EU MDR - Suggested Table of Contents for the Clinical Evaluation Report - CER

Observation 1 - This is the third installment of my series on medical device clinical evaluation. I suggest reading the first part at (http://www.medicaldevice.expert/) to have a better understanding of the concepts so the understanding of this part is easier).

Introduction

The Clinical Evaluation Report - CER is the document which contains the results of the – application of the clinical evaluation requirements and process by the manufacturer, for a medical device. The MDR and also current MEDDEV 2.7.1 Rev 4 - Clinical Evaluation contains general information on the contents of the CER (the MEDDEV also provides a suggestion for a general TOC, however, they are too general and high level. We've been using a modified TOB based on the activities mentioned in the first post of this series (http://www.medicaldevice.expert/europe/european-commission/medical-device-regulation/how-to-perform-a-clinical-evaluation-of-medical-devices-part-1-overview-and-sample-of-activities/). The suggestion is below.

Suggested Table of Contents for the Clinical Evaluation Report - CER

Part 1 - Introduction
- Introduction
- Objective
- Reference Documents
- Definition of clinical evaluation team
    - Expert in research methods and design
    - Librarian or search expert
    - Data Management Expert
    - Activities in the clinical evaluation stages
- Declaration of interests for the clinical evaluation team
- Summary
- Scope of the document

Part 2 - Scope of the clinical evaluation

Part 2.1 - Device description
- Name, models, sizes, components of the device, including software and accessories
- Device group to which the device belongs (e.g. biological artificial aortic valve)

Whether the device is being developed/ undergoing initial CE-marking/ is CE-marked
Whether the device is currently on the market in Europe or in other countries, since when, number of devices placed on the market
- Intended purpose of the device
    - Exact medical indications (if applicable)
    - Name of disease or condition/ clinical form, stage, severity/ symptoms or aspects to be treated, managed or diagnosed
    - The intended patient population, subdivided into groups if applicable, with clear indications and contraindications for each population or group
    - Detailed description of intended clinical benefits to patients with relevant and specified clinical outcome parameters, subdivided into groups if applicable
    - Detailed description of the intended performance, including the technical performance of the device intended claims regarding clinical performance and clinical safety that the manufacturer intends to use
    - Intended users (use by health care professional / lay person)
        - For each group of intended users

- Occupational description
- Demographic characteristics
- Physical characteristics
- Skills
- Potential impairments
- Performance shaping factors
- Learning style

- Organs / parts of the body / tissues or body fluids contacted by the device
- Duration of use or contact with the body
- Repeat applications, including any restrictions as to the number or duration of re-applications
- Contact with mucosal membranes/ invasiveness/ implantation
- Contraindications
- Precautions required by the manufacturer
- Single use / reusable

- General description of the medical device including
  - A concise physical and chemical description
  - Technical specifications, such as features, dimensions and performance attributes, of the device and any variants/configurations and accessories that would typically appear in the product specification made available to the user, for example in brochures, catalogues and similar publications
  - Sterility
  - Radioactivity
  - How the device achieves its intended purpose
  - Principles of operation of the device and its mode of action, scientifically demonstrated if necessary
  - A general description of the key functional elements, e.g. its parts/components (including software if appropriate), its formulation, its composition, its functionality and, where relevant, its qualitative and quantitative composition. Where appropriate, this shall include labelled pictorial representations (e.g. diagrams, photographs, and drawings), clearly indicating key parts/components, including sufficient explanation to understand the drawings and diagrams
  - A description of the raw materials incorporated into key functional elements and those making either direct contact with the human body or indirect contact with the body, e.g., during extracorporeal circulation of body fluids, and description of body parts concerned
  - Whether it incorporates a medicinal substance (already on the market or new), animal tissues, or blood components, the purpose of the component
  - An explanation of any novel features
  - A description of the accessories for a device, other devices and other products that are not devices, which are intended to be used in combination with it
  - A description or complete list of the various configurations/variants of the device that are intended to be made available on the market
  - Whether the device is intended to cover medical needs that are otherwise unmet/ if there are medical alternatives to the device / if the device is equivalent to an existing device, with a description of the situation and any new features
  - If the device is intended to enter the market based on equivalence:
    - Name, models, sizes, settings components of the device presumed to be equivalent, including software and accessories
    - Whether equivalence has already been demonstrated
  - For devices based on predecessor devices: Name, models, sizes of the predecessor device, whether the predecessor device is still on the market, description of the modifications, date of the modifications.

