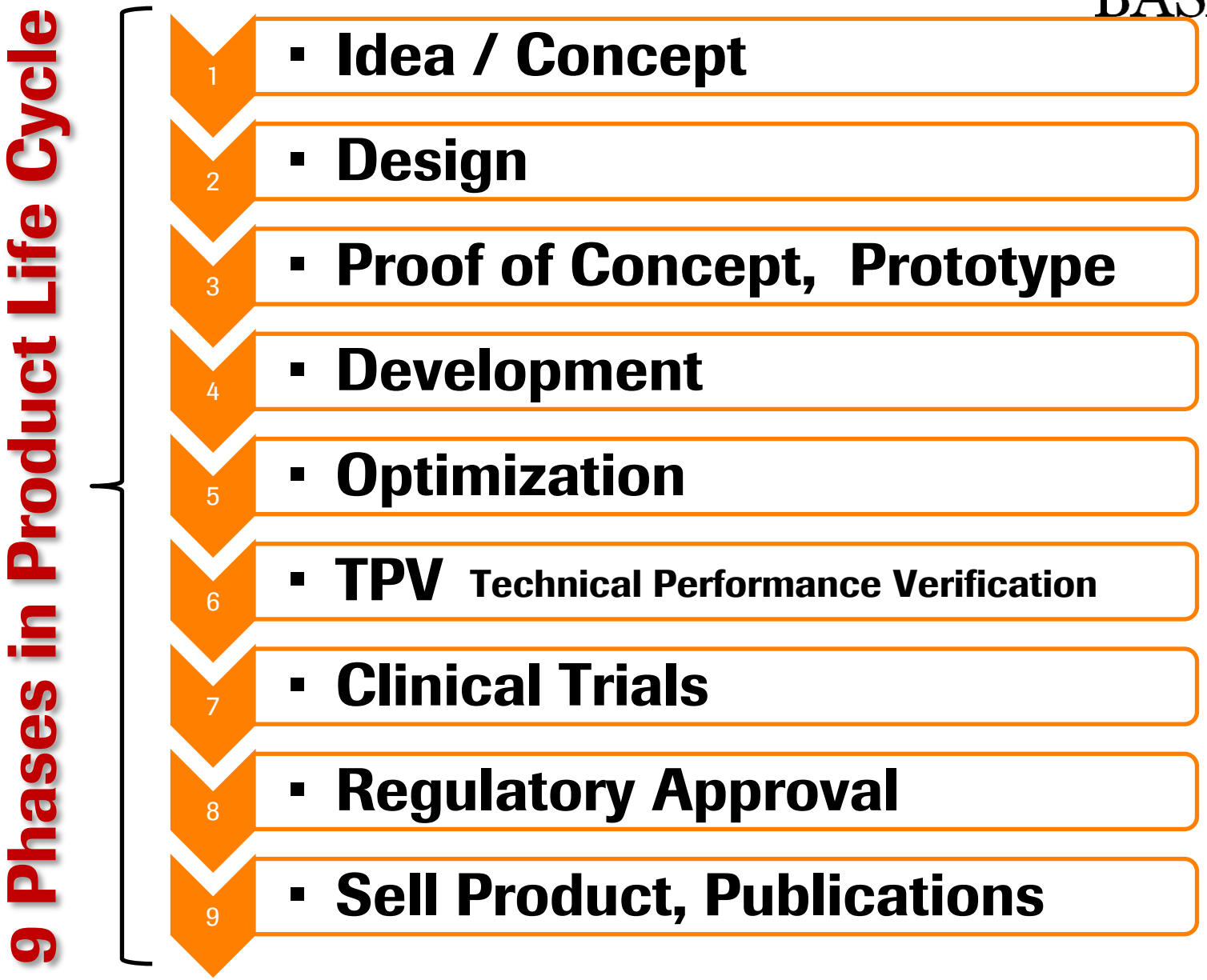
Roche

1. Idea / Concept
2. Design
3. Proof of Concept, Prototype
4. Development
5. Optimization
6. TPV Technical Performance Verification
7. Clinical Trials
8. Regulatory Approval
9. Sell Product, Publications

# General Product Life Cycles in Diagnostics

BASAS

Roche



# General Product Life Cycles in Diagnostics

BASAS

Roche

1. ▪ **Idea / Concept**
2. ▪ **Design**
3. ▪ **Proof of Concept, Prototype**

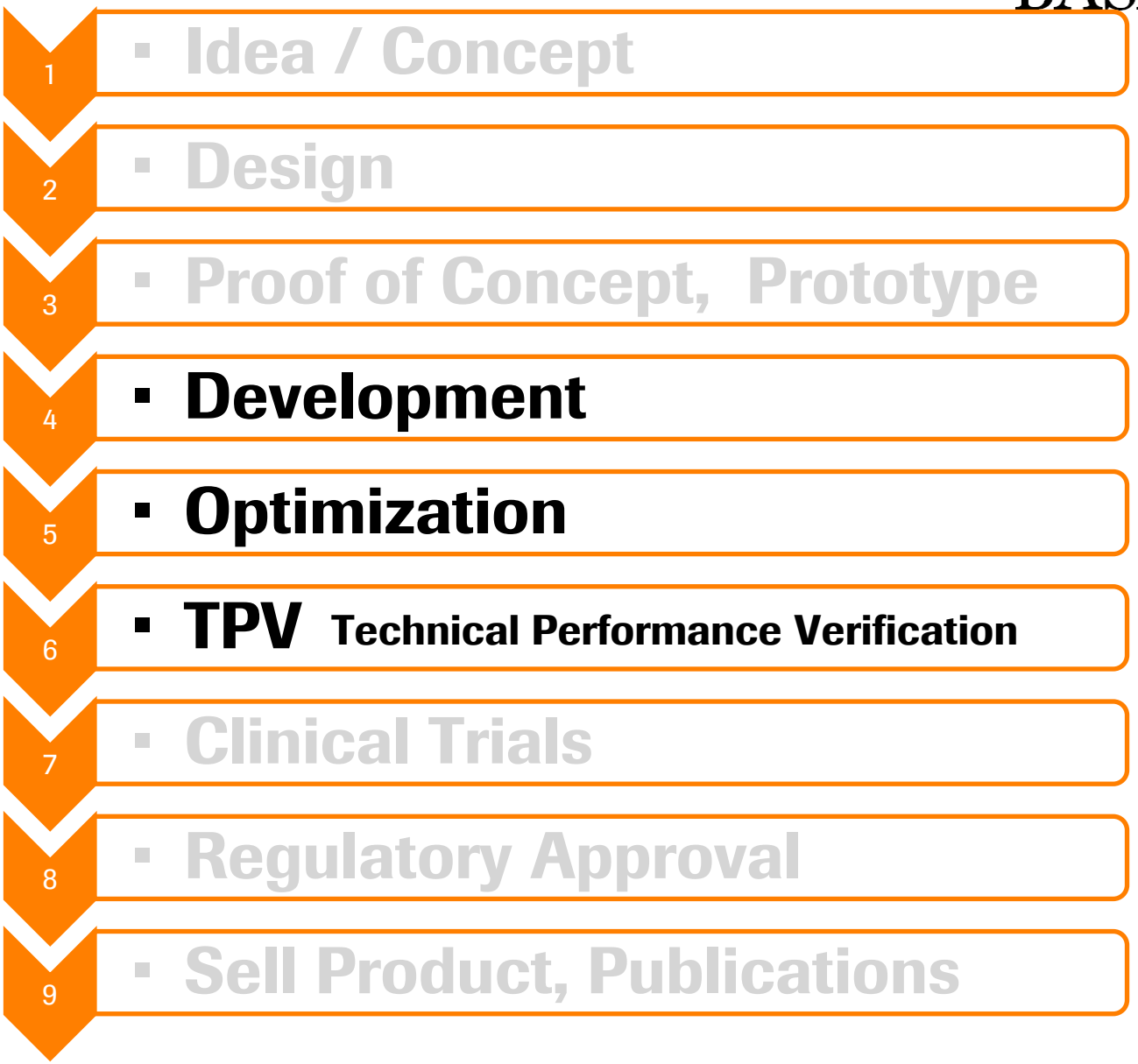
**DI**: Design Input

4. ▪ Development
5. ▪ Optimization
6. ▪ TPV Technical Performance Verification
7. ▪ Clinical Trials
8. ▪ Regulatory Approval
9. ▪ Sell Product, Publications

# General Product Life Cycles in Diagnostics

BASAS

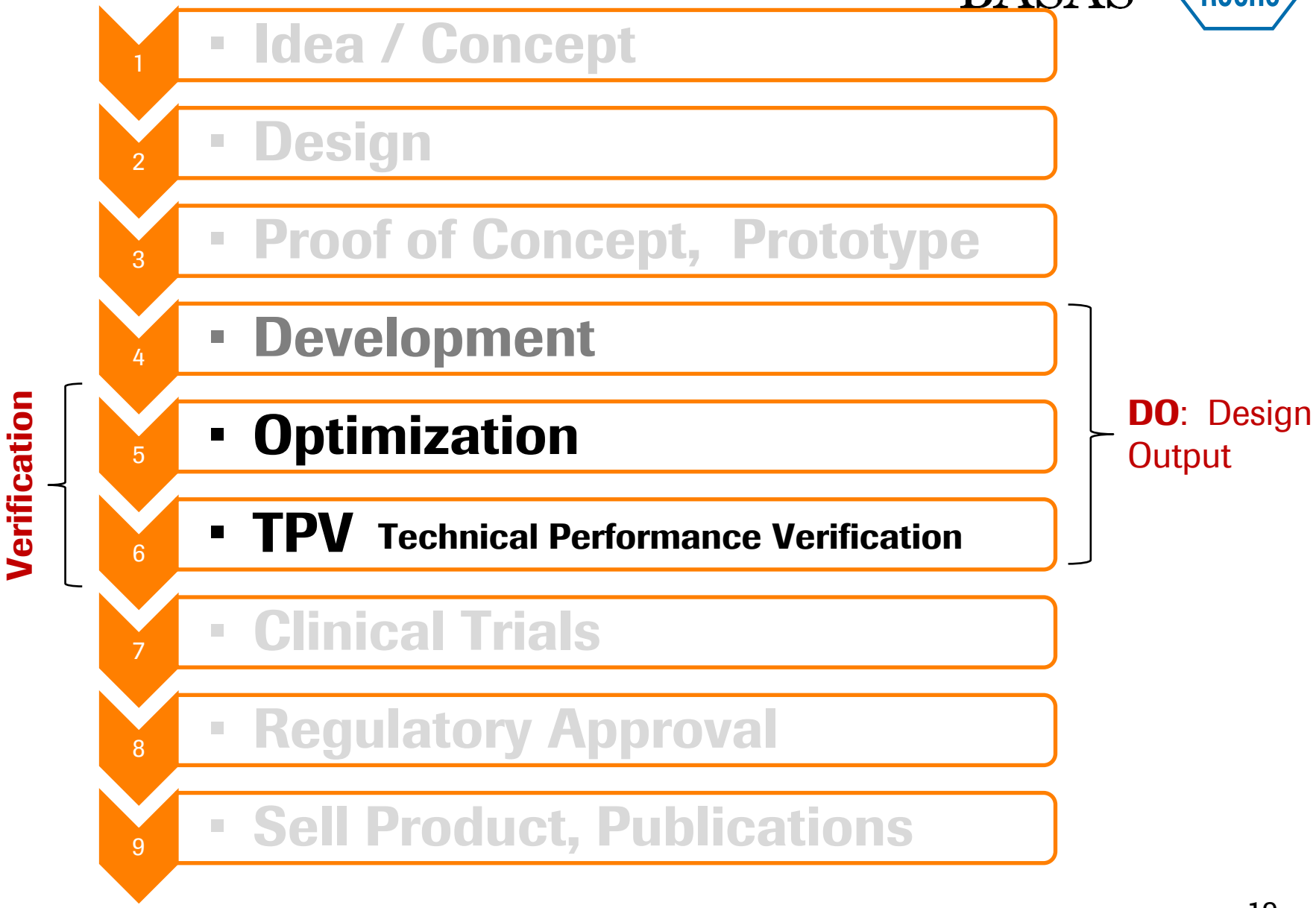
Roche



# General Product Life Cycles in Diagnostics

BASAS

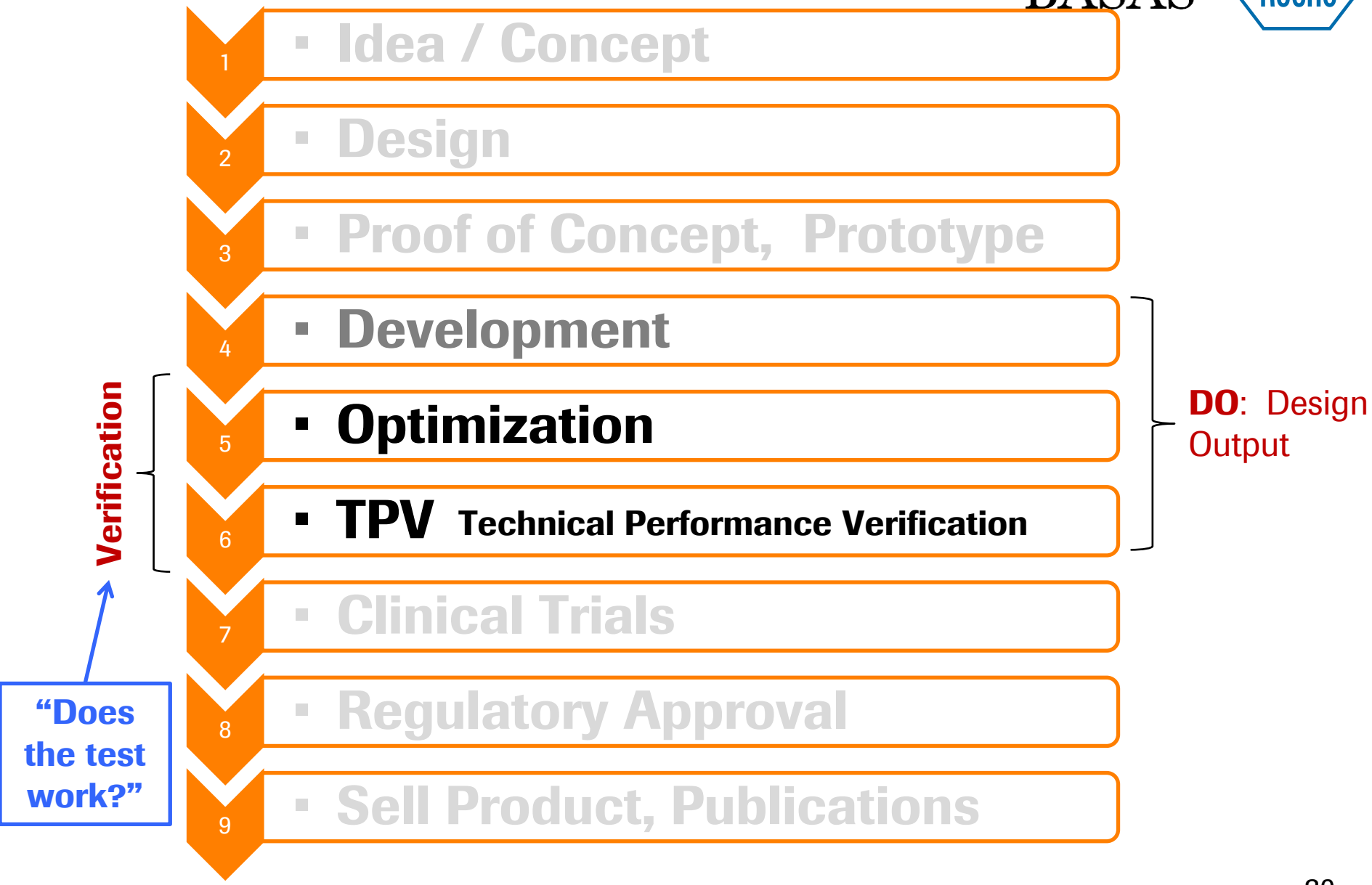
Roche



# General Product Life Cycles in Diagnostics

BASAS

Roche



# General Product Life Cycles in Diagnostics

BASAS

Roche

# General Product Life Cycles in Diagnostics

BASAS

Roche

# General Product Life Cycles in Diagnostics

BASAS

Roche

1. Idea / Concept
2. Design
3. Proof of Concept, Prototype
4. Development
5. Optimization
6. TPV Technical Performance Verification
7. Clinical Trials
8. **Regulatory Approval**
9. Sell Product, Publications

# General Product Life Cycles in Diagnostics

BASAS

Roche

1. Idea / Concept
2. Design
3. Proof of Concept, Prototype
4. Development
5. Optimization
6. TPV Technical Performance Verification
7. Clinical Trials
8. **Regulatory Approval**
9. Sell Product, Publications

FDA Center for Devices and Radiological Health

European Commission

Health Canada Santé Canada

# General Product Life Cycles in Diagnostics

BASAS

Roche

1. Idea / Concept
2. Design
3. Proof of Concept, Prototype
4. Development
5. Optimization
6. TPV Technical Performance Verification
7. Clinical Trials
8. **Regulatory Approval**
9. Sell Product, Publications

