Best Practice Guidance

for the Submission of Clinical Evaluation Documentation for Conformity Assessment by the Notified Body

By Royal Charter

Compiled and edited by Rachel Mead

July 2023
Next Update: 2 years from date of publication

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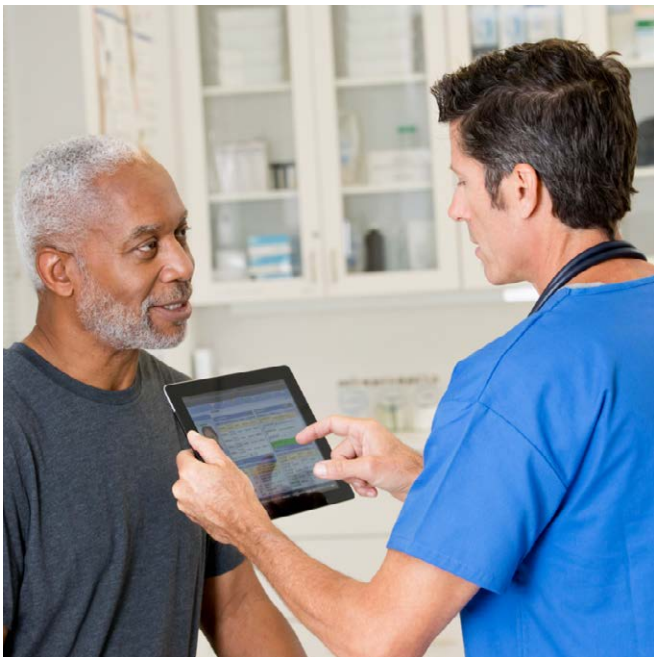
1. Scope

This document will cover the legislative aspects associated with clinical evaluation under Regulation (EU) 2017/745 (MDR) from a Notified Body perspective. The document will not describe how a clinical evaluation should be performed for individual device technologies or classifications, however it will guide manufacturers on best practice related to the development of their clinical evaluation documentation under the MDR.



2. General Considerations for Submissions

2.1 Update frequencies and alignment of documentation

Manufacturers may need to apply different cadences for updating documents within the technical file, potentially leading to their misalignment. It is vitally important to ensure that information is consistent between all documents submitted to the Notified Body as part of the conformity assessment. If the Notified Body observes that, e.g., device details, specifications, or claims differ between documents, then the manufacturer will likely be challenged on this.

The clinical evaluation documentation, including the clinical evaluation report, requires its update frequency to be defined and justified. It is important to consider, at the time of submitting documentation to the Notified Body for conformity assessment, whether the predefined update frequency of documents is appropriate considering, e.g., the classification and the risk profile of the device, combined with the level of research activity within the technical and/or medical field.

It is normally expected that clinical evaluation documentation is updated immediately prior to its submission for assessment. Updates are required whenever relevant new information is identified.[1]

2.2 Final Versions of documents

Manufacturers must always submit the final versions of documents to the Notified Body for conformity assessment. These should be version-controlled and signed as approved by all relevant stakeholders prior to being submitted. Evidence of electronic signatures is accepted by the Notified Body. If documents are updated after their submission, but prior to their assessment by the Notified Body, then the manufacturer should make efforts to inform their Scheme Manager.

1 MEDDEV 2.7/1 rev 4 Section 6.2.3

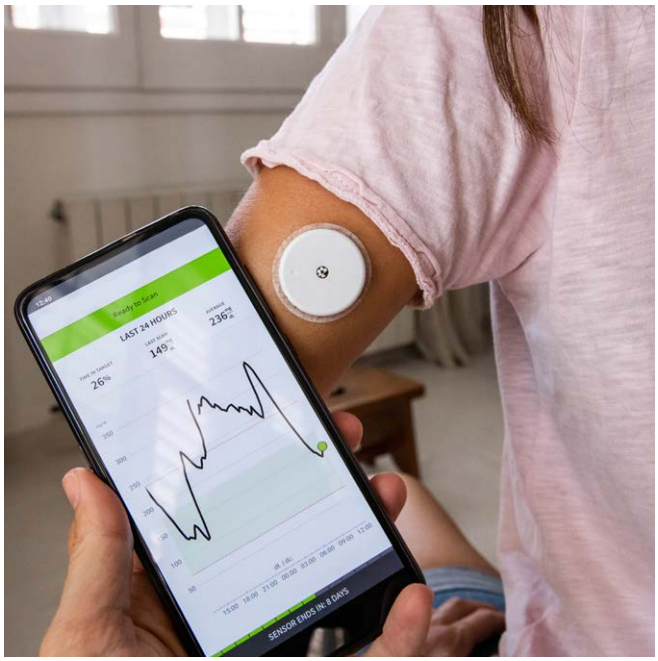
2.3 Clarity of regulatory pathway: the clinical route to conformity

Manufacturers have options in terms of how they collect the clinical data[2] they require to support the performance and safety of the device.

The default position, according to the MDR, is that all medical devices require clinical data to support the GSPRs relating to performance and safety. Clinical data should be generated by means of properly designed clinical investigations of the device subject to conformity assessment.

Alternatively, depending on several factors including the risk classification of the device, other routes to conformity may be permitted, e.g., claiming equivalence to another device. It could be that several routes to conformity are viable and it might, in some cases, be acceptable to combine clinical data obtained via multiple routes.

The choice of regulatory pathway and its justification should be clearly presented within the clinical evaluation documentation.



2 'clinical data' is defined in MDR Article 2(48)

3. The Clinical Evaluation Documentation

3.1 The Clinical Evaluation Plan

A good clinical evaluation starts with a good clinical evaluation plan (CEP): without a well-defined clinical evaluation plan the clinical evaluation report (CER) may fail to meet the requirements of the MDR. This will result in challenges from the Notified Body during the conformity assessment and may even result in refusal of the application.

The clinical evaluation should be carried out according to the CEP, while the CER should reference the CEP. There should be clear alignment of their content.

The CEP should include a plan for any clinical investigations to be conducted in support of, e.g., planned changes/modifications to the device. This is referred to as the clinical development plan, which is discussed below.

The MDR is relatively prescriptive when it comes to the content required to be covered within the clinical evaluation plan (CEP): manufacturers should refer to Annex XIV Part A 1(a). An explanation of each requirement is presented below.

a) *An identification of the general safety and performance requirements that require support from relevant clinical data*

The GSPRs relate to all aspects of safety and performance, including those related specifically to clinical safety and performance and clinical benefit(s).[3] The MDR, therefore, requires manufacturers to identify, within the CEP, which of the GSPRs require support from clinical data. It is generally accepted that, for most medical devices, a minimum of at least GSPR 1, 5 and 8 will require support in the form of relevant clinical data. Lifetime (GSPR 6) is also likely to require support from clinical data. Although not required, a justification as to why the GSPRs identified in the CEP require support from relevant clinical data can assist the Notified Body in determining whether the manufacturer has adequately identified all the applicable GSPRs that require support from relevant clinical data for the device under assessment.

3 'clinical benefit' is defined in MDR Article 2(53)

b) *A specification of the intended purpose of the device*

Manufacturers should refer to MDR Article 2, which provides a definition of 'intended purpose'. The intended purpose of the device should be clear and unambiguous. Statements that are vague or nebulous will invite scrutiny from the Notified Body and so it is important to be concise, specific and accurate. Ensure that, in all instances in which the intended purpose is cited within the technical documentation, the wording exactly matches what is stated within the CEP. If, for any reason, the intended purpose changes over the course of the clinical evaluation, this should be clearly explained and justified within the clinical evaluation report.

c) *A clear specification of intended target groups with clear indications and contra-indications*

The intended target group may be specific in the case of some devices and general in the case of others. In either case, it is important that manufacturers demonstrate an awareness of the groups of patients that will benefit from the device. Where appropriate, the specification should include details such as the grade/stage of disease that the device is indicated for, as well as any limitations that apply. For example, there may be (sub)groups of patients for which the use of the device would not be indicated and this should be clearly stated within the CEP. Where the use of a device by particular group(s) and/or under certain circumstances is deemed hazardous, the manufacturer is expected to include a list of contra-indications.

d) *A detailed description of intended clinical benefits to patients with relevant and specified clinical outcome parameters*

The MDR requires that manufacturers describe the intended clinical benefits to patients within the CEP. In many cases, these will align with the intended purpose statement. However, manufacturers can sometimes have difficulty expressing the clinical benefits as benefits afforded to the patient. It is useful therefore to ask the following questions:

- How does the use of the device improve the health of the patient?
- What is the positive outcome of using the device, from the perspective of the patient?

Further, the MDR expects that manufacturers specify the relevant outcome parameters that enable them to demonstrate that these benefits are delivered by the device. It can be thought of in the following way:

- If device x is going to have positive outcome y on the patient, what aspect of y can be measured to confirm that the outcome is achieved?

