**Clinical Evaluation Plan**

For

[Device Name]

Manufacturer Name: [Manufacturer name]

Document Number: XXXX

Revision: XXXX

# Approval

**Author Approval**

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| Title: | Signature: |

# Revision History

Table 1: History of revision

|  |  |  |
| --- | --- | --- |
| Revision | Date | Change History |
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# Table of Content

[Approval 2](#_Toc169612400)

[Revision History 3](#_Toc169612401)

[Table of Content 4](#_Toc169612402)

[Acronyms 5](#_Toc169612403)

[1. Scope of the Clinical Evaluation 6](#_Toc169612404)

[1.1. Introduction 6](#_Toc169612405)

[1.2. Manufacturer details 6](#_Toc169612406)

[1.3. Devices under evaluation 6](#_Toc169612407)

[1.4. Device description 6](#_Toc169612408)

[1.5. Intended purpose 7](#_Toc169612409)

[1.6. Clinical benefits and claims 8](#_Toc169612410)

[1.7. Device history 8](#_Toc169612411)

[1.8. Current data generated and held by the manufacturer 8](#_Toc169612412)

[2. State of the art 9](#_Toc169612413)

[2.1. State of the art search strategy 9](#_Toc169612414)

[2.2. Description of the state of the art 9](#_Toc169612415)

[2.3. Novelty & well-established technology 10](#_Toc169612416)

[2.4. Similar devices / alternative treatments 12](#_Toc169612417)

[2.5. Indicative list of safety and performance outcome parameters and acceptance criteria 13](#_Toc169612418)

[3. Safety and performance evaluation 14](#_Toc169612419)

[3.1. Equivalent device 14](#_Toc169612420)

[3.2. Clinical data search methodology 18](#_Toc169612421)

[3.3. Clinical data appraisal 20](#_Toc169612422)

[3.4. Clinical data analysis 20](#_Toc169612423)

[4. Clinical Development Plan 27](#_Toc169612424)

[4.1. Premarket Studies 29](#_Toc169612425)

[4.2. Post-market Studies 30](#_Toc169612426)

[5. Reference 32](#_Toc169612427)

[Appendix I – Appraisal plan 33](#_Toc169612428)

[Appendix II – Clinical data search protocol (only for first CEP) 34](#_Toc169612429)

[Appendix III – Literature search report for SoA (only for first CEP) 35](#_Toc169612430)

[Appendix IV – Literature search report for AC (only for first CEP) 36](#_Toc169612431)

# Acronyms

|  |  |
| --- | --- |
| AC | Acceptance criteria |
| B/R | Benefit/Risk |
| CEP | Clinical evaluation plan |
| CER | Clinical evaluation report |
| EMDN | European medical device nomenclature |
| EU | European union |
| FSN | Field safety notice |
| GSPR | General safety and performance requirements |
| IFU | Instructions for use |
| MDA | Active medical device |
| MDCG | Medical device coordinating group |
| MDN | Non-active medical device |
| MDR | Medical devices regulation |
| MEDDEV | Medical Devices Documents |
| N/A | Not applicable |
| PICO | Populations, interventions, comparators, outcomes |
| PMCF | Post-market clinical follow-up |
| PMS | Post-market surveillance |
| PSUR | Periodic safety update report |
| QMS | Quality management system |
| SoA | State of the art |
| S&P | Safety and performance |
| UDI | Unique device identification |
| UDI-DI | UDI-Device Identifier |
| WET | Well-established technology |

# Scope of the Clinical Evaluation

## Introduction

The clinical evaluation plan (CEP) is defined to establish the clinical activities for [Device Name] (hereafter named [Device Short Name]) to meet the applicable General Safety and Performance Requirements (GSPR). The clinical evaluation is intended to collect favorable and unfavorable clinical data on the subject and equivalent devices to support the safety, the claimed performances and how the benefits outweigh the risks when [Device Short Name] is used in a clinical setting taking into account the generally acknowledged state of the art. The clinical evaluation is conducted in compliance with Medical Devices Regulation (MDR), (EU) 2017/745 Article 61 and /Annex XIV as well as the manufacturer’s clinical evaluation procedure [Doc], Post-Market Clinical Follow-up (PMCF) procedure [Doc].

The clinical evaluation is also carried out according to the following Medical Device Coordinating Group (MDCG) guidance documents:

* MDCG 2019-15 for class I SC
* MDCG 2020-1 *for software*
* MDCG 2020-5 when the clinical evaluation relies on the equivalence
* MDCG 2020-6
* MDCG 2020-13

## Manufacturer details

Table 2: Manufacturer information

|  |  |
| --- | --- |
| Manufacturer name: | [Manufacturer name] (hereafter named [Manufacturer short name]) |
| Manufacturer address: |  |
| Manufacturer SRN: |  |

## Devices under evaluation

Table 3: Device details

|  |  |
| --- | --- |
| **Device Trade Name** | [Device Name] |
| **Medical devices** |
| **Model Number** | **Basic UDI-DI** | **Description** | **EMDN Code** | **MDN Code** | **Class** | **Rule** |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
| **Accessory for medical devices** |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |

