Clinical Evaluation Report

The Clinical Evaluation Report states the clinical benefits and safety characteristics of the device, based on clinical data. It is the output of the Clinical Evaluation Plan.

> While the content of the Clinical Evaluation is simple, writing it, coming up with the right structure and forming a sensible line of reasoning (equivalence) can be a bit tricky.
>
> These are the guidance documents on Clinical Evaluation. If you're the person writing it, you should read them:
>
> - MDCG 2020-1, 2020-5, 2020-6
> - MDCG 2020-13: Quite helpful as it gives you an idea of the structure.
> - MEDDEV 2.7.1 rev. 4. (mostly for MDD, but still a good starting point; especially the list of proposed headings for a report at the end of the document).
>
> Finally, this Clinical Evaluation Report is for Medical Devices. If you are an IVD manufacturer you will write a Performance Evaluation Report which has many similarities but some essential parts are different, e.g. Post-Market Performance Follow-Up and procedural descriptions of evaluation and validation).

Product

- Name: *<product name>*
- Version: *<product version>*
- Basic UDI-DI: *<insert UDI-DI, if/when available>*

Table of Contents

> A list of the sections below. You have to update this manually when you edit headings as this is a markdown file (sorry - guilty dog face).

13. Date of the Next Clinical Evaluation
14. Dates and Signatures
15. Qualification of the Responsible Evaluators
16. References

1. List of Abbreviations

Abbreviation	Explanation
AE	Adverse Event
BfArM	German Federal Institute for Drugs and Medical Devices
CE	Communauté Européenne
CER	Clinical Evaluation Report
CI	Confidence interval
DHF	Design History File
DMR	Device Master Record
EUDAMED	European Database for MEdical Devices
FDA	Food and Drug Administration (US)
IFU	Instruction for Use
LoE	Level of Evidence
MAUDE	Manufacturer and User Facility Device Experience
MEDDEV	Guideline for Clinical Evaluation of Medical Devices
MDD	Medical Device Directive, European Directive 93/42/EEC
MDR	Medical Device Directive, 2017/745
PMS	Post Market Surveillance
PMCF	Post MArket clinical Follow Up
Rev	Revision
SOP	Standard Operation Procedure
T	Tendency
C	Comparability
WHO	World Health Organization

2. Product

- Name: *<product name>*
- Version: *<product version>*
- Basic UDI-DI: *<insert UDI-DI, if/when available>*
- UMDNS-Code:
- GMDN-Code:

The classification is based on the following criteria:

Select one of these two, based on whether you're going for MDD or MDR compliance.

- Annex IX of the European Directive 93/42/EEC (MDD): *<if applicable>*

- According to the EU Regulation 2017/745 (MDR) Annex VIII Rules: *<if applicable>*.

3. Relevant Documents

- SOP Clinical Evaluation
- Clinical Evaluation Plan
- Instructions for Use (IFU)

4. Scope of the Clinical Evaluation

Note: This section is copy-pasted from the Clinical Evaluation Plan.

The following section can be part of the Clinical Evaluation Plan or pasted here with reference to the respective chapters. Remember that you can update the Clinical Evaluation Plan during your evaluation (e.g. your search criteria are not sufficient).

The approach according to the MEDDEV 2.7/1 rev. 4 includes five logical procedural stages in order to evaluate the performance and safety data of the medical device:

- Step 0 ("Scope")
- Step 1 ("Identification")
- Step 2 ("Appraisal")
- Step 3 ("Analysis")
- Step 4 ("Report")

During the working process, these five steps are iterative and influence each other. The report shows the steps in a sequential way. In the present report (step 4), the steps 0 through 3 are corresponding to the following chapters:

List sections of the Clinical Evaluation Report here which cover the steps above.

5. Device

5.1 Device Description

Copy-paste your Device Description (which includes the Intended Use) here. If it's not done yet, remember to do it later :)

Also reference your Essential Requirements Document here.

5.2 Clinical Benefits, Outcome Parameters

Medical device claims are statements from accompanying documents, marketing material, your website, etc. that include information about the performance and safety of the medical device (information by the

manufacturer). The clinical evaluation is done in order to determine whether those claims are confirmed by sufficient clinical evidence.

So, if your website claims that your device cures back pain in 50% of patients after 14 days, here's the place to list that claim and show explain how you'll prove it.

Claims that have not been stated so far (e.g. in the IFU) are described below and sorted according to their meaning for performance and safety. In this clinical evaluation, it was determined that the claims are sufficiently supported by clinical data.