The target score and follow-up interval will be defined on the basis of the current state of the art in medicine and documented within the CER. For many devices, the relevant outcome parameters will be obvious. However, for some devices, e.g., those used for imaging, it may be more challenging for manufacturers to define outcome parameters. In these cases, outcome parameters may only be *indirectly* related to the clinical benefit. Where the clinical benefit is not directly afforded to the patient, manufacturers should clearly state this and provide a justification as to why the specified outcome parameters are considered appropriate.

e) *A 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*

The MDR expects manufacturers to specify, within the CEP, the methods they will use to evaluate the risks posed by the device. It is important, therefore, to describe in detail the methods by which information relating to the risks posed by the device will be collected and analysed – both qualitatively and quantitatively. This requirement is related to the risk assessment, which should include risks that are identified as part of the clinical evaluation of the device, with the aim of defining, for example, the maximum acceptable occurrence rate based on the state of the art. Manufacturers should include details of how they intend to identify clinical risks as part of the clinical evaluation and should also make clear their intention to determine the residual risks (i.e., post-mitigation) and side-effects associated with the device.

f) *An 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*

Like the requirement to define relevant outcome parameters, manufacturers need to specify the parameters that will enable them to determine whether the device has an acceptable benefit-risk ratio. These parameters may be the same as those described in paragraph (d) above. The benefit-risk ratio needs to be assessed in relation to the current state of the art. In other words, the outcomes achieved by use of the device should be comparable to (or better than) those achieved by means of alternative devices. It is therefore important that appropriate parameters are selected in order for manufacturers to demonstrate this. It is expected that these will align with the risk acceptability parameters in the risk management file. Where it is not possible/ desirable to compare the differences between devices or alternative treatments, for example, where the relevant parameters have changed over time, efforts must be made to meet the requirements of Annex XIV, Part B, Section 6.1(d). If historically used parameters are no longer the state of the art, then PMCF studies may need to be considered.

g) *an indication how benefit-risk issues relating to specific components such as use of pharmaceutical, non-viable animal or human tissues, are to be addressed*

Some medical devices feature hazardous components such as pharmaceutical, non-viable animal or human tissues. The inclusion of these components should be justified in respect of the state of the art, especially where there exist benchmark devices that do not include such components. Since the action(s) of these may need to be considered separately from the overall device, the manufacturer should explain how they intend to assess the benefits and risks posed by these components as part of the overall clinical evaluation of the device. Where the long-term exposure of the drug or material in its particular application is not fully known, this may also point to a requirement for follow-up studies.[4] Where devices do not feature such components (or similar hazardous components), it is sufficient to confirm this within the CEP.

h) *a 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*

The final statement in the list in Section 1(a) mentions a clinical development plan (CDP). The CDP determines how a manufacturer will collect sufficient clinical data for evaluation. The clinical development plan should summarise the clinical investigations that the manufacturer plans to conduct to support the development and validation of the medical device, including any future modifications. If investigations have already been conducted, it is generally expected that these are briefly summarised. In the case of devices that have already been placed on the market, a clinical development plan is still required: in this case, the manufacturer should confirm whether all the required clinical data has been collected and summarise their plans for collecting clinical data in the post-market phase (with reference to the PMCF plan).

4 MDR Annex XIV, Part B, Section 6.1(a)

3.1.1 Defining the State of the Art (SOTA), Clinical Benefits and Safety and Performance Objectives

Within the MDR there is an expectation that manufacturers consider the acceptability of risks when weighed against benefits, taking into account the generally acknowledged state of the art[5]. Annex XIV Part A requires that the clinical evaluation plan include a specification of parameters for determining the acceptability of the benefit-risk ratio, based on state of the art.[6] The state of the art may be defined as:

"Developed stage of current technical capability and/or accepted clinical practice in regard to products, processes and patient management, based on the relevant consolidated findings of science, technology and experience."[7]

It is therefore generally considered that the state of the art embodies what is currently and generally accepted as good practice in technology and medicine. The state of the art does not necessarily imply the most technologically advanced solution.

The state of the art described here is sometimes referred to as the "generally acknowledged state of the art".

The term 'clinical benefit' is defined in the MDR.[8] It is expected that there will be sufficient clinical evidence available to support the clinical benefits claimed by the manufacturer. The required amount and quality of the evidence is dependent on the risk classification, device complexity, intended use and indications, intended users and the intended patient population.

Not all devices will have a *direct* clinical benefit attributed to them. Where there is no direct clinical benefit based upon the intended use of a device, the manufacturer should consider the level and type of clinical evidence that is required to support the clinical benefits claimed.

Manufacturers should define safety and performance objectives for their device in the context of the state of the art. The objectives should be both clinically meaningful and measurable, enabling comparison of the device with, e.g., competitor/benchmark devices and other alternatives (including pharmacological and other interventional treatments).

5 MDR Annex I, Chapter I, 1
6 MDR Annex XIV, Part A, Section 1(a)
7 IMDRF/GRRP WG/N47 Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices
8 MDR Article 2(53)

3.2 The Clinical Evaluation Report (CER)

Article 61(12) of Regulation (EU) 2017/745 requires the manufacturer to document the clinical evaluation, its results and supporting clinical evidence in a clinical evaluation report. Appendix 9 of MEDDEV 2.7/1 rev 4 provides an example of the contents of the clinical evaluation report, however it should be noted that there are additional considerations for documenting the clinical evaluation under the MDR.

3.2 1 Updating the Clinical Evaluation Report

Clinical evaluation is a continuous process and the CER should be regarded as an output of this process. There will be outputs of other activities, such as PMCF reports and periodic safety update reports (PSUR), that will necessitate updates to the CER. Refer to section 2.1 above.

When updating the report, it is expected that the manufacturer will repeat literature searches to identify new data on the device under evaluation but also to verify that the device remains the state of the art, as discussed in section 3.1.1 above. This is also a requirement of the PMS plan per Annex III.

Article 61(11) makes clear that annual updates to the clinical evaluation and supporting documentation are required for class III and implantable devices. Whilst article 61(11) does not specify any frequency for updates to the CER for Class IIa/IIb non-implantable devices, consideration should be given to other activities that impact the clinical evaluation, for example the frequency of updates to the PSUR. Justifications should be provided.

3.2.2 Competency and Declarations of Interest

The evaluators/authors of the CER should have appropriate experience of the device and/or intended patient population. It may be justifiable in the case of low-risk, standard-of-care devices for those with a general medical background to support the assessment. Typically, however, it is expected that at least one of the evaluators/authors will have appropriate specialist medical competence, especially in the case of high-risk devices.

The evaluators/authors should verify the clinical evaluation report, providing confirmation through a formal statement that they have approved the content of the report. The report should be dated and signed by all evaluators/authors.

Manufacturers should provide an updated *curriculum vitae* and a signed and dated declaration of interests for each evaluator/author involved in the evaluation.

Appendix 11 of MEDDEV 2.7/1 rev 4 provides a clear list of all aspects that should be included within the declaration of interests. Caution should be exercised when an evaluator/author of the CER has also been an investigator for any clinical studies of the device, as this presents a risk of bias. In these circumstances, manufacturers may wish to consult alternative clinical experts with appropriate competency and impartiality to approve the clinical evaluation report.

3.2.3 Documenting the Device Description in the CER

Documenting a clear and comprehensive description of the device under evaluation is critical not only to help the assessor understand your device but also to verify that you have been able to retrieve meaningful data from the literature.

Appendix 3 of MEDDEV 2.7/1 rev 4 is still valid under the Medical Device Regulations (MDR) by virtue of its citation within MDCG 2020-6 and provides a good basis for the content of the device description in the CER. For the purposes of the MDR, there are some new considerations that need attention when describing the device.

When describing the device(s) please consider the following information, which is taken from Appendix 3 of MEDDEV 2.7/1 rev 4:

- a concise physical and chemical description
- the technical specifications, mechanical characteristics
- sterility
- radioactivity
- how the device achieves its intended purpose
- principles of operation
- materials used in the device with focus on materials coming in contact (directly or indirectly) with the patient/user, 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
- other aspects

3.2.3.1 Version and regulatory/design history

Although the device description should reflect the current version/model of the device, it is equally important to consider the history of the device in the device description. This includes both its regulatory history and its design history. All previous versions of the device should be listed in the device description along with an explanation of the changes and the reasons for these.

Providing clear information about the regulatory history of the device gives the assessor an understanding not only of its current regulatory status but also of any previous placement of the device on the market. If the device is a legacy device, (i.e., a device that is certified under MDD 93/42/EEC or AIMDD 90/385/EEC) the following information should be provided:

- The date of first CE marking
- The most recent CE certificate number
- Classification/rules and any changes to the classification
- Number of units placed on the market to date
- Justification for any gaps in the history, i.e., where the device was not CE-marked

If your device is new to the EU under the MDR, consideration should be given to:

- Description of where the device has been approved and the regulatory authority that approved it, e.g., UKCA, TGA, FDA
- Date of first regulatory approval
- The status of any regulatory issues such as FSN, or open FSCA, to aid the assessor in understanding the current regulatory compliance of the device

3.2.3.2 Variants and Accessories

The CER should list the name of the device along with all available sizes and variants. The CER should also list all the devices in the scope of its use that comprise part of the evaluation. This might include accessories and software. Including images in your device description is essential. Where appropriate, images should include the steps/process required to use the device. It is important to note that clinical evidence is required to support all variants and accessories of a device. It must therefore be demonstrated that, in cases where a single body of evidence is presented in support of multiple variants, that those variants are demonstrated to be equivalent to one-another.