# General Product Life Cycles in Diagnostics

BASAS

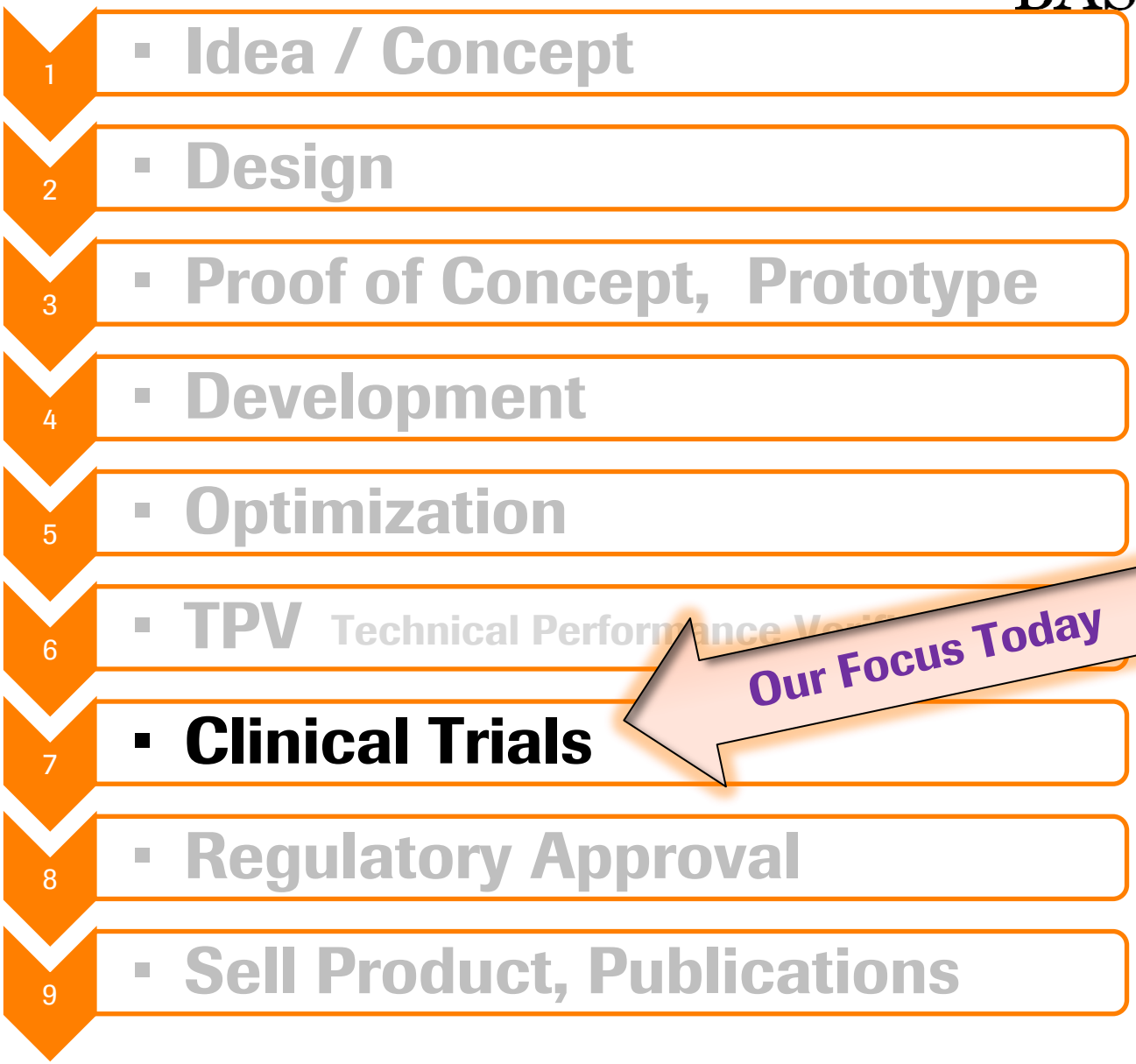
Roche

1. Idea / Concept
2. Design
3. Proof of Concept, Prototype
4. Development
5. Optimization
6. TPV Technical Performance Verification
7. Clinical Trials
8. Regulatory Approval
9. **Sell Product, Publications**

# General Product Life Cycles in Diagnostics

BASAS

Roche



## BACKGROUND APPLICATION

# Introduction to the Assay

# Assay

BASAS Roche

An **assay** is an investigative or analytic procedure in

- laboratory medicine,
- pharmacology,
- environmental biology and
- **molecular** biology

for **qualitatively assessing** or **quantitatively measuring**

the presence or amount or the functional activity of a target entity (the analyte).

*Ref: Wikipedia, from https://en.wikipedia.org/wiki/Assay accessed on 05May2016.*

# Assay

BASAS Roche

An **assay** is an investigative or analytic procedure in

- laboratory medicine,
- pharmacology,
- environmental biology and
- **molecular** biology

**i.e., detect or measure stuff like HIV, HBV, HCV, Zika, etc.**

for **qualitatively assessing** or **quantitatively measuring**

the presence or amount or the functional activity of a target entity (the analyte).

*Ref: Wikipedia, from https://en.wikipedia.org/wiki/Assay accessed on 05May2016.*

# Assay (CONTINUED)

BASAS Roche

In Molecular Diagnostics, we use the Polymerase Chain Reaction (PCR) method to detect (yes/no) and quantify (how much) the target (HIV, HCV, HBV, CMV, Zika, etc.) in your blood sample for

**HIV** = Human Immunodeficiency Virus; **HCV** = Hepatitis C; **HBV** = Hepatitis B; **CMV** = Cytomegalovirus; **Zika** = Zika Virus

# Assay (CONTINUED)

BASAS Roche

In Molecular Diagnostics, we use the Polymerase Chain Reaction (PCR) method to detect (yes/no) and quantify (how much) the target (HIV, HCV, HBV, CMV, Zika, etc.) in your blood sample for

- Screening (qualitative) and/or

**HIV** = Human Immunodeficiency Virus; **HCV** = Hepatitis C; **HBV** = Hepatitis B; **CMV** = Cytomegalovirus; **Zika** = Zika Virus

# Assay (CONTINUED)

BASAS Roche

In Molecular Diagnostics, we use the Polymerase Chain Reaction (PCR) method to detect (yes/no) and quantify (how much) the target (HIV, HCV, HBV, CMV, Zika, etc.) in your blood sample for

- Screening (qualitative) and/or
- Diagnosis and Monitoring (quantitative)

**HIV** = Human Immunodeficiency Virus; **HCV** = Hepatitis C; **HBV** = Hepatitis B; **CMV** = Cytomegalovirus; **Zika** = Zika Virus

# Assay (CONTINUED)

BASAS Roche

In Molecular Diagnostics, we use the Polymerase Chain Reaction (PCR) method to detect (yes/no) and quantify (how much) the target (HIV, HCV, HBV, CMV, Zika, etc.) in your blood sample for

- Screening (qualitative) and/or
- Diagnosis and Monitoring (quantitative)

**HIV** = Human Immunodeficiency Virus; **HCV** = Hepatitis C; **HBV** = Hepatitis B; **CMV** = Cytomegalovirus; **Zika** = Zika Virus

# General Product Life Cycles in Diagnostics

BASAS

Roche

1. Idea / Concept
2. Design
3. Proof of Concept, Prototype
4. Development
5. **Optimization**
6. **TPV** Technical Performance Verification
7. **Clinical Trials**
8. Regulatory Approval
9. Sell Product, Publications

Verification

Validation

Both Verification and Validation use Performance Metrics

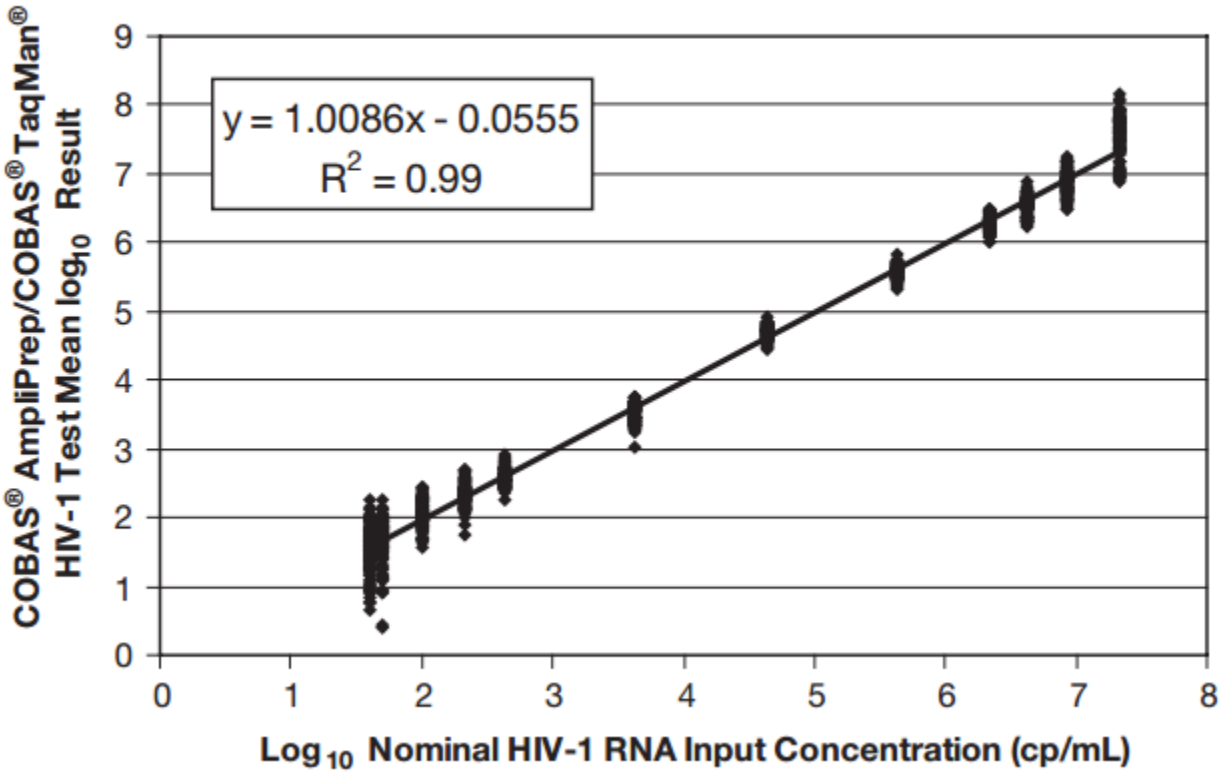
# Assay (CONTINUED)

BASAS

**First questions you may ask …**

**How good is your assay across the linear range?**

*Figure 7*
*Linear range of the COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 Test*




Ref: Package Insert for "COBAS AmpliPrep/COBAS TaqMan HIV-1 Test" http://www.fda.gov/downloads/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/PremarketApprovalsPMAs/UCM092878.pdf accessed on 05May2016.

# Assay (CONTINUED)

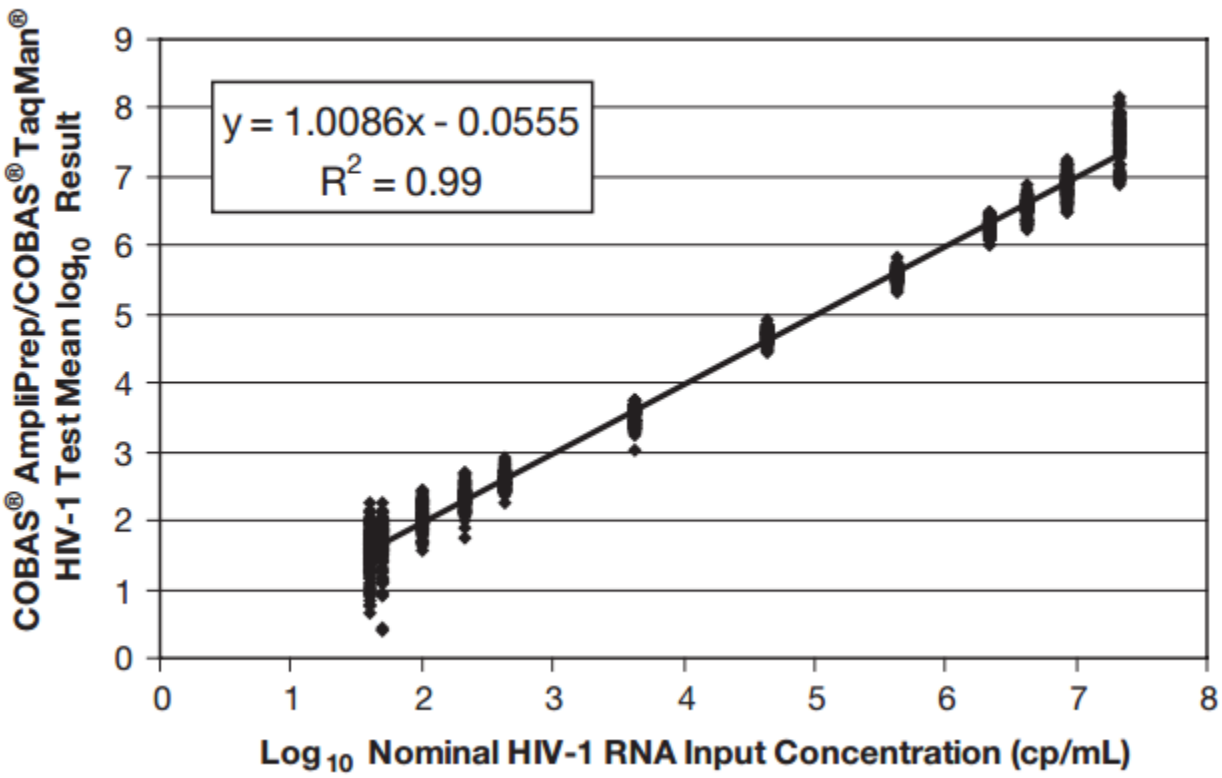
BASAS Roche

**How good is your assay across the linear range?**

**What is the linear range?**

**Linear range: measurable assay interval with acceptable precision, linearity and accuracy.**

*Figure 7*
*Linear range of the COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 Test*




Ref: Package Insert for "COBAS AmpliPrep/COBAS TaqMan HIV-1 Test" http://www.fda.gov/downloads/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/PremarketApprovalsPMAs/UCM092878.pdf accessed on 05May2016.

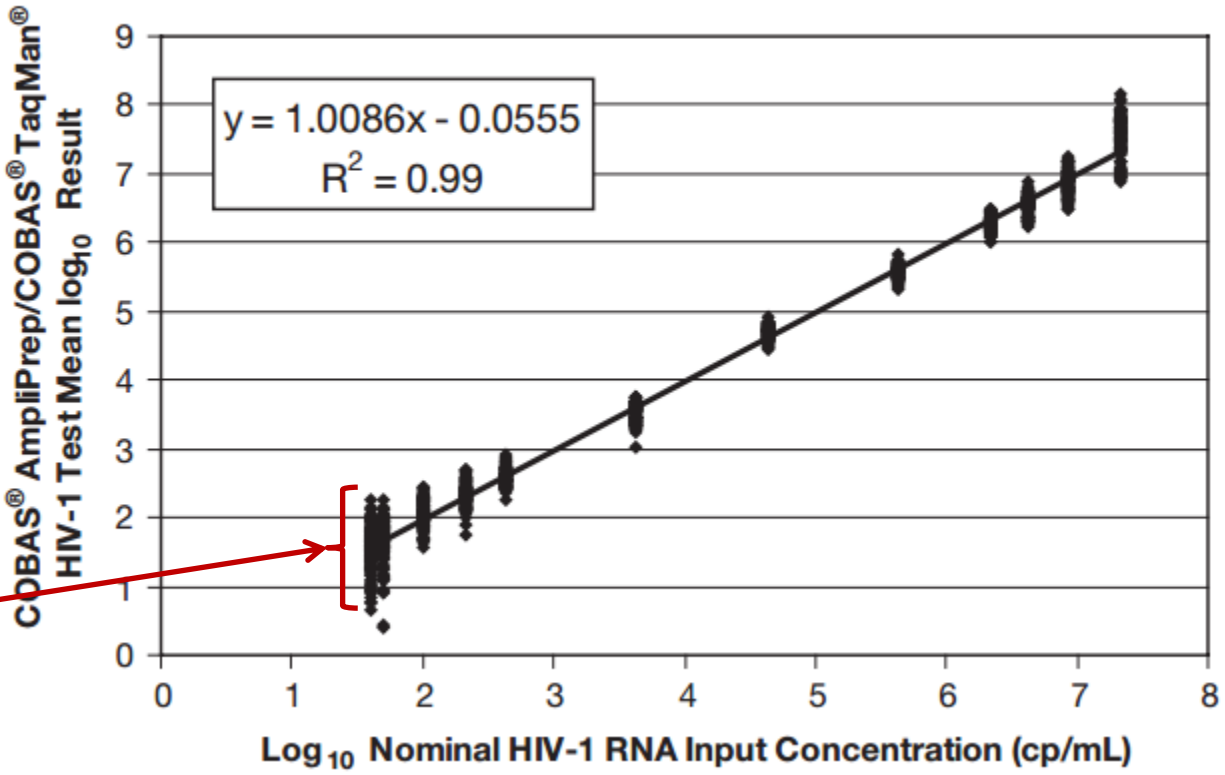
# Assay (CONTINUED)

BASAS

**How good is your assay across the linear range?**

**Linear range: measurable assay interval with acceptable precision, linearity and accuracy.**

*Figure 7*
*Linear range of the COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 Test*




Ref: Package Insert for "COBAS AmpliPrep/COBAS TaqMan HIV-1 Test" http://www.fda.gov/downloads/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/PremarketApprovalsPMAs/UCM092878.pdf accessed on 05May2016.

