# Qualitative PT data analysis with easy-to-interpret scores

**Christian Bläul and Steffen Uhlig**

## QuoData in short

- Since 1995, in Dresden (main office) and in Munich/Freising (Germany)
- Staff: 31
  - Scientific staff: 12, mainly Mathematics, Physics and Bioinformatics (9)
  - IT staff: 8

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**Our statistical services**:

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Statistically Advanced Experimental Design
Validation and certification of measurement methods, bioassays and biosensors
Interlaboratory Studies
Meta Studies

**Our products (software development)**:

Software for optimization, validation and PT („PROLab Plus“)

**Our Main Application Areas**:

Food Safety, Consumer Protection, Environmental Science, Forensics, Medical Diagnostics

## How to derive tolerance limits?

### Introduction

- Idea: Calculate the laboratory specific ROS (over all samples) and use Binomial distribution to derive tolerance limit.

- Example (PT on the Detection of Highly Infectious Pathogens)
  - n=9 replicates/samples
  - ROS=0.901 (227 out of 252 tests were successful) across laboratories
  - BINOM.INV(9;0.901;0.05)=6 (in Excel)
  - In other words: As long as a laboratory has at least 6 positive results, there is no reason to believe that this laboratory has lower competence than the average.
  - Or put it this way: the lower 95 % tolerance limit for the number of positive results for a participant with average competence is 6.
  - Therefore the assessment criterion: at least 6 positive results.

## Example: Identification of bacteria species

### PT on the Detection of Highly Infectious Pathogens

*Bacteria species that have been correctly (+) and incorrectly (-) identified by the laboratories*

| Sample (Species) | Laboratories | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 01 | 02 | 03 | 04 | 05 | 06 | 07 | 08 | 09 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 |
| HPB 1 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | no performance | no performance | no performance | + | + | + | + | + | + | + | + |
| HPB 2 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | | | | + | + | + | + | - | + | + | + |
| HPB 3 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | - | | | | + | + | + | + | + | + | + | + |
| HPB 4 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | | | | + | + | + | + | - | - | + | - |
| HPB 5 | - | + | - | + | - | + | + | - | + | + | + | - | - | + | - | - | + | + | + | + | | | | + | - | + | + | + | + | + | + |
| HPB 6 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | | | | + | + | + | + | + | + | + | + |
| HPB 7 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | - | + | + | + | + | + | | | | + | + | + | + | + | - | + | - |
| HPB 8 | + | + | - | + | + | + | + | + | + | + | + | + | + | + | - | + | + | + | + | + | | | | + | - | + | + | + | - | + | + |
| HPB 9 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | - | + | + | + | + | + | | | | + | - | - | + | + | + | + | - |

## How to derive tolerance limits?

Introduction

- Performance assessment: Based on Rate Of Success (ROS) over all samples

| Sample | Laboratory | | |
|---|---|---|---|
| | 15 | 16 | 17 |
| HPB 1 | + | + | + |
| HPB 2 | + | + | + |
| HPB 3 | + | + | + |
| HPB 4 | + | + | + |
| HPB 5 | - | - | + |
| HPB 6 | + | + | + |
| HPB 7 | - | + | + |
| HPB 8 | - | + | + |
| HPB 9 | - | + | + |
| **ROS** | **56%** | **89%** | **100%** |

- Assessment criterion?

# How to derive tolerance limits?

## Introduction

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  - n=9 replicates/samples
  - ROS=0.901 (227 out of 252 tests were successful) across laboratories
  - BINOM.INV(9;0.901;0.05)=6 (in Excel)
  - In other words: As long as a laboratory has at least 6 positive results, there is no reason to believe that this laboratory has lower competence than the average.
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# How to derive tolerance limits?

Example: PT on the Detection of Highly Infectious Pathogens

Almost all participants fulfill the performance criterion of at least 6 successful samples.