Performance-related product claims:

- Claim 1
- Claim 2

5.3 Clinical Safety, Methods for Analysis

Describe your safety parameters, i.e. which things should you product fulfil so that you consider it safe? And your methods, i.e. how will you prove that your product fulfils those safety parameters? A method could be literature search for past studies, but you could additionally do a Post-Market Clinical Follow-Up to double-check whether that's actually true for your device.

Safety-related product claims:

- Claim 1
- Claim 2

5.4 Acceptability of Benefit-Risk-Ratio

After you've defined your benefits and safety parameters, which combination of those is acceptable to you? In the case of most software devices (and apps), you'll probably have subtle benefits (e.g. better disease management, early detection of relapses) while low safety concerns (e.g. disease progression unlikely, not killing anyone).

6. Clinical Background, Current Knowledge, State of the Art

This chapter focus on literature and guidelines that describe the current state of the art and other topics. It is similar to the literature / introduction chapter of papers.

It makes sense to differentiate between "context" and "pivotal" data: * context data describes the state of the art (commonly the introduction / literature part of papers) * pivotal data is used for the appraisal,

i.e. that's the data describing the actual study and outcome(s). In the best case, the pivotal data is about the actual device you're claiming equivalence to.

6.1 Clinical Background & Current Knowledge

Describe the clinical context of the disease you're treating: How are patients currently treated? Which symptoms do they have, which diagnostic modalities are being used to establish a diagnosis, which treatment options exists? What are the benefits and drawbacks of current treatment options?

6.2 State of the Art incl. Alternative Treatments

Given the current treatment options, what is the preferred, "state of the art" treatment? What are its benefits and drawbacks? Are there recent scientific achievements (studies, new technologies, software) which may be promising to improve this state-of-the-art treatment? Also, what are alternative treatments?

7. Type of Evaluation

Note: This section is copy-pasted from the Clinical Evaluation Plan.

8. Equivalence

8.1 Equivalent Device

Describe the equivalent device you're comparing yourself to, mainly its Intended Use.

8.2 Demonstration of Equivalence (Technical, Biological, Clinical)

Here you have to demonstrate that your device is equivalent to the Equivalent Device. You accomplish that by creating a table in which you list certain characteristics, and describe those characteristics both for the Equivalent Device and for your device. The idea is that your device is mostly the same in most characteristics.

The tables are split into general stuff (first table), then Clinical, Technical and Biological equivalence as per the guidance documents. I pre-filled some of the table rows for you as they should be universal, e.g. Intended Use, Medical Indication(s) and Programming Language. But definitely feel free to add additional rows which are useful for comparing your device to the equivalent one. Maybe you're using recurrent neural networks and the equivalent device is, too? Then add that.

	Equivalent Device	This Device
Intended Use		
Medical Indication(s)		
Device Classification		
Principle of Operation	Stand-alone Software	Stand-alone Software

The level of similarity or equivalence of a comparable medical device to the evaluated medical device is divided into the three categories “clinical”, “technical” and “biological”.

Within each category there are four steps for the evaluation of the equivalence level:

Equivalence Level	Score
Very Equivalent	3
Nearly Equivalent	2
In some aspects similar	1
In some aspects similar	0

After a score has been assigned to all three categories (clinical, technical, biological), those scores are summed up. The total equivalence is determined based on the sum of those values:

Sum	Equivalence
8-9	Very Equivalent
6-7	Nearly Equivalent
3-5	In some aspects similar
0-2	Very different

Clinical Equivalence

The device is considered clinically equivalent if it is:

- used for the same clinical condition
- used for the same intended use
- used at the same site in the body
- used in a similar population
- not foreseen to deliver significantly different performances
- similar performances such as the expected clinical effect, the specific intended purpose, the duration of use, etc.

Technical Equivalence

The device is considered technically equivalent if it:

- is of similar design
- is used under the same conditions of use
- has similar specifications and properties
- has similar intensity of energy, tensile strength, viscosity, surface characteristics, wavelength
- has similar surface texture, porosity, particle size, nanotechnology, specific mass, atomic inclusions
- uses similar deployment methods
- has similar principles of operation and critical performance requirements

Biological Equivalence

For stand-alone software:

Not applicable. The device doesn't come in contact with human tissue or body fluids.

For medical devices which are a part of a hardware medical device:

Note: Medical device monitors are also medical devices according to 60601-1.

The device is considered biologically equivalent if it:

- is similar or has similar effecting materials which are contact with body tissue and fluids

Optional: Effectiveness Equivalence

The device is considered to have equivalent effectiveness, if it:

- has similar Sensitivity, Specificity, Accuracy, NNP, PPV, etc.