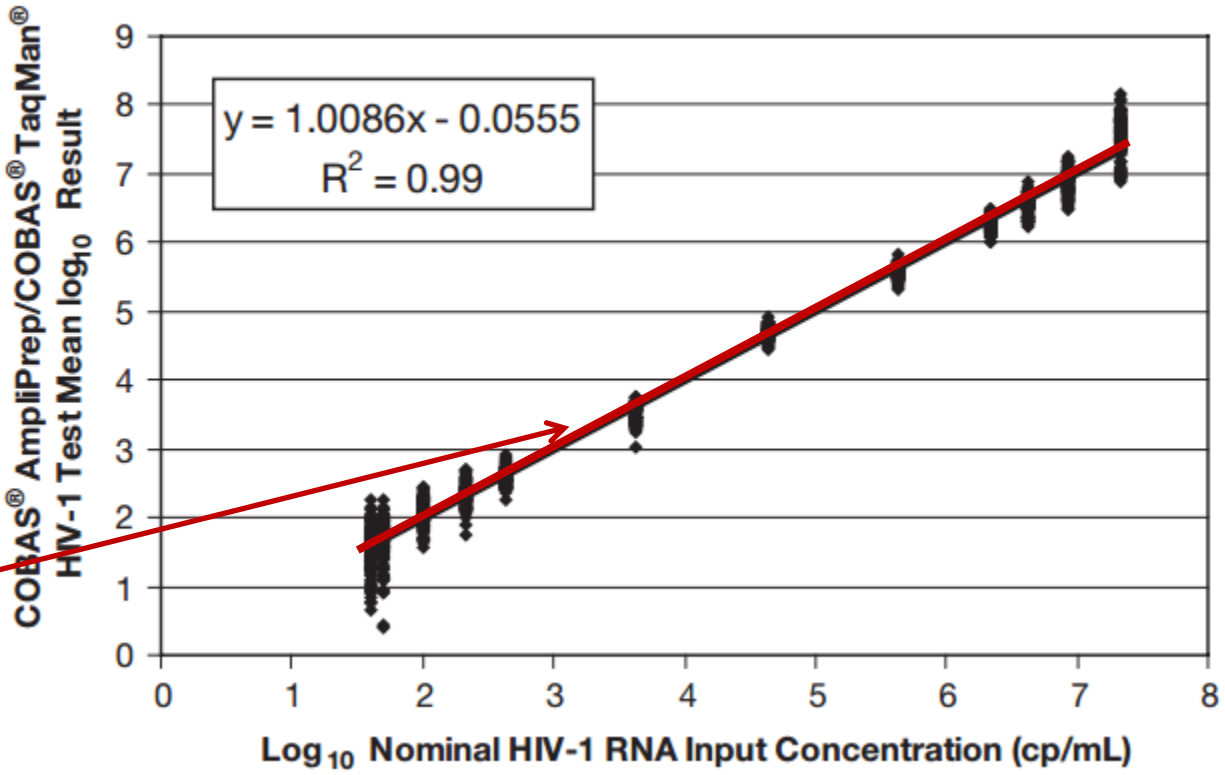
# Assay (CONTINUED)

BASAS

**How good is your assay across the linear range?**

**Linear range: measurable assay interval with acceptable precision, linearity and accuracy.**

*Figure 7*
*Linear range of the COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 Test*



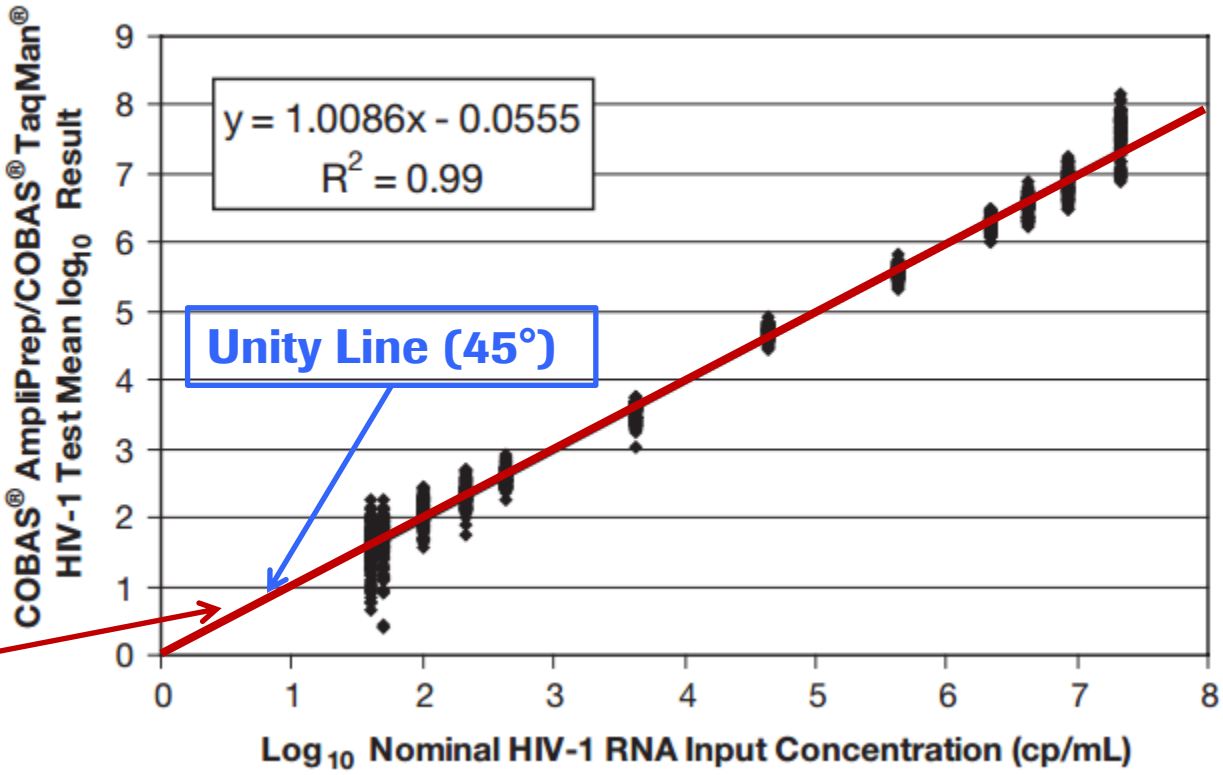

Ref: Package Insert for "COBAS AmpliPrep/COBAS TaqMan HIV-1 Test" http://www.fda.gov/downloads/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/PremarketApprovalsPMAs/UCM092878.pdf accessed on 05May2016.

# Assay (CONTINUED)

BASAS Roche

**How good is your assay across the linear range?**

*Figure 7*
*Linear range of the COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 Test*




**Linear range: measurable assay interval with acceptable precision, linearity and accuracy.**

Ref: Package Insert for "COBAS AmpliPrep/COBAS TaqMan HIV-1 Test" http://www.fda.gov/downloads/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/PremarketApprovalsPMAs/UCM092878.pdf accessed on 05May2016.

# Assay (CONTINUED)

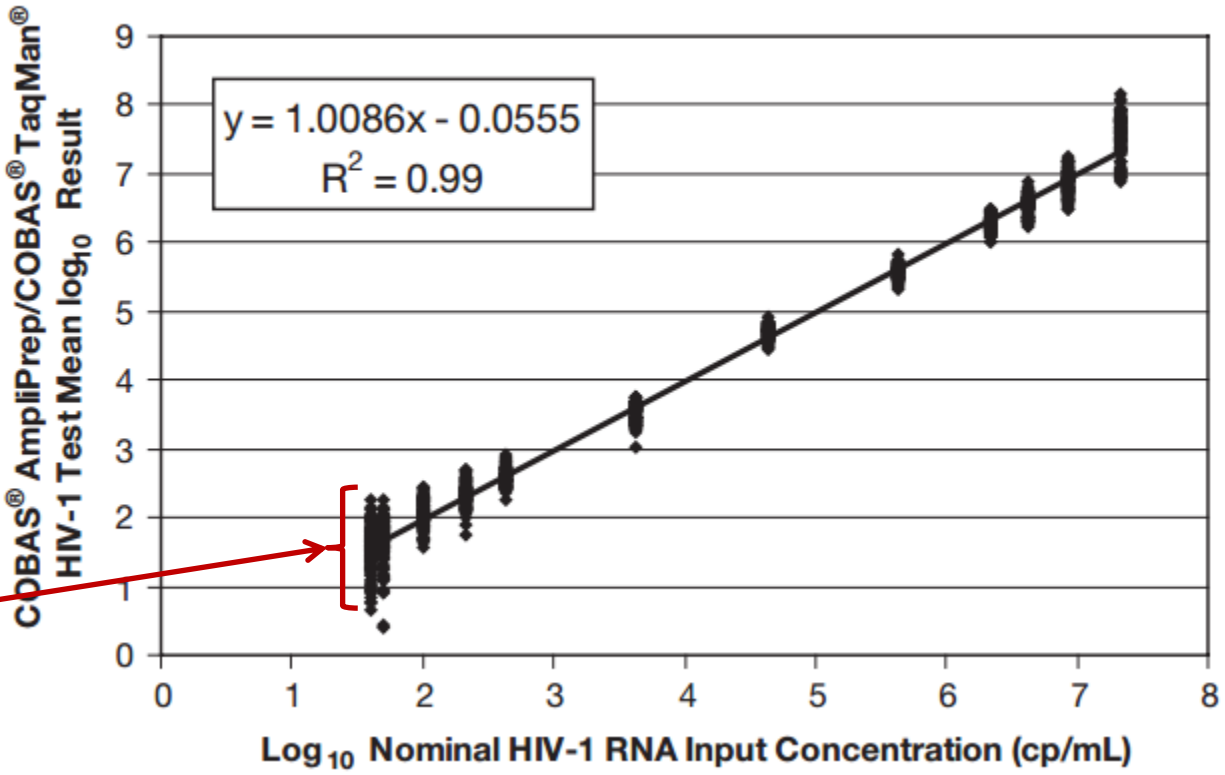
BASAS

**How good is your assay across the linear range?**

**Concentrating on Precision …**

**Linear range: measurable assay interval with acceptable precision, linearity and accuracy.**

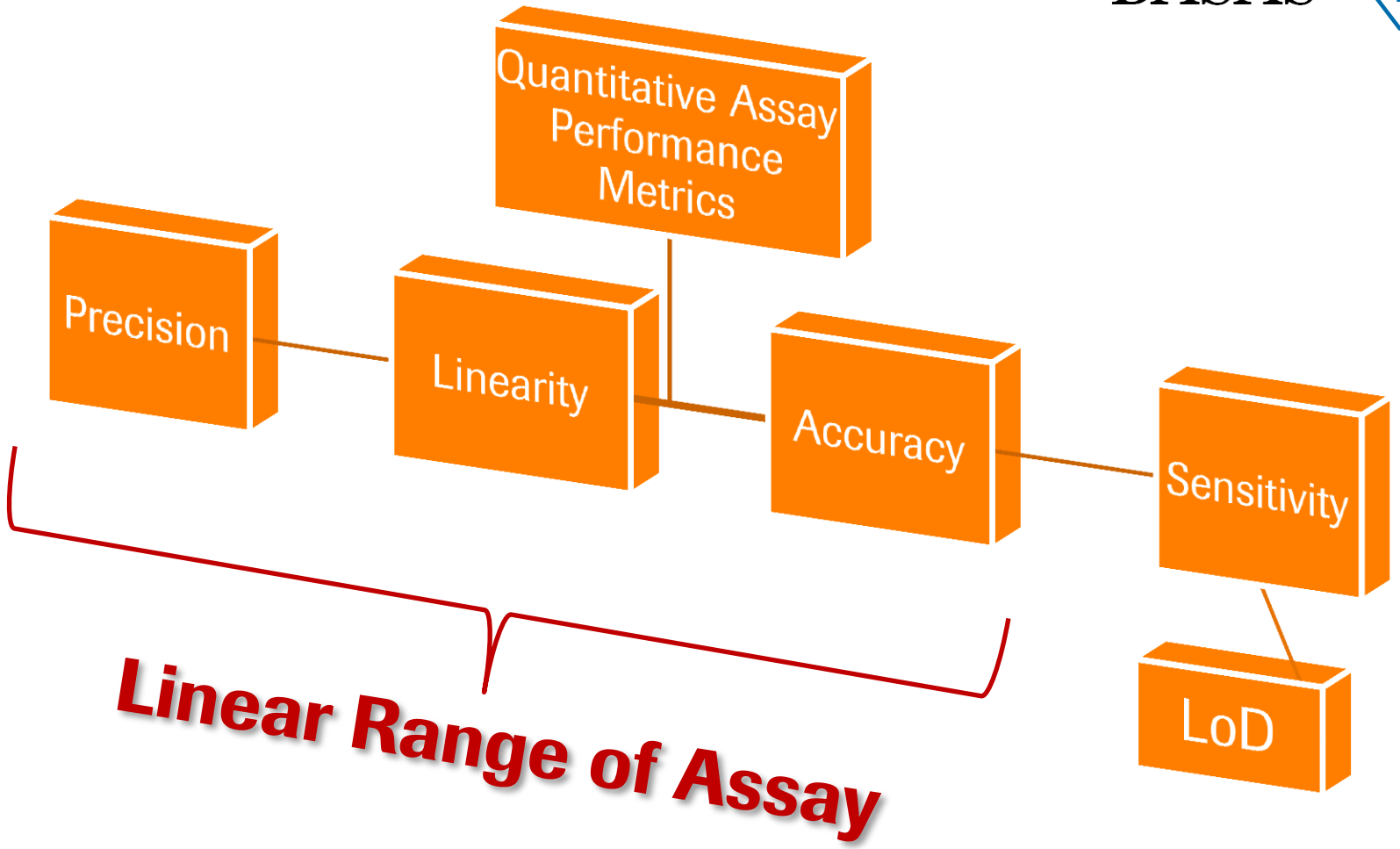
*Figure 7*
*Linear range of the COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 Test*




Ref: Package Insert for "COBAS AmpliPrep/COBAS TaqMan HIV-1 Test" http://www.fda.gov/downloads/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/PremarketApprovalsPMAs/UCM092878.pdf accessed on 05May2016.