Not successful: Lab 15

| Sample (Species) | Laboratories | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 01 | 02 | 03 | 04 | 05 | 06 | 07 | 08 | 09 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 |
| HPB 1 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | no performance | no performance | no performance | + | + | + | + | + | + | + | + |
| HPB 2 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | | | | + | + | + | + | - | + | + | + |
| HPB 3 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | - | | | | + | + | + | + | + | + | + | + |
| HPB 4 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | | | | + | + | + | + | - | - | + | - |
| HPB 5 | - | + | - | + | - | + | + | - | + | + | + | - | - | + | - | - | + | + | + | + | | | | + | - | + | + | + | + | + | + |
| HPB 6 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | | | | + | + | + | + | + | + | + | + |
| HPB 7 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | - | + | + | + | + | + | | | | + | + | + | + | + | - | + | - |
| HPB 8 | + | + | - | + | + | + | + | + | + | + | + | + | + | + | - | + | + | + | + | + | | | | + | - | + | + | + | - | + | + |
| HPB 9 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | - | + | + | + | + | + | | | | + | - | - | + | + | + | + | - |

## How to derive tolerance limits?

- What are the prerequisites of the Binomial criterion?
  - Binomial distribution applies in case of n independent Bernoulli experiments with constant probability POS per round, e.g. throwing a dice n times.
  - Therefore constant success probabilities are required for each sample.
  - This requirement is not fulfilled (PT on the Detection of Highly Infectious Pathogens):

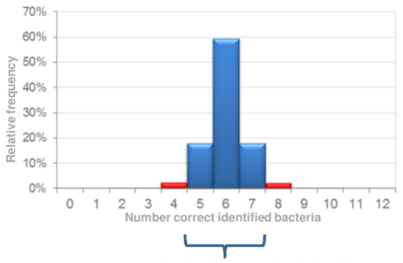
| Sample | Negative results (out of 28 participants) |
|---|---|
| HPB 1 | 0 |
| HPB 2 | 1 |
| HPB 3 | 1 |
| HPB 4 | 3 |
| HPB 5 | 9 |
| HPB 6 | 0 |
| HPB 7 | 3 |
| HPB 8 | 4 |
| HPB 9 | 4 |

## How to derive tolerance limits?

What can happen in case of unequal success probabilities?

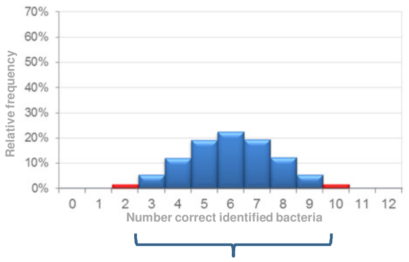
Assumption: the probability to identify a bacterium correctly is…

- 5 % for each of 6 samples (very difficult) and
- 95 % for each of 6 samples (very easy)



95 % of all laboratories identify
5 – 7 bacteria correctly (ROS: 42–58 %)

- 50 % for each of 12 samples



96 % of all laboratories identify
3 – 9 bacteria correctly (ROS: 25–75 %)

Not plausible? Then consider the situation that POS is 0 % for 6 samples and 100 % for the other 6 samples. Result: 6 bacteria will be identified correctly …

# How to derive tolerance limits?

## Conclusion of simulation study

- If the average probability of success across laboratories and samples is 0.5 and if all samples have an identical level of difficulty, then a ROS of 3/12 = 0.25  is unremarkable.
- But if the level of difficulties differs between the samples, then a ROS of 0.25 is significantly different from the average of 0.5.
- In other words: If the level of difficulties differs between the samples, the 95 % assessment criterion for the minimum number of positive results per participants (which is equivalent to Z=-2) can be stricter than with equal probabilities.
- Or put this paradox in another way: the more variability in LDT, the less variability in ROS (as long as laboratories with constant LCL are considered)

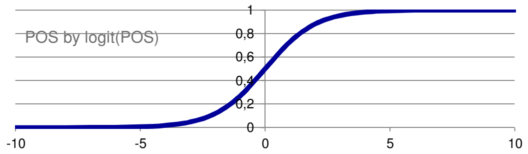
- Conclusion: Level of Competence of the Laboratory (LCL) cannot be considered without considering the Level of Difficulty of the Task (LDT)