Each UDI-DI should be listed alongside the device and its variants/accessories. This allows the assessor to cross-check the CER against other documentation, such as the summary of safety and clinical performance (SSCP). The Basic UDI-DI that covers the combination of devices within the CER should also be documented.

Where it is claimed that the device is compatible with devices of other manufacturers, these devices should be listed alongside other critical information, such as the name of the legal manufacturer and the regulatory status of the devices.

3.2.3.3 Intended Purpose and Indications

The device description should provide a clear statement of the intended purpose of the device and, where appropriate, a list of all indications. If there have been changes to the intended purpose/indications of a device, providing the context of these helps the assessor to determine their impact on the overall clinical evaluation. A clear list of all contra-indications, warnings/precautions should also be provided. Ensure this information is consistent across all the technical documentation.

When considering the indications for the device, these should be thought of as a checklist of eligible criteria that qualifies the patient to receive the device. This means they should be specific and unambiguous. Not all devices have indications: examples could be sterilisers or washer-disinfectors. However, any absence of an indication should always be strongly justified.

3.2.3.4 Patient populations/Users

The patient population for the device should be described, considering aspects such as gender, age, stage/severity of disease, along with consideration of other factors such as mobility. The intended users of the device should be specified such that it is possible to identify their profession, along with their stage of seniority and sub-speciality (in the case of intended users who are healthcare professionals).

3.2.3.5 Contraindications, Warnings, Precautions & Limitations

All contraindications, warnings, precautions, and limitations should be listed in the clinical evaluation report.

Contraindications are conditions under which the device should not be used because the risk of use clearly outweighs any possible benefit. Warnings and precautions tell the reader about hazards, other than those that are contraindications to device use. Warnings and precautions provide information on how to avoid these hazards, i.e., sources of harm in the use of the device.[9]

3.2.3.6 Novelty

When describing your device within the Clinical Evaluation Report, please consider using the table opposite. This can be used to describe any novel features of your device and the potential health or clinical impact of these; **alternatively**, it may be used to demonstrate why the device is not considered novel in these specific areas.

Note that it is not sufficient to state only that the device has already been placed on the market and that there have not been any significant changes to it: novelty should be considered both in terms of technical characteristics as well as in respect of how the device is used, or deployed.

This will help the assessor to make informed decisions regarding the applicability of the clinical evaluation consultation procedure (CECP).

Clinical or Surgical Procedure Novelty Dimensions

	Is there novelty? Yes /No	If Yes: specifically describe novel features and any potential clinical or health impact If No: provide evidence/ justification to demonstrate non-novel features
Mode of Use or Treatment Option		
Device-Patient Interface		
Interaction and Control		
Deployment Methods		

Device Related Novelty Dimensions

Medical Purpose		
Design		
Mechanism of Action		
Materials		
Site of Application		
Components		
Manufacturing Process		

3.2.3.7 Lifetime Statement

It is essential to define the lifetime for the device, which should be specified in e.g., minutes/days/months/years. This allows the assessor to ensure that the clinical data and/or PMCF plan is appropriate to meet the requirements of Annex XIV. Claims of indefinite lifetime are not acceptable.

9 Guidance on Medical Device Patient Labelling; Final Guidance for Industry and FDA Reviewers Document issued on: April 19, 2001

3.2.4 Documenting Equivalence

Claiming equivalence may be an option for manufacturers who seek to gain initial market access for their device, depending on several factors including the risk classification of the device. Note that manufacturers of legacy devices or devices for which a manufacturer already possesses sufficient clinical data are not normally expected to follow this route.

In case equivalence is being claimed, it is important to clearly identify the device to which equivalence is claimed. There should be a clear description of the claimed equivalent device, including its name, model, size, version, settings and components of the device that are presumed to be equivalent, including any software and accessories.

It is also important to document the regulatory history and the legal manufacturer of the claimed equivalent device. In terms of regulatory history, the same kind of information should be provided in respect of the claimed equivalent device as for the device under evaluation.

Whilst it is possible to claim equivalence to more than one device, for each device all aspects of equivalence need to be demonstrated in terms of technical, biological and clinical equivalence. In most cases under the MDR, it will only be feasible and/or appropriate to claim equivalence to one device.

MDCG 2020-5[10] provides a template for use when demonstrating equivalence and, where possible, this should be used. When providing scientific justifications to support differences, it is critical to include the evidence/articles with your submission and to clearly reference these within the equivalence discussion.

A clear and comprehensive analysis of why the differences do not impact clinical performance and safety is required for all sections of the table. Single-word conclusions are not acceptable and will invite scrutiny from the Notified Body.

3.2.4.1 Class III and implantable Devices claiming equivalence to the device of a different legal manufacturer

For equivalence to be claimed with a class III or implantable device of a different manufacturer the following conditions need to be met by the claimed equivalent device[11];

- Valid CE certificate **under MDR**
- Contract in place allowing full access to technical documentation
- PMCF plan includes post market studies[12]

In this situation BSI requires the following evidence that the manufacturer meets the requirements of Article 61(5):

- Copy of MDR certificate (until EUDAMED is fully-operational)
- A contract/agreement that explicitly states there is ongoing access to the technical documentation, signed by **BOTH** parties

3.2.4.2 Consideration of data from Similar Devices

MDCG 2020-6[13] defines similar devices as:

'similar device': devices belonging to the same generic device group. The MDR defines this as a set of devices having the same or similar intended purposes or a commonality of technology allowing them to be classified in a generic manner not reflecting specific characteristics.

10 MDCG 2020-5 Clinical Evaluation – Equivalence A guide for manufacturers and notified bodies April 2020

11 MDR Article 61(5)
12 MDR Article 61(4)
13 MDCG 2020-6 Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC A guide for manufacturers and notified bodies April 2020

Data pertaining to similar devices can be used as evidence of the availability of existing treatment/diagnostic options for the clinical condition under consideration, including other devices on the market. This can be advantageous in cases where there is an absence of data reported in the state of the art clinical literature and may help support the use of surrogate objectives/endpoints. When documenting the discussion of similar devices, identification of the sources of data is essential.

An understanding of similar devices in respect of their performance and safety can also help support the manufacturer with the activities mentioned in Annex III in relation to the PMS plan.

Note that it is important that manufacturers do not attempt to describe similar devices as being 'equivalent' devices: In the context of the MDR, the term 'equivalence' has a different legal interpretation. Claiming that a similar device is an equivalent device will invite scrutiny from the assessor. Furthermore, data solely from 'similar devices' may not be used as evidence of the safety and performance of the device under evaluation. It can be used, however, as supplementary evidence to support the overall clinical evaluation of the device.

3.2.5 Documenting Clinical Claims

The MDR requires that the clinical evaluation shall be thorough, objective and take into account both favourable and unfavourable data.[14] Its depth and extent shall be proportionate and appropriate to the nature, classification, intended purpose and risks of the device in question, as well as to the manufacturer's claims in respect of the device.

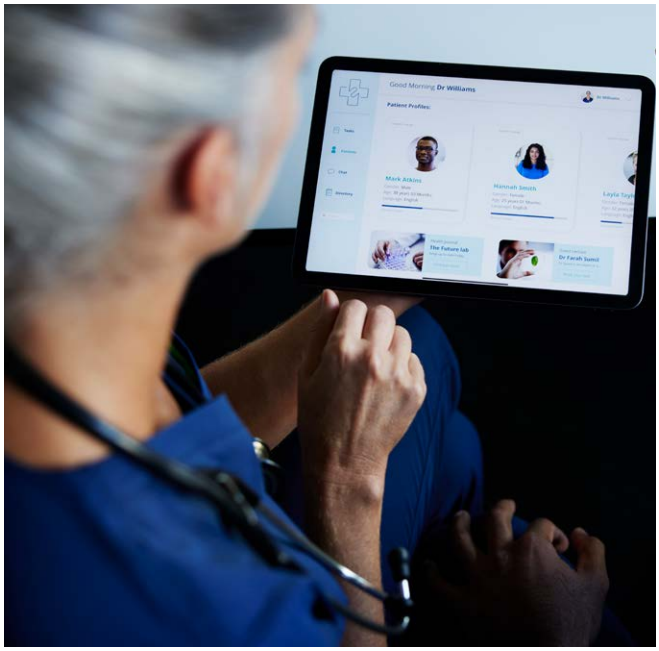
A section within the CER should be dedicated to listing all clinical and any non-clinical claims. Consider tabulating the claims with a direct reference to the data that supports each claim, so that this can be verified by the assessor.