- The current version number or date of the information materials supplied by the manufacturer (label, IFU, available promotional materials and accompanying documents possibly foreseen by the manufacturer)
- Reference to previous and similar generations of the device
    - An overview of the previous generation or generations of the device produced by the manufacturer, where such devices exist
    - An overview of identified similar devices available on the Union or international markets, where such devices exist.

Part 2.2 - Clinical evaluation plan
- Identification of the design requirements (related to applicable general safety and performance requirements) that may require verification by clinical data
- Whether there are any design features of the device, or any indications or target populations, that require specific attention
- Information required for evaluation of equivalence
- Risk management documentation
- Data source(s) and type(s) of data to be used in the clinical evaluation
- Specific clinical concerns that have newly emerged and need to be addressed
- PMS aspects that need regularly updating in the clinical evaluation report
- Parameters to be used to determine the acceptability of the risk-benefit ratio for each indication and purpose
- Risk-benefit related to specific components
- Specification of methods to be used for examination of qualitative and quantitative aspects of clinical safety with clear reference to the determination of residual risks and side-effects
- Indicative list and specification of parameters to be used to determine, based on the state of the art in medicine, the acceptability of the benefit-risk ratio for the various indications and for the intended purpose or purposes of the device
- Clinical development plan indicating progression from exploratory investigations, such as first-in-man studies, feasibility and pilot studies, to confirmatory investigations, such as pivotal clinical investigations, and a PMCF as referred to in Part B of this Annex with an indication of milestones and a description of potential acceptance criteria
- Data management
    - Bibliographic or reference management software
    - Data extraction forms
    - Data management software to use

Part 3 - Clinical background, current knowledge, state of the art
- Current knowledge / state of the art in the corresponding medical field
    - Results from initial literature review (from design phase) of current knowledge / state of the art in the corresponding medical field
    - Summary of the Medical Fields/Conditions
    - Alternative Diagnostic/Therapeutic/Management Options identified in literature
    - Opinion summary from users identified in literature
    - Regulations, Standards and Guidance Applicable for device under evaluation

Part 4 - Basis for clinical evaluation of the device under evaluation
- Rationale for need of clinical data to show compliance to design requirements (related to applicable general safety and performance requirements)
- Rationale for use of non-clinical data to show compliance to design requirements (related to applicable general safety and performance requirements)
- Evaluation of equivalence

Part 5 - Identification of pertinent data

Part 5.1 - Research question design
- Framework used to design the research question
- Identification of eligibility criteria
- Results of preliminary searches to calibrate criteria
- Definition of study types to consider based on research question
- Final feasibility analysis
- Results from term harvesting
- Evaluation of research question using FINER/TREAD/RETREAT framework

Part 5.3 - Database search
- Database search plan
    - Preliminary Search
    - Comprehensive database search
    - Manual Search
    - Contact with experts
    - Data to be documented for each type of search
- Choices of database
    - Criteria for the evaluation of accuracy of search results
    - Criteria for evaluation of recall of search results recall
    - Additional criteria for the search results evaluation
    - Initial identification of databases
        - Listing of databases based on research question
        - Verification if the research question topics are covered by each identified database
        - Results of evaluation of indexed materials of each identified database
        - Results of assessment of how each database will impact accuracy, recall and additional criteria
    - Formal definition of databases to use, with justifications
- Search strategy design
    - Translation of research question into search plan, based on framework
        - Concepts identified from research question
        - Terms harvesting for each concept
            - Results of objective term harvesting (extraction) for natural language
            - Results of conceptual term harvesting (localization) for natural language
            - Results of objective term harvesting (extraction) for controlled vocabulary
            - Results of conceptual term harvesting (localization) controlled vocabulary
            - Results of citation records retrieved from each database
            - Results from analysis and identification of search terms
            - Results of thesauri search on each database to verify completeness
            - Results of independent search on each database to verify completeness
    - Refining of search strategy
        - Floating subtitles used
        - Synonyms of natural language identified
        - Truncation used
        - Wildcards used
        - Limites used
        - Filters used, and filter validation
        - Boolean operators used
        - Refinements validation
    - Search strategy evaluation
    - Results of search strategy evaluation for each database using the PRESS tool - Peer Review of Electronic Search Strategies
- Database search results

