Probability of Detection

For the Validation of Qualitative Methods

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Qualitative (Binary) Methods

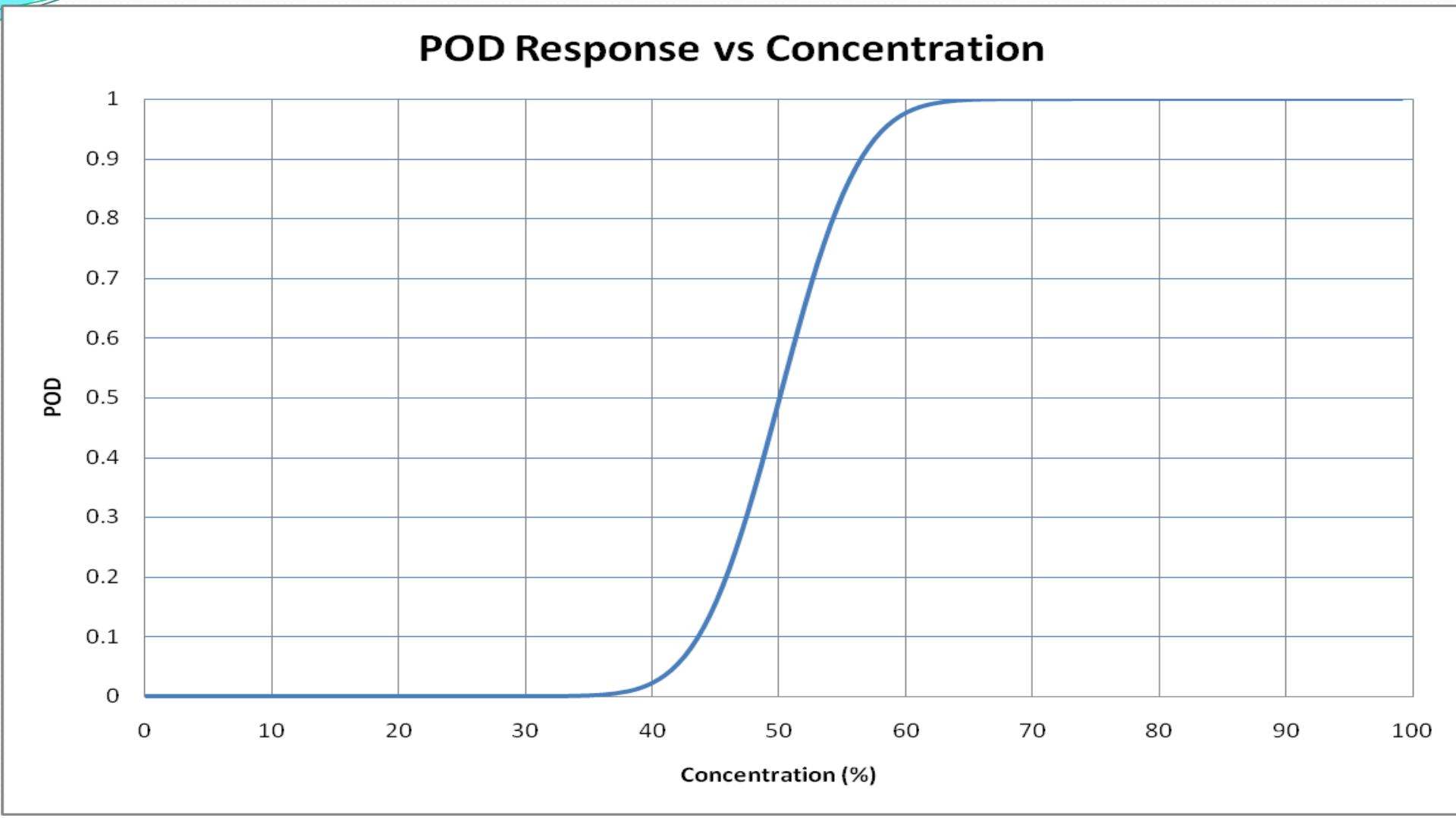
- Methods that are restricted to 2 possible outcomes:
  - Positive or Negative
  - Pass or Fail
  - Heads or Tails
  - 1 or 0
  - Yes or No
  - Presence or Absence
  - Identified or Not Identified