3.2.6 Performing and Documenting Literature Searches

Several literature searches may need to be conducted depending on the device under evaluation:

- A literature search needs to be conducted to define the state of the art for the clinical condition to be diagnosed/treated. This will help formulate the safety and performance objectives of the device under evaluation.
- A second literature search needs to be conducted on the device (or its equivalent) to identify existing favourable and unfavourable clinical data covering all sizes/variants, where data is not held by the manufacturer. This data will help support the conformity assessment and ensure there is data covering the scope of the devices under evaluation. This search may not be required where the device is new or has not been placed on the market previously. A justification should always be provided in these cases.
- Additional literature searches may be needed to specifically demonstrate safety/performance in respect of other aspects of the device and/or complications to confirm, e.g., the long-term outcomes of an undesirable side effect. This evidence can help to build a stronger body of evidence for the device under evaluation.

There is an expectation that the search protocol is comprehensive, i.e., that effort should be made to retrieve all available data, including, e.g., published guidance, to demonstrate that selection bias has been minimised. In principle, it should be possible for the assessor to replicate the searches, based on the information presented in the CER.



The protocol should include the following as a minimum:

- The use of multiple databases with clear justifications for choosing those databases 
- A clear search protocol which employs a validated method such as PICO or PRISMA 
- Clear and exact search terms to ensure appropriate identification of the data 
- Details of additional methods used to identify articles, e.g., internet searches for unpublished information such as competitor IFUs, along with their justification 
- Dates of data searches and justifications for publication date ranges 
- Clear exclusion and inclusion criteria and justification for these choices 
- A clear strategy for considering data already held by the manufacturer and supplication of returned results 
- A data collection plan that defines data management practices to ensure data integrity during extraction (e.g., quality control/second review of extracted data by additional reviewer) 

3.2.6.1 Appraisal Plan

The appraisal plan needs to be clear and applied consistently. It should take into consideration the following:

- **Suitability** - Is the data *clinical data* as defined in MDR Article 2(48)?
- **Applicability** - Is the data on the device under evaluation or the equivalent device?
- **Population** - Is the population reflective of the intended purpose and indications of the device?
- **Sufficiency** - Is the data of sufficient quality and quantity?

MEDDEV 2.7/1 rev. 4, Appendix 6 guides the manufacturer in identifying potential flaws in the data, such as:

- A lack of information on elementary aspects, such as methods, patient population, side-effects, or clinical outcomes
- Statistically insignificant data or improper statistical methods
- A lack of adequate controls leading to bias or confounding
- The improper collection of mortality and serious adverse events data
- Misinterpretation of data by the authors, such as when the conclusions they draw are not in line with the results section of the report
- Any illegal activities, such as clinical investigations that were not conducted in compliance with local regulations

3.2.6.2 Documenting the Results of the Clinical Literature Search

The focus of the analysis should be on the data that holds the highest sufficiency (quality and quantity). These are the articles that the appraisal plan has identified as having the heaviest weighting. Therefore, these articles should support the overall conclusions.

The data should be reported in a scientific manner, avoiding any bias. Stratifying the data in a table format with consideration of the indications is an option when the intended purpose of the device concerns multiple populations and/or variants. The analysis should be based on the full text of included articles. It is expected that copies of key articles included in the analysis are submitted to the Notified Body along with the CER. The Notified Body may request copies of other referenced articles as part of the conformity assessment process.

3.2.7 Documenting Clinical Investigations

Clinical investigations are mandatory for all new class III and implantable devices under the MDR. There are some exemptions mentioned in article 61(4) of the EU MDR, including:

- where there is a successful claim of equivalence
- when modifications are made to a device already marketed by the same manufacturer
- devices considered WET per article 61(6)(b)

Article 61(7) requires manufacturers who have not conducted clinical investigations for class III and implantable devices due to the exemptions mentioned above to provide a justification within the CER. Please note this does not exempt class IIa and IIb non-implantable devices from performing clinical investigations and due consideration of the requirement for clinical investigations should always be given to the device under evaluation.

The Notified Body is required to assess all clinical investigations as part of the conformity assessment. Documenting sufficient detail of the clinical investigations and ensuring the correct documentation accompanies the CER is essential to ensure the Notified Body assessment can confirm the data provided.

Clinical investigations initiated on or after 26th May 2021 must be conducted to the requirements of Articles 62-82 and Annex XV of the Medical Device Regulation EU 2017/745 or ISO14155. Clinical investigations initiated before 26th May 2021 shall have been conducted in accordance with Directive 93/42/EEC, Directive 90/385/EEC or ISO14155.[15]

Note that ISO14155 was updated in 2020 to reflect the changes in requirements related to clinical investigations under the MDR. Compliance to ISO14155:2020 is considered compliance to the MDR (although we are yet to see an official announcement of its adoption, other than its reference within MDCG 2020-13). Compliance to ISO14155:2020 is typically required when clinical investigations are conducted outside of the EU and consideration should always be given to local authority requirements.

When submitting clinical investigation data, the Notified Body is required to verify the following supporting documentation as a minimum:

- Clinical Investigation Plan(s)
- Completed Clinical Investigation Reports, signed by the Principal Investigator
- Evidence of communication - and of no objections - from the ethics committee
- All regulatory approvals of the clinical investigation (from all countries, including outside of the EU)
- Investigator brochure
- Sample of the informed consent
- Statistical analysis plan
- Evidence of public registration (if applicable)

15 MDR Article 120(11)

If any deviations from the protocol occurred, then justifications should be provided with copies of the original and amended protocols, together with evidence of relevant approvals.

If there is missing or incomplete information, then the manufacturer should always provide an explanation. Note that in cases where legacy devices rely upon data from historic clinical investigations (and where the outcomes of these were not published), the Notified Body will expect to receive all relevant documentation as per the above list.

The Notified Body assessment will focus on seven key aspects of clinical investigations:

- Ethics
- Study design
- Study locations
- Patient population
- Patient numbers
- Objectives and endpoints
- Length of follow-up and intervals

3.2.7.1 Ethics

Annex XV Chapter I Section 1 of the MDR requires clinical investigations to have been carried out in accordance with recognised ethical principles:

- The initial study design, through to publication should consider ethical principles
- Ethics and the practice of obtaining consent should be considered, also where vulnerable populations are involved[16]
- *Recognised ethical principles* should be considered in respect of the most recent version of the Declaration of Helsinki[17]
- Evidence of ethics committee approval/no objection and a sample of the consent form are always required for conformity assessment

3.2.7.2 Study Design

Annex XV, Section 2 of the MDR discusses the need for the procedures and design of the study to be appropriate to the device under investigation. The design of the study should be appropriate to the device under investigation, e.g., RCT, single-blind, double-blind, retrospective or prospective, interventional or observational, etc.

It can be difficult for the Notified Body to understand the rationale behind the chosen design. Therefore, always provide a rationale in the CER, considering aspects such as why the design was more likely to confirm or refute the claims related to safety or performance compared with other designs. The rationale may also point to clinical investigations of other, similar devices to demonstrate that the design of the study is common for the type of device.

3.2.7.3 Patient Population

Annex XV, Section 2.4 of the MDR requires clinical investigations to be performed in a clinical environment that is representative of the intended

17 World Medical Association Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects, Adopted by the 18 WMA General Assembly, Helsinki, Finland, June 1964

16 MDR Articles 63-69

use of the device under normal conditions and in the *target patient population.* The patient population should be clearly defined and include the stage and severity of disease, age, co-morbidities and discussion of how these compare with the intended purpose. This information should align with the clinical evaluation plan.

Consideration and justification should be given as to why certain inclusion and exclusion criteria have been applied, particularly in cases where the intended purpose includes patients who were excluded from investigations.

3.2.7.4 Patient Numbers

Annex XV, Section 2.1 of the MDR requires that the clinical investigation shall include a minimum number of observations to guarantee scientific validity (note the term 'observations' rather than 'subjects'). A statistical analysis plan (SAP) is always required alongside the clinical investigation plan as part of the conformity assessment. A strong rationale for the SAP design and chosen methodology is always required. Ensure a biostatistician has had input to the SAP. An SAP that includes the use of rare methods will invite scrutiny from the Notified Body and will likely require an additional review by an expert biostatistician.

3.2.7.5 Objectives and Endpoints

Section 2.6 of Annex XV requires that clinical investigations address the intended purpose, clinical benefits, safety and performance of the device and that all endpoints are scientifically validated. The primary endpoint must be appropriate and clinically relevant. Note that a feasibility study is not considered a confirmatory investigation of intended purpose, clinical benefits, safety or performance.

The primary endpoint should reflect the clinical benefit and be both quantifiable and meaningful. Primary endpoints that are safety-orientated are typically associated with feasibility studies. The CER should discuss why endpoints were chosen and how they have been scientifically validated.

3.2.7.6 Length of Follow-Up and Intervals

Annex XV Sections 2.2. and 2.3 of the MDR discuss the need for the research methodologies and procedures to be appropriate for the device under evaluation.

Consideration should be given to the follow-up methods and intervals between data collection. The duration of follow up should be appropriate to capture the correct data at clinically meaningful timepoints. A justification should be documented as to why follow-up was conducted at the chosen timepoints.

The study duration should be sufficient considering the device under investigation.