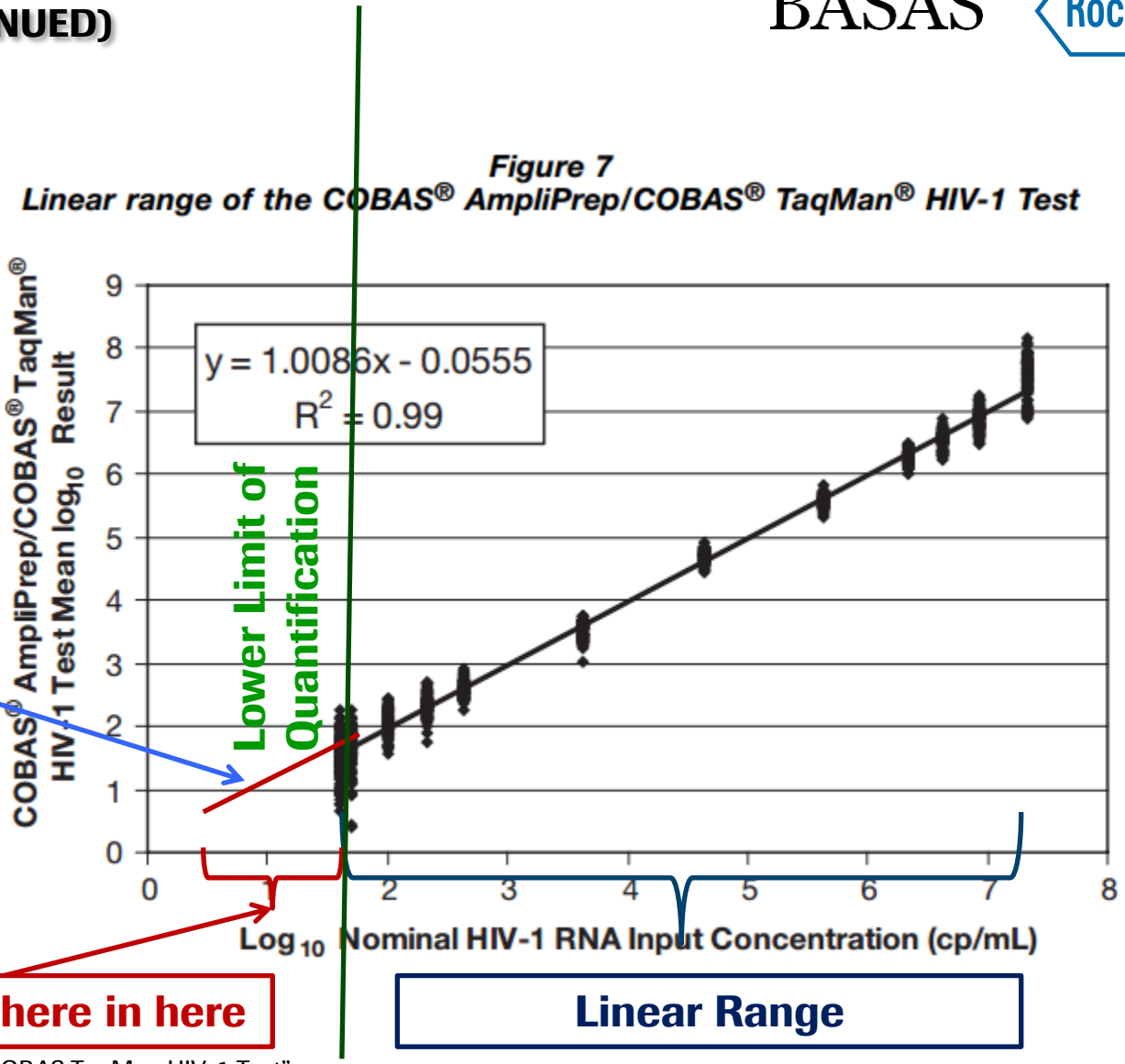
# Performance Metrics

BASAS Roche



# Assay (CONTINUED)

BASAS Roche




**Sensitivity answers the question: "How low can you go?"**

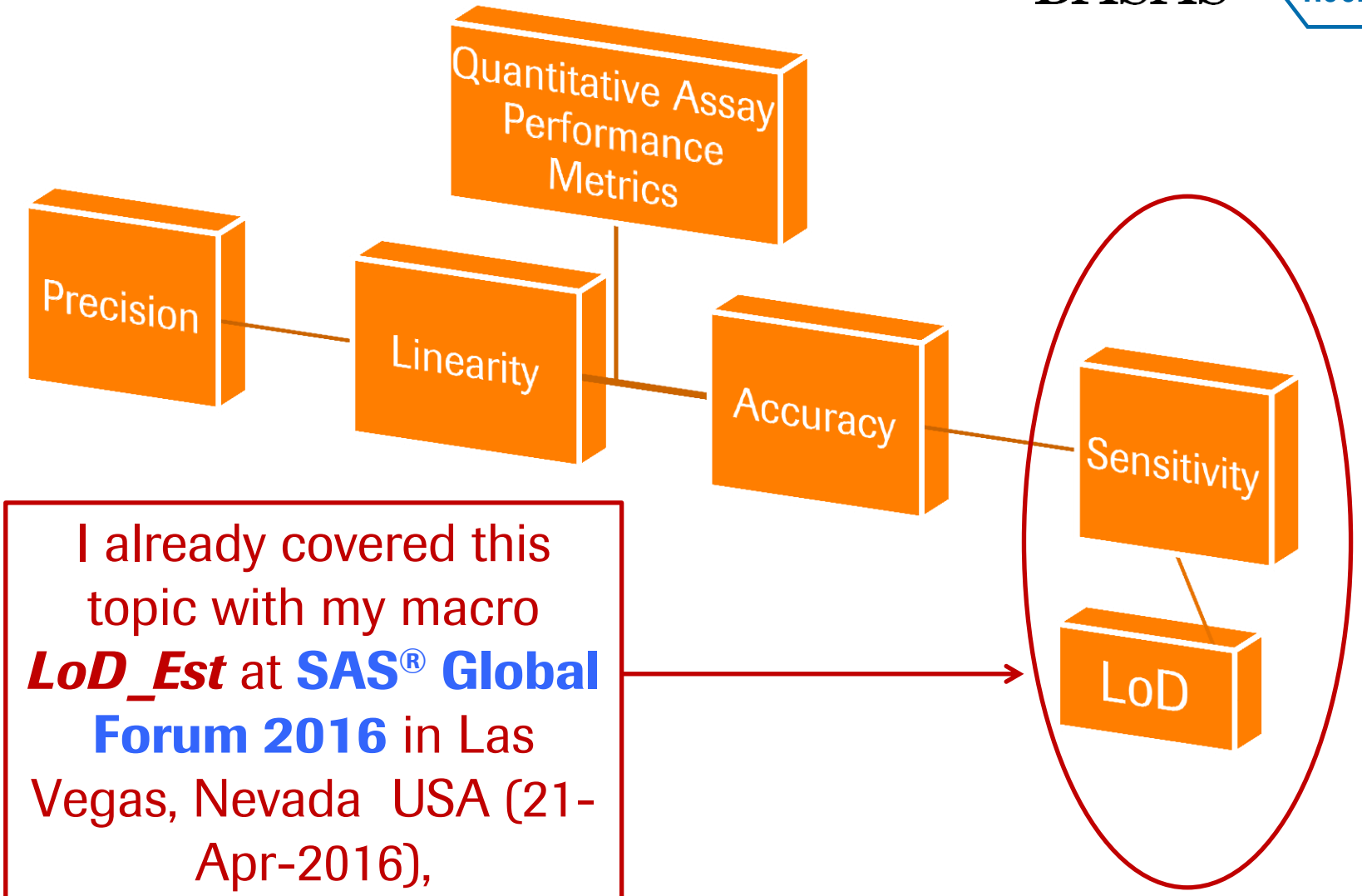
**LoD somewhere in here**

**Linear Range**

Ref: Package Insert for "COBAS AmpliPrep/COBAS TaqMan HIV-1 Test" http://www.fda.gov/downloads/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/PremarketApprovalsPMAs/UCM092878.pdf accessed on 05May2016.

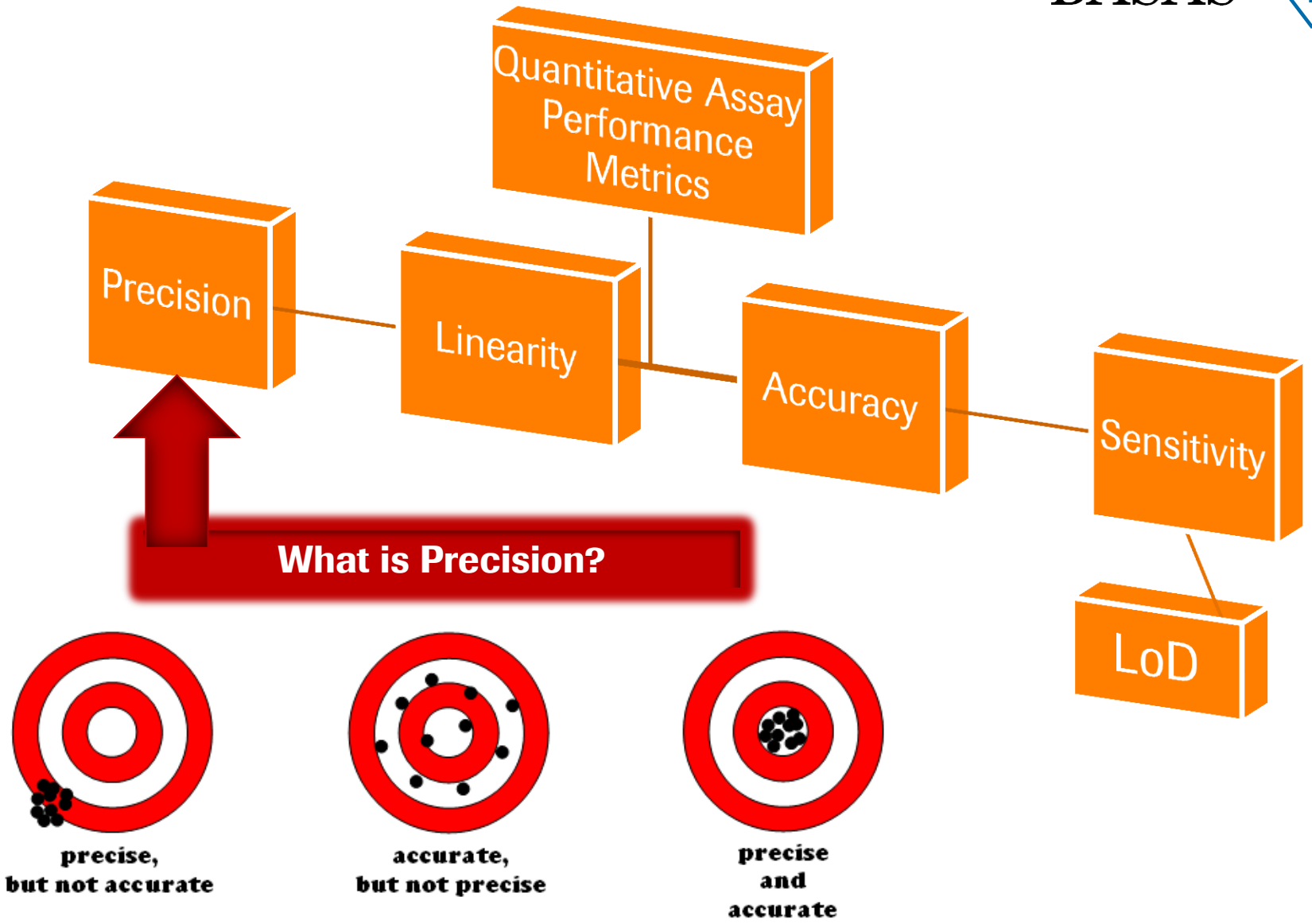
# Performance Metrics

BASAS Roche



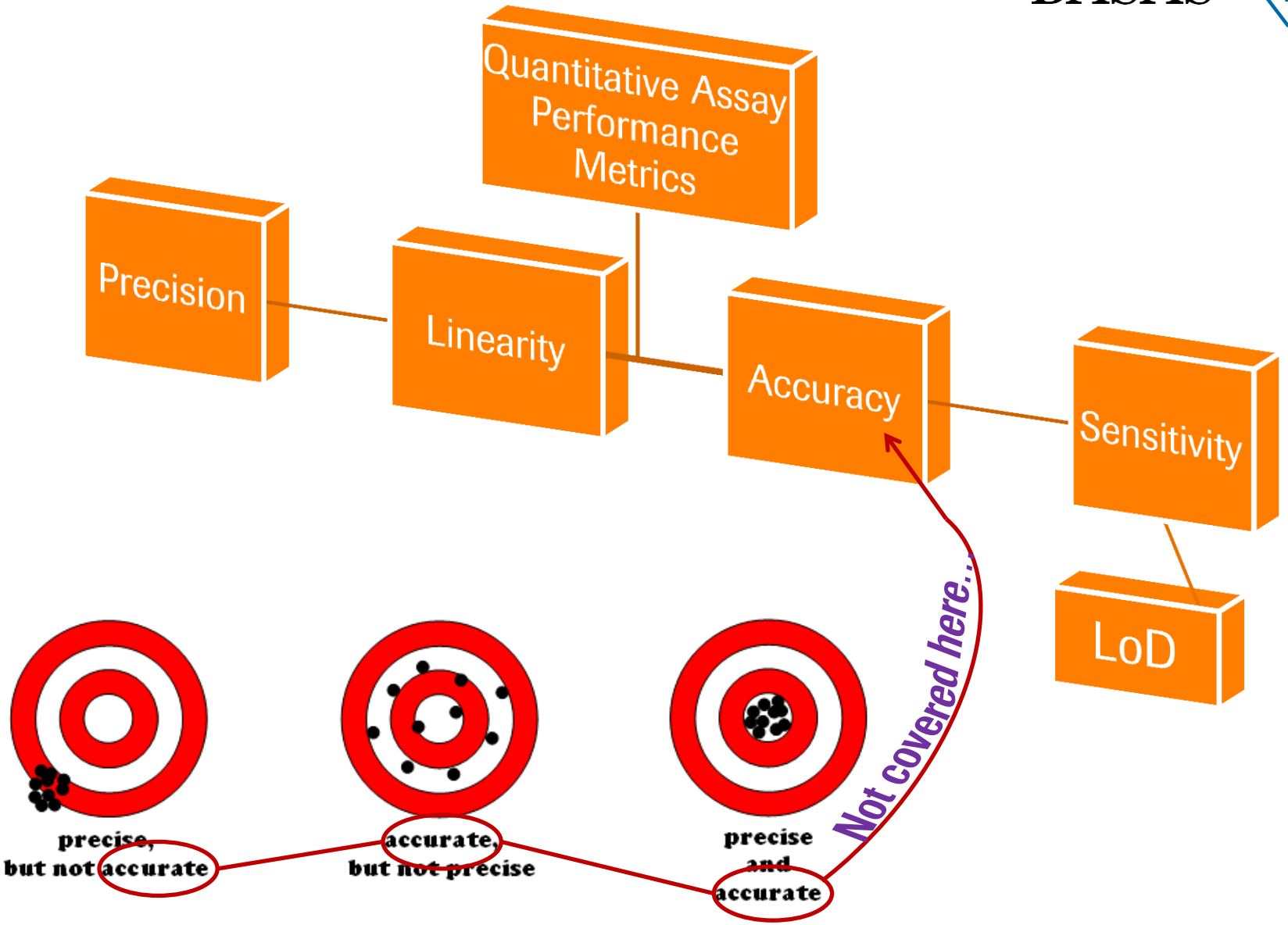
# Performance Metrics

BASAS



# Performance Metrics

BASAS



# Performance Metrics

BASAS Roche

- We now look at a few dry definitions then expand on each…

# Performance Metrics: Definitions

BASAS Roche

- Precision (EP05-A2): …is the closeness of agreement between independent test/measurement results obtained under stipulated conditions.

BASAS Roche

# Motivation

Whenever decisions are based on analytical or clinical results, it's important to assess the quality of the results…

BASAS Roche

# Motivation

…that is, the extent to which the results can be relied upon for the purpose at hand.

-OR-

BASAS Roche

# Motivation

In other words,

“Can I believe the results I got from the lab or my doctor?”

# Performance Metrics: Precision

BASAS Roche

Another (more accessible) Precision Definition (ICH 1994):

- The precision of an analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions.

ICH = International Conference on Harmonisation

# Performance Metrics: Precision

BASAS

Roche

- Example of the types of conditions are (but not limited to):

# Performance Metrics: Precision

BASAS Roche

- Example of the types of conditions are (but not limited to):

⇨ Between-site

⇨ Between-lot

⇨ Between-instrument

⇨ Between-operator

⇨ Between-run

⇨ Between-batch

⇨ Within-run

# Performance Metrics: Precision

BASAS Roche

- Example of the types of conditions are (but not limited to):

⇨ Between-site

⇨ Between-lot

⇨ Between-instrument

⇨ Between-operator

⇨ Between-run

⇨ Between-batch

⇨ Within-run

# Performance Metrics: Precision

BASAS Roche

- Example of the types of conditions are (but not limited to):

⇨ Between-site

⇨ Between-lot

⇨ Between-instrument

⇨ Between-operator

⇨ Between-run

⇨ Between-batch

⇨ Within-run

# Performance Metrics: Precision

BASAS Roche

- Example of the types of conditions are (but not limited to):

⇨ Between-site

⇨ Between-lot

⇨ Between-instrument

⇨ Between-operator

⇨ Between-run

⇨ Between-batch

⇨ Within-run

# Performance Metrics: Precision

BASAS Roche

- Example of the types of conditions are (but not limited to):

⇨ Between-site

⇨ Between-lot

⇨ Between-instrument

⇨ Between-operator

⇨ Between-run

⇨ Between-batch

⇨ Within-run

# Performance Metrics: Precision

BASAS Roche

- Example of the types of conditions are (but not limited to):

⇨ Between-site

⇨ Between-lot

⇨ Between-instrument

⇨ Between-operator

⇨ Between-run

⇨ Between-batch

⇨ Within-run

# Performance Metrics: Precision

BASAS

- Example of the types of conditions are (but not limited to):

⇨ Between-site

⇨ Between-lot

⇨ Between-instrument

⇨ Between-operator

⇨ Between-run

⇨ Between-batch

⇨ Within-run

# Performance Metrics: Precision

BASAS Roche

- Example of the types of conditions are (but not limited to):

⇨ Between-site
⇨ Between-lot
⇨ Between-instrument
⇨ Between-operator
⇨ Between-run
⇨ Between-batch
⇨ Within-run

# Performance Metrics: Precision

BASAS Roche

- The terms “repeatability” and “reproducibility” have specific definitional intents from CLSI

CLSI = Clinical & Laboratory Standards Institute

# Performance Metrics: Precision

BASAS Roche

- For example:
  - "repeatability" measures variation within site and
  - "reproducibility" measures variation across sites, lots, instruments, operators, runs, etc.).

$\Rightarrow$ See also the guidance CLSI EP05-A2:

"Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline - Second Edition"

CLSI = Clinical & Laboratory Standards Institute

# Performance Metrics: Precision

BASAS Roche

- Precision is usually expressed in terms of ***imprecision***, and computed as either:
  - Standard Deviation (SD) or $Log_{10}$(SD),
  - Variance, or
  - Percent Coefficient of Variation (%CV) of the test results,
  - Attributable Percent of the total variation.

with less precision reflected as large standard deviations, variances or large %CVs.

# Performance Metrics: Precision

BASAS Roche

- Precision is usually expressed in terms of ***imprecision***, and computed as either:
  - Standard Deviation (SD) or $Log_{10}$(SD),
  - Variance, or
  - Percent Coefficient of Variation (%CV) of the test results,
  - Attributable Percent of the total variation.

with less precision reflected as large standard deviations, variances or large %CVs.

# Performance Metrics: Precision

BASAS Roche

- Precision is usually expressed in terms of ***imprecision***, and computed as either:
  - Standard Deviation (SD) or $Log_{10}$(SD),
  - Variance, or
  - Percent Coefficient of Variation (%CV) of the test results,
  - Attributable Percent of the total variation.

with less precision reflected as large standard deviations, variances or large %CVs.

# Performance Metrics: Precision

BASAS Roche

- Precision is usually expressed in terms of ***imprecision***, and computed as either:
  - Standard Deviation (SD) or $Log_{10}$(SD),
  - Variance, or
  - Percent Coefficient of Variation (%CV) of the test results,
  - Attributable Percent of the total variation.

with less precision reflected as large standard deviations, variances or large %CVs.

# Performance Metrics: Precision

BASAS Roche

- Precision is usually expressed in terms of ***imprecision***, and computed as either:
  - Standard Deviation (SD) or $Log_{10}$(SD),
  - Variance, or
  - Percent Coefficient of Variation (%CV) of the test results,
  - Attributable Percent of the total variation.

with less precision reflected as large standard deviations, variances or large %CVs.

# Performance Metrics: Precision

BASAS Roche

- Precision is usually expressed in terms of ***imprecision***, and computed as either:
  - Standard Deviation (SD) or $Log_{10}$(SD),
  - Variance, or
  - Percent Coefficient of Variation (%CV) of the test results,
  - Attributable Percent of the total variation.

with less precision reflected as large standard deviations, variances or large %CVs.

# Performance Metrics: Precision

BASAS Roche

- Precision is usually expressed in terms of ***imprecision***, and computed as either:
  - Standard Deviation (SD) or $Log_{10}$(SD),
  - Variance, or
  - Percent Coefficient of Variation (%CV) of the test results,
  - Attributable Percent of the total variation.

with less precision reflected as large standard deviations, variances or large %CVs.

# Performance Metrics: Precision

BASAS Roche

- **Estimation of Precision**

- Precision is usually expressed in terms of %CV (percent coefficient of variation) or $Log_{10}SD$ scale.

- In general, the %CV is estimated as follows (for non-log transformed data):

$$\%CV = \left(\frac{SD}{mean}\right) \cdot 100\%$$

where SD is the standard deviation of the quantitation.

- However, on the $log_{10}$ scale, the %CV is defined as the approximation:

$$\%CV = \sqrt{10^{SD^2 \cdot \ln(10)} - 1} \cdot 100\%$$

where the SD in this case is the $Log_{10}SD$ $log_{10}$ transformed quantitation and ln(·) is the natural logarithm.

# Performance Metrics: Precision

BASAS Roche

- **Estimation of Precision**

- Precision is usually expressed in terms of %CV (percent coefficient of variation) or $Log_{10}SD$ scale.

- In general, the %CV is estimated as follows (for non-log transformed data):

$$\%CV = \left(\frac{SD}{mean}\right) \cdot 100\%$$

where SD is the standard deviation of the quantitation.