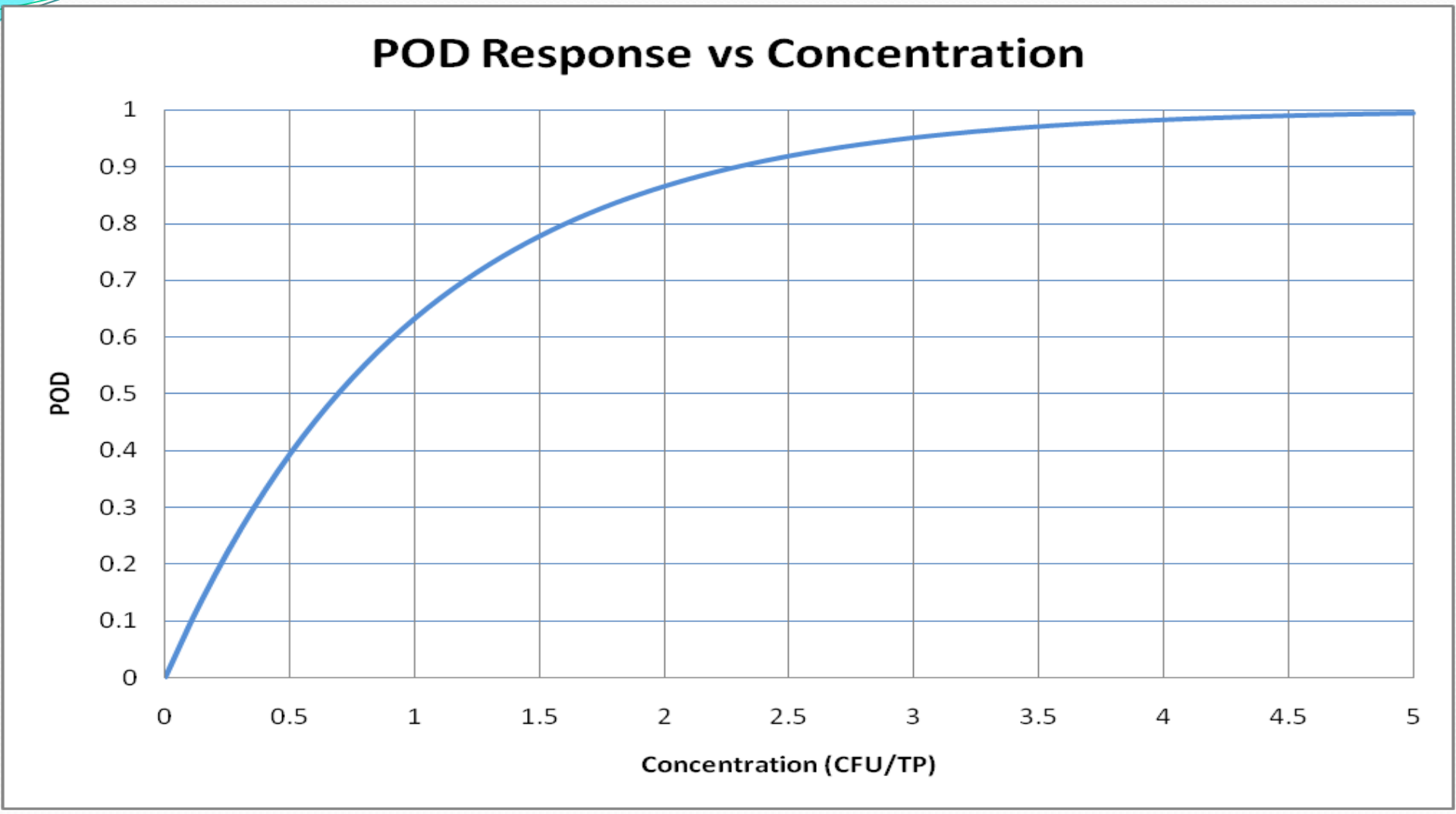
POD

- Parameter – Probability of Detection
- General – Designed to be used by any Qualitative (Binary) Method
  - Microbiological
  - Chemical
  - Bio Threat Agent Methods
  - Botanical Identification
  - Allergens