# The Logit approach

## Modeling success rates

- The probability p=POS (Prob. Of Success) for a positive results depends on Level of Competence of the Laboratory (LCL) and Level of Difficulty of the Task (LDT):

  ln[ POS/(1-POS)] = logit(POS) = LCL – LDT



- The higher LCL, the higher POS. The higher LDT, the lower POS
- If LCL is tending to –infinity, POS is tending to 0
- If LCL is tending to +infinity, POS is tending to 1
- Ref.: Schilling, Powilleit, Uhlig: Macrozoobenthos interlaboratory comparison on taxonomical identification and counting of marine invertebrates in artificial sediment samples including testing various statistical methods of data evaluation. ACQUAL 2006, 422–429

# The Logit approach

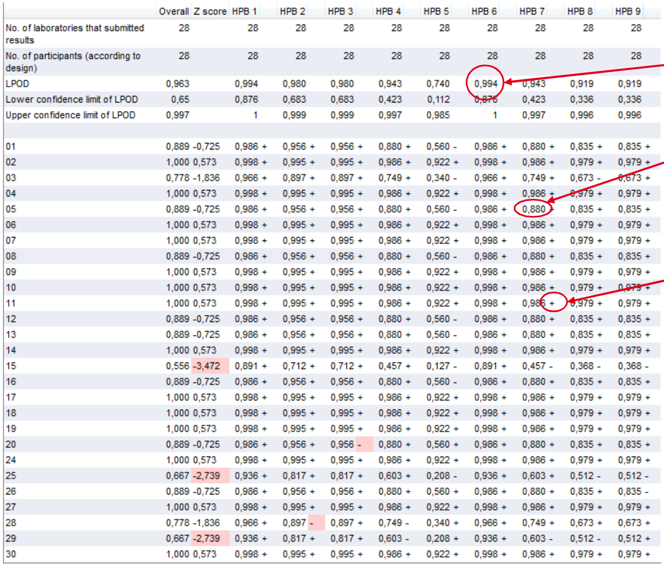
Logit approach

| Parameter | Explanation |
|---|---|
| **Probability POS** | Probability of fulfilling a task correctly (e.g. correct identification) |
| **Chance (odds)** | Ratio of the probability for being successful to the probability for not being successful<br>Chance (odds) = exp(mean + level of competence - level of difficulty) |
| **LCL**<br>**Level of Competence** | Depending on the relative knowledge, experience and practise of the laboratory<br>– laboratory with average competence → level of competence is set to 0<br>– laboratories with higher competence → positive level of competence<br>– laboratories with lower competence → negative level of competence |
| **LDT**<br>**Level of Difficulty** | Depending on the relative difficulty of the task<br>– depends on e.g. sample or species (so the probability of correct identification for an average laboratory can vary from species to species) |

- LCL and LDT are estimated by means of Maximum-Likelihood

# The Logit approach

Example continued (Identification of bacteria species)