- However, on the $log_{10}$ scale, the %CV is defined as the approximation:

$$\%CV = \sqrt{10^{SD^2 \cdot \ln(10)} - 1} \cdot 100\%$$

where the SD in this case is the $Log_{10}SD$ $log_{10}$ transformed quantitation and ln(·) is the natural logarithm.

# Performance Metrics: Precision

BASAS Roche

## Estimation of Precision

- For quant assays (as we call them), we typically evaluate precision at several concentration levels across the assay quantitation range
- To do this, we use a contrived dilution panel (what we might call a quality control panel or QC Panel).
- The same panel may be tested multiple times across randomly selected lots, instruments, runs, etc.
- Using a statistical model (variance component model), we fit the data from each panel member to estimate the variation (Variance, SD or %CV) of the quantitations due to the relevant random effects (lots, instruments, runs, etc.)

# Performance Metrics: Precision

BASAS Roche

## Estimation of Precision

- For quant assays (as we call them), we typically evaluate precision at several concentration levels across the assay quantitation range

- To do this, we use a contrived dilution panel (what we might call a quality control panel or QC Panel).

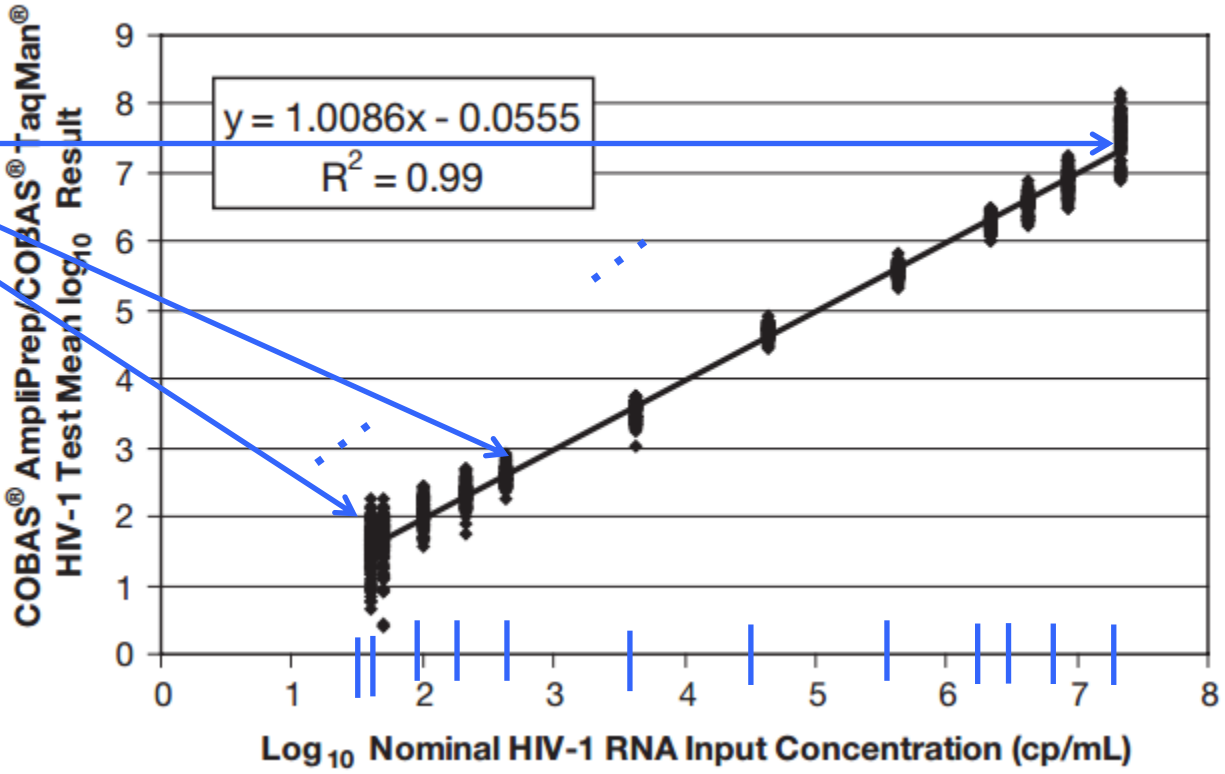
- The same panel may be tested multiple times across randomly selected lots, instruments, runs, etc.

- Using a statistical model (variance component model), we fit the data from each panel member to estimate the variation (Variance, SD or %CV) of the quantitations due to the relevant random effects (lots, instruments, runs, etc.)

# Assay

**Example:**
**12 contrived panel levels/members**

***Figure 7***
***Linear range of the COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 Test***




Ref: Package Insert for "COBAS AmpliPrep/COBAS TaqMan HIV-1 Test" http://www.fda.gov/downloads/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/PremarketApprovalsPMAs/UCM092878.pdf accessed on 05May2016.

# Performance Metrics: Precision

BASAS Roche

## Estimation of Precision

- For quant assays (as we call them), we typically evaluate precision at several concentration levels across the assay quantitation range
- To do this, we use a contrived dilution panel (what we might call a quality control panel or QC Panel).
- The same panel may be tested multiple times across randomly selected lots, instruments, operators, runs, etc.
- Using a statistical model (variance component model), we fit the data from each panel member to estimate the variation (Variance, SD or %CV) of the quantitations due to the relevant random effects (lots, instruments, runs, etc.)

# Performance Metrics: Precision

BASAS Roche

## Estimation of Precision

- For quant assays (as we call them), we typically evaluate precision at several concentration levels across the assay quantitation range
- To do this, we use a contrived dilution panel (what we might call a quality control panel or QC Panel).
- The same panel may be tested multiple times across randomly selected lots, instruments, runs, etc.
- Using a statistical model (variance components model), we fit the data from each panel member to estimate the variation (Variance, SD or %CV) of the quantitations due to the relevant random effects (lots, instruments, runs, etc.)

## Performance Metrics: Precision

BASAS Roche

## Estimation of Precision:

## The Random Effects (RE) Linear Model

$$y_{lsodre} = \mu + L_l + S_s + O_o + D_d + R_r + \varepsilon_{lsodre}$$

**Where** $L_l \overset{\text{iid}}{\sim} N(0, \sigma_L^2)$ **is the RE due to lot;**

$S_s \overset{\text{iid}}{\sim} N(0, \sigma_S^2)$ **is the RE due to site;**

$O_o \overset{\text{iid}}{\sim} N(0, \sigma_O^2)$ **is the RE due to operator;**

$D_d \overset{\text{iid}}{\sim} N(0, \sigma_D^2)$ **is the RE due to day;**

$R_r \overset{\text{iid}}{\sim} N(0, \sigma_R^2)$ **is the RE due to run/batch.**

# Performance Metrics: Precision

BASAS Roche

**The SAS MIXED procedure is used to fit the random effects model using the restricted maximum likelihood (REML) or maximum likelihood (ML) methods.**

```
proc mixed data = DataIn method = &method ;
   class &ClassVars ;
   model &DepVar  = / solution cl
                      ddfm=satterth ;
   random &Random;
   where LevelVar = &index ;
run ;
```

# Performance Metrics: Precision

BASAS Roche

**The SAS MIXED procedure is used to fit the random effects model using the restricted maximum likelihood (REML) or maximum likelihood (ML) methods.**

```
proc mixed data = DataIn method = &method ;
    class &ClassVars ;
    model &DepVar  = / solution cl
                       ddfm=satterth ;
    random &Random;
    where LevelVar = &index ;
run ;
```

# Performance Metrics: Precision

BASAS Roche

## The SAS PrecMod Macro call:

```
%PrecMod(InData = ,
   ByVars    = ,
   ClassVars = ,
   DepVar    = ,
   IndepVars = ,
   Random    = ,
   Method    = REML ,
   OutData   = ,
   FlagVar   = ,
   FlagValue = ,
   EquTest   = N    ,
   Alpha     = 0.05 ,
   InsType   = ,
   Logged    = "Yes") ;
```

⇦ SAS Input Data Set

# Performance Metrics: Precision

BASAS Roche

## The SAS PrecMod Macro call:

```
%PrecMod(InData = ,
   ByVars     = ,
   ClassVars  = ,
   DepVar     = ,
   IndepVars  = ,
   Random     = ,
   Method     = REML ,
   OutData    = ,
   FlagVar    = ,
   FlagValue  = ,
   EquTest    = N    ,
   Alpha      = 0.05 ,
   InsType    = ,
   Logged     = "Yes") ;
```

⇦ SAS Input Data Set

⇦ "By" Processing variable

# Performance Metrics: Precision

BASAS Roche

## The SAS PrecMod Macro call:

```
%PrecMod(InData = ,   ⇦ SAS Input Data Set
   ByVars     = ,   ⇦ "By" Processing variable
   ClassVars  = ,   ⇦ Categorical or class variables
   DepVar     = ,
   IndepVars  = ,
   Random     = ,
   Method     = REML ,
   OutData    = ,
   FlagVar    = ,
   FlagValue  = ,
   EquTest    = N    ,
   Alpha      = 0.05 ,
   InsType    = ,
   Logged     = "Yes") ;
```

# Performance Metrics: Precision

BASAS Roche

## The SAS PrecMod Macro call:

```
%PrecMod(InData = ,  ⇦ SAS Input Data Set
   ByVars     = ,  ⇦ "By" Processing variable
   ClassVars  = ,  ⇦ Categorical or class variables
   DepVar     = ,  ⇦ Dependent variable
   IndepVars  = ,
   Random     = ,
   Method     = REML ,
   OutData    = ,
   FlagVar    = ,
   FlagValue  = ,
   EquTest    = N    ,
   Alpha      = 0.05 ,
   InsType    = ,
   Logged     = "Yes") ;
```

# Performance Metrics: Precision

BASAS Roche

## The SAS PrecMod Macro call:

```
%PrecMod(InData = ,  ⇦ SAS Input Data Set
   ByVars     = ,  ⇦ "By" Processing variable
   ClassVars  = ,  ⇦ Categorical or class variables
   DepVar     = ,  ⇦ Dependent variable
   IndepVars  = ,  ⇦ Independent fixed variables
   Random     = ,
   Method     = REML ,
   OutData    = ,
   FlagVar    = ,
   FlagValue  = ,
   EquTest    = N    ,
   Alpha      = 0.05 ,
   InsType    = ,
   Logged     = "Yes") ;
```

# Performance Metrics: Precision

BASAS Roche

## The SAS PrecMod Macro call:

```
%PrecMod(InData = ,  ⇦ SAS Input Data Set
   ByVars     = ,  ⇦ "By" Processing variable
   ClassVars  = ,  ⇦ Categorical or class variables
   DepVar     = ,  ⇦ Dependent variable
   IndepVars  = ,  ⇦ Independent fixed variables
   Random     = ,  ⇦ Independent random variables
   Method     = REML ,
   OutData    = ,
   FlagVar    = ,
   FlagValue  = ,
   EquTest    = N    ,
   Alpha      = 0.05 ,
   InsType    = ,
   Logged     = "Yes") ;
```

# Performance Metrics: Precision

BASAS Roche

## The SAS PrecMod Macro call:

```
%PrecMod(InData = ,   ⇦ SAS Input Data Set
   ByVars     = ,   ⇦ "By" Processing variable
   ClassVars  = ,   ⇦ Categorical or class variables
   DepVar     = ,   ⇦ Dependent variable
   IndepVars  = ,   ⇦ Independent fixed variables
   Random     = ,   ⇦ Independent random variables
   Method     = REML ,  ⇦ Optimization method
   OutData    = ,
   FlagVar    = ,
   FlagValue  = ,
   EquTest    = N    ,
   Alpha      = 0.05 ,
   InsType    = ,
   Logged     = "Yes") ;
```

# Performance Metrics: Precision

BASAS Roche

## The SAS PrecMod Macro call:

```
%PrecMod(InData = ,  ⇦ SAS Input Data Set
   ByVars     = ,  ⇦ "By" Processing variable
   ClassVars  = ,  ⇦ Categorical or class variables
   DepVar     = ,  ⇦ Dependent variable
   IndepVars  = ,  ⇦ Independent fixed variables
   Random     = ,  ⇦ Independent random variables
   Method     = REML ,  ⇦ Optimization method
   OutData    = ,  ⇦ Output SAS data set
   FlagVar    = ,
   FlagValue  = ,
   EquTest    = N    ,
   Alpha      = 0.05 ,
   InsType    = ,
   Logged     = "Yes") ;
```

# Performance Metrics: Precision

BASAS Roche

## The SAS PrecMod Macro call:

```
%PrecMod(InData = ,  ⇦ SAS Input Data Set
   ByVars     = ,  ⇦ "By" Processing variable
   ClassVars  = ,  ⇦ Categorical or class variables
   DepVar     = ,  ⇦ Dependent variable
   IndepVars  = ,  ⇦ Independent fixed variables
   Random     = ,  ⇦ Independent random variables
   Method     = REML ,  ⇦ Optimization method
   OutData    = ,  ⇦ Output SAS data set
   FlagVar    = ,  ⇦ Any data flag or indicator variable
   FlagValue  = ,
   EquTest    = N    ,
   Alpha      = 0.05 ,
   InsType    = ,
   Logged     = "Yes") ;
```

# Performance Metrics: Precision

BASAS Roche

## The SAS PrecMod Macro call:

```
%PrecMod(InData = ,  ⇦ SAS Input Data Set
   ByVars     = ,  ⇦ "By" Processing variable
   ClassVars  = ,  ⇦ Categorical or class variables
   DepVar     = ,  ⇦ Dependent variable
   IndepVars  = ,  ⇦ Independent fixed variables
   Random     = ,  ⇦ Independent random variables
   Method     = REML ,  ⇦ Optimization method
   OutData    = ,  ⇦ Output SAS data set
   FlagVar    = ,  ⇦ Any data flag or indicator variable
   FlagValue  = ,  ⇦ Value for FlagVar or indicator
   EquTest    = N     ,
   Alpha      = 0.05  ,
   InsType    = ,
   Logged     = "Yes")  ;
```

# Performance Metrics: Precision

BASAS Roche

## The SAS PrecMod Macro call:

```
%PrecMod(InData = ,  ⇦ SAS Input Data Set
   ByVars     = ,  ⇦ "By" Processing variable
   ClassVars  = ,  ⇦ Categorical or class variables
   DepVar     = ,  ⇦ Dependent variable
   IndepVars  = ,  ⇦ Independent fixed variables
   Random     = ,  ⇦ Independent random variables
   Method     = REML ,  ⇦ Optimization method
   OutData    = ,  ⇦ Output SAS data set
   FlagVar    = ,  ⇦ Any data flag or indicator variable
   FlagValue  = ,  ⇦ Value for FlagVar or indicator
   EquTest    = N ,  ⇦ Y/N Test for equivalency
   Alpha      = 0.05 ,
   InsType    = ,
   Logged     = "Yes") ;
```

# Performance Metrics: Precision

BASAS Roche

## The SAS PrecMod Macro call:

```
%PrecMod(InData = ,  ⇦ SAS Input Data Set
   ByVars     = ,  ⇦ "By" Processing variable
   ClassVars  = ,  ⇦ Categorical or class variables
   DepVar     = ,  ⇦ Dependent variable
   IndepVars  = ,  ⇦ Independent fixed variables
   Random     = ,  ⇦ Independent random variables
   Method     = REML ,  ⇦ Optimization method
   OutData    = ,  ⇦ Output SAS data set
   FlagVar    = ,  ⇦ Any data flag or indicator variable
   FlagValue  = ,  ⇦ Value for FlagVar or indicator
   EquTest    = N     ,  ⇦ Y/N Test for equivalency
   Alpha        = 0.05 ,  ⇦ Significance level
   InsType    = ,
   Logged     = "Yes") ;
```

# Performance Metrics: Precision

BASAS Roche

## The SAS PrecMod Macro call:

```
%PrecMod(InData = ,  ⇦ SAS Input Data Set
   ByVars     = ,  ⇦ "By" Processing variable
   ClassVars  = ,  ⇦ Categorical or class variables
   DepVar     = ,  ⇦ Dependent variable
   IndepVars  = ,  ⇦ Independent fixed variables
   Random     = ,  ⇦ Independent random variables
   Method     = REML ,  ⇦ Optimization method
   OutData    = ,  ⇦ Output SAS data set
   FlagVar    = ,  ⇦ Any data flag or indicator variable
   FlagValue  = ,  ⇦ Value for FlagVar or indicator
   EquTest    = N    ,  ⇦ Y/N Test for equivalency
   Alpha      = 0.05 ,  ⇦ Significance level
   InsType     = ,  ⇦ Variable containing instruments
   Logged     = "Yes") ;
```

# Performance Metrics: Precision

BASAS Roche

## The SAS PrecMod Macro call:

```
%PrecMod(InData = ,   ⇦ SAS Input Data Set
   ByVars     = ,   ⇦ "By" Processing variable
   ClassVars  = ,   ⇦ Categorical or class variables
   DepVar     = ,   ⇦ Dependent variable
   IndepVars  = ,   ⇦ Independent fixed variables
   Random     = ,   ⇦ Independent random variables
   Method     = REML ,  ⇦ Optimization method
   OutData    = ,   ⇦ Output SAS data set
   FlagVar    = ,   ⇦ Any data flag or indicator variable
   FlagValue  = ,   ⇦ Value for FlagVar or indicator
   EquTest    = N     ,  ⇦ Y/N Test for equivalency
   Alpha      = 0.05  ,  ⇦ Significance level
   InsType    = ,   ⇦ Variable containing instruments
   Logged     = "Yes") ;  ⇦ Uses correct math form if data
                          log-transformed
```

# Performance Metrics: Precision

BASAS Roche

## The SAS PrecMod Macro call:

```
%PrecMod(InData = ,      ⇦ SAS Input Data Set
   ByVars     = ,      ⇦ "By" Processing variable
   ClassVars  = ,      ⇦ Categorical or class variables
   DepVar     = ,      ⇦ Dependent variable
   IndepVars  = ,      ⇦ Independent fixed variables
   Random     = ,      ⇦ Independent random variables
   Method     = REML ,    ⇦ Optimization method
   OutData    = ,      ⇦ Output SAS data set
   FlagVar    = ,      ⇦ Any data flag or indicator variable
   FlagValue  = ,      ⇦ Value for FlagVar or indicator
   EquTest    = N      ,    ⇦ Y/N Test for equivalency
   Alpha      = 0.05 ,    ⇦ Significance level
   InsType    = ,      ⇦ Variable containing instruments
   Logged     = "Yes") ;    ⇦ Uses correct math form if data
                                log-transformed
```

BASAS Roche

# Practical Example

We present an analysis of 1855 reproducibility data samples for an HIV-1 PCR assay test evaluated at six titer/concentration levels across the following factors:

PCR = Polymerase Chain Reaction

BASAS Roche

# Practical Example

**Lot:** 3 manufactured reagent lots

BASAS Roche

# Practical Example

**Lot:** 3 manufactured reagent lots

**Site/Instrument:** 3 test sites,
1 instrument per site

BASAS Roche

# Practical Example

**Lot:** 3 manufactured reagent lots

**Site/Instrument:** 3 test sites; 1 instrument per site

**Operator:** 2 operators performing testing at each site

BASAS Roche

# Practical Example

**Lot:** 3 manufactured reagent lots

**Site/Instrument:** 3 test sites; 1 instrument per site

**Operator:** 2 operators performing testing at each site

**Day/Run:** 5 days per lot for each operator, 1 run per day

BASAS Roche

# Practical Example

**Lot:** 3 manufactured reagent lots

**Site/Instrument:** 3 test sites; 1 instrument per site

**Operator:** 2 operators performing testing at each site

**Day/Run:** 5 days per lot for each operator; 1 run per day

**Within-Day/run:** 3 replicates for each HIV-1 RNA concentration level

BASAS Roche

# Practical Example: Study

We present an analysis of 1855 reproducibility data samples for an HIV-1 PCR assay test evaluated at six titer/concentration levels across the following factors:

**Lot:** 3 manufactured reagent lots

**Site/Instrument:** 3 test sites; 1 instrument per site

**Operator:** 2 operators performing testing at each site

**Day/Run:** 5 days per lot for each operator; 1 run per day

**Within-Day/run:** 3 replicates for each HIV-1 RNA concentration

Two different operators are at each of 3 test sites each performed 5 days of testing with each of 3 lots of reagents.