Part 5.4 - Searches beyond databases
- Additions sources searched
    - Data generated and maintained by the manufacturer
    - Gray literature
        - Event Annals
        - Dissertations / Theses
        - Internet Search
        - Government, IGOs, NGOs
        - Search Records
        - Clinical Trial Records
        - Advertising / Contact
        - Manual Search
        - Search by quote
- Document to be extracted from each data source (MECIR or PRISMA)
- Searches beyond databases search results
- Verification if results are indexed
    - Determination of reason indexed data was not retrieved
    - Terms not included
    - Revised database search strategies
- Revised database search results

Part 5.5 - Evaluation of search results
Results of the evaluation using the capture-mark-recapture (CRM) method

Part 5.6 - Study selection
- Results of pilot test of eligibility criteria
- Results of screening of results
- Results of evaluation of eligibility criteria and included data sets
- Results of verification of degree of agreement between reviewers

Part 6 - Appraisal of pertinent data

Part 6.1 - Critical appraisal plan

Part 6.2 - Evaluation of methodological quality and scientific validity
- Types of data sets identified
    - Harm
    - Cause / Risk Factors
    - Screening / Diagnosis
    - Prognosis
    - Prevention
    - Experience / perceptions of patient / consumer / participant
    - Service Delivery
    - Cost-effectiveness
- Critical appraisal worksheets to be used for each type of data set identified
    - Validation of critical appraisal worksheets
- Results of application of critical appraisal worksheets to each data set (evaluation of

Part 6.3 - Evaluation of contribution of each data set to the clinical evaluation
- Results of the evaluation of contribution
    - Pivotal data sets
    - Other data

Part 6.4 - Evaluation of weighting of the contribution of each pivotal data set to the clinical evaluation

- Results of the evaluation of weighting of the contribution of each pivotal data set to the clinical evaluation

Part 7 - Analysis of the clinical data

- Synthesis Planning
    - Type of synthesis chosen
    - Data elements codification
    - Methods for data collection used
    - Conflict resolution, including vague or missing data
    - Data collection tool used - Systematic Review Data Repository (SRDR)
    - Data collection forms
- Data Synthesis
    - General Overview
    - Summary of data related to safety requirements conformity assessment (MDD ER1 / AIMDD ER1)
    - Summary of data related to conformity assessment with acceptable benefit / risk profile requirement (MDD ER1 / AIMDD ER1)
    - Summary of data related to the assessment of compliance with performance requirements
    - Summary of data related to conformity assessment with requirement for acceptability of undesirable side effects
- Explanation of the results and findings
    - General findings
    - Analysis of safety related conformity assessment data (MDD ER1 / AIMDD ER1)
    - Analysis of data related to conformity assessment with acceptable benefit / risk profile requirement (MDD ER1 / AIMDD ER1)
    - Analysis of performance related conformity assessment data (MDD ER3 / AIMDD ER2)
    - Analysis of data related to conformity assessment with requirement for acceptance of undesirable side effects (MDD ER6 / AIMDD ER5)

Part 8 - Conclusion of the clinical evaluation

Part 9 - Post Market Clinical Follow Up (PMCF) requirements

Part 10 - Date of the next update to the clinical evaluation

Part 11 - Qualification of the responsible evaluators

Part 12 - Dates and signatures