POD Parameter

- Method Parameter that describes and predicts method behavior
- Probability of Detection or POD
- The probability of getting a positive result at a given concentration of analyte.
- POD is a function of concentration


POD Response vs Concentration
POD
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
10
20
30
40
50
60
70
80
90
100
Concentration (%)


POD Response vs Concentration
POD
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5
Concentration (CFU/TP)

POD

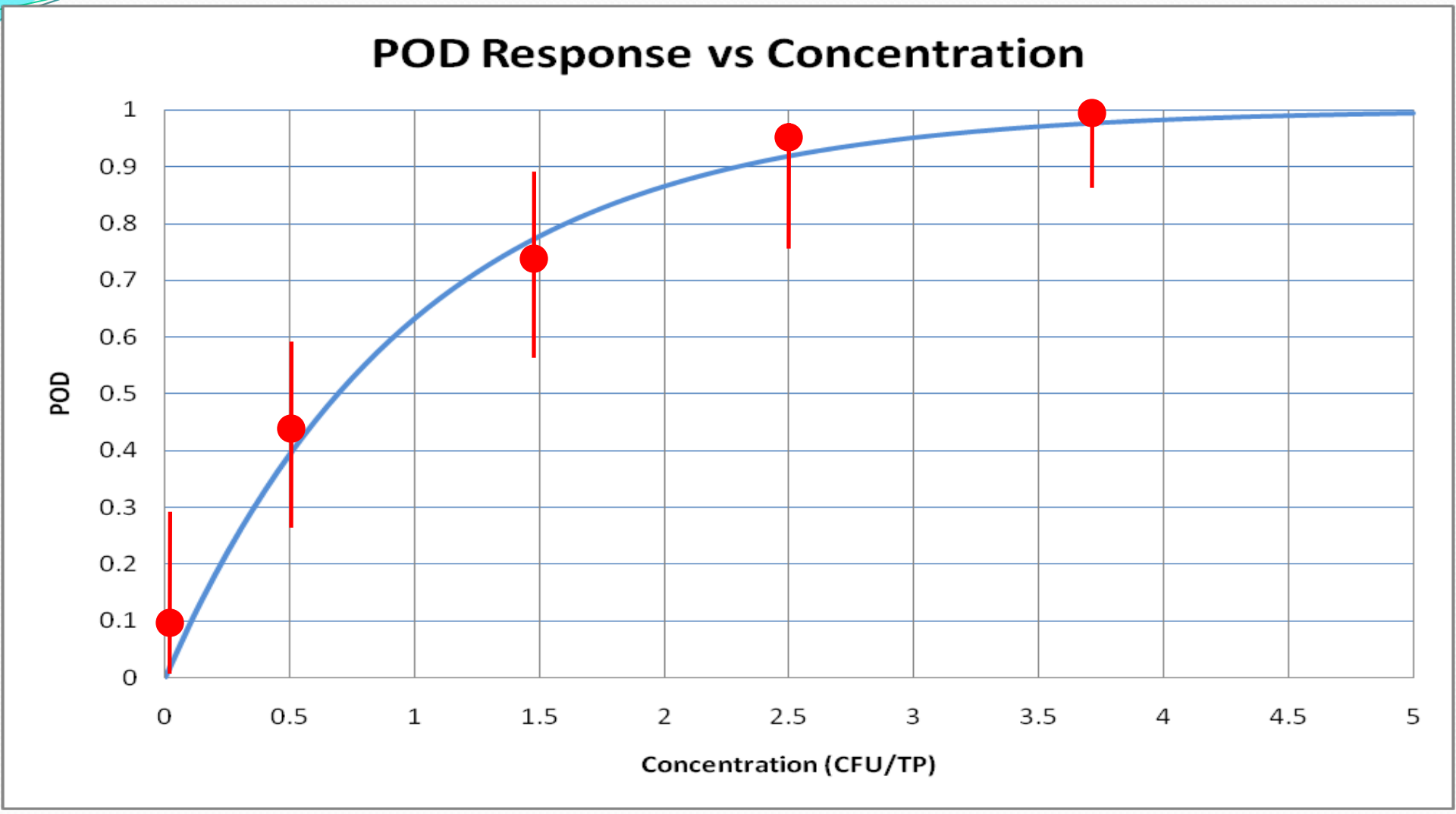
- A simple descriptive statistic that describes the method performance at a given concentration.
- It is a calculation of proportion of observed positive outcomes per total trials.
- This simple statistic is inherent in all other systems, such as Chi-Square, LOD, RLOD.
- The “POD Concept” is only new in that it recognizes the POD as a key parameter and plots a graph of POD vs concentration.