BASAS Roche

# Practical Example: Macro Call

For this example, the specification for the PrecMod SAS macro is as follows:

```
%PrecMod(InData    = DataSetIn ,
         ByVars    = titer_n titer_c logexp  ,
         ClassVars = dslot site operator day ,
         DepVar    = logconc ,
         IndepVars = ,
         Random    = dslot site operator day ,
         Method    = REML ,
         OutData   = ResultsDat ,
         FlagVar   = dvlflag ,
         FlagValue = DVL ,
         EquTest   = N    ,
         Alpha     = 0.05 ,
         InsType   = ,
         Logged    = "Yes") ;
```

BASAS Roche

# Practical Example: Macro Call

For this example, the specification for the PrecMod SAS macro is as follows:

```
%PrecMod(InData    = DataSetIn ,
         ByVars    = titer_n titer_c logexp  ,
         ClassVars = dslot site operator day ,
         Random    = dslot site operator day ,
         Method    = REML ,
         OutData   = ResultsDat ,
         FlagVar   = dvlflag ,
         FlagValue = DVL ,
         EquTest   = N    ,
         Alpha     = 0.05 ,
         InsType   = ,
         Logged    = "Yes") ;
```

**Enter SAS data set**

BASAS Roche

# Practical Example: Macro Call

For this example, the specification for the PrecMod SAS macro is as follows:

```
%PrecMod(InData    = DataSetIn ,
         ByVars    = titer_n titer_c logexp  ,
         ClassVars = dslot site operator day ,
         DepVar    = loggeng
         OutData   = ResultsDat ,
         FlagVar   = dvlflag ,
         FlagValue = DVL ,
         EquTest   = N    ,
         Alpha     = 0.05 ,
         InsType   = ,
         Logged    = "Yes") ;
```

**Enter "By" Variables *(to iterate over and obtain results for each level)***

BASAS Roche

# Practical Example: Macro Call

For this example, the specification for the PrecMod SAS macro is as follows:

```
%PrecMod(InData    = DataSetIn ,
         ByVars    = titer_n titer_c logexp  ,
         ClassVars = dslot site operator day ,
         DepVar    = logresp
```

**Enter "By" Variables *(to iterate over and obtain results for each level)***

**titer_n = concentration level as numeric**

**titer_c = concentration level as character**

**logexp = logarithm base 10 of titer_n**

BASAS Roche

# Practical Example: Macro Call

For this example, the specification for the PrecMod SAS macro is as follows:

```
%PrecMod(InData    = DataSetIn ,
         ByVars    = titer_n titer_c logexp  ,
         ClassVars = dslot site operator day ,
         DepVar    = logexp
```

**Enter "By" Variables *(to iterate over and obtain results for each level)***

titer_n = concentration level as numeric

**titer_c = concentration level as character**

logexp = logarithm base 10 of titer_n

BASAS Roche

# Practical Example: Macro Call

For this example, the specification for the PrecMod SAS macro is as follows:

```
%PrecMod(InData    = DataSetIn ,
         ByVars    = titer_n titer_c logexp  ,
         ClassVars = dslot site operator day ,
         DepVar    = logexp
```

**Enter "By" Variables *(to iterate over and obtain results for each level)***

titer_n = concentration level as numeric

titer_c = concentration level as character

**logexp = logarithm base 10 of titer_n**

BASAS Roche

# Practical Example: Macro Call

For this example, the specification for the PrecMod SAS macro is as follows:

```
%PrecMod(InData    = DataSetIn ,
         ByVars    = titer_n titer_c logexp  ,
         ClassVars = dslot site operator day ,
         DepVar    = logexp
```

**Enter "By" Variables *(to iterate over and obtain results for each level)***

**titer_n = concentration level as numeric**
**titer_c = concentration level as character**
**logexp = logarithm base 10 of titer_n**

BASAS Roche

# Practical Example: Macro Call

For this example, the specification for the PrecMod SAS macro is as follows:

```
%PrecMod(InData    = DataSetIn ,
         ByVars    = titer_n titer_c logexp  ,
         ClassVars = dslot site operator day ,
         DepVar    = logconc ,
```

**Enter "Class" Variables**

```
         Method    = REML ,
         OutData   = ResultsDat ,
         FlagVar   = dvlflag ,
         FlagValue = DVL ,
         EquTest   = N    ,
         Alpha     = 0.05 ,
         InsType   = ,
         Logged    = "Yes") ;
```

BASAS Roche

# Practical Example: Macro Call

For this example, the specification for the PrecMod SAS macro is as follows:

```
%PrecMod(InData    = DataSetIn ,
         ByVars    = titer_n titer_c logexp  ,
         ClassVars = dslot site operator day ,
         DepVar    = logconc ,
```

## Enter "Class" Variables

**dslot = lot variable**

**site = site variable**

**operator = operator variable**

**day = day variable**

BASAS Roche

# Practical Example: Macro Call

For this example, the specification for the PrecMod SAS macro is as follows:

```
%PrecMod(InData    = DataSetIn ,
         ByVars    = titer_n titer_c logexp  ,
         ClassVars = dslot site operator day ,
         DepVar    = logconc ,
```

## Enter "Class" Variables

dslot = lot variable

**site = site variable**

operator = operator variable

day = day variable

BASAS Roche

# Practical Example: Macro Call

For this example, the specification for the PrecMod SAS macro is as follows:

```
%PrecMod(InData    = DataSetIn ,
         ByVars    = titer_n titer_c logexp  ,
         ClassVars = dslot site operator day ,
         DepVar    = logconc ,
```

## Enter "Class" Variables

dslot = lot variable

site = site variable

**operator = operator variable**

day = day variable

BASAS Roche

# Practical Example: Macro Call

For this example, the specification for the PrecMod SAS macro is as follows:

```
%PrecMod(InData    = DataSetIn ,
         ByVars    = titer_n titer_c logexp  ,
         ClassVars = dslot site operator day ,
         DepVar    = logconc ,
```

## Enter "Class" Variables

dslot = lot variable

site = site variable

operator = operator variable

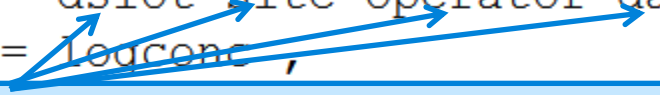
**day** = day variable

BASAS Roche

# Practical Example: Macro Call

For this example, the specification for the PrecMod SAS macro is as follows:

```
%PrecMod(InData    = DataSetIn ,
         ByVars    = titer_n titer_c logexp  ,
         ClassVars = dslot site operator day ,
         DepVar    = logconc ,
```



**Enter "Class" Variables**

**dslot = lot variable**
**site = site variable**
**operator = operator variable**
**day = day variable**

BASAS Roche

# Practical Example: Macro Call

For this example, the specification for the PrecMod SAS macro is as follows:

```
%PrecMod(InData     = DataSetIn ,
         ByVars     = titer_n titer_c logexp  ,
         ClassVars  = dslot site operator day ,
         DepVar     = logconc ,
         IndepVars  = ,
         InsType    = ,
         Logged     = "Yes") ;
```

**Enter "Dependent" Variable**

**logconc = logarithm base 10 of observed quantitation value**

BASAS Roche

# Practical Example: Macro Call

For this example, the specification for the PrecMod SAS macro is as follows:

```
%PrecMod(InData    = DataSetIn ,
         ByVars    = titer_n titer_c logexp  ,
         ClassVars = dslot site operator day ,
         DepVar    = logconc ,
         IndepVars = ,
         Random    = dslot site operator day ,
         Method    = REML
         InsType   = ,
         Logged    = "Yes") ;
```

**Enter any "Independent" Variables**

**None here.**

BASAS Roche

# Practical Example: Macro Call

For this example, the specification for the PrecMod SAS macro is as follows:

```
%PrecMod(InData    = DataSetIn ,
         ByVars    = titer_n titer_c logexp  ,
         ClassVars = dslot site operator day ,
         DepVar    = logconc ,
         IndepVars = ,
         Random    = dslot site operator day ,
         Method    = REML ,
         OutData   = ResultsDat ,
```

**Enter "Random Variable" names**

*These are the same names as in the "ClassVars" statement.*

BASAS Roche

# Practical Example: Macro Call

For this example, the specification for the PrecMod SAS macro is as follows:

```
%PrecMod(InData    = DataSetIn ,
         ByVars    = titer_n titer_c logexp  ,
         ClassVars = dslot site operator day ,
         DepVar    = logconc ,
         IndepVars = ,
         Random    = dslot site operator day ,
         Method    = REML ,
         OutData   = ResultsDat ,
```

**Enter "Random Variable" names**

***These are the same names as in the "ClassVars" statement.***

BASAS Roche

# Practical Example: Macro Call

For this example, the specification for the PrecMod SAS macro is as follows:

```
%PrecMod(InData    = DataSetIn ,
         ByVars    = titer_n titer_c logexp  ,
         ClassVars = dslot site operator day ,
         DepVar    = logconc ,
         IndepVars = ,
         Random    = dslot site operator day ,
         Method    = REML ,
         OutData   = ResultsDat ,
         FlagVar   = dylflag ,
```

## Enter estimation "Method"

***Two main ones:***

**REML = Restricted Maximum Likelihood**

**ML = Maximum Likelihood**

BASAS Roche

# Practical Example: Macro Call

For this example, the specification for the PrecMod SAS macro is as follows:

```
%PrecMod(InData    = DataSetIn ,
         ByVars    = titer_n titer_c logexp  ,
         ClassVars = dslot site operator day ,
         DepVar    = logconc ,
         IndepVars = ,
         Random    = dslot site operator day ,
         Method    = REML ,
         OutData   = ResultsDat ,
         FlagVar   = dvlflag ,
         FlagValue = DVL
         InsType   = ,
         Logged    = "Yes") ;
```

**Enter output SAS data set name.**

BASAS Roche

# Practical Example: Macro Call

For this example, the specification for the PrecMod SAS macro is as follows:

```
%PrecMod(InData    = DataSetIn ,
         ByVars    = titer_n titer_c logexp  ,
         ClassVars = dslot site operator day ,
         DepVar    = logconc ,
         IndepVars = ,
         Random    = dslot site operator day ,
         Method    = REML ,
         OutData   = ResultsDat ,
         FlagVar   = dvlflag ,
         FlagValue = DVL
```

**Enter output SAS data set name.**

**ResultsDat = work.ResultsDat SAS data set**

BASAS Roche

# Practical Example: Macro Call

For this example, the specification for the PrecMod SAS macro is as follows:

**Enter any "flag" variables for subsetting …**

**dvlflag = flag variable**

```
IndepVars = ,
Random    = dslot site operator day ,
Method    = REML ,
OutData   = ResultsDat ,
FlagVar   = dvlflag ,
FlagValue = DVL ,
EquTest   = N     ,
```

**…and corresponding "flag" value**

**FlagValue = DVL**

**Where DVL is the value of "FlagVar".**

BASAS Roche

# Practical Example: Macro Call

**For the moment, ignore the optional "Equivalency Testing" option, "EquTest".**

**Tests for equivalency between the two comparison items via a variance ratio test.**

```
OutData   = ResultsDat ,
FlagVar   = dvlflag ,
FlagValue = DVL ,
EquTest   = N    ,
Alpha     = 0.05 ,
InsType   = ,
Logged    = "Yes") ;
```

BASAS Roche

# Practical Example: Macro Call

For this example, the specification for the PrecMod SAS macro is as follows:

**… and ignore associated options:**

**Alpha = Significance Level for Variance Ratio Test for Equivalency Testing of two compared items;**

**InstType = Variable that identifies the two compared items, here, "Instrument Type".**

```
FlagVal   = DVLFlag ,
FlagValue = DVL ,
EquTest   = N     ,
Alpha     = 0.05 ,
InsType   = ,
Logged    = "Yes") ;
```

BASAS Roche

# Practical Example: Macro Call

**Indicate whether your outcome/dependent variable is logged (“Yes”) or on original scale (“No”).**

**This is important in order to use the correct formula for the percent coefficient of variation (%CV).**

```
Method    = REML ,
OutData   = ResultsDat ,
FlagVar   = dvlflag ,
FlagValue = DVL ,
EquTest   = N    ,
Alpha     = 0.05 ,
InsType   = ,
Logged    = "Yes") ;
```

# Performance Metrics: Precision

BASAS Roche

- **Estimation of Precision**

- Precision is usually expressed in terms of %CV (percent coefficient of variation) or $Log_{10}SD$ scale.

- In general, the %CV is estimated as follows (for non-log transformed data):

$$\%CV = \left(\frac{SD}{mean}\right) \cdot 100\%$$

where SD is the standard deviation of the quantitation.

- However, on the $log_{10}$ scale, the %CV is defined as the approximation:

$$\%CV = \sqrt{10^{SD^2 \cdot \ln(10)} - 1} \cdot 100\%$$

where the SD in this case is the $Log_{10}SD$ $log_{10}$ transformed quantitation and ln(·) is the natural logarithm.

# Performance Metrics: Precision

BASAS Roche

- **Estimation of Precision**

- Precision is usually expressed in terms of %CV (percent coefficient of variation) or $Log_{10}SD$ scale.

- In general, the %CV is estimated as follows (for non-log transformed data):

$$\%CV = \left(\frac{SD}{mean}\right) \cdot 100\%$$

where SD is the standard deviation of the quantitation.

- However, on the $\log_{10}$ scale, the %CV is defined as the approximation:

$$\%CV = \sqrt{10^{SD^2 \cdot \ln(10)} - 1} \cdot 100\%$$

where the SD in this case is the $Log_{10}SD$ $\log_{10}$ transformed quantitation and ln(·) is the natural logarithm.

# Performance Metrics: Precision

BASAS Roche

- **Estimation of Precision**

- Precision is usually expressed in terms of %CV (percent coefficient of variation) or $Log_{10}SD$ scale.

- In general, the %CV is estimated as follows (for non-log transformed data):

$$\%CV = \left(\frac{SD}{mean}\right) \cdot 100\%$$

where SD is the standard deviation of the quantitation.

- However, on the $log_{10}$ scale, the %CV is defined as the approximation:

$$\%CV = \sqrt{10^{SD^2 \cdot \ln(10)} - 1} \cdot 100\%$$

where the SD in this case is the $Log_{10}SD$ $log_{10}$ transformed quantitation and ln(·) is the natural logarithm.

BASAS Roche

# Practical Example: Macro Call

For this example, the specification for the PrecMod SAS macro is as follows:

```
%PrecMod(InData    = DataSetIn ,
         ByVars    = titer_n titer_c logexp  ,
         ClassVars = dslot site operator day ,
         DepVar    = logconc ,
         IndepVars = ,
         Random    = dslot site operator day ,
         Method    = REML ,
         OutData   = ResultsDat ,
         FlagVar   = dvlflag ,
         FlagValue = DVL ,
         EquTest   = N    ,
         Alpha     = 0.05 ,
         InsType   = ,
         Logged    = "Yes") ;
```

BASAS Roche

# Practical Example: Macro Call

For this example, the specification for the PrecMod SAS macro is as follows:

```
%PrecMod(InData    = DataSetIn ,
         ByVars    = titer_n titer_c logexp  ,
         ClassVars = dslot site operator day ,
                                              day ,
         EquTest   = N    ,
         Alpha     = 0.05 ,
         InsType   = ,
         Logged    = "Yes") ;
```

BASAS Roche

# Practical Example: Results

Table 3 shows the results as formatted using the DATA step and PROC REPORT code in APPENDIX B.

| HIV-1 RNA Concentration ($log_{10}$ cp/mL) | | | Random Effects Model Components Contribution to Total Variance (%) | | | | | Total Precision |
|---|---|---|---|---|---|---|---|---|
| Expected | Observed (average) | # of Results[a] | Lot | Site | Operator | Day | Within-Day | Standard Deviation (Lognormal %CV)[b] |
| 1.699 | 1.644 | 3 | 5.3% | 0.7% | 0.0% | 2.5% | 91.4% | 0.16 (66.1%) |
| 1.699** | 1.646 | 3 | 4.4% | 2.7% | 0.0% | 0.9% | 92.0% | 0.25 (63.1%) |
| 2.301 | 2.260 | 7 | 1.1% | 1.1% | 1.1% | 0.0% | 96.7% | 0.13 (32.3%) |
| 2.602 | 2.538 | 7 | 2.3% | 1.3% | 1.4% | 0.5% | 84.5% | 0.10 (23.3%) |
| 3.000 | 2.983 | 66 | 0.0% | 0.0% | 4.6% | 0.0% | 94.9% | 0.12 (28.6%) |
| 5.000 | 4.961 | 265 | 9.0% | 11.2% | 2.7% | 0.0% | 78.1% | 0.09 (21.3%) |
| 6.699 | 6.673 | 29 | 7.7% | 1.1% | 2.0% | 0.0% | 23.7% | 0.16 (39.7%) |

Note: Results with detectable viral load are included in this table.

