

Clinical Affairs

Requirements for clinical data

A) Clinical report

A clinical report for a medical device calling for CE marking shall fulfill the requirements of MEDDEV 2.7.1. The following hints which are generally checked during an in-house review of a clinical report are based on our experience with documentations submitted in the past; they give additional advice for the demands outlined in the MEDDEV.

Content-related aspects

1. The report should contain a technical description as well as a detailed description of the intended use of the device. A mere reference to the technical documentation cannot be regarded as adequate.
2. Any clinical risk associated with the use of the device and the medical procedure wherein the device is used shall be identified and assessed in the clinical report. In that context, the severity of any hazard as well as the probability of occurrence of the harm shall be characterized. A mere reference to the formal risk analysis cannot be regarded as adequate.
3. The acceptability of any identified risk shall be assessed adequately. Such a process may include a systematic literature review, bench testing, pre-clinical or clinical studies.
4. In case the "literature route" is used, transferability of device technology used in publications to the device under assessment is often critical.

Notes:
 - In the majority of cases, a pure literature review will not be sufficient. Rather, the equivalence shall be demonstrated.
 - The adequacy of methods used in the discussed publications shall also be taken into account.
5. In case a clinical study is performed, attention should be paid to:
 - the fulfillment of requirements outlined in EN 14155-1 and -2;
 - the adequacy of the study follow-up regarding the evaluation of safety and performance of the device;
 - the adequacy of primary and secondary objectives regarding the evaluation of safety and performance;
 - the adequacy of inclusion/exclusion criteria regarding the evaluation of safety and performance;
 - the adequacy of statistical methods employed, including sample size estimation;
 - intent-to-treat and per-protocol analysis.

6. Bench tests, pre-clinical and clinical studies, if used for the demonstration of safety and performance of the device, shall be detailed and discussed in the clinical report. A mere reference to the technical documentation cannot be regarded as adequate.

Notes:

- The adequacy of pre-clinical or clinical testing depends on the novelty of the device or treatment procedure, compared to established devices or methods.
- It should be taken into account that statistical issues might also be relevant for the assessment of the adequacy of such tests.

7. In that equivalence with the current “state of the art” shall be demonstrated for any medical device calling for CE marking, not only the identified risks of the device itself may be evaluated for the overall risk-to-benefit assessment of the device.

Rather, an adequate “state of the art” review shall be included in the clinical report.

8. “State of the art” review:
- “State of the art” is understood as detailed description and discussion of all currently available treatment options and medical devices for the same intended use as the device calling for CE marking, reflecting current medical practice and the acknowledged technologies.
- To document a systematic “state of the art” review, a protocol for the identification, selection, collation and review of scientific literature including search databases, search terms, selection criteria and rationale shall be attached to the clinical report.

- Reasons for believing that all relevant references, both favorable and unfavorable, are included in the review, shall be given.
- The acceptability of publications quoted (i.e. reviewed journal, publication year, qualification of the author) shall also be included in the discussion.

9. In case there are comparable or predecessor devices, this clinical experience shall also be included in the report.

10. The overall risk-to-benefit assessment of the device shall include the comparison of the device under assessment and the established treatment options/medical devices mentioned in the “state of the art” section.

The author’s conclusions shall be substantiated by the presented data.

Formal aspects

1. The quotation index of the referenced literature shall be attached to the clinical report.
2. Intended use/indications/contraindications shall be conclusive in the different parts of the documentation.
3. The claimed intended use/indications/contraindications shall be substantiated by the provided clinical data.
4. Relevance of the background and expertise of the author of the clinical report in relation to the particular device and/or medical procedure involved shall be demonstrated by a scientific curriculum vitae.
5. The data provided in the different parts of the documentation should be consistent (e.g. indications, technical parameters, etc.)

B) Other documents to be included in the clinical data documentation

1. Copies of the publications quoted in the clinical report
2. Reports of all bench tests quoted in the clinical report
3. Study protocols and study reports in case pre-clinical or clinical studies have been performed. In case a clinical study has been performed, the "letter of no objection" from the Competent Authority as well as the Ethics Committee opinion have to be included.
4. Instructions for use, including indications, contraindications, risks, side effects, adverse events
5. Risk analysis, including clinical risks
6. Post-market experience data of predecessor devices, if applicable
7. PMCF plan, if applicable

Post-market clinical follow-up (PMCF)

The MEDDEV 2.12-2 provides guidance on how to fulfill the requirements of the Directives regarding post market surveillance obligations. It emphasizes the limitations of premarket conformity assessments, in that infrequent complications may not be detected. Adequate post-marketing strategies are therefore to be regarded as of utmost importance.

Due to the fact that the "literature route" to demonstrate safety and performance of a medical device prior to CE marking is particularly associated with major limitations (i.e. transferability of clinical data to the device under assessment), a rigorous post market surveillance is essential.

Miscellaneous

For some time past, an additional mode for the review of clinical data in case of shortage of time prior to the desired CE marking date has been offered (for more details see our previous Med-Infos). Please take into account that only if an appointment with Clinical Affairs is made six to eight weeks prior to the desired assessment date, a review within five working days from this date can be guaranteed.

At the same time, the client is responsible for the availability of the complete set of documentation as hardcopies in our office on the scheduled date.

In general, documents submitted for review should be provided as hardcopies to speed up the review process.



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