Best Practices For Writing An IVDR-Compliant Performance Evaluation Report

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A legally non-compliant performance evaluation of an in-vitro diagnostic medical device (IVD) not only poses a risk of problems with the product during the authorization process but also risks patient safety. This paved the path for strict and robust IVDR requirements on performance evaluation of IVD products.

What Is Clinical Evidence?

As per the new European regulation 2017/746 on in vitro diagnostic devices (the EU-IVDR), "'Clinical evidence' means clinical data and performance evaluation results, … of a sufficient amount and quality to allow a qualified assessment of whether the device is safe and achieves the intended clinical benefit(s) when used as intended by the manufacturer."[1]

In short, clinical evidence is the data that supports the use of the device, which is required for all IVDs irrespective of class, based on assessed data used to demonstrate compliance with the general safety and performance requirements (GSPRs) laid out in Annex I of the regulation. As the IVDs are classified in accordance with the rules set out in Annex VIII of the regulation in a risk-based approach, the amount and quality of the clinical data varies among the device classes.

How To Gather Clinical Data For An IVD

The building blocks of the clinical evidence are based on three integral pillars for an in-vitro diagnostic device, namely:

- Scientific validity
- Analytical performance
- Clinical performance

Scientific Validity: Scientific validity means the association of an analyte or marker with a clinical condition or a physiological state. This can be demonstrated through a literature search if enough information with adequate quality can be found to establish the validity.[2]

Additionally, consensus expert opinions result from proof of concept, and clinical performance studies may be utilized as sources of data. The scientific validity of the analyte or marker is documented in the scientific validity report.

Analytical Performance: Analytical performance is the ability of a device to correctly detect or measure a particular analyte. The analytical performance of the device shall be demonstrated in relation to the following parameters (unless any of them can be justified as not applicable): analytical sensitivity, analytical specificity, trueness (bias), precision (repeatability and reproducibility), accuracy (resulting from trueness and precision), limits of detection and quantitation, measuring range, linearity, cut-off (including determination of appropriate criteria for specimen collection and handling and control of known relevant endogenous and exogenous interference), and cross-reactions.

Generally, analytical performance is demonstrated based on analytical performance studies and is demonstrated and documented in the analytical performance report.

Clinical Performance: Clinical performance is the ability of a device to yield results that are correlated with a particular clinical condition or a physiological or pathological process or state in accordance with the target population and intended user. The clinical performance of the device shall be demonstrated using the following parameters (unless any of them can be justified as not applicable): diagnostic sensitivity, diagnostic specificity, positive predictive value, negative predictive value, likelihood ratio, and expected values in normal and affected populations.

Demonstration of clinical performance must be based on the clinical performance studies, scientific peer-reviewed literature, and/or publishing experience gained by routine diagnostic testing. Clinical performance studies should always be performed unless it can be justified that a demonstration based on other sources of clinical data is sufficient. The clinical performance should be demonstrated and documented in the clinical performance report.

The clinical evidence gathered from these elements occurs throughout the lifetime of the device, which results in a rule of thumb as depicted below:

A performance evaluation plan or PEP consists of the procedures and methods to correctly perform and appropriately report the performance evaluation. According to the EU-IVDR, the PEP should cover at least the following:

Performance Evaluation Plan

- The intended purpose of the IVD
- Description of the analyte
- Target population
- Description of the state-of-the-art
- Steps for demonstrating the scientific validity, clinical performance, and analytical performance
- Determination of the acceptability of the benefit-risk ratio

Performance Evaluation Report (PER)

The performance evaluation report is an output of the process of performance evaluation activities populated from the results of applying the performance evaluation plan. Annex XIII, Part A (1.3.2) of the IVDR outlines the specific components of the PER and specifies that it must include:

- The scientific validity report
- The analytical performance report
- The clinical performance report and
- An assessment of all these reports supporting that the demonstration of the clinical evidence is sufficient to decide on the benefit-risk ratio.

Performance evaluation reports for Class C and D devices[3,4] must be updated at least annually, whereas PERs for Class A and B[5] devices should be updated as needed, although at least a three-year review cycle is recommended. Along with the above-mentioned elements of the performance evaluation, this should include continuous planning and gathering reports of post-market surveillance, as well as identifying and assessing any new/upcoming/residual risks as per the risk-mitigation activities.

The practical considerations to be taken into account while preparing a PER include:

- The reasoning behind the clinical evidence gathering methods used, including literature searches (related protocols and reports)
- A description of the technology behind the IVD
- The intended purpose and associated claims
- The actual scientific validity and the analytical and clinical performance data that have been evaluated
- The clinical evidence supporting the use of the device when assessed in the context of the current state-of-the-art
- Any new conclusions coming from post-market performance follow-up or other sources.

Conclusion

The impact of European In-Vitro Diagnostic Regulation 2017/746 (IVDR) on the device industry is more profound than the impact of European Medical Device Regulation 2017/745 (MDR). The majority of IVDs under the earlier IVD directives were self-certified and did not involve any notified bodies for conformity assessment. In contrast, around 90%

of IVDs now require the involvement of notified bodies. Also, new requirements for establishing the performance of an IVD have been introduced in the EU IVDR, adding a significant volume of regulatory work for IVD manufacturers. Receipt of insufficient or irrelevant data will result in the issuance of major non-conformities by notified bodies. You should take into account all the practical considerations described above when building the performance reports for your IVDs.

References

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Priya Ray Chaudhuri is a medical writing lead at the Medical Devices Centre of Excellence (COE) at Freyr Solutions. She drafts end-to-end clinical reports on IVDRs and MDRs and has a deep knowledge of IVDs, and their classification, testing, and post-marketing compliance requirements. She is highly skilled in good clinical practice (GCP) and pharmacovigilance and is knowledgeable about the medical device and pharmaceutical industries. Priya also has a very good understanding of Software as Medical Devices (SaMDs). With her diverse expertise, Priya manages the medical writing team and helps to deliver various projects.