



# Contents

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- Background of Calibration
- Calibration Evaluation
- Computer Simulation
- Comments



# What is Calibration?

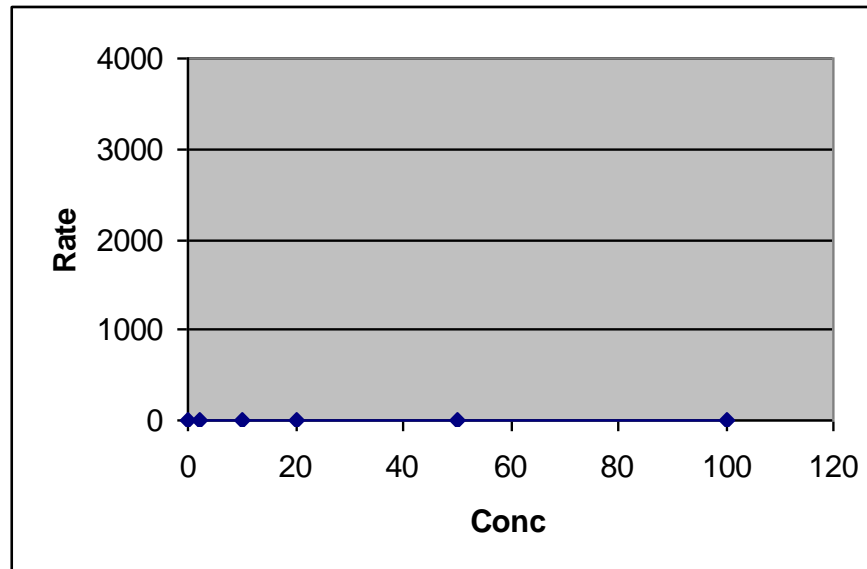
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- Definition (ANSI/NCSL,1994)

The set of operations which establish, under specified conditions, the relationship between values indicated by a measuring instrument or measuring system, and the corresponding standard or known values derived from the standard.

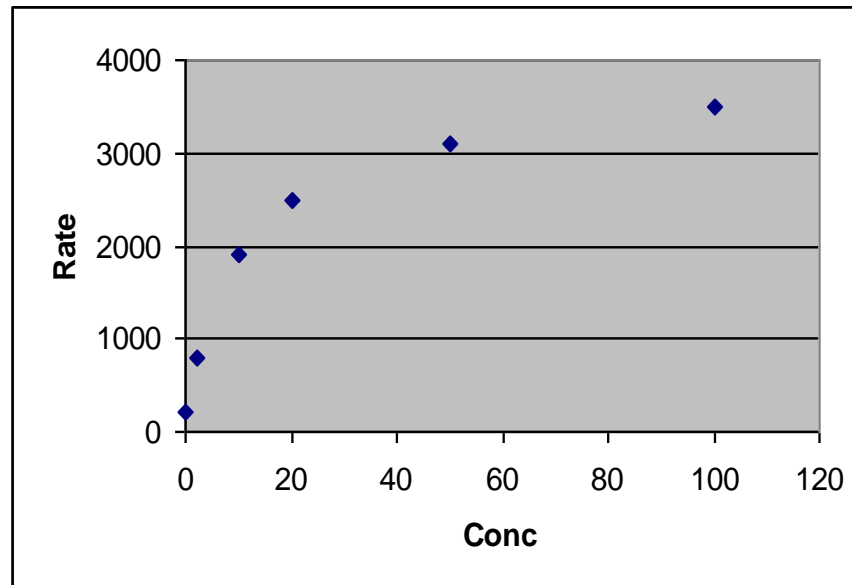
# Calibration Process

- Reference standard with known values (**calibrators**) to cover the range of interest.