8.2.1 Clinical Equivalence

Note: The MDR doesn't explicitly state that the device needs to be used for the same medical indication, gender and duration of use. But it should be used for the same clinical condition or purpose including similar severity and stage of disease.

	Equivalent Device	This Device
Clinical Condition		
Disease Stage		
Site in Body		
Population: Age, Anatomy, Physiology		
Clinical Effect		
Duration of Use		

	Equivalent Device	This Device
Significant Performance Difference		

Clinical Equivalence Score: <enter number between 0 and 3>

8.2.2 Technical Equivalence

	Equivalent Device	This Device
Software Algorithm		
Programming Language		
Graphical User Interface (GUI)		
Web-based Application		
Inputs		
Outputs		

The following table can be added if it is a hardware-related Medical Device:

	Equivalent Device	This Device
Design		
Dimension		
Operating Condition		
Physical Characteristics (e.g. weight)		
Data transmission		

Technical Equivalence Score: <enter number between 0 and 3>

8.2.3 Biological Equivalence

For stand-alone software:

Not applicable. The device doesn't come in contact with human tissue or body fluids.

For medical devices which are a part of a hardware medical device:

	Equivalent Device	This Device
Material/ Radiation in Contact With Body (User/ Patient)		

Biological Equivalence Score: <enter number between 0 and 3>

8.2.4 Conclusion

Describe your conclusion based on the sum of numbers values that you gave for each aspect of your equivalence evaluation.

It would be also goodp to describe, on a high level, the outcome of your evaluation from the following processes:

- Risk Management
- Biocompatibility investigation (if applicable)
- Performance Testing
- Usability Testing (formative / summative evaluation)
- Post-Market Surveillance/ Post-Market Clinical Follow-up

Total Equivalence Score: <enter number between 0 and 9>

9. Literature Search

9.1 Literature Search Methods

Copy-paste from Clinical Evaluation Plan.

9.2 Literature Appraisal Criteria

Copy-paste from Clinical Evaluation Plan.

You can describe it as a flow chart. e.g.

1. Initial search with all publications from the relevant databases. 2.1 Potentially relevant papers (from the first skimming of article titles / abstracts) 2.2 Irrelevant papers
2. Potentially relevant papers found in irrelevant papers 4.1 Relevant paper used for context 4.2 Relevant paper used for single appraisal (pivotal data)

9.3 Literature Search Protocol

A table which lists your actual literature search results. For each entry, you should decide whether it's acceptable (based on your appraisal criteria) or not. I pre-wrote some tables to give you an idea of the structure below. You could separate the tables based on the database where you did the search (PubMed, Google Scholar).

It could make sense to put this in a separate document (rather: a spreadsheet).

Here are some bullet points from the guidance: * Literature search protocol provided * Literature search reports provided * Full list of retrieved articles provided * Full list of excluded articles provided, with reasons for exclusion Full text copies of relevant documents available

9.4 Database Search Overview

Database	Search term	# Hits	# Evaluated Abstracts	# Potential Relevant Publications

9.5 Database: PubMed

Title	Author	Year	Summary	Relevant?	Why?
					e.g. similar design, similar features

9.6 Database: Google Scholar

Title	Author	Year	Summary	Relevant?	Why?

9.7 Database: Cochrane

Title	Author	Year	Summary	Relevant?	Why?

9.8 Literature Search Report

Briefly summarize how many studies you reviewed, how many you deemed acceptable and why you didn't include the unacceptable ones (probably because they didn't conform to the appraisal criteria).

Describe a gap analysis which information could not be found during your search e.g. specific functionalities of your device, limited number of clinical data in publications.

9.10 Evaluation of study Quality

9.10.1 Level of Evidence (LoE)

Take a sufficient classification to evaluate the quality of your study. You can use the LoE from MDCG 2020-6 or from the american heart association.

9.10.2 Tendency (T)

The MEDDEV 2.7/1 rev. 4 requires that literature is used that confirms as well as questions the suitability of the evaluated medical device.

- positive: + (Confirms clinical suitability)
- negative: - (Does not confirm clinical suitability)
- indifferent: i (No statement to the clinical suitability possible)

9.10.3 Comparability (C)

For the consideration of the relevance of literature data of the clinical evaluation it is necessary to make a statement about the comparability to the medical device to be evaluated. This statement about the comparability is made according to the described criteria from chapter "Equivalence" above.

9.10.4 Single Appraisal of Searched Clinical Studies

This chapter is highly important for the medical device evaluation. Here you take all the publication from the literature search and evaluate them to prove equivalence with your device and prove the respective product claims. The latter can also be proven by other activities (e.g. PMS, equivalent device, usability testing, result of adverse events etc.).