| | Overall | Z score | HPB 1 | HPB 2 | HPB 3 | HPB 4 | HPB 5 | HPB 6 | HPB 7 | HPB 8 | HPB 9 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| No. of laboratories that submitted results | 28 | | 28 | 28 | 28 | 28 | 28 | 28 | 28 | 28 | 28 |
| No. of participants (according to design) | 28 | | 28 | 28 | 28 | 28 | 28 | 28 | 28 | 28 | 28 |
| LPOD | 0,963 | | 0,994 | 0,980 | 0,980 | 0,943 | 0,740 | 0,994 | 0,943 | 0,919 | 0,919 |
| Lower confidence limit of LPOD | 0,65 | | 0,876 | 0,683 | 0,683 | 0,423 | 0,112 | 0,876 | 0,423 | 0,336 | 0,336 |
| Upper confidence limit of LPOD | 0,997 | | 1 | 0,999 | 0,999 | 0,997 | 0,985 | 1 | 0,997 | 0,996 | 0,996 |
| | | | | | | | | | | | |
| 01 | 0,889 | -0,725 | 0,986 + | 0,956 + | 0,956 + | 0,880 + | 0,560 - | 0,986 + | 0,880 + | 0,835 + | 0,835 + |
| 02 | 1,000 | 0,573 | 0,998 + | 0,995 + | 0,995 + | 0,986 + | 0,922 + | 0,998 + | 0,986 + | 0,979 + | 0,979 + |
| 03 | 0,778 | -1,836 | 0,966 + | 0,897 + | 0,897 + | 0,749 + | 0,340 - | 0,966 + | 0,749 + | 0,673 - | 0,673 + |
| 04 | 1,000 | 0,573 | 0,998 + | 0,995 + | 0,995 + | 0,986 + | 0,922 + | 0,998 + | 0,986 + | 0,979 + | 0,979 + |
| 05 | 0,889 | -0,725 | 0,986 + | 0,956 + | 0,956 + | 0,880 + | 0,560 - | 0,986 + | 0,880 + | 0,835 + | 0,835 + |
| 06 | 1,000 | 0,573 | 0,998 + | 0,995 + | 0,995 + | 0,986 + | 0,922 + | 0,998 + | 0,986 + | 0,979 + | 0,979 + |
| 07 | 1,000 | 0,573 | 0,998 + | 0,995 + | 0,995 + | 0,986 + | 0,922 + | 0,998 + | 0,986 + | 0,979 + | 0,979 + |
| 08 | 0,889 | -0,725 | 0,986 + | 0,956 + | 0,956 + | 0,880 + | 0,560 - | 0,986 + | 0,880 + | 0,835 + | 0,835 + |
| 09 | 1,000 | 0,573 | 0,998 + | 0,995 + | 0,995 + | 0,986 + | 0,922 + | 0,998 + | 0,986 + | 0,979 + | 0,979 + |
| 10 | 1,000 | 0,573 | 0,998 + | 0,995 + | 0,995 + | 0,986 + | 0,922 + | 0,998 + | 0,986 + | 0,979 + | 0,979 + |
| 11 | 1,000 | 0,573 | 0,998 + | 0,995 + | 0,995 + | 0,986 + | 0,922 + | 0,998 + | 0,986 + | 0,979 + | 0,979 + |
| 12 | 0,889 | -0,725 | 0,986 + | 0,956 + | 0,956 + | 0,880 + | 0,560 - | 0,986 + | 0,880 + | 0,835 + | 0,835 + |
| 13 | 0,889 | -0,725 | 0,986 + | 0,956 + | 0,956 + | 0,880 + | 0,560 - | 0,986 + | 0,880 + | 0,835 + | 0,835 + |
| 14 | 1,000 | 0,573 | 0,998 + | 0,995 + | 0,995 + | 0,986 + | 0,922 + | 0,998 + | 0,986 + | 0,979 + | 0,979 + |
| 15 | 0,556 | -3,472 | 0,891 + | 0,712 + | 0,712 + | 0,457 + | 0,127 - | 0,891 + | 0,457 - | 0,368 - | 0,368 - |
| 16 | 0,889 | -0,725 | 0,986 + | 0,956 + | 0,956 + | 0,880 + | 0,560 - | 0,986 + | 0,880 + | 0,835 + | 0,835 + |
| 17 | 1,000 | 0,573 | 0,998 + | 0,995 + | 0,995 + | 0,986 + | 0,922 + | 0,998 + | 0,986 + | 0,979 + | 0,979 + |
| 18 | 1,000 | 0,573 | 0,998 + | 0,995 + | 0,995 + | 0,986 + | 0,922 + | 0,998 + | 0,986 + | 0,979 + | 0,979 + |
| 19 | 1,000 | 0,573 | 0,998 + | 0,995 + | 0,995 + | 0,986 + | 0,922 + | 0,998 + | 0,986 + | 0,979 + | 0,979 + |
| 20 | 0,889 | -0,725 | 0,986 + | 0,956 + | 0,956 - | 0,880 + | 0,560 + | 0,986 + | 0,880 + | 0,835 + | 0,835 + |
| 24 | 1,000 | 0,573 | 0,998 + | 0,995 + | 0,995 + | 0,986 + | 0,922 + | 0,998 + | 0,986 + | 0,979 + | 0,979 + |
| 25 | 0,667 | -2,739 | 0,936 + | 0,817 + | 0,817 + | 0,603 + | 0,208 - | 0,936 + | 0,603 + | 0,512 - | 0,512 - |
| 26 | 0,889 | -0,725 | 0,986 + | 0,956 + | 0,956 + | 0,880 + | 0,560 + | 0,986 + | 0,880 + | 0,835 + | 0,835 - |
| 27 | 1,000 | 0,573 | 0,998 + | 0,995 + | 0,995 + | 0,986 + | 0,922 + | 0,998 + | 0,986 + | 0,979 + | 0,979 + |
| 28 | 0,778 | -1,836 | 0,966 + | 0,897 - | 0,897 + | 0,749 - | 0,340 + | 0,966 + | 0,749 + | 0,673 + | 0,673 + |
| 29 | 0,667 | -2,739 | 0,936 + | 0,817 + | 0,817 + | 0,603 - | 0,208 + | 0,936 + | 0,603 - | 0,512 - | 0,512 + |
| 30 | 1,000 | 0,573 | 0,998 + | 0,995 + | 0,995 + | 0,986 + | 0,922 + | 0,998 + | 0,986 + | 0,979 + | 0,979 + |