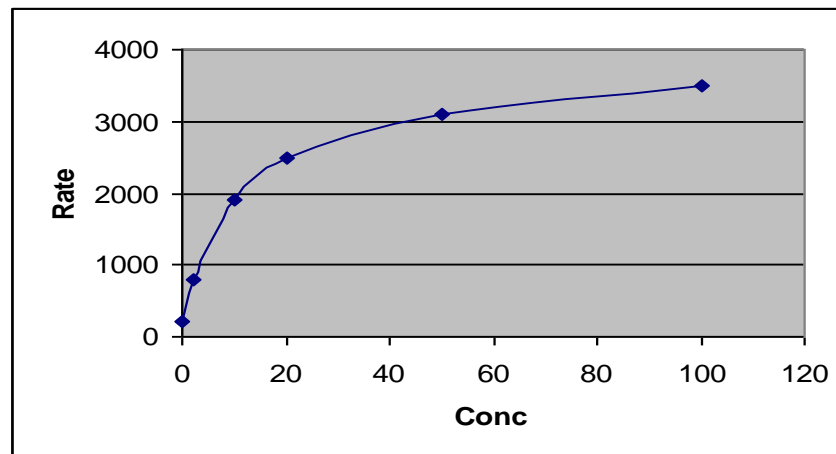
# Calibration Process

- Measurements on the calibrators with the instrument/reagent lot to be calibrated.



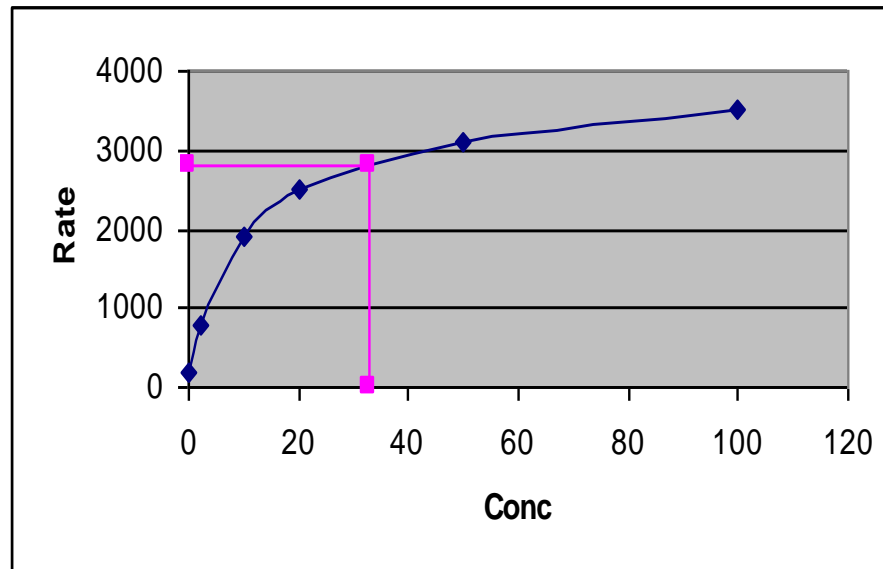
# Calibration Process

- Mathematical function relationship between the measured responses and the known values of the reference standards, called a **Calibration Curve**.

