CLINICAL EVALUATION REPORT

An expert opinion....

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Here's What the Medical Device Manufacturers Need to Know!

ABSTRACT

This write up is to enlighten the medical device manufacturers to document Clinical Evaluation Report (CER) based on MEDDEV 2.7/1 Rev. 4 guidance. Here, it explains how an evaluation is performed, what information is required and how this information should be appraised, analyzed and presented in the CER.

The essentiality of an overall evaluation of the device is also highlighted with the precise focus on establishing that clinical data are evaluated in a systematic and objective way, that the benefit risk profile is satisfactorily acceptable and that any gaps in clinical evidence are identified and addressed.

A. CLINICAL EVALUATION and the NEED OF CLINICAL EVALUATION REPORT (CER)

As per MEDDEV 2.7/1 Rev.4, Clinical Evaluation is a specialized robust method to collect, appraise and analyze clinical data related to a medical device and to interpret if there is satisfactory clinical information (evidence) to establish conformity with pertinent essential requirements for safety and performance when employing the medical device as per the manufacturer’s instructions for use.

The evaluation should be based on a broad analysis of pre- and post-market clinical data relevant to the device under evaluation as well as any data disclosing about the devices claimed as equivalent or benchmark by the manufacturer.

The requirements of clinical evaluation are imperative to all classes of medical devices. The evaluation should be true to the device under evaluation, its specific properties, and its intended purpose.

Clinical Evaluation Report is one of the key documents for your CE Certification !!!

Clinical evaluation is an obligation of the manufacturer and the CLINICAL EVALUATION REPORT (CER) where all the clinical evaluation processes are documented (favorable and unfavorable), is an essential aspect of the technical documentation for CE marking of the medical device in accordance with the requirements shown in Article 61 and Annex XIV of Official Journal of the European Union- Regulations (Council Regulation 2017/745 of 5 April 2017), including a PMCF*. 
* The manufacturer should take-charge of collecting clinical data of the CE marked Medical device in-use on humans with the objective of confirming the safety and performance as intended continuously during the expected lifetime of the device to confirm the continued acceptability of identified risks and to detect any emerging risks based on the real and correct clinical evidence. A PMCF plan and PMCF Evaluation Report should be maintained and when required, preventive and/or corrective measures must be identified and the manufacturer should implement them.

B. VARIOUS STAGES OF CLINICAL EVALUATION

B1 STAGE 0: Scoping And The Clinical Evaluation Plan

Scoping is defined based on the Essential Requirements that are vital to be addressed from a clinical context and the type and history of the device.

The Clinical Evaluation Plan should include different aspects, considering the stages in the lifecycle of the product.

Device description, Design features, Risk Management documents, current knowledge/ state of the art in the corresponding medical field data source input(s) and type(s) of data to be used in the clinical evaluation are included in all CERs whereas few aspects are specific to CERs before and after CE marking.
<table>
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<th>Before CE marking</th>
<th>For CE marked devices</th>
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| Equivalent device data **, if claimed | Any relevant changes such as:  
- design changes,  
- changes to materials and manufacturing procedures,  
- changes to the information materials supplied by the manufacturer (label, IFU, available promotional materials including accompanying documents possibly foreseen by the manufacturer) or other claims,  
- and whether the claim of equivalence to an existing device is still appropriate |
| Any specific clinical concerns that have newly emerged and need to be addressed | PMS Data (new) |
| PMS Plan including PMCF | |

**The demonstration of equivalence should be considered based on Technical, Biological and Clinical characteristics and the equivalence identification should be provided with proper justification.**

### B2 STAGE 1: Identification Of Pertinent Data

#### a) Data that are generated and held by the manufacturer:
- pre-market clinical investigations  
- clinical data generated from risk management activities and the PMS programmes (PMCF, Complaint reports, Incident reports and so on..)  
- relevant pre-clinical studies (bench test reports- verification and validation data)

#### b) Data derived from Literatures
- Clinical data relevant to the device under evaluation or to the equivalent device (if equivalence is claimed)  
- Current knowledge/ the state of the art

### B3 STAGE 2: Appraisal of Pertinent Data

The evaluators should appraise each individual document identified in Stage 1 in terms of its scientific validity, relevance, and weighting of its contribution to the evaluation of the clinical performance and safety of the device.
B4  STAGE 3: Analysis Of The Data, whereby conclusions are reached about
- in concurrence with Essential Requirements (including ER1, ER3, ER6) on performance and safety of the device, including its benefit-risk profile,
- the contents of information and materials given by the manufacturer (including the IFU, labels of the device, promotional materials, including accompanying documents possibly anticipated by the manufacturer),
- residual risks and uncertainties or unanswered questions (including on rare complications, long-term performance, safety under widespread use), whether these are acceptable for CE-marking, and whether they are required to be addressed during PMS.

B5  STAGE 4: Clinical Evaluation Report (CER)
Clinical Evaluation report (CER) has the summary and inferences of the evaluation of all the relevant clinical data documented or referenced in other parts of the Technical File documentation.

"The clinical evaluation report and the relevant clinical data constitute the clinical evidence for conformity assessment"

Clinical Evaluation is a paramount aspect of CE Mark certification process because it guarantees that the evaluation of safety and performance of the device is based on adequate clinical evidence throughout the lifetime that the medical device is on the market.

