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Medical Device + Diagnostic Industry

Meeting Medical Device Clinical Evidence Requirements

Staying On Top of CE Marking Regulation

Clinical Evaluations are required by the Medical Device Directive to ensure the safety of devices marketed in the European Union. The requirements are clearly outlined. However, many manufacturers are challenged by the process and rejections by the reviewers are not uncommon. Industry expert, Chris Henza, shares her insights on compiling Clinical Evaluations, including tips from a recent submission which was approved in just 22 hours.

MDD 93/42/EEC Annex 1 (Medical Device Directive), amended by the 2007/47/EC, outlines the Essential Requirements that have been established by the European Union. The 2007 amendment includes the clinical requirement in the general section (essential requirement 6a) and does not allow an answer of "not applicable"

The What, When, and Why of Clinical Evaluations

A clinical evaluation is the assessment and analysis of clinical data pertaining to a medical device in order to verify its clinical safety and performance.

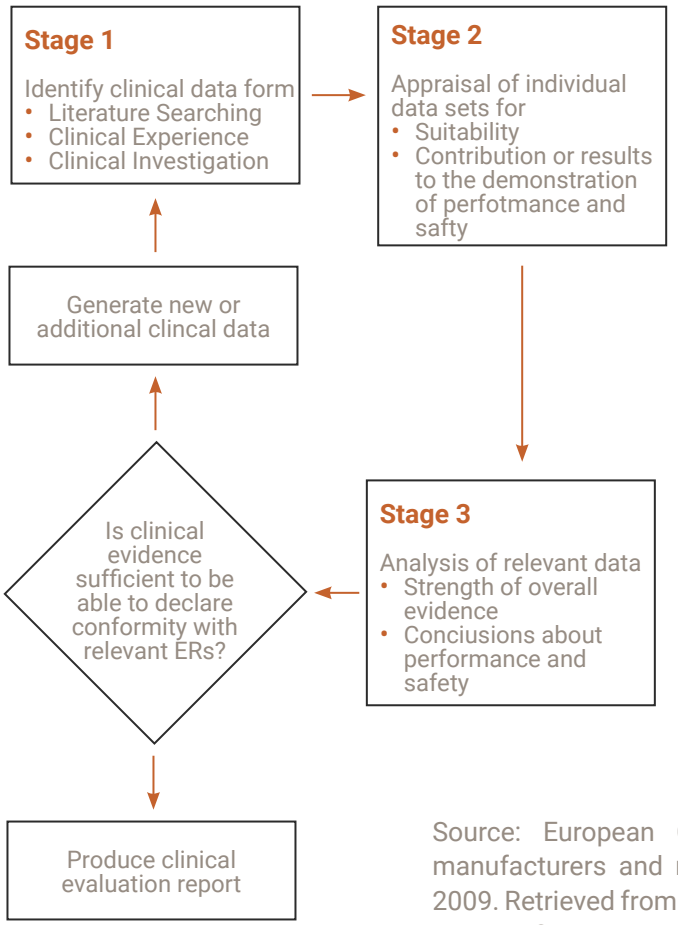
Clinical evaluations are first performed prior to marketing of a medical device and then repeated periodically as new clinical safety and performance information about the device is obtained.

The manufacturer demonstrates the device achieves its intended performance and the risks and any adverse events are minimized and acceptable when weighed against the benefits. Claims made about the device's performance and safety are supported by suitable evidence.

With regard to post-market activities, manufacturers are expected to implement and maintain surveillance programs which routinely monitor the clinical performance and safety of the device as part of their Quality Management System (QMS). The QMS should use data generated from safety reports, including adverse event reports, results from published literature, any further clinical investigations and formal post-market surveillance studies.

The stages of a clinical evaluation are outlined in Figure 1, below.

Figure 1: Stages of Clinical Evaluations



The Clinical Evaluation Process

Identify the Essential Requirements that require support from relevant clinical data;

Identify available clinical data relevant to the device and its intended use;

Evaluate data in terms of its suitability for establishing the safety and performance of the device;

Generate any clinical data needed to address outstanding issues;

Bring all the clinical data together to reach conclusions about the clinical safety and performance of the device.

Source: European Commission: Clinical Evaluation: a guide for manufacturers and notified bodies, MEDDEV. 2.7.1 Rev.3, December 2009. Retrieved from: http://ec.europa.eu/consumers/sectors/medical-devices/files/meddev/2_7_1rev_3_en.pdf

Collecting Data

The literature review must be complete, covering pre- and post-market data and any clinical investigations. Common sources for data are:

- Competitive products
- Complaints
- MAUDE database
- Internal clinical testing
- MedWatch
- Published literature using common databases such as PUBMED and Science Direct, etc.

In collecting data, it's helpful to print search pages including the search terms and exact logic used in the search. Boolean logic operators such as "AND" and "OR" show repeatability and helps the reviewers in analyzing the resulting clinical evaluation.

For published literature, it is not uncommon for thousands of data sources to be identified.

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Data Evaluation:

The Heavy Lifting in Clinical Evaluations

After data collection, the next step is assessing content and determining whether the data is considered for the clinical evaluation.

A scoring table can be useful for determining whether or not to include data. For example, the data might be scored on factors such as device equivalency, application equivalency, similarity of operator and demographic equivalency.

Studies which pass the scoring table must be summarized on how they support the Essential Requirements (see sidebar page 1). A common mistake is simply copying the conclusion of the study instead of describing how it relates to the Essential Requirements.

Insights from the Experts

The clinical evaluation must be re-creatable by third parties based on the process and scoring system outlined in the report. If the notified body can't re-create it, they have no recourse except to find deficiency.

Make it easy for the reviewers to check off each step. Highlight what they are looking for relative to what you are covering. Refer to guidances and standards such as, *The European Commission: Clinical Evaluation: a guide for manufacturers and notified bodies*[1] which features helpful appendices.

Common Errors:

- Missing inclusion / exclusion criteria
- Omitting applicable papers
- Summarizing papers instead of evaluating them. Although a summary is required, the more important (and often omitted) portion is to explain how the data supports the Essential Requirements.
- Forgetting summary tables
- Forgetting a concluding argument. Explain how the document fulfills the requirements for the clinical evaluation.

Case Study:

Class II device for breast biopsies

The manufacturer of the existing device changed notified bodies who alerted them of numerous deficiencies in the clinical evaluation. The manufacturer decided it was beneficial to submit a new clinical evaluation.

The data collection resulted in 2211 papers. After an extensive analysis and scoring system, 27 papers were included in the clinical evaluation. A summary table was prepared for the clinical evaluation which featured each paper and outlined the support of the Essential Requirements. The resulting clinical evaluation was approved without deficiency within 22 hours of submission.

Conclusion

Clinical evaluations include the assessment and analysis of the medical device's clinical data to verify its clinical safety and performance. The stages are well-defined, but can be intensive. A thorough clinical evaluation can involve thousands of data sources and significant time for proper assessment. Manufacturers should submit evaluations which are re-creatable and make it easy for reviewers to follow.

Resources:

1. European Commission: clinical evaluation: a guide for manufacturers and notified bodies, MEDDEV. 2.7.1 Rev.3, December 2009. Retrieved from: http://ec.europa.eu/consumers/sectors/medical-devices/files/meddev/2_7_1rev_3_en.pdf

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