Justify the bundling of devices in a single CEP/CER

## Device description

The [Device Short name] is a Include a general description (Sourced from the TD)

The [Device Short name] is intended for Include intended use (Sourced from the IFU)

The [Device Short name] consists of Include mode of action (Sourced from the TD)

The [Device Short name] is illustrated in the following Figure(s):

Figure 1: [Device Short Name]

XXX

The following tables describe the general device characteristics. (Sourced from the TD)

Table 4: General device characteristics

|  |  |
| --- | --- |
| Materials: |  |
| Sterility: |  |
| Main Mechanical characteristics: |  |
| Main Physicochemical characteristics: |  |
| Invasiveness: |  |
| Nature of contact:*Identification of organs, tissues or body fluids contacted by the device* |  |
| Duration of use / nature of contact with the body: |  |
| Other |  |

The [Device Short name] is available in various models for which the critical technical characteristics are the following:

Table 5: Critical device characteristics

| Device Model | … | … | … | … | … |
| --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |

## Intended purpose

### Indications

As specified in the IFU

### Targeted patient population

As specified in the IFU

### Contra-indications

As specified in the IFU

### Warning and precautions

As specified in the IFU

### Undesirable side-effects

As specified in the IFU

## Clinical benefits and claims

The clinical benefits for [Device Short Name] are presented in the following table.

Table 6: Clinical benefits

| **Claims** | **Clinical claims** | **Non-clinical claims**  | **Justification** |
| --- | --- | --- | --- |
| Benefits |
|  | X |  |  |
|  |  | X |  |
| Performances |
|  | X |  |  |
|  |  | X |  |
| Safety |
|  | X |  |  |
|  |  | X |  |

## Device history

[Device Short Name] is a legacy/MDR device marketed in EU under 93/42/EEC / (EU) 2017/745 since XXXX and has transitioned to MDR on DD/MM/YYYY.

Following the first commercialization/Since compliance to the MDR, the device has been modified several times as shown in the table below.

Table 7: History of changes

| **Design Change Number** | **Date of Implementation** | **Description** | **Clinical Impact** |
| --- | --- | --- | --- |
|  |  |  |  |
|  |  |  |  |

The changes identified in **bold** are those implemented since the last revision of the CEP. As described, the clinical data collected before the implementation of changes are still applicable to the current [Device Short Name].

## Current data generated and held by the manufacturer

The following documents generated by [Manufacturer Short Name] have been considered in the clinical evaluation plan:

Table 8: Documents of reference

| **Documents** | **Document Number** | **Comments** |
| --- | --- | --- |
| Instructions for use | Doc + Rev |  |
| Risk management file | - | - |
| * Risk management plan
 | Doc + Rev |  |
| * Risk analysis
 | Doc + Rev |  |
| * Risk management report
 | Doc + Rev |  |
| Clinical evaluation plan (CEP) | Doc + Rev |  |
| PMCF Plan | Doc + Rev |  |
| PMCF Evaluation Report | Doc + Rev |  |
| PMS Plan | Doc + Rev |  |
| PSUR/PMS report | Doc + Rev |  |
| Technical Documentation (TD) | Doc + Rev |  |
| Summary of safety and clinical performance (SSCP) | Doc + Rev |  |
| Expert panel consultation reference | Doc + Rev |  |

The documents are available in the [Manufacturer Short Name]’s QMS and available on request.

# State of the art

## State of the art search strategy

For the first CEP

As part of this CEP, a literature search strategy has been carried out to establish the current state of the art (SoA) of the medical conditions for which [device short name] is intended to be used. The strategy has been defined in the clinical data search protocol [Doc+Rev] and implemented in the literature search reports for SoA, [Doc+Rev], and for safety and performance (S&P) acceptance criteria (AC), [Doc+Rev], respectively in Appendix II – Clinical data search protocol, Appendix III – Literature search report for SoA and Appendix IV – Literature search report for AC.

The clinical evaluation is defined based on a methodologically sound procedure that also aims at providing a list of parameters and specifications to determine, based on the state of the art, the acceptability of the benefit-risk profile for [device short name]. As a result, **Section 2.2** summarizes the key information from the state of the art of medical conditions for which [device short name] is intended to be used and **Section 2.5** lists the clinical benefits, performance and safety outcome parameters and specifications defined based on similar devices/and therapeutic alternatives.

With the most recent clinical data, the clinical evaluation report (CER) will confirm or update the state of the art as well as the parameters and specifications for the evaluation of clinical benefits, performance and safety of [device short name].

For CEP updates

The state of the art (SoA) has been established in the last CER based on a defined methodologically sound procedure, [Doc+rev], and summarized with the key information in **Section 2.2**. The last CER also describes the list of parameters and specifications to determine, based on the state of the art, the acceptability of the benefit-risk profile for [device short name]. As a result, parameters and specifications for the evaluation of clinical benefits, performance and safety of [device short name] as justified in the last CER, have been summarized in **Section 2.5**.

With the most recent clinical data, the new CER will confirm or update the state of the art as well as the parameters and specifications for the evaluation of clinical benefits, performance and safety of [device short name].