This continuous process enables manufacturers to handover the notified bodies and competent authorities with sufficient clinical evidence for the demonstration of conformity of the device with the Essential Requirements throughout its lifetime (for example: for CE marking, completion of post-market surveillance and reporting necessities, or during surveillance processes).
C. RIGHT TIME FOR CLINICAL EVALUATION

C1. Clinical Evaluation During the Development of A Medical Device

Mostly, clinical evaluation is first performed during the development of a medical device in order to:

a) Interpret needs regarding clinical safety and clinical performance of the device - sufficient clinical evidence to establish conformity with the Essential Requirements covering clinical performance and clinical safety;

b) Determine what data need to be generated for European market entry by carrying out a gap analysis - Post-market Surveillance (PMS), E.g. in post-market clinical follow-up studies (PMCF Studies) required under the medical device directives [MEDDEV 2.12/2]. Generally, these aspects include estimation of residual risks and uncertainties or unanswered questions (such as rare complications, uncertainties regarding long-term performance, safety under wide-spread use) [EN ISO 14971:2012];

c) Find out whether clinical investigations are necessary and if so, to define the study design [EN ISO 14155:2011]

d) Decide desirable equivalence to an existing device thorough available clinical data

“The Clinical Evaluation Report is essential for initial CE-marking and it must be actively updated since that time onwards. It is conducted during the whole of the life cycle of a medical device, as a continuous process”
C2. Updating the Clinical Evaluation Report

The manufacturer should specify and substantiate the frequency at which the clinical evaluation needs to be actively updated.

The clinical evaluation should be actively updated:

1. When the manufacturer collects new information from PMS that has the potential to change the current evaluation. As a manufacturer, one should establish a PMS system with a well-defined scope and nature in line with the intended purpose of the device that consistently monitors the clinical performance and clinical safety of the device as part of their quality management system. PMS should systematically generate new data, such as safety reports, results from published literatures, registries, PMCF studies, and other data about device usage. Those data need to be evaluated for information that has a potential to change the evaluation of the benefit-risk profile, and the clinical performance and clinical safety of the device. These data are required to be fed into the clinical evaluation files in a timely manner. In agreement with the Regulatory Directives, the clinical evaluation and the clinical evaluation report must be actively updated with data obtained from post-market surveillance.

"Clinical Evaluation can therefore lead to changes to the Manufacturer's Risk Management Documents, Instructions For Use (IFU) and PMS Activities."

2. If no such information is received, then CER should be updated:
   • at least annually if the device carries serious risks or is not yet well established; or
   • every 2-5 years, if the device is not expected to transmit serious risks and is well established, a justification should be provided.

When involvement of notified bodies is required, updates are usually coordinated with the notified body. Usually, they are lined up with the timetable for surveillance audits and the renewal of the certificates.
D. ROLE OF CLINICAL EVALUATOR(S) Few Points to Note!

Clinical evaluation should be conducted by a well-qualified individual or a team and the evaluator(s) should own experience and expertise in research methodology, information management, regulatory requirements, medical writing, proficiency of the technology of device under evaluation and its application, diagnosis and management of the conditions intended to be diagnosed or managed by the device, familiarity of medical alternatives, medical care standards and technology (e.g. specialist clinical expertise in the relevant medical specialty).

"The evaluator(s) should have 5-10 years of documented professional experience in the relevant field".

In cases where the level of evaluator expertise may be less or different, it should be recorded and properly justified.

"DECLARATION OF INTEREST and CURRICULUM VITAE" of the EVALUATOR(S) must be submitted with Clinical Evaluation Files to the Notified Body.
E. WHAT THE NOTIFIED BODY WOULD CHECK FROM THE MANUFACTURER’S CLINICAL EVALUATION REPORT!

- device description and product specification
- intended purpose of the device
- classification proposed for the device
- pre-clinical evaluation data presented by the manufacturer
- risk analysis and risk management and alignment with the clinical evaluation report
- clinical evaluation process
- clinical evaluation report’s authors
- equivalence assessment – if data from equivalent is used
- clinical investigation plans and reports etc.

F. I 3 CONSULTING HELPS WITH EFFICIENT PREPARATION (BUT NOT LIMITED):

- a new CER with well tailored SOPs and templates for each stages
- updating your existing CER
- upgrading your CER to comply with the latest regulatory requirements [MDD superseded by MDR]
- assisting and training QA/RA team in your organization effectively to conduct Clinical evaluation, including PMS, PMCF, Risk Management Files and so on.

G. REFERENCES

H. ABOUT I 3 CONSULTING

We are a group of qualified and experienced Regulatory Affairs Specialists (Consultants) for Highly Regulated Markets such as Medical Devices, Pharmaceuticals, Cosmetics, Food and Nutraceutical regulatory requirements, working across the America, Europe, Middle East and Asia-Pacific. Despite the reach and capabilities of our offices, we are large enough to guide fortune 500 companies and small enough to guide individually owned companies, making us one of the most accepted regulatory service providers. No wonder, the proof of our ability is answered by our massive number of customers which is increasing day by day mainly from client references!

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