[a] Number of tests with detectable viral load.
[b] Lognormal %CV = 100% • square root of {10^[variance • ln(10)]-1}, where ln() is the natural logarithm
** Results < 3.40E+1 cp/mL were calculated based on the validated in-house software from ΔCt values for test results that were below LLoQ.

Data Source: Appendix X, Table Y.1, Table Y.2.

**Table 3. Attributable percentage of total variance, total precision standard deviation and lognormal %CV of HIV-1 RNA concentration (log10 cp/mL) from tests with detectable viral load.**

BASAS Roche

# Practical Example: Results

Table 3 shows the results as formatted using the DATA step and PROC REPORT code in APPENDIX B.

| HIV-1 RNA Concentration ($log_{10}$ cp/mL) | | | Random Effects Model Components Contribution to Total Variance (%) | | | | | Total Precision |
|---|---|---|---|---|---|---|---|---|
| Expected | Observed (average) | No. of Tests[a] | Lot | Site | Operator | Day | Within-Day | Standard Deviation (Lognormal %CV)[b] |
| 1.699 | 1.624 | 263 | 5.3% | 0.7% | 0.0% | 2.5% | 91.4% | 0.26 (66.1%) |
| 1.699** | 1.646 | 263 | 4.4% | 2.7% | 0.0% | 0.9% | 92.0% | 0.25 (63.1%) |
| 2.301 | 2.260 | 267 | 1.1% | 1.1% | 1.1% | 0.0% | 96.7% | 0.13 (32.3%) |
| 2.602 | 2.538 | 267 | 2.3% | 1.3% | 11.4% | 0.5% | 84.5% | 0.10 (23.3%) |
| 3.000 | 2.983 | 266 | 0.5% | 0.0% | 4.6% | 0.0% | 94.9% | 0.12 (28.6%) |
| 5.000 | 4.961 | 265 | 0.9% | 17.2% | 2.7% | 0.4% | 78.7% | 0.09 (21.3%) |
| 6.699 | 6.673 | 264 | 1.7% | 71.5% | 2.8% | 0.3% | 23.7% | 0.16 (39.7%) |

Note: Results with detectable viral load are included in this table.

[a] Number of tests with detectable viral load.
[b] Lognormal %CV = 100% • square root of {10^[variance • ln(10)]-1}, where ln() is the natural logarithm
** Results < 3.40E+1 cp/mL were calculated based on the validated in-house software from ΔCt values for test results that were below LLoQ.

Data Source: Appendix X, Table Y.1, Table Y.2.

**Table 3. Attributable percentage of total variance, total precision standard deviation and lognormal %CV of HIV-1 RNA concentration (log10 cp/mL) from tests with detectable viral load.**

BASAS Roche

# Practical Example: Results

Table 3 shows the results as formatted using the DATA step and PROC REPORT code in APPENDIX B.

| HIV-1 RNA Concentration ($log_{10}$ cp/mL) | | | Random Effects Model Components Contribution to Total Variance (%) | | | | | Total Precision |
|---|---|---|---|---|---|---|---|---|
| Expected | Observed (average) | No. of Tests[a] | Lot | Site | Operator | Day | Within-Day | Standard Deviation (Lognormal %CV)[b] |
| 1.699 | 1.624 | 263 | 5.3% | 0.7% | 0.0% | 2.5% | 91.4% | 0.26 (66.1%) |
| 1.699** | 1.646 | 263 | 4.4% | 2.7% | 0.0% | 0.9% | 92.0% | 0.25 (63.1%) |
| 2.301 | 2.260 | 267 | 1.1% | 1.1% | 1.1% | 0.0% | 96.7% | 0.13 (32.3%) |
| 2.602 | 2.538 | 267 | 2.3% | 1.3% | 11.4% | 0.5% | 84.5% | 0.10 (23.3%) |
| 3.000 | 2.983 | 266 | 0.5% | 0.0% | 4.6% | 0.0% | 94.9% | 0.12 (28.6%) |
| 5.000 | 4.961 | 265 | 0.9% | 17.2% | 2.7% | 0.4% | 78.7% | 0.09 (21.3%) |
| 6.699 | 6.673 | 264 | 1.7% | 71.5% | 2.8% | 0.3% | 23.7% | 0.16 (39.7%) |

Note: Results with detectable viral load are included in this table.

[a] Number of tests with detectable viral load.
[b] Lognormal %CV = 100% • square root of {10^[variance • ln(10)]-1}, where ln() is the natural logarithm
** Results < 3.40E+1 cp/mL were calculated based on the validated in-house software from ΔCt values for test results that were below LLoQ.

Data Source: Appendix X, Table Y.1, Table Y.2.

**Table 3. Attributable percentage of total variance, total precision standard deviation and lognormal %CV of HIV-1 RNA concentration (log10 cp/mL) from tests with detectable viral load.**

BASAS Roche

# Practical Example: Results

Table 3 shows the results as formatted using the DATA step and PROC REPORT code in APPENDIX B.

| HIV-1 RNA Concentration ($log_{10}$ cp/mL) | | | Random Effects Model Components Contribution to Total Variance (%) | | | | | Total Precision |
|---|---|---|---|---|---|---|---|---|
| Expected | Observed (average) | No. of Tests[a] | Lot | Site | Operator | Day | Within-Day | Standard Deviation (Lognormal %CV)[b] |
| 1.699 | 1.624 | 263 | 5.3% | 0.7% | 0.0% | 2.5% | 91.4% | 0.26 (66.1%) |
| 1.699** | 1.646 | 263 | 4.4% | 2.7% | 0.0% | 0.9% | 92.0% | 0.25 (63.1%) |
| 2.301 | 2.260 | 267 | 1.1% | 1.1% | 1.1% | 0.0% | 96.7% | 0.13 (32.3%) |
| 2.602 | 2.538 | 267 | 2.3% | 1.3% | 11.4% | 0.5% | 84.5% | 0.10 (23.3%) |
| 3.000 | 2.983 | 266 | 0.5% | 0.0% | 4.6% | 0.0% | 94.9% | 0.12 (28.6%) |
| 5.000 | 4.961 | 265 | 0.9% | 17.2% | 2.7% | 0.4% | 78.7% | 0.09 (21.3%) |
| 6.699 | 6.673 | 264 | 1.7% | 71.5% | 2.8% | 0.3% | 23.7% | 0.16 (39.7%) |

Note: Results with detectable viral load are included in this table.

[a] Number of tests with detectable viral load.
[b] Lognormal %CV = 100% • square root of {10^[variance • ln(10)]-1}, where ln() is the natural logarithm
** Results < 3.40E+1 cp/mL were calculated based on the validated in-house software from ΔCt values for test results that were below LLoQ.

Data Source: Appendix X, Table Y.1, Table Y.2.

**Table 3. Attributable percentage of total variance, total precision standard deviation and lognormal %CV of HIV-1 RNA concentration (log10 cp/mL) from tests with detectable viral load.**

BASAS Roche

# Practical Example: Results

Table 3 shows the results as formatted using the DATA step and PROC REPORT code in APPENDIX B.

| HIV-1 RNA Concentration ($log_{10}$ cp/mL) | | | Random Effects Model Components Contribution to Total Variance (%) | | | | | Total Precision |
|---|---|---|---|---|---|---|---|---|
| Expected | Observed (average) | No. of Tests[a] | Lot | Site | Operator | Day | Within-Day | Standard Deviation (Lognormal %CV)[b] |
| 1.699 | 1.624 | 263 | 5.3% | 0.7% | 0.0% | 2.5% | 91.4% | 0.26 (66.1%) |
| 1.699** | 1.646 | 263 | 4.4% | 2.7% | 0.0% | 0.9% | 92.0% | 0.25 (63.1%) |
| 2.301 | 2.260 | 267 | 1.1% | 1.1% | 1.1% | 0.0% | 96.7% | 0.13 (32.3%) |
| 2.602 | 2.538 | 267 | 2.3% | 1.3% | 11.4% | 0.5% | 84.5% | 0.10 (23.3%) |
| 3.000 | 2.983 | 266 | 0.5% | 0.0% | 4.6% | 0.0% | 94.9% | 0.12 (28.6%) |
| 5.000 | 4.961 | 265 | 0.9% | 17.2% | 2.7% | 0.4% | 78.7% | 0.09 (21.3%) |
| 6.699 | 6.673 | 264 | 1.7% | 71.5% | 2.8% | 0.3% | 23.7% | 0.16 (39.7%) |

Note: Results with detectable viral load are included in this table.

[a] Number of tests with detectable viral load.
[b] Lognormal %CV = 100% • square root of {10^[variance • ln(10)]-1}, where ln() is the natural logarithm
** Results < 3.40E+1 cp/mL were calculated based on the validated in-house software from ΔCt values for test results that were below LLoQ.

Data Source: Appendix X, Table Y.1, Table Y.2.

**Table 3. Attributable percentage of total variance, total precision standard deviation and lognormal %CV of HIV-1 RNA concentration (log10 cp/mL) from tests with detectable viral load.**

BASAS Roche

# Practical Example: Results

Table 3 shows the results as formatted using the DATA step and PROC REPORT code in APPENDIX B.

| HIV-1 RNA Concentration ($log_{10}$ cp/mL) | | | Random Effects Model Components Contribution to Total Variance (%) | | | | | Total Precision |
|---|---|---|---|---|---|---|---|---|
| Expected | Observed (average) | No. of Tests[a] | Lot | Site | Operator | Day | Within-Day | Standard Deviation (Lognormal %CV)[b] |
| 1.699 | 1.624 | 263 | 5.3% | 0.7% | 0.0% | 2.5% | 91.4% | 0.26 (66.1%) |
| 1.699** | 1.646 | 263 | 4.4% | 2.7% | 0.0% | 0.9% | 92.0% | 0.25 (63.1%) |
| 2.301 | 2.260 | 267 | 1.1% | 1.1% | 1.1% | 0.0% | 96.7% | 0.13 (32.3%) |
| 2.602 | 2.538 | 267 | 2.3% | 1.3% | 11.4% | 0.5% | 84.5% | 0.10 (23.3%) |
| 3.000 | 2.983 | 266 | 0.5% | 0.0% | 4.6% | 0.0% | 94.9% | 0.12 (28.6%) |
| 5.000 | 4.961 | 265 | 0.9% | 17.2% | 2.7% | 0.4% | 78.7% | 0.09 (21.3%) |
| 6.699 | 6.673 | 264 | 1.7% | 71.5% | 2.8% | 0.3% | 23.7% | 0.16 (39.7%) |

Note: Results with detectable viral load are included in this table.

[a] Number of tests with detectable viral load.
[b] Lognormal %CV = 100% • square root of {10^[variance • ln(10)]-1}, where ln() is the natural logarithm
** Results < 3.40E+1 cp/mL were calculated based on the validated in-house software from ΔCt values for test results that were below LLoQ.

Data Source: Appendix X, Table Y.1, Table Y.2.

**Table 3. Attributable percentage of total variance, total precision standard deviation and lognormal %CV of HIV-1 RNA concentration (log10 cp/mL) from tests with detectable viral load.**

BASAS Roche

# Practical Example: Results

Table 3 shows the results as formatted using the DATA step and PROC REPORT code in APPENDIX B.

| HIV-1 RNA Concentration ($log_{10}$ cp/mL) | | | Random Effects Model Components Contribution to Total Variance (%) | | | | | Total Precision |
|---|---|---|---|---|---|---|---|---|
| Expected | Observed (average) | No. of Tests[a] | Lot | Site | Operator | Day | Within-Day | Standard Deviation (Lognormal %CV)[b] |
| 1.699 | 1.624 | 263 | 5.3% | 0.7% | 0.0% | 2.5% | 91.4% | 0.26 (66.1%) |
| 1.699** | 1.646 | 263 | 4.4% | 2.7% | 0.0% | 0.9% | 92.0% | 0.25 (63.1%) |
| 2.301 | 2.260 | 267 | 1.1% | 1.1% | 1.1% | 0.0% | 96.7% | 0.13 (32.3%) |
| 2.602 | 2.538 | 267 | 2.3% | 1.3% | 11.4% | 0.5% | 84.5% | 0.10 (23.3%) |
| 3.000 | 2.983 | 266 | 0.5% | 0.0% | 4.6% | 0.0% | 94.9% | 0.12 (28.6%) |
| 5.000 | 4.961 | 265 | 0.9% | 17.2% | 2.7% | 0.4% | 78.7% | 0.09 (21.3%) |
| 6.699 | 6.673 | 264 | 1.7% | 71.5% | 2.8% | 0.3% | 23.7% | 0.16 (39.7%) |

Note: Results with detectable viral load are included in this table.

[a] Number of tests with detectable viral load.
[b] Lognormal %CV = 100% • square root of {10^[variance • ln(10)]-1}, where ln() is the natural logarithm
** Results < 3.40E+1 cp/mL were calculated based on the validated in-house software from ΔCt values for test results that were below LLoQ.

Data Source: Appendix X, Table Y.1, Table Y.2.

**Table 3. Attributable percentage of total variance, total precision standard deviation and lognormal %CV of HIV-1 RNA concentration (log10 cp/mL) from tests with detectable viral load.**

BASAS Roche

# Practical Example: Results

Table 3 shows the results as formatted using the DATA step and PROC REPORT code in APPENDIX B.

| HIV-1 RNA Concentration ($log_{10}$ cp/mL) | | | Random Effects Model Components Contribution to Total Variance (%) | | | | | Total Precision |
|---|---|---|---|---|---|---|---|---|
| Expected | Observed (average) | No. of Tests[a] | Lot | Site | Operator | Day | Within-Day | Standard Deviation (Lognormal %CV)[b] |
| 1.699 | 1.624 | 263 | 5.3% | 0.7% | 0.0% | 2.5% | 91.4% | 0.26 (66.1%) |
| 1.699** | 1.646 | 263 | 4.4% | 2.7% | 0.0% | 0.9% | 92.0% | 0.25 (63.1%) |
| 2.301 | 2.260 | 267 | 1.1% | 1.1% | 1.1% | 0.0% | 96.7% | 0.13 (32.3%) |
| 2.602 | 2.538 | 267 | 2.3% | 1.3% | 11.4% | 0.5% | 84.5% | 0.10 (23.3%) |
| 3.000 | 2.983 | 266 | 0.5% | 0.0% | 4.6% | 0.0% | 94.9% | 0.12 (28.6%) |
| 5.000 | 4.961 | 265 | 0.9% | 17.2% | 2.7% | 0.4% | 78.7% | 0.09 (21.3%) |
| 6.699 | 6.673 | 264 | 1.7% | 71.5% | 2.8% | 0.3% | 23.7% | 0.16 (39.7%) |

Note: Results with detectable viral load are included in this table.

[a] Number of tests with detectable viral load.
[b] Lognormal %CV = 100% • square root of {10^[variance • ln(10)]-1}, where ln() is the natural logarithm
** Results < 3.40E+1 cp/mL were calculated based on the validated in-house software from ΔCt values for test results that were below LLoQ.

Data Source: Appendix X, Table Y.1, Table Y.2.

**Table 3. Attributable percentage of total variance, total precision standard deviation and lognormal %CV of HIV-1 RNA concentration (log10 cp/mL) from tests with detectable viral load.**

BASAS Roche

# Practical Example: Results

Table 3 shows the results as formatted using the DATA step and PROC REPORT code in APPENDIX B.

| HIV-1 RNA Concentration ($log_{10}$ cp/mL) | | | Random Effects Model Components Contribution to Total Variance (%) | | | | | Total Precision |
|---|---|---|---|---|---|---|---|---|
| Expected | Observed (average) | No. of Tests[a] | Lot | Site | Operator | Day | Within-Day | Standard Deviation (Lognormal %CV)[b] |
| 1.699 | 1.624 | 263 | 5.3% | 0.7% | 0.0% | 2.5% | 91.4% | 0.26 (66.1%) |
| 1.699** | 1.646 | 263 | 4.4% | 2.7% | 0.0% | 0.9% | 92.0% | 0.25 (63.1%) |
| 2.301 | 2.260 | 267 | 1.1% | 1.1% | 1.1% | 0.0% | 96.7% | 0.13 (32.3%) |
| 2.602 | 2.538 | 267 | 2.3% | 1.3% | 11.4% | 0.5% | 84.5% | 0.10 (23.3%) |
| 3.000 | 2.983 | 266 | 0.5% | 0.0% | 4.6% | 0.0% | 94.9% | 0.12 (28.6%) |
| 5.000 | 4.961 | 265 | 0.9% | 17.2% | 2.7% | 0.4% | 78.7% | 0.09 (21.3%) |
| 6.699 | 6.673 | 264 | 1.7% | 71.5% | 2.8% | 0.3% | 23.7% | 0.16 (39.7%) |

Note: Results with detectable viral load are included in this table.