WHY PLOT POD?

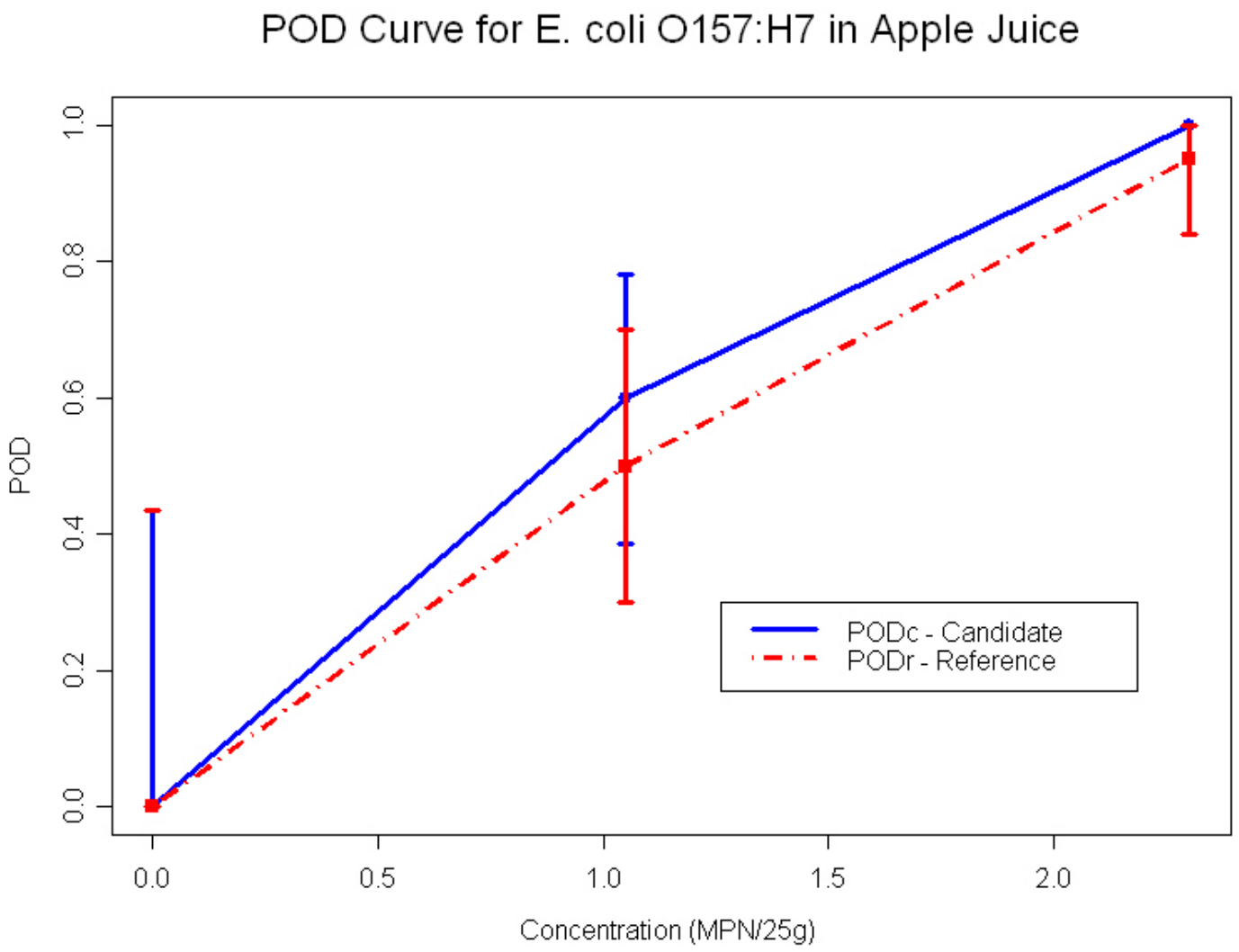
- Plot of POD Curves are intended to assist method users
  - To assist users in selecting best method for intended use.
  - Understanding POD Curve is crucial for interpretation of results.
  - The POD curve can be an indicator of the "usefulness" of the method.
  - If POD were constant across all concentrations, the method would not be useful.

