Case Study | 11th April 2023

Evaluation of Precision of Quantitative Measurement Procedures : Support for CE IVD Marking for an Immunoassay Instrument

CE IVD Marking | Analytical Performance | Precision Study | Data Management | Biostatistics

The Case

The concept of analytical performance includes different parameters that must be considered in the context of ensuring the quality, safety, and efficacy of an IVD device before placing it on the market. One of these parameters is precision (repeatability and reproducibility) which is summarized as the agreement between different independent measurement results of a sample in a series of measurements or between different series of measurements.

Our customer sought our expertise to meet predetermined accuracy requirements on 26 parameters in the areas of bacterial infectious diseases, prenatal screening, oncology, and endocrinology to obtain CE marking for this instrument.

The Challenges

Design, monitor, and data analysis of the single-site precision & the multi-site precision study performed in accordance with the CLSI EP05-A3.

This single-site study was conducted according to the following design per parameter :

- 20 days ; 2 runs ; 2 replicates
- 20 Samples : 17 samples & 3 QC
- 3 lots of reagent
- 3 lots of calibrator
- 4 instruments

➔ 1600 data to manage per parameter
➔ ~40000 data to manage for the full study

This multi-site study was conducted according to the following design :

- 5 days ; 3 instruments ; 5 replicates
- 16 Samples : 13 samples & 3 QC
- 1 lot of reagent
- 1 lot of calibrator

➔ 1200 data to manage per parameter
➔ ~30000 data to manage for the full study

Access to a dedicated team of 7 technicians, a clean room, and the rental of 7 instruments to perform the different evaluation studies.

How We Responded

Establishment of a working group of experts dedicated to the project (head of IVD-R, testing project manager, 7 technicians, data manager and biostatistician as well as the setting up of a clean room on different sites) to carry out the different analytical performances

Successful implementation of a clean room on different sites to carry out the different analytical performances.

Management and centralization of more than 70,000 data and analyze of the precision using analysis of variance NIST (Two-Way Nested ANOVA).

Successful completion of the single-site precision study for repeatability as well as the multi-site study for reproducibility.

Top Takeaways

This study is part of a complete IVD-R validation plan for our client's instrument in order to obtain its CE marking. Following these two studies aimed at validating the analytical performance, a clinical performance study was conducted including retrospective and prospective sample collection of the 26 parameters studied. Following this, comparative studies with the Standard Of Care were conducted.

Successful completion of the entire study within the time limit set by the client and obtaining the CE mark.

Cerba Research

Single-Site Precision Study : Extract From The Data Analysis

Example of results of single site precision study						
Sample ID	N	"Average pg/mL"	Repeatability		Specification	Conclusion
			SD pg/mL	CV%		
1	80	29.1	5.71	NA	Average<120pg/mL	within specifications
2	80	36.5	5.65	NA		within specifications
3	80	54.1	7.7	NA		within specifications
4	80	67.9	7.34	NA		within specifications
5	80	83.7	7.48	NA		within specifications
6	80	113	7.55	7%	≤12%	within specifications
7	80	162	7.18	4%	≤12%	within specifications
8	80	179	8.17	5%	≤12%	within specifications
9	80	219	10.4	5%	≤12%	within specifications
10	80	262	8.16	3%	≤10%	within specifications
11	80	304	10.5	3%	≤10%	within specifications
12	80	372	12.5	3%	≤10%	within specifications
13	80	445	11.2	3%	≤10%	within specifications
14	80	610	12.8	2%	≤10%	within specifications
15	80	748	16	2%	≤10%	within specifications
16	80	882	17.9	2%	≤10%	within specifications
17	80	1165	27	2%	≤6%	within specifications
18	80	2674	46.2	2%	≤6%	within specifications
19	80	4247	84.6	2%	≤6%	within specifications
20	80	5077	164	3%	≤6%	within specifications

Acceptance criteria for Repeatability	
Repeatability	
[ ] pg/mL	Specification
< 100	Individual values should remain below 120pg/mL
[100 - 250]	CV ≤ 12%
]250 - 1000]	CV ≤ 10%
> 1000	CV ≤ 6%

Conclusion :

The results of the single-site precision study, carried out according to CLSI guideline EP05-A3, met the acceptance criteria. The imprecision profil was described graphically and showed the trend of the results: [X]↗& CV%↘