## Description of the state of the art

The following subsections are evaluated to be the minimum SoA information for the CEP. However, more sub-sections can be included as needed (e.g., device concept, prevalence, etc.).

### Historical context and development

To be defined based on the literature articles included for the SoA.

### Description of medical conditions

To be defined based on the literature articles included for the SoA.

### Targeted user

To be defined based on the literature articles included for the SoA.

### Description of alternative treatments

To be defined based on the literature articles included for the SoA.

## Novelty & well-established technology

### Novelty

The novelty of [Device short name] has been evaluated for the criteria evaluated critical regarding safety and performance of the device with the consideration of clinical, technical and biological criteria as defined in Annex XIV of the MDR and described in the following table.

Table 9: Justification of novelty

|  |  |  |  |
| --- | --- | --- | --- |
| **Critical device characteristics** | **Any Novelty?** | **Description of novelty or justification for absence of novelty** | **Clinical impact of any novelty** |
| **Clinical characteristics** |
| Medical purpose | Yes / No | If yes, specifically describe novel featuresIf no, provide evidence/justification to demonstrate non-novel features (e.g., based on similar devices) | If yes, describe the clinical impact and how this will be addressed in the CERIf no, indicate N/A – no novelty |
| Indications for use |  |  |  |
| Targeted type of procedure |  |  |  |
| Principles of operations |  |  |  |
| Condition of use |  |  |  |
| Targeted patients |  |  |  |
| Targeted users |  |  |  |
| Environment of use |  |  |  |
| Deployment Methods |  |  |  |
| … |  |  |  |
| **Technical characteristics** |
| Design characteristics (e.g., shape, size, components) |  |  |  |
| Design characteristics (e.g., shape, size, components) |  |  |  |
| Mechanism of action |  |  |  |
| Device-Patient Interface |  |  |  |
| Compatibility with other devices |  |  |  |
| Manufacturing process |  |  |  |
| … |  |  |  |
| **Biological characteristics** |
| Materials |  |  |  |
| Site of application |  |  |  |
| Duration of contact |  |  |  |
| … |  |  |  |
|  |  |  |  |
|  |  |  |  |

No novelty has been defined with [Device short name].

OR

The device includes the following novelty according to the current state of the art:

* XXXX
* XXXX
* XXXX

The novelty brought with [Device short name] has a significant/non-significant clinical impact because XXXX Include a summary the clinical impact of the novelty and how this will be addressed in the CER.

### Well-established technology (WET)

This section can be removed if the device does not meet the WET definition

MDCG 2020-6 defines a WET as a device in the category listed in Article 61(6b) as amended by Delegated Acts (Article 61(8)). The list currently includes: sutures, staples, dental fillings, dental braces, tooth crowns, screws, wedges, plates, wires, pins, clips or connectors.

[Device short name] meets the definition of WET and is recognized as a device:

* with relatively simple, common and stable designs with little evolution.

Include the rationale

* with well-known clinical performance characteristics

Include the rationale

* with a long history on the market

Include the rationale

* belonging to a generic device group:
	+ with a well-known safety not associated with safety issues in the past

Include the rationale

* + recognized standard of care devices where there is little evolution in indications and the state of the art.

Include the rationale

Conclusion for WET device

[Device short name] is part of the WET devices described in Article 61(6b) and meets the WET criteria in the definition of MDCG 2020-6. Hence the cumulative evidence from Rank 5 to Rank 12, including Rank 6 (i.e., clinical data (based on SoA) can be used to support the safety and performance of [Device short name]).

/OR

Conclusion for devices that are not in WET list but meet the definition.

Though [Device short name] is not part of the WET devices described in Article 61(6b), [Device short name] meets the WET definition described in MDCG 2020-6. Hence, the device is recognized in the current treatment strategy as defined in the state of the art for the treatment/diagnosis of XXXX. Indicate the medical condition to be treated/diagnosed.

## Similar devices / alternative treatments

As part of the therapeutic alternatives, the following devices have been considered similar to [Device Short Name]. They have been deemed similar as they do not meet the clinical, technical and biological criteria as detailed in Annex XIV section 3 of the MDR but share a similar device technology under the same EMDN code and are intended to be used for the same indication and patient’s medical conditions, in the same environment and by the same type of user.

Table 10: Similar devices

| **Similar devices** | **Manufacturer Name** |
| --- | --- |
| **[similar device 1]** |  |
| **[similar device 2]** |  |
| … |  |

Optional As the parameters and specifications for the clinical benefits, safety and performance of [device short name] cannot be established solely based on similar devices, [Manufacturer short name] also considered the following therapeutic alternatives:

* XXX
* XXX

**Description of [similar device 1]**

Include a general description

A comparison between [device short name] and [similar device 1] is presented in the table below per the criteria described in MDCG 2020-5. A simplified version of comparison table is also acceptable.