3.2.7.7 Study Locations

Per Annex XV, Section 2.4 of the MDR, which requires that clinical investigations be performed in a clinical environment that is representative of the intended use of the device under normal conditions and in the target patient population, it is important to include the following details:

- clinical investigation sites, including locations and the type of environment, e.g., the surgical theatre or minor surgery room, tertiary care centre, etc.
- differences in patient populations between sites: even across the EU there can be significant differences between patients
- differences in surgical techniques or post-operative care between sites
- Reference to national/society guidance that confirms the location/skill-set/post-operative care for such procedures and, where applicable, confirmation that the investigation adheres to this
- where the device is novel, how it will be placed on the market, e.g., if a phased market launch is required to allow for adequate training

3.2.7.8 Stratifying the Clinical Data

Stratification of data within the CER can help provide transparency, particularly when there are multiple variants associated with a device. Taking this approach can result in fewer questions from the Notified Body and, consequently, a more efficient conformity assessment.

Stratification of data can be applied to all variants for all classifications. An example table has been provided overleaf but other formats may be acceptable. By stratifying the data, the evaluator is immediately able to identify the data held for each variant and can also understand where PMCF activities may be required to complement existing data.

Variant 1: name/image/description	
Data sources/ quality/CER location	Name the source of data for the variant, including data from the literature, clinical investigations and PMS/PMCF and provide details of where the evidence can be located within the CER
Safety data summary	Provide a summary of safety information derived from all sources of clinical data
Performance data summary	Provide a summary of performance information derived from all sources of clinical data
Comparison to state of the art	Consider whether the clinical data for each variant is aligned with the safety and performance objectives, based on the state of the art
Claims supported	Provide information on any clinical benefit claims for the variant and whether the clinical data is supportive
Indications supported	Consider whether the clinical data covers all indications for the variant
Cohort/lifetime, PMCF follow-up appropriate	Consider whether there is sufficient data to support the claimed lifetime of the variant, with reference to the type of PMCF activity to be conducted to capture additional data, where necessary
Compatibility considered	Clarify whether the clinical data for the variant considers any claimed compatibility or configuration options
New risks observed Adverse events/ complications considered in risk management	Identify any new risks associated with the variant, describe how these have been considered within risk management and, where appropriate, how new risks will be considered in the context of PMS/PMCF

It is unlikely that manufacturers would have a substantial amount of data for a device that has low rates of use, e.g., in the treatment of rare conditions. The situation can be similar for variants of devices that are at the extreme ends of the size range. Careful consideration needs to be given, therefore, to determining a sufficient quantity of data in such cases. In accordance with Article 61(1), manufacturers should always provide a robust justification along with data on incidence and sales volumes.

3.2.8 Overall benefit-risk analysis and conclusions

As part of the clinical evaluation process the manufacturer should conduct a scientific analysis of the benefit-risk ratio of the device(s) under evaluation, based on all available data. Brief statements summarising the benefit-risk ratio that do not consider all the available evidence will invite scrutiny by the Notified Body.

The purpose of the benefit-risk analysis is to consider holistically all clinical data to be able to draw conclusions confirming that the benefits outweigh the risks. Consideration should also be given to the state of the art and how the device compares as a treatment/diagnostic option, as well as to any additional risks identified and how these are deemed acceptable when weighed against the benefits of the device. Note that when documenting the benefit-risk, it is not sufficient to merely reference the risk management file, since the CER is a stand-alone document.[18,19]

Involving those with medical qualifications who have experience of using the device in the analysis can be helpful in drawing benefit-risk conclusions: healthcare professionals who use the device will understand its benefits to patients and whether risks can be deemed acceptable.

The documentation of risk within the CER should discuss key risks (e.g., use in high-risk populations), the likelihood of occurrence, any mitigations and objective evidence that the benefit-risk ratio meets pre-defined acceptance criteria. This information should align with the risk management file.

The clinical risks identified when defining the state of the art should be considered within the risk analysis and occurrence rates should be quantitative and align with any post-market surveillance data. Residual risks must be communicated within the IFU.

18 MEDDEV 2.7/1 rev 4, Sections 8.1, 10.2(b) and A12.2.2
19 MDCG 2020-6

3.3 PMS & PMCF

3.3.1 The PMS Plan

The PMS plan shall comply with (and is assessed against) the requirements of the technical documentation: Annex III, Section 1.1(b) of the MDR lays out the minimum requirements and refers to other sections of the MDR, all of which must be clearly and comprehensively addressed within the manufacturer's PMS plan or via direct referencing and summarisation of procedures.

Referring to Annex III, Section 1.1(b), as a minimum, the PMS plan must describe:

a) a proactive and systematic process to collect any information referred to in point 1.1(a). The process shall allow a correct characterisation of the performance of the devices and shall also allow a comparison to be made between the device and similar products available on the market

The PMS plan should include details of the proactive methods used to collect the information referred to in Annex III, Section 1,1(b), including the frequency the process occurs and with whom the responsibility lies to collect such information. Note that the term 'proactive' implies that the manufacturer does not wait for information to be received (e.g., via customer complaints) to collect and evaluate performance or safety data. Proactive methods generally include, e.g., PMCF, user surveys, focus groups and other activities that *generate new data*. Reactive methods include inputs such as from vigilance,[20] complaints analysis and literature searches. This part of the plan should demonstrate how the manufacturer will compare the post-market experience of their device against identified benchmark devices.

b) effective and appropriate methods and processes to assess the collected data

It should be clear from the PMS plan how each source of data is assessed, including details of how the methods and processes employed are effective at assessing the type of data and are appropriate for the medical device under evaluation, considering classification, risk profile, etc. A higher risk device may require, for example, specific PMCF activities.

c) suitable indicators and threshold values that shall be used in the continuous reassessment of the benefit-risk analysis and of the risk management as referred to in Section 3 of Annex I

Indicators and threshold values to be used during the reassessment of the benefit-risk analysis should be clearly specified. It should be explained why indicators and threshold values are appropriate considering the state of the art and the conclusions of the clinical evaluation.

d) effective and appropriate methods and tools to investigate complaints and analyse market-related experience collected in the field

The PMS plan should directly reference procedures for complaint investigation and for the analysis of market-related experience. The summary of the procedures within the PMS plan should clarify why such methods are appropriate and effective.

e) methods and protocols to manage the events subject to the trend report as provided for in Article 88, including the methods and protocols to be used to establish any statistically significant increase in the frequency or severity of incidents as well as the observation period

MDR Article 88 outlines requirements associated with trend reporting, which is performed by the manufacturer when there is a *statistically significant* increase in (the number or severity of) incidents that are either not serious or are expected side effects of the device under evaluation. A manufacturer must possess sufficient data to be able to categorise incidents as expected side effects.

For incidents to which MDR Article 88 applies, it must be described within the PMS plan how incidents will be appropriately identified and how a statistically significant increase will be detected. The PMS plan should describe an appropriate process for reporting such incidents. References to procedures implementing MDR Article 88 should be accompanied by sufficient summary in the PMS plan.

20 MEDDEV 2.12/1 rev.8 - Guidelines on a Medical Devices Vigilance System

f) methods and protocols to communicate effectively with competent authorities, notified bodies, economic operators and users

The manufacturer is required to notify the stakeholders identified above in respect of trends, vigilance, field safety issues and corrective actions, as well updates to the device,[21] the PSUR and SSCP.[22] The PMS plan shall provide reference and summary of the procedures for implementing these requirements.

g) reference to procedures to fulfil the manufacturers obligations laid down in Articles 83, 84 and 86

Article 83 specifies the requirements of the Post Market System: Section 3 lists ways in which the collected data shall be used. The manufacturer shall provide reference to procedures that implement these requirements. Article 84 states the requirements for the PMS plan and Article 86 outlines the requirements of the PSUR. The manufacturer shall reference the procedure, and within the procedure itself, clearly detail *how* each requirement will be satisfied.

h) *systematic procedures to identify and initiate appropriate measures including corrective actions*

As a result of the analysis of the data collected in the post-market phase, to ensure that risks are minimised as far as possible, corrective actions may be required. Procedures to identify and initiate corrective actions shall be referenced and summarised within the PMS plan.

i) *effective tools to trace and identify devices for which corrective actions might be necessary*

References to tools used to track and identify devices that might require corrective actions shall be provided in the PMS plan, along with clarification as to why such methods are appropriate and effective.

j) *a PMCF plan as referred to in Part B of Annex XIV, or a justification as to why a PMCF is not applicable*

The manufacturer may choose to present the detailed PMCF plan in a separate document, in which case a reference shall be provided, along with a brief summary. If a PMCF study is not applicable, the justification shall be clearly presented within the PMS and/or PMCF plan but note that a PMCF plan is always required.

3.3.2 The PMCF Plan

The PMCF plan is a document that clearly outlines how the post market aspects of the clinical evaluation are to be executed. PMCF is used as a method of addressing gaps in the evidence supporting the clinical safety and performance of a device (and its accessories), particularly in relation to residual risks. It should also be used to help identify new/emergent risks, e.g., those associated with misuse. In cases where a device has multiple indications or target populations, PMCF can be used as a source of additional clinical data where this was relatively scarce at the time of applying the CE mark to the device. However, in the absence of sufficient pre-market data, a PMCF plan alone is not sufficient for confirming the safety and performance of the device for the purposes of conformity assessment.