VALIDATION

- The task of validating a qualitative (binary) method is characterizing the POD curve at critical concentration points.
  1. Make up a series of test materials at concentrations of interest.
  2. Analyze with replication
  3. Calculate the proportion of positive responses at the concentrations.
  4. Plot observed proportions as POD curve by concentration.


POD Response vs Concentration
POD
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5
Concentration (CFU/TP)

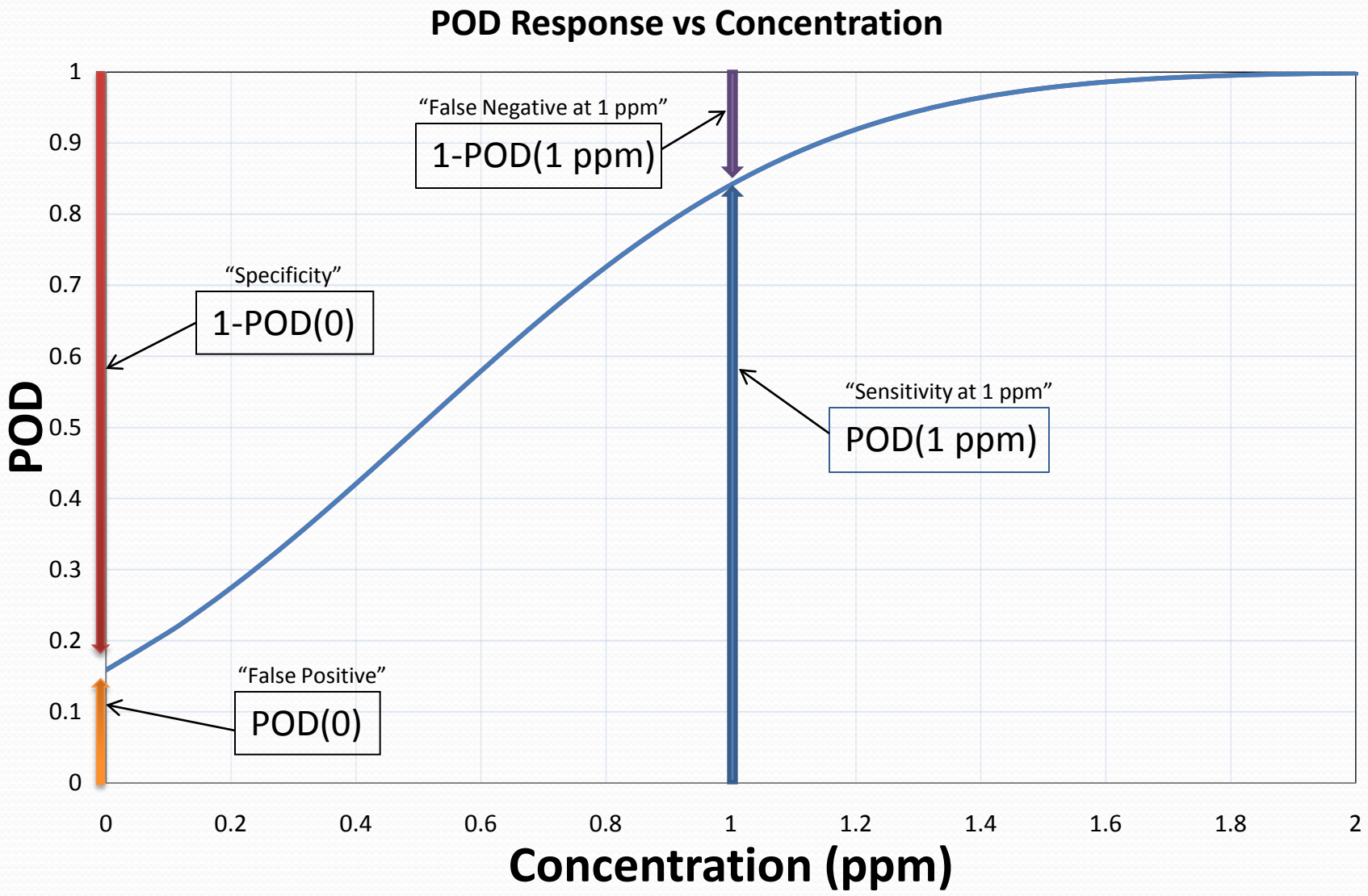
Example POD Response Curve



A BIT ABOUT POD

- POD is a combination of sensitivity, specificity, false positives, false negatives.
- Where did they all go?

“Where’s my False Negative?”



Some Statistics

- To do Classical Collab Statistics, Code Results
  - "Positive" = 1
  - "Negative" = 0

Use AOAC Calculations from Quantitative Stats to estimate

- Mean = POD
- Reproducibility Standard Deviation
- Repeatability Standard Deviation
- Laboratory Standard Deviation

POD = Mean

	LAB1	LAB2	LAB3	
Trial1	1	1	0	
Trial2	0	1	1	
Trial3	1	1	1	
Trial4	0	0	0	
Trial5	1	0	0	
Trial6	1	0	1	
Trial7	0	0	1	
Trial8	0	1	0	
Trial9	1	1	0	
Trial10	0	1	0	
Mean	0.5	0.6	0.4	LPOD = 0.50