Table 11: Comparison between [device short name] and [similar device 1]

| **Critical characteristics** | **Subject device** | **Similar device** |
| --- | --- | --- |
| Device Name | [device short name] | [similar device 1] |
| Device Manufacturer | [manufacturer short name] |  |
| CE marking |  |  |
| **Clinical criteria** |
| Intended purpose / indication for use |  |  |
| Clinical conditions |  |  |
| Disease treated (including severity / stage) |  |  |
| Application site |  |  |
| Patient population |  |  |
| User |  |  |
| Relevant clinical performance in view of expected clinical effect |  |  |
| *…* |  |  |
| **Technical criteria** |
| *Design characteristics (shape, size, etc.)* |  |  |
| *Physico-chemical properties (e.g. strength, viscosity)* |  |  |
| *Principle of use (e.g. deployment)* |  |  |
| *…* |  |  |
| **Biological criteria** |
| Body Contact |  |  |
| Material or substances |  |  |
| Duration of body contact |  |  |
| Release characteristics of substances (degradation product, leachable) |  |  |
| *…* |  |  |

**Description of [similar device 2]**

Include a general description

A comparison between [device short name] and [similar device 2] is presented in the table below per the criteria described in MDCG 2020-5. Simplified version of comparison table is also acceptable.

Table 12: Comparison between [device short name] and [similar device 2]

| **Critical characteristics** | **Subject device** | **Similar device** |
| --- | --- | --- |
| Device Name | [device short name] | [similar device 2] |
| Device Manufacturer | [manufacturer short name] |  |
| CE marking |  |  |
| **Clinical criteria** |
| Intended purpose / indication for use |  |  |
| Clinical conditions |  |  |
| Disease treated (including severity / stage) |  |  |
| Application site |  |  |
| Patient population |  |  |
| User |  |  |
| Relevant clinical performance in view of expected clinical effect |  |  |
| *…* |  |  |
| **Technical criteria** |
| *Design characteristics (shape, size, etc.)* |  |  |
| *Physico-chemical properties (e.g. strength, viscosity)* |  |  |
| *Principle of use (e.g. deployment)* |  |  |
| *…* |  |  |
| **Biological criteria** |
| Body Contact |  |  |
| Material or substances |  |  |
| Duration of body contact |  |  |
| Release characteristics of substances (degradation product, leachable) |  |  |
| *…* |  |  |

## Indicative list of safety and performance outcome parameters and acceptance criteria

The literature search implemented on similar devices and therapeutic alternatives aimed to establish the parameters and specifications for the evaluation of clinical benefits, performance and safety of [device short name]. The outcome parameters and acceptance criteria have been defined based on a literature search methodology with the results presented in Appendix IV – Literature search report for AC.

For the first CEP

Data resulting from the searches have been extracted and the following indicative list of clinical outcome parameters and specifications for the evaluation of [device short name], has been established based on similar devices and therapeutic alternatives.

For CEP updates

The list of relevant clinical outcome parameters and specifications for the evaluation of [device short name], has been defined based on the state of the art and documented in the last CER as reported in the following table.

Table 13: Indicative list of parameters and specifications for the evaluation of [device short name]

| **Clinical claims** | **List of clinical outcome parameters** | **Specifications** |
| --- | --- | --- |
| Clinical benefits |
|  |  | From X[Z] to Y[Z] |
|  |  |  |
| Clinical performances |
|  |  |  |
|  |  |  |
| Safety |  |  |
|  |  |  |
|  |  |  |

Indicate the source for the specifications[Z]

The outcome parameters/specification should be stratified by indications/patients as needed

With the most recent clinical data, the CER will confirm or update the parameters and specifications for the evaluation of clinical benefits, performance and safety of [device short name].

# Safety and performance evaluation

## Equivalent device

To support the safety and performance of [device short name], [manufacturer short name] has decided to consider a route of equivalence per MDR Article 61(5) with [Equivalent device name] manufactured by [Equivalent device manufacturer name]. [Equivalent Device Name] meets the criteria defined in Annex XIV section 3 of the MDR and [Manufacturer Short name] has a sufficient access to the data related [Equivalent Device Name] in order to justify the claims of equivalence as identified in **Table 14**.

For class III/implantable devices only As [device short name] is a class III /or implantable device and the equivalent device (certified under MDR) is not manufactured by [manufacturer short name], an agreement [Doc+Rev] has been signed between [manufacturer short name] and [equivalent device manufacturer name] to give full access to the technical documentation of [equivalent device name] on an ongoing basis.

### Equivalent device description

General equivalent device description

The following figure represents [Equivalent Device Name]

Figure 2: Representative pictures of equivalent device

XXX

### Justification of equivalence

The following table considers the critical relevant characteristics for the purpose of comparing [Device Short Name] and its equivalent device based on clinical, technical and biological criteria as established in Annex XIV section 3 of the MDR and MDCG 2020-5