Where equivalence is claimed in the CER, the following are expected to be included in the PMCF plan:

- appropriate studies to cover any differences between the subject and equivalent device, patient populations and indications, etc. Data from these studies will form the basis of the scientific justification as to why differences do not negatively impact the benefit-risk profile of the device
- appropriate confirmatory studies to cover modifications intended to improve the safety or performance of the device

Importantly, the PMCF plan must address all the individual requirements listed in Annex XIV, Part B, Section 6.1. It should be clear how the PMCF plan addresses each requirement, with details of clinical study and/or survey designs, their timings/durations and relevant endpoints in respect of the state of the art, such that the quality and quantity of evidence that will be generated by the plan can be determined by the assessor. This will also facilitate future assessments, when the assessor will verify whether the post-market clinical follow-up activities were carried out according to the PMCF plan.

Note that Annex XIV, Part B, Section 6.2 refers to both 'general' and 'specific' methods and provides examples of these. Additional guidance is also provided in MDCG 2020-7.[23] Where the manufacturer deems that PMCF is not required, this must be clearly documented along with an appropriate justification.

21 MDR Annex VII, Section 4.9
22 MDR Articles 32, 86-88
23 MDCG 2020-7 Guidance on PMCF plan template

It is acceptable for the manufacturer to reference additional documentation, such as clinical study/survey protocols, if applicable. However, it is not acceptable to submit only a clinical study/survey protocol: the PMCF plan must address all requirements within Annex XIV, Part B.

The PMCF plan should be updated as a necessary consequence of any changes in the state of the art. Procedures relating to the development and update of the PMCF plan should be referenced in the plan and, ideally, mapped to the requirements of the MDR.

Note that a PMCF plan is always required, even in cases where the manufacturer provides justification that no PMCF clinical studies are required.

3.3.3 PMCF Evaluation Report

Incorporated within the CER, the PMCF Evaluation Report documents the outputs of the PMCF plan[24] and, in the case of class III and implantable devices, is required to be updated at least annually.[25] It should provide an analysis of any ongoing PMCF activities and document and justify any deviations from the established PMCF plan.

Results of activities undertaken as part of the PMCF plan, including, e.g., interim analysis of clinical study data, should be used as input for updating the CER (and risk management) accordingly.[26] Evidence of off-label use should be documented and there should be clear consideration of this when updating the CER and the risk management documentation. It is also important to include data on claimed equivalent devices (where applicable) and similar devices as necessary, to demonstrate that the objectives of the PMCF plan have been adequately addressed.

MDCG 2020-8[27] provides a template for the PMCF evaluation report.

Note that where more frequent updates of the PMCF evaluation are necessary, it may be acceptable to provide the PMCF evaluation report as a separate document.

3.4 Additional documentation and procedures applicable to certain classes of medical devices

3.4.1 Summary of Safety & Clinical Performance (SSCP)

Article 32(1) of the MDR requires manufacturers to draw up a summary of safety and clinical performance (SSCP) for all implantable devices and class III devices, other than custom-made or investigational devices. The SSCP is written specifically for the intended user and, where relevant, the patient for the purpose of transparency and provision of safety and clinical performance information. The SSCP is an important source of information for the intended users: both healthcare professionals and patients.

The draft SSCP is included in the technical documentation and is first validated by the Notified Body during the initial Conformity Assessment. After validation, the Notified Body is responsible for uploading the SSCP to EUDAMED where it will be made available for public access. The instructions for use for all implantable and class III devices is required to include a reference or link to where the SSCP is available.[28]

3.4.1.1 Healthcare Professional Section

The SSCP should always have a section which is written for the intended user or healthcare professional. The provision of up to date, clear and appropriately-presented safety and clinical performance information enables the healthcare professional to make informed decisions in relation to the device.

3.4.1.2 Patient Section

The SSCP will include a second section which is written specifically for the patient, only where it is considered relevant. A patient section is considered relevant for the following:

- Implantable devices for which patients will be provided with an Implant Card. This includes all implantable devices with the exception of those identified as well-established technologies and listed within Article 52(4)
- Class III devices that are intended to be used directly by patients
- Devices listed in Annex XVI without an intended medical purpose and which are either class III or implantable devices

24 MDR Annex XIV, Part B, Section 7
25 MDR Article 61(11)
26 MDR Annex XIV, Part B, Section 8
27 MDCG 2020-8 Guidance on PMCF evaluation report template
28 Annex I, GSPR 23.4(d)

For all other devices requiring an SSCP, the manufacturer should consider whether it is relevant to provide information specifically for the patient. Where a patient SSCP is not considered relevant, the manufacturer should provide a justification in the technical documentation for not including a patient section within the SSCP. This justification should focus on the actual device and why the safety and clinical performance information is not deemed to be relevant or of interest to the patient. Simply stating that a device does not fall into one of the patient-relevant categories listed above is not sufficient. For example, stating that the device does not require an implant card and therefore a patient SSCP is not relevant will be challenged by the Notified Body. The onus is on the manufacturer to fully rationalise why the patient would not need the device-related information the SSCP is intended to convey.

Each SSCP should be provided as a single document which contains a section clearly aimed at the intended user or healthcare professional and, if relevant, a second section written for the patient. The two sections should be separated by a page break. The SSCP will be uploaded to EUDAMED and made available to the public as a single document.

3.4.1.3 Initial SSCP Validation by the Notified Body

All information presented in the SSCP must be sourced from the technical documentation and may reference the instructions for use. Note that The SSCP should not contain any promotional content.

Per MDR Article 32, the Notified Body is responsible for validating the SSCP before it is uploaded to EUDAMED for public access. The term 'validate' in the context of the SSCP means that the NB should undertake the following:

- At the end of a conformity assessment, ensure the data in the SSCP has been verified and aligns to the data that has been assessed within the manufacturer's technical documentation
- Check that the minimum required elements for an SSCP as outlined in MDR Article 32(2) have been included, along with the stylistic and readability recommendations provided in MDCG 2019-9[29]

When the Notified Body has confirmed that all the required elements are included in the draft SSCP, that these are accurately presented and are in alignment with the most current version of the technical documentation, the SSCP is considered to have been validated by the Notified Body. All other elements of the conformity assessment process must then be completed before the final SSCP is uploaded to EUDAMED at the time of certificate registration.

3.4.1.4 SSCP Updates

The SSCP is intended to provide user, patient and public access to an updated summary of clinical data. For this reason, in addition to the initial SSCP validation, updates to the SSCP must be validated by the Notified Body and made available according to defined timescales:

Article 61(11) requires the SSCP for all eligible devices to be updated annually by the manufacturer with clinical data obtained from the implementation of the PMS and PMCF plan. When updating the SSCP all sections should be updated to maintain alignment with the current version of the technical documentation.

Whereas SSCP updates by the manufacturer are required at least annually, submission of the SSCP to the Notified Body is aligned with the periodic safety update report (PSUR) submission timing, which is annually except in the case of class IIa implantable devices, where PSUR submission is required at least every 2 years.

29 MDCG 2019-9 - Summary of safety and clinical performance A guide for manufacturers and notified bodies

The SSCP is expected to be submitted to the Notified Body along with the PSUR if it includes new or updated information. If the SSCP has been validated previously, the Notified Body should validate the updated SSCP against the submitted and evaluated PSUR. If the SSCP has not been validated, the Notified Body may defer validation until the technical documentation is reviewed as per the sampling plan. A draft SSCP that was not validated during the initial conformity assessment (which is possible in the case of class IIa implantable and class IIb implantable WET devices listed in Article 52(4)) shall be validated against the technical documentation at least once during the period of validity of the CE certificate.

Whereas the manufacturer can and should continue to revise the SSCP annually and as required throughout the device lifecycle, versions should only be submitted to the Notified Body for validation to coincide with a certificate change or a scheduled PSUR evaluation.

At the time of a PSUR evaluation it is possible to conduct an SSCP validation for information which is presented in the PSUR and any editorial or administrative updates to the SSCP. It is important to remember that the SSCP validation is aimed at verifying alignment of data in the SSCP with data that has been assessed by the Notified Body, which at the time of a PSUR evaluation will be the updated PSUR only. For any SSCP updates that are sourced from sections of the technical documentation outside of the PSUR, a change notification will need to be submitted to BSI outlining the changes. The change notification will be reviewed by a Scheme Manager to decide what action needs to be taken. Where changes are classified as significant or substantial, updated technical documentation will need to be submitted for a supplementary conformity assessment. Where the change has resulted in updates to the SSCP, the SSCP can be validated as part of the supplementary conformity assessment.

Editorial or administrative changes to the SSCP can be made and approved by the manufacturer at any time without Notified Body approval (assuming the change is non-significant). Non-significant administrative and editorial changes to an SSCP should only ever be validated at the time of a PSUR evaluation or at the time of a supplementary conformity assessment in support of a certificate change. Requests to validate administrative or editorial changes alone will be deferred until the next scheduled PSUR evaluation or conformity assessment, where this occurs first.