POS across laboratories

Laboratory specific POS

(+) correctly or (-) uncorrectly identified bacterium

## Calculation of z scores

Normalised LCL

$$\text{z score} = \frac{\text{LCL} - \text{Average LCL}}{\text{Standard error}} = \frac{\text{LCL}}{\text{Standard error}}$$

- LCL = level of competence of the laboratory
- Average LCL = average level of competence over all laboratories = 0
- Standard error = standard error of the estimated level of competence of the laboratory (derived from Maximum Likelihood estimation; no explicit formula available)

- PT on the Detection of Highly Infectious Pathogens:
  - Four participants are below z=-2
  - Therefore the Logit approach is stricter than the Binomial approach (where only one participant is not succeeding). This is in line with the simulation study presented before.

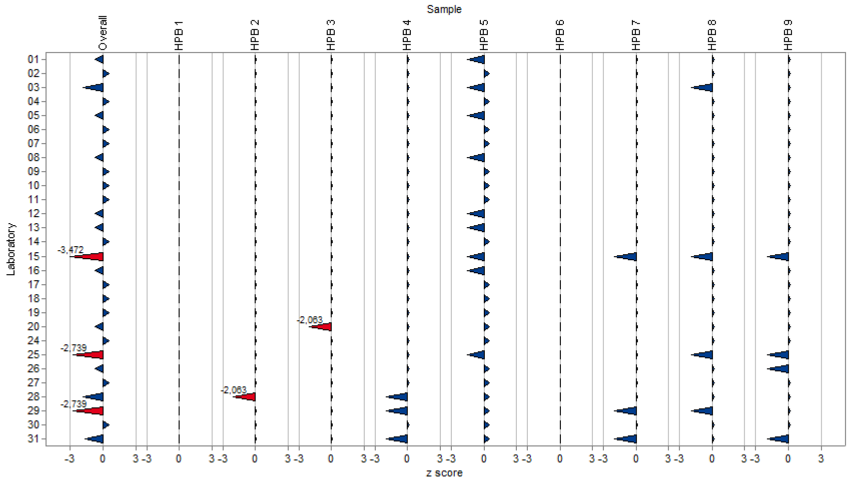
## Calculation of z scores

Interpretation is different from z scores of quantitative methods

| z score | Interpretation | |
|---|---|---|
| < -2 | Competence is significantly lower | 🟥 |
| -2 ... +2 | Laboratory result is not significant different from average | 🟦 |
| > 2 | Competence is significantly higher | 🟩 |

# Calculation of z scores

## Example continued (Identification of bacteria species)



*PROLab Smart for qualitative tests*

# Interpretation of results

- Z scores across samples (left column) measure relative competence of the laboratories.
- Z scores for specific samples (columns 2…10):
  - only two outcomes per sample
  - Significant deviations (z <-2) possible only when the probability of a negative result is less than 5 % (only for two tasks with very high LDT, HBP 3+4)

## Discussion

- z score is equivalent to LCL, normalized by standard error
- Interpretation of z scores for qualitative methods is **not equivalent** to z scores for quantitative methods
- If LDT is equal for all samples, the Binomial approach and the Maximum Likelihood method provide similar results.
- However, both easy and difficult tasks are required to differentiate between laboratories with lower and higher competence
- If LDT varies considerably between samples, the Maximum Likelihood method provides stricter assessment criteria (allows better identification of lower competence)
- Maximum Likelihood method is available in several software packages and in PROLab POD (www.quodata.de)
- Similar procedures are available for repeated tests (method validation) – also in PROLab POD

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