

ISO/TS 16393:2019 (E)

Molecular biomarker analysis — Determination of the performance characteristics of qualitative measurement methods and validation of methods

Contents

	Foreword
	Introduction
1	Scope
2	Normative references
3	Terms and definitions
4	Characterization of a qualitative method via a validation experiment
4.1	Criteria for a standard measurement method
4.2	Performance of a validation experiment
4.3	Nature of test materials
4.4	Requirements for replicate test samples
4.5	Robustness (ruggedness)
4.6	Applicability
4.7	Selectivity
4.8	Experimental design for a multi-laboratory study
4.8.1	Participating laboratories
4.8.2	Number of laboratories
4.8.3	Number of levels
4.8.4	Number of replicates per level and laboratory
4.9	Validation experiment under intermediate conditions
4.10	Expressing the results of a validation experiment
4.10.1	General
4.10.2	Graphical representation of the data
4.11	Calculation of the confidence interval for the general mean, confidence interval and prediction interval
4.12	Calculation of prediction interval for PODs in each laboratory
5	Statistical model for test result
5.1	General
5.2	Basic model
5.3	Constraints in the model
5.4	General mean, m
5.5	Variance parameters
5.6	Relationship of qualitative model to the quantitative model
5.7	Derivation of a limit of detection
Annex A	(informative) Estimation of the mean and variance
A.1	Single laboratory experiment
A.2	Multi-laboratory experiment
A.3	Calculation of variances of a multi-laboratory experiment
Annex B	(informative) Hybrid modified Wilson interval model
B.1	General
B.2	Method for estimating LPOD, $P \alpha \lambda$ 95 % confidence intervals
B.3	Transition point on x (number positive)
Annex C	(informative) Maximum profile likelihood based on the probit model
Annex D	(informative) Maximum likelihood estimate based on beta binomial distribution
Annex E	(informative) Testing of the models via simulation