[a] Number of tests with detectable viral load.
[b] Lognormal %CV = 100% • square root of {10^[variance • ln(10)]-1}, where ln() is the natural logarithm
** Results < 3.40E+1 cp/mL were calculated based on the validated in-house software from ΔCt values for test results that were below LLoQ.

Data Source: Appendix X, Table Y.1, Table Y.2.

**Table 3. Attributable percentage of total variance, total precision standard deviation and lognormal %CV of HIV-1 RNA concentration (log10 cp/mL) from tests with detectable viral load.**

BASAS Roche

# Practical Example: Results

Table 3 shows the results as formatted using the DATA step and PROC REPORT code in APPENDIX B.

| HIV-1 RNA Concentration ($log_{10}$ cp/mL) | | | Random Effects Model Components Contribution to Total Variance (%) | | | | | Total Precision |
|---|---|---|---|---|---|---|---|---|
| Expected | Observed (average) | No. of Tests[a] | Lot | Site | Operator | Day | Within-Day | Standard Deviation (Lognormal %CV)[b] |
| 1.699 | 1.624 | 263 | 5.3% | 0.7% | 0.0% | 2.5% | 91.4% | 0.26 (66.1%) |
| 1.699** | 1.646 | 263 | 4.4% | 2.7% | 0.0% | 0.9% | 92.0% | 0.25 (63.1%) |
| 2.301 | 2.260 | 267 | 1.1% | 1.1% | 1.1% | 0.0% | 96.7% | 0.13 (32.3%) |
| 2.602 | 2.538 | 267 | 2.3% | 1.3% | 11.4% | 0.5% | 84.5% | 0.10 (23.3%) |
| 3.000 | 2.983 | 266 | 0.5% | 0.0% | 4.6% | 0.0% | 94.9% | 0.12 (28.6%) |
| 5.000 | 4.961 | 265 | 0.9% | 17.2% | 2.7% | 0.4% | 78.7% | 0.09 (21.3%) |
| 6.699 | 6.673 | 264 | 1.7% | 71.5% | 2.8% | 0.3% | 23.7% | 0.16 (39.7%) |

Note: Results with detectable viral load are included in this table.

[a] Number of tests with detectable viral load.
[b] Lognormal %CV = 100% • square root of {10^[variance • ln(10)]-1}, where ln() is the natural logarithm
** Results < 3.40E+1 cp/mL were calculated based on the validated in-house software from ΔCt values for test results that were below LLoQ.

Data Source: Appendix X, Table Y.1, Table Y.2.

**Table 3. Attributable percentage of total variance, total precision standard deviation and lognormal %CV of HIV-1 RNA concentration (log10 cp/mL) from tests with detectable viral load.**

BASAS Roche

# Practical Example: Results

Table 3 shows the results as formatted using the DATA step and PROC REPORT code in APPENDIX B.

| HIV-1 RNA Concentration ($log_{10}$ cp/mL) | | | Random Effects Model Components Contribution to Total Variance (%) | | | | | Total Precision |
|---|---|---|---|---|---|---|---|---|
| Expected | Observed (average) | No. of Tests[a] | Lot | Site | Operator | Day | Within-Day | Standard Deviation (Lognormal %CV)[b] |
| 1.699 | 1.624 | 263 | 5.3% | 0.7% | 0.0% | 2.5% | 91.4% | 0.26 (66.1%) |
| 1.699** | 1.646 | 263 | 4.4% | 2.7% | 0.0% | 0.9% | 92.0% | 0.25 (63.1%) |
| 2.301 | 2.260 | 267 | 1.1% | 1.1% | 1.1% | 0.0% | 96.7% | 0.13 (32.3%) |
| 2.602 | 2.538 | 267 | 2.3% | 1.3% | 11.4% | 0.5% | 84.5% | 0.10 (23.3%) |
| 3.000 | 2.983 | 266 | 0.5% | 0.0% | 4.6% | 0.0% | 94.9% | 0.12 (28.6%) |
| 5.000 | 4.961 | 265 | 0.9% | 17.2% | 2.7% | 0.4% | 78.7% | 0.09 (21.3%) |
| 6.699 | 6.673 | 264 | 1.7% | 71.5% | 2.8% | 0.3% | 23.7% | 0.16 (39.7%) |

Note: Results with detectable viral load are included in this table.

[a] Number of tests with detectable viral load.
[b] Lognormal %CV = 100% • square root of {10^[variance • ln(10)]-1}, where ln() is the natural logarithm
** Results < 3.40E+1 cp/mL were calculated based on the validated in-house software from ΔCt values for test results that were below LLoQ.

Data Source: Appendix X, Table Y.1, Table Y.2.

**Table 3. Attributable percentage of total variance, total precision standard deviation and lognormal %CV of HIV-1 RNA concentration (log10 cp/mL) from tests with detectable viral load.**

## Table Formatting Code

BASAS Roche

We provide table formatting code for formatting the results of your precision estimation run.

## Table Formatting Code (cont'd)

As every model is different AND so would be the formatted tables you create so an automatic table is not quite possible here … without additional programming.

## Table Formatting Code (cont'd)

BASAS Roche

The output data set will create variables of the form:

## Table Formatting Code (cont'd)

BASAS Roche

(ResultsDat in our code)

# The output data set will create variables of the form:

## Table Formatting Code (cont'd)

(**ResultsDat** in our code)

The output data set will create variables of the form:

**<Characteristic>**

## Table Formatting Code (cont'd)

BASAS Roche

(ResultsDat in our code)

# The output data set will create variables of the form:

**<Characteristic>_**

## Table Formatting Code (cont'd)

BASAS Roche

(ResultsDat in our code)

The output data set will create variables of the form:

**<Characteristic>_<Model Effect>**

# Table Formatting Code (cont'd)

BASAS

Roche

## Where <Characteristic> will be:

## Table Formatting Code (cont'd)

BASAS Roche

# Where <Characteristic> will be:

**VAR** for variance estimate;

**PC** for percent contribution to the variance;

**SD** for standard deviation estimate;

**CV** for percent coefficient of variation estimate.

## Table Formatting Code (cont'd)

BASAS Roche

# Where <Characteristic> will be:

VAR for variance estimate;

**PC for percent contribution to the variance;**

SD for standard deviation estimate;

CV for percent coefficient of variation estimate.

## Table Formatting Code (cont'd)

BASAS Roche

# Where <Characteristic> will be:

VAR for variance estimate;

PC for percent contribution to the variance;

**SD for standard deviation estimate;**

CV for percent coefficient of variation estimate.

## Table Formatting Code (cont'd)

BASAS Roche

# Where <Characteristic> will be:

VAR for variance estimate;

PC for percent contribution to the variance;

SD for standard deviation estimate;

**CV for percent coefficient of variation estimate.**

## Table Formatting Code (cont'd)

BASAS Roche

# Where <Characteristic> will be:

**VAR** for variance estimate;

**PC** for percent contribution to the variance;

**SD** for standard deviation estimate;

**CV** for percent coefficient of variation estimate.

# Table Formatting Code (cont'd)

BASAS Roche

## And where <Model Effect> is the variable name *as specified in our model*:

```
%PrecMod(InData     = DataSetIn ,
         ByVars     = titer_n titer_c logexp  ,
         ClassVars  = dslot site operator day ,
         DepVar     = logconc ,
         IndepVars  = ,
         Random     = dslot site operator day ,
         Method     = REML ,
         OutData    = ResultsDat ,
         FlagVar    = dvlflag ,
         FlagValue  = DVL ,
         EquTest    = N    ,
         Alpha      = 0.05 ,
         InsType    = ,
         Logged     = "Yes") ;
```

## Table Formatting Code (cont'd)

BASAS Roche

**And where <Model Effect> is the variable name *as specified in our model*:**

## Table Formatting Code (cont'd)

BASAS Roche

**And where <Model Effect> is the variable name *as specified in our model*:**

**DSLOT = Lot variable name**

**SITE = Site variable name**

**OPERATOR = Operator variable name**

**DAY = Day variable name**

## Table Formatting Code (cont'd)

BASAS Roche

**And where <Model Effect> is the variable name *as specified in our model*:**

DSLOT = Lot variable name

SITE = Site variable name

OPERATOR = Operator variable name

DAY = Day variable name

## Table Formatting Code (cont'd)

BASAS Roche

**And where <Model Effect> is the variable name *as specified in our model*:**

DSLOT = Lot variable name

SITE = Site variable name

**OPERATOR = Operator variable name**

DAY = Day variable name

## Table Formatting Code (cont'd)

BASAS Roche

**And where <Model Effect> is the variable name *as specified in our model*:**

DSLOT = Lot variable name

SITE = Site variable name

OPERATOR = Operator variable name

**DAY = Day variable name**

## Table Formatting Code (cont'd)

BASAS Roche

**And where <Model Effect> is the variable name *as specified in our model*:**

**DSLOT = Lot variable name**

**SITE = Site variable name**

**OPERATOR = Operator variable name**

**DAY = Day variable name**

## Table Formatting Code (cont'd)

BASAS Roche

**<Characteristic>_<Model Effect>**

**In our *ResultsDat* output file becomes:**

VARIANCE

**VAR_DSLOT**

**VAR_SITE**

**VAR_OPERATOR**

**VAR_DAY**

# Table Formatting Code (cont'd)

BASAS Roche

## <Characteristic>_<Model Effect>

## In our *ResultsDat* output file becomes:

PERCENT CONTRIBUTION

PC_DSLOT

PC_SITE

PC_OPERATOR

PC_DAY

## Table Formatting Code (cont'd)

BASAS Roche

**<Characteristic>_<Model Effect>**

**In our *ResultsDat* output file becomes:**

STANDARD DEVIATION

**SD_DSLOT**

**SD_SITE**

**SD_OPERATOR**

**SD_DAY**

## Table Formatting Code (cont'd)

BASAS Roche

**<Characteristic>_<Model Effect>**

**In our *ResultsDat* output file becomes:**

COEFFICIENT OF VARIATION

**CV_DSLOT**

**CV_SITE**

**CV_OPERATOR**

**CV_DAY**

# Additional Variables Created:

**TotVariance = Total Variance (sum of the individual variance terms)**

**PC_TotVariance (this is 100% down the column)**

**TotSD = square root of the Total Variance**

**CV_TotSD = Total SD in %CV terms.**

**PROC REPORT** is then used to format the results.

# see SAS code in Appendix B applied to our example to give …

BASAS Roche

# Practical Example: Results

Table 3 shows the results as formatted using the DATA step and PROC REPORT code in APPENDIX B.

| HIV-1 RNA Concentration ($log_{10}$ cp/mL) | | | Random Effects Model Components Contribution to Total Variance (%) | | | | | Total Precision |
|---|---|---|---|---|---|---|---|---|
| Expected | Observed (average) | No. of Tests[a] | Lot | Site | Operator | Day | Within-Day | Standard Deviation (Lognormal %CV)[b] |
| 1.699 | 1.624 | 263 | 5.3% | 0.7% | 0.0% | 2.5% | 91.4% | 0.26 (66.1%) |
| 1.699** | 1.646 | 263 | 4.4% | 2.7% | 0.0% | 0.9% | 92.0% | 0.25 (63.1%) |
| 2.301 | 2.260 | 267 | 1.1% | 1.1% | 1.1% | 0.0% | 96.7% | 0.13 (32.3%) |
| 2.602 | 2.538 | 267 | 2.3% | 1.3% | 11.4% | 0.5% | 84.5% | 0.10 (23.3%) |
| 3.000 | 2.983 | 266 | 0.5% | 0.0% | 4.6% | 0.0% | 94.9% | 0.12 (28.6%) |
| 5.000 | 4.961 | 265 | 0.9% | 17.2% | 2.7% | 0.4% | 78.7% | 0.09 (21.3%) |
| 6.699 | 6.673 | 264 | 1.7% | 71.5% | 2.8% | 0.3% | 23.7% | 0.16 (39.7%) |

Note: Results with detectable viral load are included in this table.

[a] Number of tests with detectable viral load.
[b] Lognormal %CV = 100% • square root of {10^[variance • ln(10)]-1}, where ln() is the
** Results < 3.40E+1 cp/mL were calculated based on the validated in-house software for test results that were below LLoQ.

Data Source: Appendix X, Table Y.1, Table Y.2.

**Table 3. Attributable percentage of total variance, total precision standard deviation and lognormal %CV of HIV-1 RNA concentration (log10 cp/mL) from tests with detectable viral load.**

BASAS Roche

# Conclusion

- PrecMod SAS Macro:

BASAS Roche

# Conclusion

- PrecMod SAS Macro:
  - **Fits Random Effects Linear Models to estimate variance components using the SAS MIXED procedure:**

BASAS Roche

# Conclusion

- PrecMod SAS Macro:
  - Fits Random Effects Linear Models to estimate variance components using the SAS MIXED procedure:
    - **For multiple factors**

BASAS Roche

# Conclusion

- PrecMod SAS Macro:
  - Fits Random Effects Linear Models to estimate variance components using the SAS MIXED procedure:
    - For multiple factors
    - **At one or more grouping levels.**

BASAS Roche

# Conclusion

- PrecMod SAS Macro:
  - Fits Random Effects Linear Models to estimate variance components using the SAS MIXED procedure:
    - For multiple factors
    - At one or more grouping levels.
    - **The variance estimates are then used to:**
      - **derive the standard deviation,**

BASAS Roche

# Conclusion

- PrecMod SAS Macro:
  - Fits Random Effects Linear Models to estimate variance components using the SAS MIXED procedure:
    - For multiple factors
    - At one or more grouping levels.
    - **The variance estimates are then used to:**
      - derive the standard deviation,
      - **calculate percent coefficient of variation,**

BASAS Roche

# Conclusion

- PrecMod SAS Macro:
  - Fits Random Effects Linear Models to estimate variance components using the SAS MIXED procedure:
    - For multiple factors
    - At one or more grouping levels.
    - **The variance estimates are then used to:**
      - derive the standard deviation,
      - calculate percent coefficient of variation,
      - **calculate attributable percentage of total variance and**

BASAS Roche

# Conclusion

- PrecMod SAS Macro:
  - Fits Random Effects Linear Models to estimate variance components using the SAS MIXED procedure:
    - For multiple factors
    - At one or more grouping levels.
    - **The variance estimates are then used to:**
      - derive the standard deviation,
      - calculate percent coefficient of variation,
      - calculate attributable percentage of total variance and
      - **calculate confidence intervals for the variance components using the correct effective degrees of freedom (Satterthwaite, 1946).**

BASAS Roche

# Conclusion

- PrecMod SAS Macro:
  - Fits Random Effects Linear Models to estimate variance components using the SAS MIXED procedure:
    - For multiple factors
    - At one or more grouping levels.
    - The variance estimates are then used to:
      - derive the standard deviation,
      - calculate percent coefficient of variation,
      - calculate attributable percentage of total variance and
      - calculate confidence intervals for the variance components using the correct effective degrees of freedom (Satterthwaite, 1946).
  - **Easy to use and**

BASAS Roche

# Conclusion

- PrecMod SAS Macro:
  - Fits Random Effects Linear Models to estimate variance components using the SAS MIXED procedure:
    - For multiple factors
    - At one or more grouping levels.
    - The variance estimates are then used to:
      - derive the standard deviation,
      - calculate percent coefficient of variation,
      - calculate attributable percentage of total variance and
      - calculate confidence intervals for the variance components using the correct effective degrees of freedom (Satterthwaite, 1946).
  - Easy to use and
  - **Provides a clear and concise path towards efficient and timely calculations ready for reporting.**

BASAS Roche

# Conclusion

- PrecMod SAS Macro:
  - Fits Random Effects Linear Models to estimate variance components using the SAS MIXED procedure:
    - For multiple factors
    - At one or more grouping levels.
    - The variance estimates are then used to:
      - derive the standard deviation,
      - calculate percent coefficient of variation,
      - calculate attributable percentage of total variance and
      - calculate confidence intervals for the variance components using the correct effective degrees of freedom (Satterthwaite, 1946).
  - Easy to use and
  - Provides a clear and concise path towards efficient and timely calculations ready for reporting.

# References


- Agresti A, Coull BA. Approximate is better than “exact” for interval estimation of binomial proportions. The Americal Statistician. 1988; 52(2): 119-126.
- Clinical Laboratory Standards Institute (CLSI) document EP05-A2, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition. 2004. Wayne, PA.
- Clincial Labroratory Standards Institute (CLSI) document EP12-A2. “User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline - Second Edition”. January; 2008.
- Clopper CJ, Pearson ES. The use of confidence or fiducial limits illustrated in the case of the binomial. Biometrika 1934; 26: 404–13.
- Guidance for Industry and FDA: “Statistical Guidance on Reporting Results from Studies Evaluating Diagnostic Tests” March 13, 2007.
- Nelson W. Applied Life Data Analysis. In. New York, NY: John Wiley and Sons; 1982.
- Neter J, Kutner MH, Nachtsheim CJ, Wasserman W (1996). Applied Linear Statistical Models. pp. 976-977. Boston, MA: IRWIN.
- SAS Enterprise Guide v5.1. Copyright © 2012 by SAS Institute Inc., Cary, NC, USA. All rights reserved. product or service names are registered trademarks or trademarks of SAS Institute Inc., Cary, NC, USA.
- Wilson EB. Probable inference, the law of succession and statistical inference, JASA. 1927; 22: 209-212.
- Satterthwaite, F. E. (1946), "An Approximate Distribution of Estimates of Variance Components.", *Biometrics Bulletin* **2**: 110–114,doi:10.2307/3002019
- SAS Institute Inc. 2011. SAS/STAT® 9.3 User’s Guide. Cary, NC: SAS Institute Inc.

# Contact Info:

BASAS Roche

**NOTE: PrecMod SAS Macro available in appendix of paper.**

**Jesse A. Canchola**
Roche Molecular Systems, Inc.

**Address**:
4300 Hacienda Drive
Pleasanton, California, 94588

**eMail**: Jesse.Canchola@Roche.Com

**Web**: http://usdiagnostics.roche.com/en/index.html

# Questions

# *Doing now what patients need next*