Updates to the patient version of the SSCP will be required to meet the required stylistic and readability recommendations.

3.4.1.5 Draft and Final Versions of the SSCP

A draft SSCP is provided to the Notified Body for validation purposes during an initial conformity assessment or certification change review. The content of this draft SSCP often needs to be revised during the conformity assessment process to ensure the content fully aligns with the technical documentation and includes the minimum required elements for an SSCP including the stylistic and readability recommendations.

The final SSCP is the SSCP which has been released in the manufacturers document control system and is the document which will be made available to the intended user, patients and the public. The final SSCP should:

- be a stand-alone document provided in PDF format
- not incorporate any red lines, track changes or confidentiality markings
- be identical to the content validated by BSI using the draft SSCP
- have a complete revision history including the following details:
  - SSCP revision number
  - date of issue for the revision in date, month, year format
  - change description
  - indication of whether the SSCP revision has been validated
  - the validation language (if validated)

Once the SSCP validation is completed by the Notified Body the assessor will request a final copy of the SSCP. This final copy must be provided to the Notified Body prior to completion of the conformity assessment process. The final SSCP is uploaded to EUDAMED at the time of certificate registration once the conformity assessment is complete.

3.4.1.6 Provision of the SSCP to the Notified Body – Conformity Assessment

A draft SSCP should be included in the technical documentation submitted to the Notified Body for initial conformity assessment. Once the draft is validated the final SSCP will be requested by the Notified Body.

When submitting technical documentation in support of a change, a red-lined SSCP should be included in the technical documentation which highlights all changes made to the SSCP since a final version was last submitted to the Notified Body, along with any

updates related to the proposed change. Once the Notified Body completes the conformity assessment to support the proposed change and validates the updates to the SSCP, a final copy of the SSCP will be requested from the manufacturer.

For technical documentation which is subject to sampling (class IIa implantable devices and class IIb implantable WET per Article 52(4)) at least one SSCP is validated against the relevant technical documentation during the initial conformity assessment. The manufacturer is responsible for providing the final SSCP for all devices in the group, prior to completion of the initial conformity assessment. Regardless of validation status, all SSCPs for each group will be uploaded and made available through EUDAMED at the time of certificate registration. The SSCP validation status is transparent to the public via the SSCP revision history. Draft SSCPs that are not validated during the initial conformity assessment will be validated against the technical documentation at least once during the period of validity of the certificate. Once validated against the technical documentation, the SSCP will be uploaded to EUDAMED thus replacing the SSCP uploaded at the time of initial certification with the currently validated version.

3.4.1.7 Provision of the SSCP to the Notified Body – PSUR Evaluation

Outside of the normal conformity assessment process (which includes initial, surveillance and supplementary conformity assessments for the approval of certification changes) submission of SSCP updates to the Notified Body is aligned with the PSUR evaluation schedule. When submitting an SSCP which includes new or updated information collected as an output of the PMS or PMCF plans (or editorial or administrative changes), the current version of the SSCP should be submitted to the Notified Body at the same time as the PSUR. The BSI eVigilance portal has been adapted for the purpose of receiving PSURs and SSCPs, which have been updated to incorporate the output of the PMS and PMCF activities.

3.4.1.8 Guidance on SSCP Content and Structure

Article 32(2) of the MDR outlines the minimum requirements for the SSCP. Further guidance in relation to the content of each section is provided in MDCG 2019-9, which also includes a template.

It is important to note the following:

- If a single device is placed on the market by multiple legal manufacturers, each legal manufacturer will need to produce a separate SSCP for that device, specifying a single legal manufacturer name, address and SRN: like the Declaration of Conformity and the CE certificate, the SSCP is unique to one legal manufacturer
- Whereas the SSCP is a device-specific document, it is acceptable to include more than one Basic-UDI in each SSCP. This is most feasible in the case of systems.[30] It is also possible to combine multiple Basic-UDIs in a single SSCP where the nature of the devices means it is possible and sensible to assess the technical documentation together within the same conformity assessment
- **It is NOT possible to partially validate SSCP content. The conformity assessment must be complete for all devices included in each SSCP before the SSCP validation can be finalised.** For this reason, careful consideration is required when grouping multiple devices in an SSCP
- Having a unique identifier for each SSCP, which remains unchanged for its lifetime, is critical to ensure that SSCPs can be uploaded and updated within EUDAMED. The identifier itself can consist of any combination of letters, numbers or other characters to refer to the document and the revision fields (e.g., SSCP2023 rev 3). Regardless of the identifier used, it must remain unchanged on all future versions of the SSCP, with the only change allowed being to the actual physical revision number. Translations of each SSCP must be assigned the exact same identifier and revision number as the master SSCP.

30 MDR Article 2(11)

3.4.1.9 Link to the IFU

The information in the SSCP is targeted at the intended user and patient and shall be made available to the public via EUDAMED. In MDR Annex I, GSPR 23.4(d) requires a link between the instructions for use and the SSCP. Although the guidance in MDCG 2019-9 suggests the use of the Basic-UDI as a solution for linking the IFU to the SSCP, the MDR does not mandate the use of a Basic-UDI in the IFU and alternative methods can be used by the manufacturer for the purposes of linking the device to the correct SSCP.

The SSCP is written for the purposes of providing information and transparency to the intended user or healthcare professional and, if relevant, the patient. The intent of the MDR is clear in that SSCPs need to be accessible to the intended user, patients and the public. Until EUDAMED is fully-functional, it is the responsibility of the manufacturer to have an appropriate system in place to ensure SSCPs are made available to interested stakeholders without undue delay. Compliance to GSPR 23.4(d) will be assessed during technical documentation assessment. In addition, the process for making the SSCPs available will be subject to assessment during initial and surveillance QMS assessments.

3.4.2 Clinical Evaluation Consultation procedure (CECP)

As outlined in MDR Article 54(1), the Clinical Evaluation Consultation Procedure (CECP) is applicable when performing a conformity assessment of class III implantable and class IIb rule 12 devices that are intended to administer or remove a medicinal substance.

Article 54(2)(a-c) presents three scenarios in which CECP can be justified as not required. The first is in relation to MDR certificate renewals; the second to the modification of a device already marketed by the same manufacturer and where the device and intended purpose is unchanged, with no modifications that adversely affect the benefit-risk ratio of the device; and the third exemption is for devices where the clinical evaluation for the device type has been addressed within a Common Specification.

The guidance in MDCG 2019-3 places limitations on the modifications permitted to be made to MDD/AIMDD legacy devices in order for the exception in Art 54(2)(b) to apply. The EU Commission and Expert Panels have made it clear that the legal provision in the MDR must be followed but that the Notified Body should not submit for review dossiers that do not apply, particularly legacy devices that have remained "essentially unchanged".

It is critical that the CECP process is taken into consideration both by the manufacturer and the Notified Body when conducting (initial and supplementary) conformity assessments for all MDR class III implantable and class IIb rule 12 devices intended to administer or remove a medicinal substance. If the exemption outlined in Article 54(2)(b) is to be applied, the manufacturer must provide the following within the technical documentation:

- A statement that it has marketed the device in question for the same intended purpose under the relevant Directive
- A copy of the last issued certificate(s) together with the certificate history (or, where the certificate is issued by BSI, a reference to the certificate number)
- A clear description of all modifications introduced at the time of MDR application

During the clinical evaluation assessment, the Notified Body will verify that:

- The device in question had a valid certificate under the Directives
- In case the certificate has been withdrawn, suspended or expired, whether there is an impact on compliance with the GSPRs

- There is no pending assessment of changes for the device or outstanding non-compliance

The Notified Body will also carefully consider all modifications to verify that the exemption in Article 54(2)(b) is indeed applicable.

For this group of devices, all changes will be considered on a case-by-case basis to determine whether CECP is required. Modifications to legacy devices which go beyond ensuring compliance with the MDR requirements do not automatically trigger CECP. Where a change to a legacy device requires the assessment of new/additional clinical data, CECP will be required. Typical reasons for the requirement for CECP in the case of legacy devices include:

- Changes to the legal manufacturer
- Indication expansion
- Changes to the intended use
- Changes to the intended patient population
- Design and material changes

Class III implantable or class IIb Rule 12 devices that are intended to administer or remove a medicinal substance and are new to the market will require CECP.

It is worth noting:

Clinical data needs to be assessed for all class IIb rule 12 devices that are intended to administer or remove a medicinal substance before a certificate can be issued. No sampling of the clinical data is allowed throughout the certification cycle for this class of device.[31]

The CECP process only applies to positive certificate recommendations. It does not apply to clinical evaluation assessments that resulted in a certificate refusal.

In cases where the CECP process is applicable, the manufacturer will be informed of this decision as early in the clinical evaluation assessment process as possible. The EU Commission expects that the CEAR is finalised prior to CECP review, meaning that all other components of the BSI conformity assessment and any external consultations (where applicable) must be completed before the CECP process can be initiated.

The following documents will need to be provided by the Notified Body to the Expert Panels for review:

- Clinical Evaluation Plan
- Clinical Evaluation Report
- PMCF Plan
- PMCF Report
- CEAR

All documents should be stand-alone, revision-controlled and final versions.