Analogous Parameters

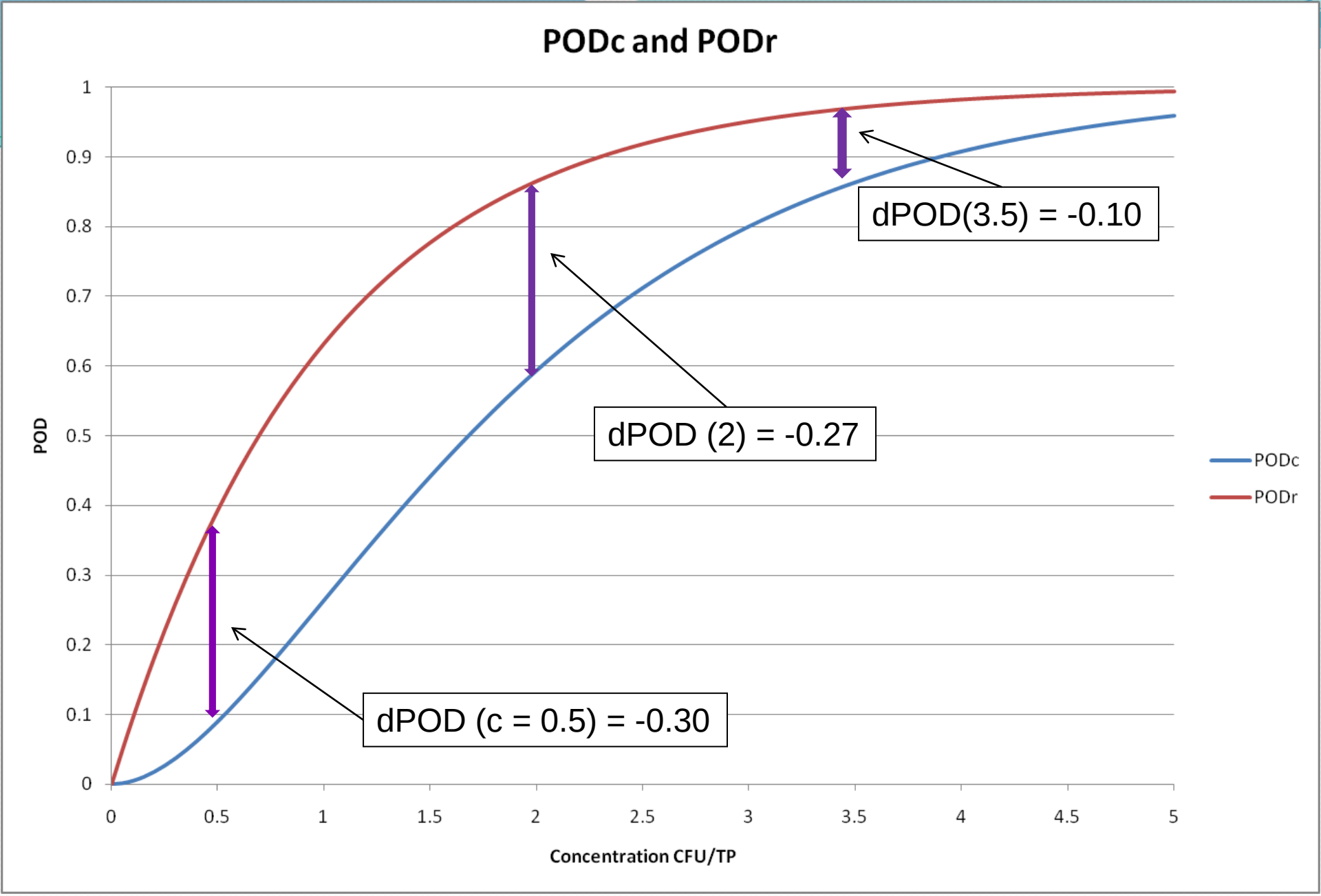
Method Attribute	Quantitative Parameter	Quantitative Estimate	Qualitative Parameter	Qualitative Estimate
General Mean or Expectation	Mean, μ	Mean, $\overline{x}$	POD	POD or $LPOD$
Repeatability Variance	σ_r^2	s_r^2	σ_r^2	s_r^2
Reproducibility Variance	σ_R^2	s_R^2	σ_R^2	s_R^2
Laboratory Variance	σ_L^2	s_L^2	σ_L^2	s_L^2
Expected difference between Two Methods*	Bias, B	$\overline{x}_1 - \overline{x}_2$	dPOD	$POD_1 - POD_2$