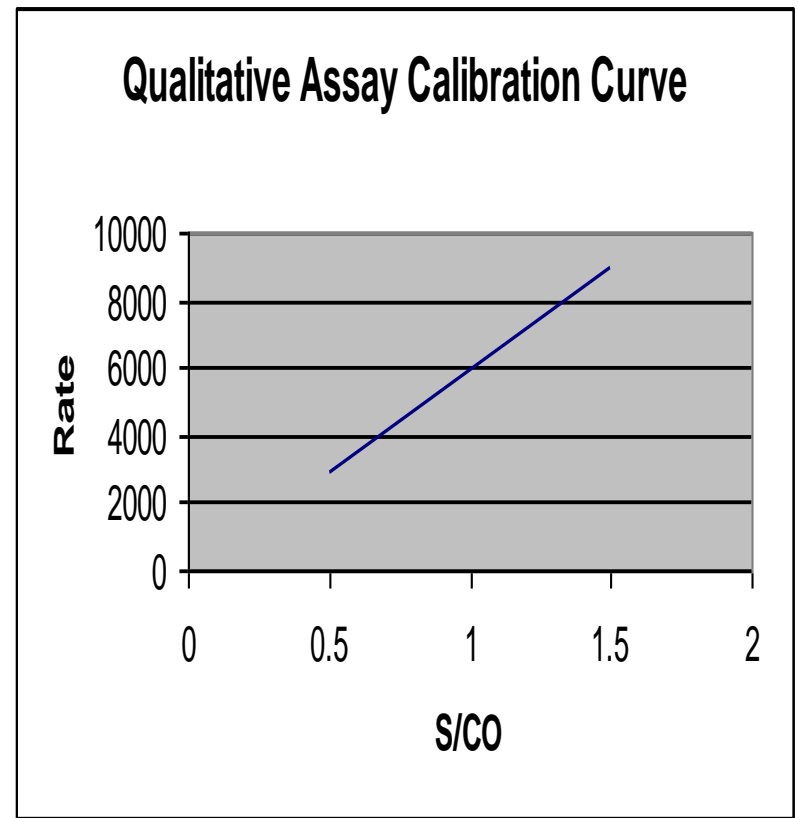
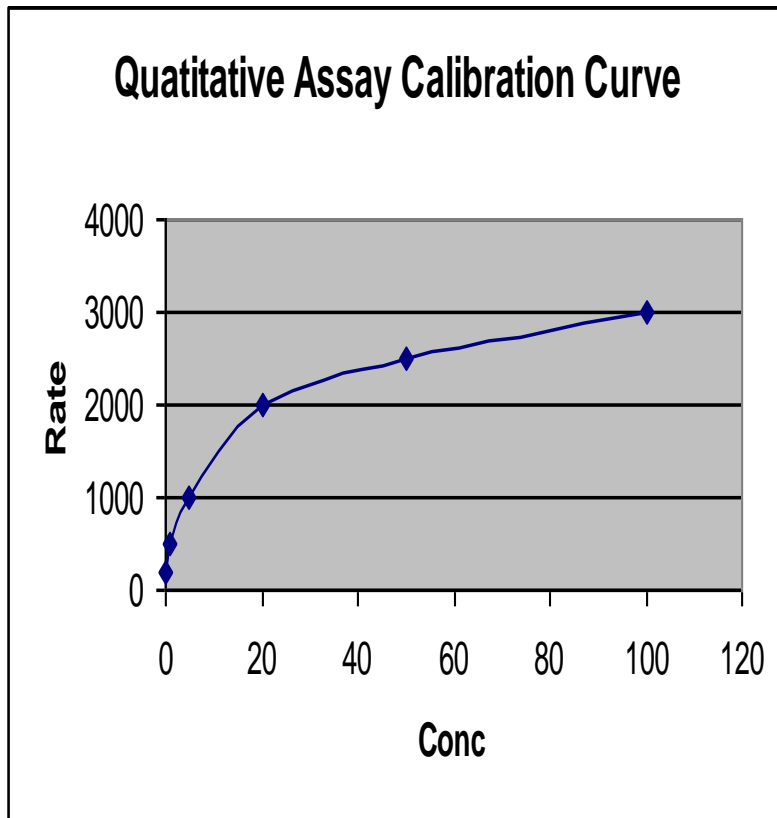


# Calibration Process

- Translation of the measurements of samples to the values of interest by the inverse of the calibration curve.



# Calibration Curves





# Calibration Determination

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- Calibrator values
- Model and weight in calibration curve fitting
- Number of replicate at each calibrator level
- Stored calibration curve use





# Evaluation of Calibration

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- Accuracy - Bias
- Precision - Variance Components (of calibration, and more important, of instrument, reagent lot, run, etc.)
- Sensitivity
- Specificity



# Problems

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- Very limited calibration curves available due to:
  - Instrument capacity
  - Testing material limitation
  - Time limitation
  - Manpower/Laboratory availability