It is important to note that the Expert Panels are providing an opinion on the Notified Body assessment as documented within the CEAR. Annex IX of the MDR is clear that the CEAR will document the Notified Body conclusion on the outcome of the assessment. The Expert Panel process is part of the conformity assessment and BSI will only provide a copy of the CEAR to the manufacturer once the conformity assessment is complete, including consideration of the Expert Panel decision and feedback.

From the manufacturer perspective, attention to detail is important within the technical documentation. Any discrepancies identified will be questioned by the Expert Panels with updates requested to ensure consistency. Device names should be reported consistently throughout the documentation and the device/variant which is the subject of CECP should be easily identifiable.

Novelty is a key consideration for determining whether devices are subject to CECP. **The Expert Panels have requested that the ANSM card is not used for the assessment of novelty as it is considered insufficient.** When considering and documenting novelty the table outlined in section 3.2.3.6 of this guidance should be utilised.

Robust PMS and PMCF plans are always important. Within the PMCF plan, ensure that there is long-term follow-up which is appropriate considering the lifetime of the device.

As per Article 54(3), the Notified Body is required to notify the Commission of all certificates issued for class III implantable, or class IIb rule 12 devices that are intended to administer or remove a medicinal substance, and that are not submitted for CECP. This notification will include a copy of the CEAR.

31 MDR Annex IX, Section 5.1(a)

The MDCG have confirmed that the provisions of the Regulation should not apply beyond its wording. This means that the Article 54 is not applicable to Class III devices under rule 22 that are intended to administer or remove a medicinal substance.

When to consider Article 61(10)

In the case of certain devices, the applicability of MDR Article 61(10) should be considered. Note, however, that such cases require robust justification to explain why clinical data is not deemed "appropriate."

Justifications will need to address the following:

- **Clinical claims:** Where clinical benefit claims are made, it is not possible to apply Article 61(10). Also, where a manufacturer does not intend to make specific clinical claims about a medical device, this does not necessarily justify the use of Article 61(10). Note that measuring, diagnostic, and therapeutic devices are generally considered to have direct clinical benefits and therefore require clinical data
- **Outputs from risk management activities**: Where it would be unethical to perform clinical investigations, Article 61(10) may apply but only where the other requirements of Article 61(10) are met. In cases where the patient population is limited, the manufacturer is instead encouraged to apply for Derogation from the Competent Authority
- **Consideration of the interaction between the device and the human body:** In the case of patient-contacting and invasive devices, it will be more challenging to demonstrate that pre-clinical testing alone is sufficient to demonstrate conformity with the MDR
- **Intended clinical performance:** The manufacturer shall duly substantiate why it considers a demonstration of conformity with GSPRs based on the results of non-clinical testing methods alone to be adequate

For software devices, manufacturers should refer to MDCG 2020-1.[32] For example, picture archiving software that does not modify images may not require clinical data, whereas clinical data is expected in the case of, e.g., procedure planning software.

Article 61(10) will not be accepted for the following devices and situations:

- Class III devices
- Implantable devices (other than those listed in Article 52(4), for which clinical investigations may be exempted)
- Devices for which the particular standard expressly states that clinical adequacy is not covered (e.g., Annex ZZ of IEC 60601-2-2[33]; IEC 60601-2-34[34])
- Devices for which a clinical study is expressly required by the standard (e.g., IEC 81060-2[35], IEC 60601-2-61[36])

Article 61(10) will generally not be accepted for devices where the function cannot be verified without clinical data, for example:

- Concentrators and other devices that create medicinal substances (e.g., nitric oxide, oxygen)
- Imaging/monitoring devices that drive clinical management (e.g., endoscopes, MRI, ECG monitors)
- Devices that treat problems, which tend to self-resolve, or which are associated with strong placebo effects, and thus require robust controlled studies (e.g., wound care, pain management)
- Devices for the transportation of organs

Note that in the case of legacy devices, the expectation is that data obtained via PMS will be available in support of devices. If there exists published data on the device under evaluation, or on similar devices, then this may indicate that it is appropriate to collect clinical data: Article 61(10) will therefore not be applicable in this situation.

32 MDCG 2019-1 - Guidance on Clinical Evaluation (MDR) / Performance Evaluation (IVDR) of Medical Device Software

33 IEC 60601-2-2 Medical electrical equipment - Part 2-2: Particular requirements for the basic safety and essential performance of high frequency surgical equipment and high frequency surgical accessories

34 IEC 60601-2-34 Medical electrical equipment - Part 2-34: Particular requirements for the basic safety and essential performance of invasive blood pressure monitoring equipment

35 IEC 81060-2 Non-invasive sphygmomanometers - Part 2: Clinical investigation of intermittent automated measurement type

36 IEC 60601-2-61 Medical electrical equipment — Part 2-61: Particular requirements for basic safety and essential performance of pulse oximeter equipment

Where Article 61(10) is considered applicable, any Common Specifications, standards, guidance and other solutions applied should be cited and justified where appropriate (e.g., in the case of non-harmonized versions of standards).

4. The Clinical Oversight Process at BSI

Under the requirements of MDR Annex VII, Section 3.2.4, the Notified Body is required to have permanent availability of personnel with relevant clinical expertise for the conformity assessment of clinical data. BSI interprets this requirement as the Notified Body requiring individuals with appropriate clinical education and skills that are familiar with the devices under the evaluation. BSI typically employs currently practicing clinicians to support the conformity assessment of medical devices. We refer to these individuals as Internal Clinicians.

The Internal Clinician ensures that that there are appropriate personnel involved in the assessment of the device and clinical data.[37] If the Internal Clinician identifies that additional expertise is required to support the conformity assessment, then an External Clinician may be requested to support the assessment. If this occurs, the manufacturer will be informed of this process in advance and will have the opportunity to review a select number of External Clinicians and to declare if there are any conflicts of interest.

37 MDR Annex VII section 3.2.4, first indent

4.1 How does the clinical oversight process work?

The clinical evaluation assessment begins with the Internal Clinician and Clinical Evaluation Specialist (or Technical Specialist) defining the scope of the assessment, based on the type of conformity assessment and the documentation provided by the manufacturer.

The Internal Clinician then confirms whether or not external expertise is required for the assessment and also confirms that the Clinical Evaluation Specialist (or Technical Specialist) has the appropriate competence to undertake the assessment. If the Internal Clinicians do not have experience with the device (e.g., the device is novel) then, as described above, an External Clinician may need to be consulted, which will increase the cost and duration of the assessment.

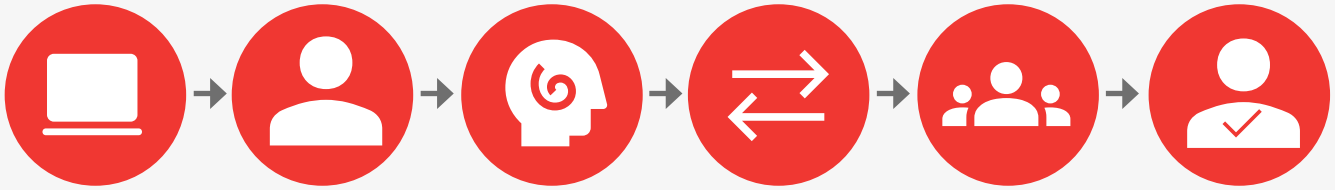
The Clinical Evaluation Specialist (or Technical Specialist) then reviews the clinical evaluation documentation and compiles the CEAR. During this phase of the assessment the Clinical Evaluation (or Technical Specialist) will raise questions for the manufacturer and will have the opportunity to liaise with the Internal Clinician to discuss any concerns during the assessment.

Once the assessment of the clinical data is completed the assessment documentation, including the CEAR, is submitted for review by the Internal Clinician who will provide a final conclusion and, if appropriate, a positive recommendation for certification based on the Clinical Evaluation documentation.

For all conformity assessments of the clinical evaluation conducted under (EU) 2017/745, the manufacturer will receive a CEAR summarising the assessment following the conclusion of the Clinical Oversight process.

Please note that for certain assessments the person conducting the clinical evaluation assessment may not be the same person assessing the technical documentation. This may be due to the requirement for additional competency when reviewing the clinical data. When this occurs, please be aware that you may receive separate rounds of questions from assessors, related to either the technical or the clinical documentation.

Whilst this may occasionally result in some overlap of questions, please be aware that certain aspects of the documentation require assessment for both the purposes of technical and clinical conformity, e.g., risk management, equivalence, PMS and the instructions for use.



Manufacturer documentation received. Clinician is assigned to the assessment.

Internal Clinician defines scope of assessment and resource required.

External Experts engaged if required, this may include Biostasticians, MRI experts.

Clinical Evaluation/ Technical Specialist engaged.

Up to 3 rounds of Questions are sent to the Manufacturer during the assessment.

Internal Clinician performs a final approval assessment.

5. Where to find additional resources

BSI publishes a range of resources for manufacturers on its website:

https://www.bsigroup.com/en-GB/medical-devices/resources

bsi.

Read more about
standards at:
knowledge.bsigroup.com