9.10.5 Literature Data on the Performance of the Medical Device

Focus here on equivalent devices that support your performance claims.

Do the paper description in the same way e.g.:

- First describe the study with its main characteristics regarding the quality and relevance are made. (Study design, patient number, mean age inclusion and exclusion criteria, used product, end point, results of performance, conclusion of the author).
- Complications, side-effects, adverse events.
- A consideration of the study according to the criteria. (LoE, T, C)

In the following, the selected literature references, which were categorized as "relevant" (appraisal), are evaluated. This was done according to the following scheme:

9.10.6 Literature Data about the Safety of the Medical Device

Focus here on equivalent devices that support your Safety claims. So you do not need to describe the LoE since potential risks can also arise from case studies (which might have a low LoE).

10. Clinical Data

10.1 Clinical Data From Literature

List all the clinical data you got from studies which matched your appraisal criteria.

10.2 Clinical Data from Clinical Study Databases

List all the clinical data you got from studies (clinical trials.gov, ANCTR, DRKS, WHO etc.).

10.3 Clinical Data From Adverse Event Databases

List all the clinical data you got from studies which matched your appraisal criteria (BfArM, MAUDE, FDA Medical Device Recall, EUDAMED (when applicable)).

10.4 Summary and Appraisal of Clinical Data

Summarize all the clinical data from above :)

10.5 Analysis of the Clinical Data

Analyze the clinical data with a focus on whether your targets of clinical benefits and safety were fulfilled.

11. Post-Market Activities

This chapter is used to summarize your PMS/ PMCF activities. During the clinical evaluation you evaluate the information of your safety and performance claims as well as general requirements on safety & performance. If you can not cover certain aspects you might need to add them to your PMS/ PMCF - Plan.

Summarize your post-market activities. You can copy-paste a lot of those here. At the minimum, you'll have a Post-Market Surveillance Plan and Report. If this is your initial certification, your report may be empty as you haven't brought your device to market yet.

Additionally, you may have a Post-Market Clinical Follow-Up (PMCF) Plan and Report which essentially has the content of "we'll be tracking some data to make sure that our claims of clinical benefits and safety are actually true".

Here's what the guidance states about it: Describe how the manufacturer will verify the presumption that there would be no clinically significant difference in the safety and clinical performance of the device under evaluation compared with the equivalent device by post market surveillance or post market clinical follow-up?

- PMS Plan
- PMS Report
- PMCF Plan
- PMCF Report
- PSUR (if relevant)

12. Conclusions

Your conclusion whether the clinical data shows that your goals (benefit/ performance and safety) are fulfilled. Reference your claims you stated before.

13. Date of the Next Clinical Evaluation

When will you be doing the next clinical evalulation and updating this report?

14. Dates and Signatures

Date and sign the report. If your document management system supports it, you can digitally sign by typing e.g. your initials in the "Signature" field. Otherwise, you can still sign it the old-school way (print it and sign sheet of paper, ugh).

Activitiy	Name	Signature
Creation		
Review		
Approval		

15. Qualification of the Responsible Evaluators

Attach CVs of the people who were involved in writing the Clinical Evaluation. They must fulfil some critieria (it's complicated), so I'll just copy-paste MEDDEV 2.7.1 rev. 4 here:

- The manufacturer defines requirements for the evaluators that are in line with the nature of the device under evaluation and its clinical performance and risks.
- The manufacturer should be able to justify the choice of the evaluators through reference to their qualifications and documented experience, and to present a declaration of interest for each evaluator.

As a general principle, the evaluators should possess knowledge of the following: * research methodology (including clinical investigation design and biostatistics); MEDDEV 2.7/1 revision 4 page 14 of 65 *

information management (e.g. scientific background or librarianship qualification; experience with relevant databases such as Embase and Medline); * regulatory requirements; and * medical writing (e.g. post-graduate experience in a relevant science or in medicine; training and experience in medical writing, systematic review and clinical data appraisal).

With respect to the particular device under evaluation, the evaluators should in addition have knowledge of: * the device technology and its application; * diagnosis and management of the conditions intended to be diagnosed or managed by the device, knowledge of medical alternatives, treatment standards and technology (e.g. specialist clinical expertise in the relevant medical specialty).

The evaluators should have at least the following training and experience in the relevant field: * a degree from higher education in the respective field and 5 years of documented professional experience; or * 10 years of documented professional experience if a degree is not a prerequisite for a given task.

There may be circumstances where the level of evaluator expertise may be less or different; this should be documented and duly justified.

16. References

Papers and other references which you cite go here.