Table 14: Justification of equivalence

| **Characteristics** | **[Device Name]** | **Equivalent device name** | **Identified differences or conclusion that there are no differences in the characteristic** |
| --- | --- | --- | --- |
| **Manufacturer Name** |  |  | N/A |
| **Picture** |  |  | N/A |
| **CE marking** |  |  |  |
| 1. **Technical characteristics**
 |
| Indicate the critical design characteristics |  |  | No differences in the characteristicOR short summary of the difference (refer to 1.X) |
| Condition of use |  |  |  |
| Indicate the critical specifications / technical features |  |  |  |
| Principles of operation |  |  |  |
| Other |  |  |  |
| **Scientific justification why there would be no clinically significant difference in the safety and clinical performance of the device, OR a description of the impact on safety and or clinical performance** | **Clinically significant difference** **Yes / No** |
| 1.1.  |  |
| 1.2. |  |
| 1. **Biological characteristics**
 |
| Materials in contact with the human tissue/body |  |  | No differences in the characteristicOR short summary of the difference (refer to 2.X) |
| Duration of contact |  |  |  |
| Other (e.g., degradation characteristics if applicable) |  |  |  |
| **Scientific justification why there would be no clinically significant difference in the safety and clinical performance of the device, OR a description of the impact on safety and or clinical performance** | **Clinically significant difference** **Yes / No** |
| 2.1.  |  |
| 2.2.  |  |
| 1. **Clinical characteristics**
 |
| Medical condition |  |  | No differences in the characteristicOR short summary of the difference (refer to 3.X) |
| Indication for use |  |  |  |
| Targeted patients |  |  |  |
| Intended users |  |  |  |
| Indicate the critical performances with a medical effect |  |  |  |
| **Scientific justification why there would be no clinically significant difference in the safety and clinical performance of the device, OR a description of the impact on safety and or clinical performance** | **Clinically significant difference** **Yes / No** |
| 3.1.  |  |
| 3.2.  |  |
| **Summary** |
| In the circumstance that more than one non-significant difference is identified, provide a justification whether the sum of differences may affect the safety and clinical performance of the device. |

The characteristics listed above are identical or similar to the extent that there would be no clinically significant difference in the safety and clinical performance of the device.

[Device Short name] and [Equivalence Device Name] are considered equivalent for the purpose of this CER.

## Clinical data search methodology

### Pre-clinical data

Pre-clinical data /or non-clinical data are generated and held by [manufacturer short name] with the purpose to support the compliance to common specifications, European pharmacopeia, applicable harmonized standards under MDR, European or internationally recognized standards that represent the state of the art for [device short name] when used as intended. Pre-clinical data /or non-clinical data are in the form of bench testing, animal testing, and other design/process verification & validation activities.

After appraisal of the pre-clinical /or non-clinical evidence as specified in **Section 3.3**, the data that may impact the clinical safety and performance will be summarized in a tabular format to describe the tests, methods, standards, results and evidence of conformity to support how [device short name] meets the technical requirements recognized in Europe.

### Clinical investigation if applicable

Results of clinical investigations are pivotal data generated and held by [manufacturer short name] with the purpose to support the safety and performance of [device short name]. [manufacturer short name] conducted the following clinical investigations that are today complete:

* XXXX

In addition, the following clinical investigations are still ongoing with the purpose of XXX Indicate the reason of the clinical investigations (e.g., additional models, extension of the indications/population):

* XXXX

After appraisal of the results of clinical investigations as specified in **Section 3.3**, the clinical evidence of safety and performance will be summarized with the identification of critical information as defined in Section 5.2 of MDCG 2019-9. The key safety and performance outcome parameters will be specifically emphasized to ensure a comparison with the acceptable limits defined based on the state of the art (see **Section 2.5**).

### PMCF investigation if applicable

Results of PMCF investigations are data generated after the device has been commercialized and held by [manufacturer short name] with the purpose to support and confirm the safety and performance of [device short name]. [manufacturer short name] conducted the following PMCF investigations that are today complete:

* XXXX

In addition, the following PMCF investigations are still ongoing with the purpose of XXX Indicate the PMCF objective according to the PMCF plan:

* XXXX

After appraisal of the results of PMCF investigations as specified in **Section 3.3**, the clinical evidence of safety and performance will be summarized with the identification of critical information as defined in Section 5.2 of MDCG 2019-9. The key safety and performance outcome parameters will be specifically emphasized to ensure a comparison with the acceptable limits defined based on the state of the art (see **Section 2.5**).

### Other PMCF specific procedures and methods if applicable

Specific PMCF procedures and methods have been defined with the following objectives:

* XXXX indicate the specific PMCF specific procedure (e.g., surveys, registries)

The specific PMCF procedure has been planned with the objective to XXX Indicate the PMCF objective according to the PMCF plan.

* XXXX indicate the specific PMCF specific procedure (e.g., surveys, registries)

The specific PMCF procedure has been planned with the objective to XXX Indicate the PMCF objective according to the PMCF plan.

After appraisal of the results of PMCF specific procedures and methods as specified in **Section 3.3**, the clinical evidence of safety and performance will be summarized in a tabular format with the critical information ensuring the understanding of the PMCF activity, including the clinical outcome parameters and results evaluated. If the PMCF specific procedures and methods include key safety and performance outcome parameters, they will be specifically emphasized to ensure a comparison with the acceptable limits defined based on the state of the art (see **Section 2.5**).

