



12 Keys to Meeting Revised Clinical Evaluation Report Requirements

In the recent revision to the Medical Devices Directive (MDD) 93/42/EEC (as amended by 2007/47/EC) there was a change to the requirements for the clinical evaluation report that must be submitted to the Notified Body as part of the technical file review that have been challenging and / or confusing to some manufacturers.

For the Regulatory Affairs manager that has the experience and expertise to interpret the requirements, the documentation may be found online. Fortunately, guidance is available, published as MEDDEV 2.7.1 Rev 3 (December 1999)ⁱ. Specifically, UL's Notified Body staff expects that the clinical evaluation reports will be provided in accordance with this guidance and will use the checklist provided in Appendix F to conduct the assessment.

The following are some of the key requirements manufacturers need to remember when submitting their clinical evaluation reports to the Notified Body.

Clinical Literature Evaluations

1. Clinical literature evaluations must be conducted using a full search protocol to find all relevant literature
2. Clinical literature evaluations must include and discuss matters arising from both favorable and unfavorable datasets. *The tendency is to only document those datasets (which may include technical papers and/or documentation of clinical trials) that support or favor the technical file submission.*
3. Clinical literature evaluations must be written or reviewed by an objective (i.e. independent) clinical expert in the area of the product. The clinical expert review is provided by the manufacturer not the notified body.
 - a. The Curriculum Vitae of authors and reviewers must be provided together with justification as to why manufacturers believe they are qualified to conduct/review the study.
4. The critical evaluation of the report must describe the qualitative or quantitative weighting given to each dataset and identify the pivotal datasets for the conclusion of the study.
5. Clinical Studies must demonstrate the equivalency of devices under evaluation to devices used in the individual datasets. Equivalency must be demonstrated with regards to:
 - a. Clinical Effectiveness (with regards to clinical condition, purpose, diagnosis or treatment; anatomical site, tissue type, physiology, target population)
 - b. Performance (similar conditions or use, accuracy, principles of operation, mechanical properties)
 - c. Biological (same materials in contact with same human tissues/body fluids for same duration)

6. Clinical Experience is a particular type of literature study used where the device is a long established product with well understood and characterized technology. In this case the datasets include manufacturer generated post market surveillance reports (including Field Safety Corrective Actions), registries or cohort studies, and/or searches of adverse event databases held by regulatory authorities (in EU as well as elsewhere). Each dataset must still be appraised for equivalency and how the manufacturer has included such matters in their risk management, and then critically analyzed as per the literature study.

Clinical Investigations

7. Clinical investigations must also provide an evaluation of available clinical literature to demonstrate what new information was needed as the objectives the investigation.
 8. Clinical investigations must always be provided by evidence of approval by a Research Ethics Committee (aka Investigation Review Board) regardless of where the investigation took place.
 9. Clinical investigations must follow the harmonized standard ISO 14155 for the process of the investigation in addition to any local regulations even if the study occurred outside of the EEA.
 10. Clinical investigations conducted outside of the EEA must show the relevance of the study towards a European population (considering for example any differences in diet, endemic diseases and environment). Justification must also be provided to show that the process of the trial meets current clinical practice in the EEA.
 11. The statistical hypothesis to be proven by the study must be clearly stated in the Clinical Investigation Plan and approved prior to the commencement of the trial.
 12. For both clinical literature studies and clinical investigations, a post-market clinical follow up plan must be provided or appropriate justification should be stated.
-

What has changed from previous requirements:

Applies to All Classes

The M5 amendment to the MDD, in Annex X (section 1.1) states that conformity with specific essential requirements must be based on a clinical evaluation following a defined and methodically sound procedure. This requires a manufacturer to provide clinical evidence through literature, experience or investigation (trial) to demonstrate conformity with the essential requirements. This is a 'general rule' relevant to all classes of devices and not just higher risk devices, although there is an increased emphasis that clinical data for implants and class III products must be based on a clinical investigation unless duly justified.

Post Market Review

Additionally the clinical evaluation must be considered a body of knowledge that must be actively updated with data obtained from the post market phase (Annex X, Section 1.1c). This is referenced by section 3.1 of Annexes II and V which require “...the manufacturer to institute and keep up to date a systematic procedure to review experience gained from devices in the post-production phase, including the provisions referred to in Annex X.” Your Notified Body will evaluate the implementation of this procedure and the manufacturer’s ability to update their clinical evidence for the device during audits and subsequent periodic sampling of technical files.

What this means to you, the manufacturer:

You will need to demonstrate that these requirements have been met through documented evidence, which the Notified Body will review. The MEDDEV 2.7.1 rev 3 document contains excellent guidance on how report this information and how to keep it up to date with post market surveillance information (additionally refer to clause 9 of harmonized standard ISO 14971:2007 and the associated guidance in the annexes).

More Information - UL Notified Body

UL offers local services for CE Marking under the MDD and IVDD and provides a simple way to transfer from your existing Notified Body or ISO 13485 Registrar. For more information, please visit UL’s website at www.ul.com/medical-cemark or send us an email at Medical.Inquiry@us.ul.com .

ⁱ MEDDEV 2.7.1 Rev 3 http://ec.europa.eu/consumers/sectors/medical-devices/documents/guidelines/index_en.htm