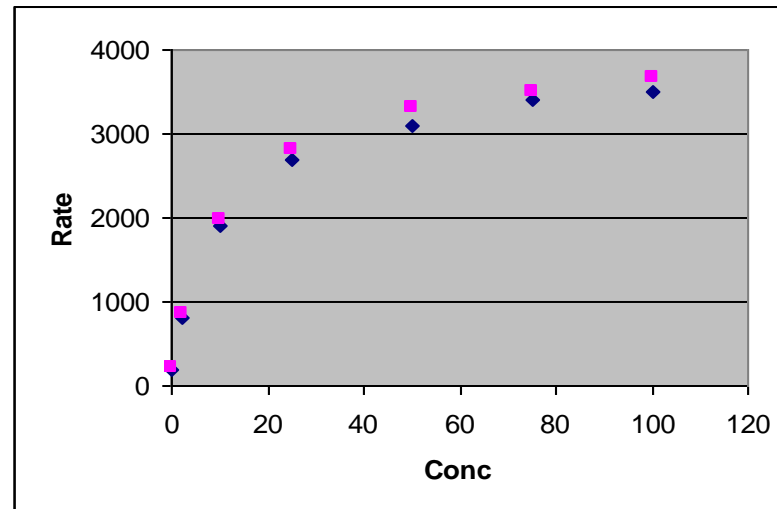
# Simulation Approach

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- Build mean and SD profiles
- Simulate calibration curves based on the profiles
- Evaluate and select calibration methods

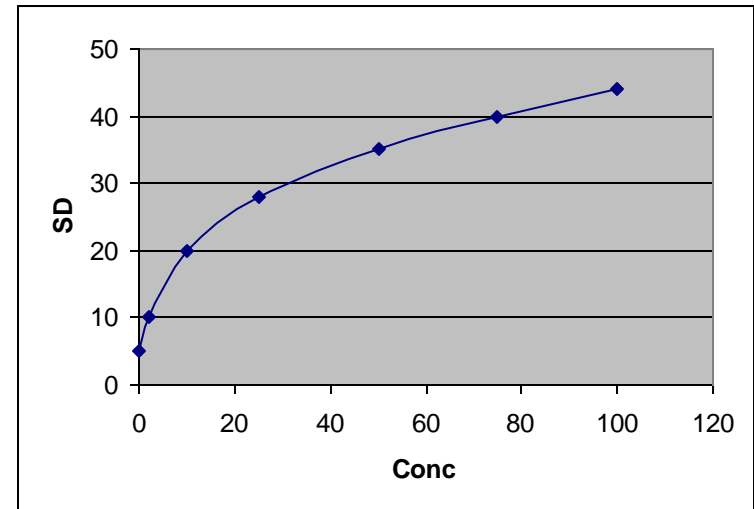
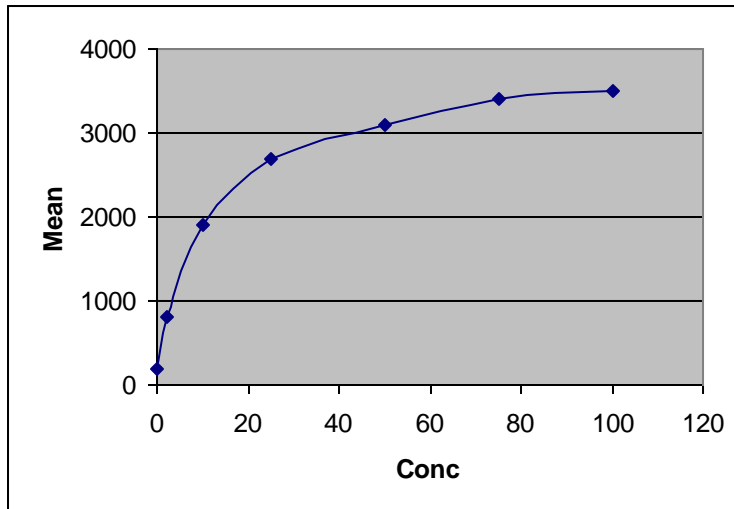
# Mean and SD Profiles

- Run multiple replicates at each of several samples with known values across assay dynamical region.



# Mean and SD Profiles

- Build mean and SD profiles of response variable over the region based on the test results.