### Published and non-published clinical literature

A literature search will be implemented and documented in the CER to detect the published and unpublished articles related to [device short name] or equivalent devices and bring clinical evidence for the demonstration of safety and performance.

The literature search methodology will be carried out in compliance with Section A5 of MEDDEV 2.7/1 rev.4. Research questions will be constructed using a PICO (Populations, Interventions, Comparators, Outcomes) process to justify the selection of relevant keywords. In the selected literature and clinical trial databases, the search queries will be defined using the selected keywords in a way to match with the language of each database used and the relevant limitations.

The result of literature search will be a list of articles/studies that will be screened in two stages:

* Level-1 screening is based on the titles and abstracts
* Level-2 screening is based on the full articles

The screening process consists of the review of each collected article/study to confirm if it should be included or excluded based on the inclusion/exclusion criteria.

After appraisal of literature articles as specified in **Section 3.3**, the clinical evidence of safety and performance will be summarized with the identification of critical information such as:

* Objective
* Method
* Statistical technique
* Follow-up
* Demographic data (number of patients, age, sex, medical condition, etc.)
* Device involved
* Safety and performance data
* Author’s conclusion

The key safety and performance outcome parameters will be specifically emphasized to ensure a comparison with the acceptable limits defined based on the state of the art (see **Section 2.5**).

### Vigilance/recall databases if applicable

A vigilance / recall search will be implemented to detect the clinical risks (i.e., device problem, patient problems) related to the subject or equivalent devices and bring additional clinical evidence for the demonstration of safety.

The vigilance / recall search methodology will be carried out using an approach similar to the literature search methodology described in **Section 3.2.5**. Research questions will be constructed using a PICO process to justify the selection of relevant keywords. In the selected vigilance / recall databases, the search queries will be defined using the selected keywords in a way to match with the language of each database used and the relevant limitations.

The result of vigilance / recall search will be a list of events that will be screened to determine if applicable to the subject/equivalent devices.

After appraisal of vigilance and recall data as specified in **Section 3.3**, the risks will be qualified, and as much as possible quantified via a number of occurrences over a reporting period.

### Internal PMS data if applicable

Post-Market Surveillance (PMS) data including serious and non-serious complaints as well as known undesirable side-effects as reported in the last Period Safety Update Report (PSUR), will be summarized to emphasize the quantitative data via a number of occurrences over a reporting period out of the sales or number of uses. The rates will be calculated per year and will consider the device problems, investigation root-causes and health impacts. PMS data will also include a review of field safety corrective actions (Field Safety Notice (FSN), recalls) implemented for [device short name] including the status of planned actions.

After appraisal of internal PMS data as specified in **Section 3.3**, conclusions of the last PSUR regarding rates exceeding the threshold values and statistical increase in trends will be summarized in the CER.

## Clinical data appraisal

All clinical data set will be appraised using the method described in the appraisal plan available in Appendix I – Appraisal plan

## Clinical data analysis

### Applicable GSPRs

Per Article 61, at least GSPRs 1 and 8 are required. Include solely the applicable GSPRs as identified in the GSPR checklist.

#### GSPR 1

*Devices shall achieve the performance intended by their manufacturer and shall be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose. They shall be safe and effective and shall not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art.*

#### GSPR 2

*The requirement in this Annex to reduce risks as far as possible means the reduction of risks as far as possible without adversely affecting the benefit-risk ratio.*

#### GSPR 4

*Risk control measures adopted by manufacturers for the design and manufacture of the devices shall conform to safety principles, taking account of the generally acknowledged state of the art. To reduce risks, Manufacturers shall manage risks so that the residual risk associated with each hazard as well as the overall residual risk is judged acceptable. In selecting the most appropriate solutions, manufacturers shall, in the following order of priority:*

1. *eliminate or reduce risks as far as possible through safe design and manufacture;*
2. *where appropriate, take adequate protection measures, including alarms if necessary, in relation to risks that cannot be eliminated; and*
3. *provide information for safety (warnings/precautions/contra-indications) and, where appropriate, training to users.*

*Manufacturers shall inform users of any residual risks.*

#### GSPR 6

*The characteristics and performance of a device shall not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer's instructions.*

#### GSPR 8

*All known and foreseeable risks, and any undesirable side-effects, shall be minimised and be acceptable when weighed against the evaluated benefits to the patient and/or user arising from the achieved performance of the device during normal conditions of use.*

### Level of clinical data required

#### Exemption of clinical investigation only applicable to class III and implantable devices

Legacy device

[Device short name] is transitioning to the MDR but was lawfully placed on the market in accordance to the MDD. No common specifications have been published for the clinical evaluation of [device short name] /OR This clinical evaluation report has been defined based on the common specifications applicable to [device short name]. Finally, the clinical data currently available on [Device short name] are assumed to be sufficient and the conclusion of the clinical evaluation report will confirm this assumption.

As a result, according to Article 61(6a) of the MDR, no clinical investigation is evaluated required as long as there is sufficient clinical evidence on [device short name] to comply with the applicable GSPRs.