Difference Between Methods - dPOD

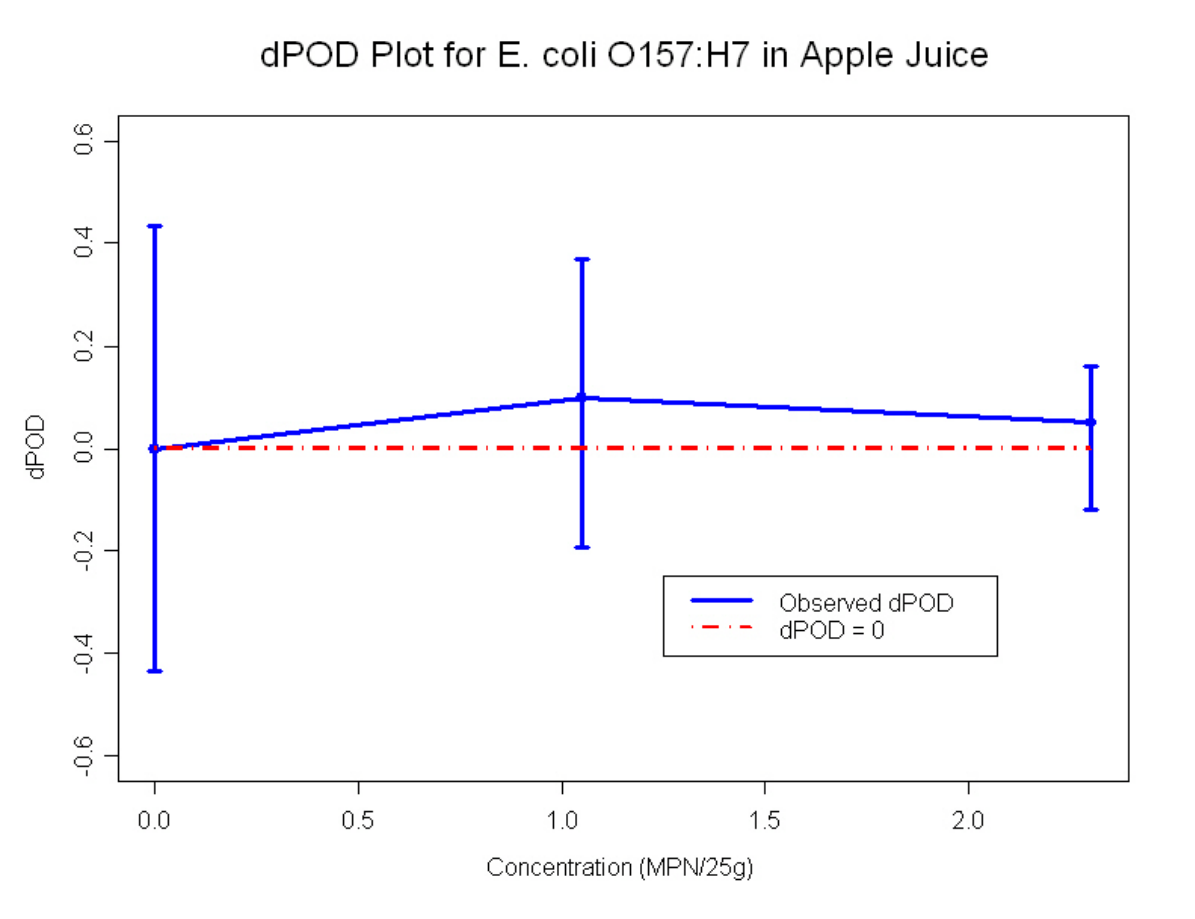
- Compare any two methods by comparing POD values at a given concentration.
- Difference by subtraction

- dPOD = PODc – PODr

- dPOD is always dependent on concentration


PODc and PODr
POD
Concentration CFU/TP
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5
dPOD(3.5) = -0.10
dPOD (2) = -0.27
dPOD (c = 0.5) = -0.30
PODc
PODr

dPOD Curve vs Concentration



Big Ideas

- Combine sensitivity, specificity, false positive, false negative into 1 parameter – Probability of Detection or 'POD'
- Graph POD vs. Concentration with Confidence Intervals
- Compare methods by difference of POD at same concentration
- Use the classic statistical model and descriptive stats for quantitative methods as the tool for calculating qualitative stats.

POD Concept

- Works for single lab and Multilab experiments.
- Works for paired and unpaired designs.
- Provides harmonization across qualitative/quantitative methodologies.
- Does comparisons and hypothesis tests via confidence interval analysis – equivalent to chi-squared tests.
- POD Curve plots mean response and uncertainty on the same graph.