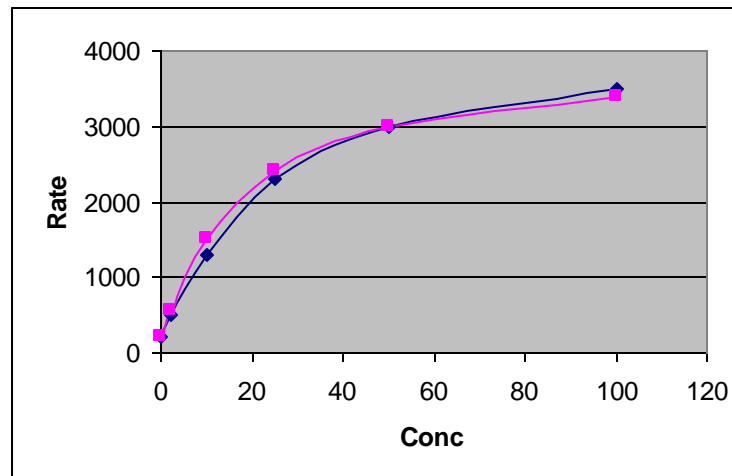
# Calibration Curve Simulation

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- Simulate a sample mean at each of six calibrator concentration levels based on the profiles
- $\text{sample\_mean} = \text{mean} + \text{SD} / \sqrt{n} * \text{random}(\text{seed})$

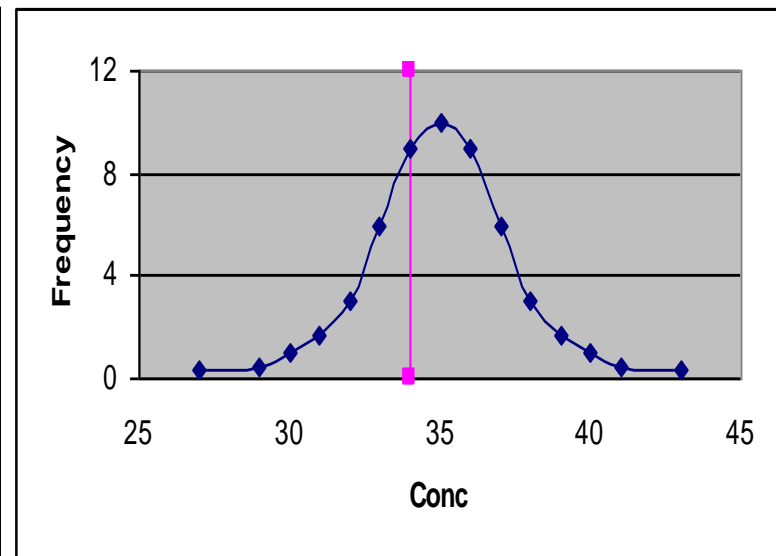
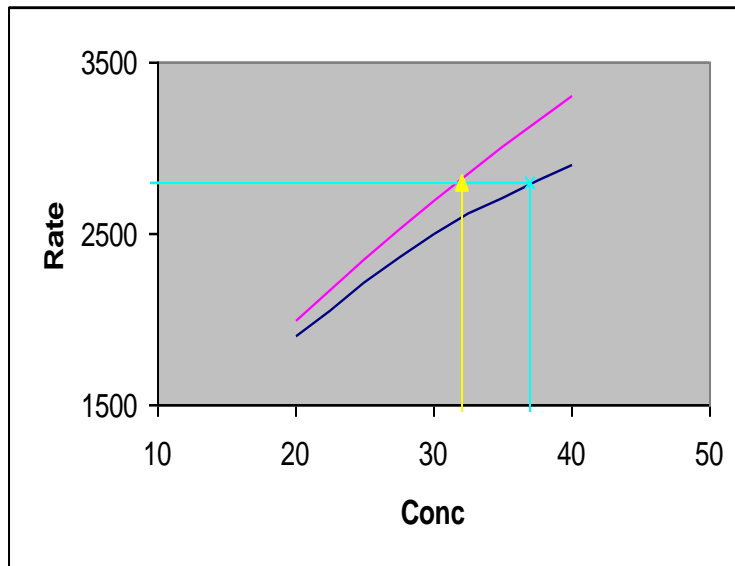
# Calibration Curve Simulation

- Fit the calibration curve
- Replicate the process to get multiple simulated calibration curves



# Calibration Method Evaluation

- Evaluate bias, precision, sensitivity and specificity for each calibration method.







# Comments

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- The same approach applies to other calibration methods such as the ones used in qualitative assays.
- When evaluating calibration curves, different criteria might be used in different region due to clinical importance.