WET device

[Device short name] is considered to be a WET device as it meets the definition from MDCG 2020-6 as described in **Section** Error! Reference source not found. and is part of the list of WET in Article 61(6b) of the MDR. No common specifications have been published for the clinical evaluation of [device short name] /OR This clinical evaluation report has been defined based on the common specifications applicable to [device short name]. Finally, the clinical data currently available for the GSPR compliance of [Device short name] are assumed to be sufficient and the conclusion of the clinical evaluation report will confirm this assumption.

As a result, according to Article 61(6b) of the MDR, no clinical investigation is evaluated required as long as there is sufficient clinical evidence to comply with the applicable GSPRs.

Equivalent device with the same manufacturer

[Device short name] has been design by modifications of a device manufactured by [manufacturer short name] and both are considered equivalent per requirements from MDCG 2020-5 as described in **Section** Error! Reference source not found.. As a result [manufacturer short name] has defined a specific PMCF procedure to confirm the safety and performance of [Device short name] (see PMCF plan referenced in **Section** Error! Reference source not found.).

In conclusion, according to Article 61(4) of the MDR, no clinical investigation is evaluated required as long as there is sufficient clinical evidence on [Equivalent device name] to support the compliance of [device short name] with the applicable GSPRs.

Equivalent device with another manufacturer

As described in **Section** Error! Reference source not found., [device short name] has been demonstrated to be equivalent to [Equivalent device name] not manufactured by [manufacturer short name] and currently commercialized in compliance to the MDR. **Section** Error! Reference source not found. provides the details of the contract in place that allows the [manufacturer short name] full access to the technical documentation of [Equivalent device name] on an ongoing basis.

As a result, according to Article 61(5) of the MDR, no clinical investigation is evaluated required as long as there is sufficient clinical evidence on [Equivalent device name] to support the compliance of [device short name] with the applicable GSPRs.

#### Determination of minimum level of clinical evidence required

When article 61(10) applies

Article 61(1) of the MDR requires [Manufacturer short name] to justify the sufficient level of clinical evidence required to support the compliance to applicable GSPR. Using the criteria of Article 61(10), clinical data for the [Device short name] were not deemed appropriate for the demonstration of conformity to GSPRs. The following table describes the justification drawn up by [Manufacturer short name]:

Table 15: Justification for meeting the criteria of Article 61(10)

| **Article 61(10) criteria** | **Justification** | **Conclusion** |
| --- | --- | --- |
| Results of the manufacturer's risk management | Verify the possible patient harms for the risks identified in the risk analysis to verify if they need to be monitor by clinical data or preclinical data are sufficient.The approach is not acceptable for class III or implantable devices | [Device short name] is a class I/Is/Im/Ir/IIa/IIb non-implantable device.The risks resulting from the risk management activities are technical by nature and does not need to be substantiated by clinical data. |
| Interaction between the device and the human body | Devices without patient contact do not require clinical data. For devices with a limited contact (nature + duration), the rationale shall be discussed for the clinical significance and need (or no need) of clinical evidence. (E.g., justification difficult for a contact lense, devices in direct contact with blood or brain; justification possible for transient contact such as with scalpel for which the interaction should not have a clinical impact). | The interaction between the device and patients have been analyzed, are non-clinically significant and can be substantiated by non-clinical data. |
| Clinical performance intended | All performances and benefits shall be reviewed to confirm they are technical by nature and should not be verified with clinical data.  | The review of performances claimed by the manufacturer did not emphasis any clinical performances leading to clinical benefits. All performances are technical by nature and does not need to be substantiated by clinical data |
| Claims of the manufacturer | All claims shall be reviewed to verify they can be achieved with preclinical data. E.g., claims for reduction of pain, surgery time, complications are not technical by nature. Claims for using a specific technology, compliance with preclinical standard, sterility, compatibility with MRI, … can be substantiated with preclinical data. | [Manufacturer short name] does not have any claim/does not have any claim that require to be substantiated by clinical data. All claims are technical by nature. |

If the rationale needs a long elaboration, the tabular format can be removed to include bullet points.

In conclusion, per the MDCG 2020-6 guidance document and considering [Device short name] meets the article 61(10) criteria, the minimum level of clinical evidence required will be from Rank 10 to 12, as applicable, with Rank 10 if common specifications have been published and with Rank 11 if preclinical tests with healthcare professionals/users are deemed required.

When article 61(10) does not apply

Article 61(1) of the MDR requires [Manufacturer short name] to justify the sufficient level of clinical evidence required to support the compliance to applicable GSPR. As described in the following table, MDCG 2020-6 Appendix III provides a suggested hierarchy of clinical evidence for the confirmation of conformity with applicable GSPRs under MDR.

