Updates to the European Medical Device Clinical Evaluation Report Guidelines

The Role of Literature Searches in Obtaining Regulatory Approval

September 2016

Introduction

In June 2016, the updated Medical Device Clinical Evaluation Report (CER) guidelines came into effect (Revision 4 of ***MEDDEV 2.7/1:*** *Clinical Evaluation: Guide for Manufacturers and Notified Bodies*). These guidelines align very closely with regulations expected to come into effect in the next few years.

The European Commission provides a range of guidance documents to assist stakeholders in implementing directives related to medical devices. It is expected that the relevant guidelines should be applied to all medical devices sold in European Union, including those manufactured elsewhere.

Revision 4 of the guidelines includes detailed information on where and how to search for literature and how to record the process of collecting, appraising and analyzing the items found.

Search strategies, full search results, appraisal strategy and results, analysis of the data and a clear and functional list of references must be included in the CER.

This document gives an overview of some of the major points from Revision 4.

Clearer definition of device equivalence

As in Revision 3, the allowance is made to establish clinical evidence based on clinical experience and literature reports on the safety and performance of a device that is considered equivalent. This reduces the need for clinical data generation via investigation of the device under evaluation.

However, Revision 4 defines equivalence more clearly than Revision 3 and gives stricter guidance on where this rule can be applied.

Guidance for systematic reviews of biomedical literature in CER creation

Sources

Appendix A4, Sources of Literature, highlights the important literature databases to be used as sources, specifically stating:

- MEDLINE® or PubMed® can provide a good starting point for a search. However, with potentially incomplete coverage of European journals and reduced search features, comprehensiveness is not necessarily guaranteed.

- Additional databases may need to be used to ensure adequate coverage of devices and therapies in use in Europe, to identify relevant clinical trials and publications of user experience, and to facilitate searches by device name and manufacturer. Listed additional databases include Embase® and the Cochrane Central Trials Register.

Items for inclusion and protocol

Section 7 and Appendix 5 give detailed guidance on what should be included in a CER. The objectives of the CER must be linked to specific safety, performance and risk–benefit endpoints. Appendix 5 speficically pertains to the literature review, suggesting types of structured literature search that can be performed with guidelines on content.

The protocol should specify the search elements, addressing the background, objective and methods for identification, selection and collection of the relevant publications to address the literature review questions.

Types of search

Appendix 5 states:

Objective, non-biased, systematic search and review methods should be used. Examples are:

- **PICO (patient characteristics, type of intervention, control and outcome queries)**
- Cochrane Handbook for Systematic Reviews of Interventions
- PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Statement
- MOOSE Proposal (Meta-analysis Of Observational Studies in Epidemiology)

How Embase addresses these requirements

Embase is a biomedical literature database containing comprehensive, up-to-date and deeply indexed information, with over 32 million records from more than 8,500 journals and 6,000 conferences. It covers all the content contained in MEDLINE and unique coverage, including conference abstracts and European journals. The database currently has over 2,900 journals that cannot be found in MEDLINE.

Crucially for medical device CERs, Embase has a specific focus on medical devices. Emtree®, the Embase thesaurus used for indexing, includes over 3,000 medical device terms It also has a dedicated medical device search form and device subheadings that show relationships to related terms (e.g., adverse device events, device comparison, device economics). Device trade names and manufacturer names are also indexed.

Moreover, the ability to build searches in Embase.com using a structured PICO framework, which also allows easy incorporation of Emtree terms and synonyms, supports manufacturers in the creation of comprehensive CERs, enabling them to get regulatory approval faster and accelerating the time to market.

Further reading

1. European Commission website, Medical Devices section, Guidance subsection: http://ec.europa.eu/growth/sectors/medical-devices/guidance_en

2. European Commision, Health Technology and Cosmetics. MEDDEV 2.7/1 revision 4, Guidelines on Medical Devices: Clinical Evaluation: A Guide for Manufacturers and Notified Bodies Under Directives 93/42/EEC and 90/385/EEC. 2016. http://ec.europa.eu/DocsRoom/documents/17522/attachments/1/translations/en/renditions/pdf

3. BSI Group. The top ten changes in MEDDEV 2.7.1 Rev 4. 2016. http://www.bsigroup.com/meddev/LocalFiles/en-GB/Documents/MedDev-brochure.pdf

4. Elsevier website, Embase for Medical Devices page: https://www.elsevier.com/solutions/embase-biomedical-research/medical-device

5. Elsevier. Boost the Success of Medical Device Development with Systematic Literature Reviews. 2015. https://www.elsevier.com/__data/assets/pdf_file/0015/109212/R_D-Solutions_Embase_White-Paper_MedicalDevice_DIGITAL.pdf