Table 16: Hierarchy of clinical evidence under the MDR

| **Rank** | **Types of clinical data and evidence** |
| --- | --- |
| 1 | Results of high-quality clinical investigations covering all device variants, indications, patient populations, duration of treatment effect, etc |
| 2 | Results of high-quality clinical investigations with some gaps |
| 3 | Outcomes from high quality clinical data collection systems such as registries |
| 4 | Outcomes from studies with potential methodological flaws but where data can still be quantified and acceptability justified |
| 5 | Equivalence data (reliable / quantifiable) |
| 6 | Evaluation of state of the art, including evaluation of clinical data from similar devices |
| 7 | Complaints and vigilance data; curated data |
| 8 | Proactive PMS data, such as that derived from surveys |
| 9 | Individual case reports on the subject device |
| 10 | Compliance to non-clinical elements of common specifications considered relevant to device safety and performance  |
| 11 | Simulated use / animal / cadaveric testing involving healthcare professionals or other end users |
| 12 | Pre-clinical and bench testing / compliance to standards |

Considering [device short name] is a legacy/MDR class X device, exempted from clinical investigation as described in **Section 3.4.2** only for class III/implantable devices, is/is not a well-established technology and the lack of novelty/or the novelty identified **Section 2.3**, [manufacturer short name] determined the minimum level of clinical evidence necessary to demonstrate the conformity to applicable GSPRs is:

* Rank X clinical evidence
* Rank Y clinical evidence
* Rank Z clinical evidence

The clinical evaluation report will assess, appraise and analyze the clinical data available to confirm the sufficient level of clinical evidence is achieved regarding the safety and performance of [device short name] for the medical condition(s) for which the device is intended to be used.

To support the decision, see the suggested recommendations (to be customized with the device):

| **Scenario** | **Device class** | **Estimated minimum level of clinical evidence required** |
| --- | --- | --- |
| 1 | Class I/IIa/IIb meeting requirements from Article 61 (10) | Rank 10-12 (non-clinical evidence) |
| **Legacy devices or already commercialized MDR devices** |
| 2 | Class I (Is, Im, Ir)\* | Rank 10-12 (non-clinical evidence) + Rank 7 (complaints and vigilance) |
| 3 | Class IIa non-implantable | Rank 10-12 (non-clinical evidence) + Rank 7 (complaints and vigilance) + Planned Rank 8 (PMCF activities, e.g., patient/user survey) |
| 4 | Class IIb non-implantable | Rank 10-12 (non-clinical evidence) + Rank 7 (complaints and vigilance) + * Rank 4 (data from subject device) or
* Rank 5 (data from equivalent device2) +
	+ Planned Rank 8 (PMCF activities, e.g., patient/user survey)
 |
| 5 | Implantable/Class III | Rank 10-12 (non-clinical evidence) + Rank 7 (complaints and vigilance) + * Rank 4 (data from subject device) or
* Rank 5 (data from equivalent device1) +
	+ Planned Rank 4 or higher (PMCF activities, e.g., PMCF study/investigation)
 |
| 6 | Implantable/Class III and WET | Rank 10-12 (non-clinical evidence) + Rank 7 (complaints and vigilance) + Rank 6 (data from similar devices) + * Rank 4 (data from subject device) or
* Rank 5 (data from equivalent device1) +
	+ Planned Rank 8 (PMCF activities, e.g., patient/user survey)
 |
| **New MDR devices** |
| 7 | Class I | Rank 10-12 (non-clinical evidence) + Rank 5 (data from equivalent device) |
| 8 | Class I (Is, Im, Ir) and Class IIa non-implantable | Rank 10-12 (non-clinical evidence) + Rank 5 (data from equivalent device) + * Planned Rank 8 (PMCF activities, e.g., patient/user survey)
 |
| 9 | Class IIb non-implantable | Rank 10-12 (non-clinical evidence) + * Rank 4 (clinical investigation), OR
* Rank 5 (data from equivalent device) +
	+ Planned Rank 8 (PMCF activities, e.g., patient/user survey), or
	+ Planned Rank 4 or higher (PMCF activities, e.g., PMCF study/investigation)
 |
| 10 | Implantable/Class III | Rank 10-12 (non-clinical evidence) + * Rank 4 (clinical investigation), OR
* Rank 5 (data from equivalent device4) +
	+ Planned Rank 4 or higher (PMCF activities, e.g., PMCF study/investigation)
 |

### Safety evaluation (GSPR 1, 2, 3)

The clinical evaluation report will examine the safety of [device short name] using the clinical data available as described in **Section 3.2** such as results of clinical/PMCF investigation, literature article, vigilance & recalls or internal complaint.

All clinical risks (i.e., device problem and patient problem) will be qualitatively identified through the data generated and held by the manufacturer and the clinical data search strategy implemented. Clinical risks will be gathered in a list that will be reviewed in comparison to the risk management file to confirm the risk mitigation measures implemented are appropriate and carried out as far as possible without adversely affecting the benefit-risk ratio. Hence, the review of qualitative aspects of [device short name] safety will consist of the examination of residual risks and side-effects reported for [device short name] when the device is used as intended in clinical settings.

Finally, as manufacturers shall inform users of any residual risks, the qualitative aspects of the [device short name] safety will also consist of reviewing the device labeling to confirm all residual risks including unknown undesirable side-effects, have been delineated in the instructions for use (e.g., warnings, precautions, or contra-indications).

### Acceptability of known and foreseeable risks (GSPR 1, 8)

The clinical evaluation report will examine the quantitative aspects of [device short name] safety through an analysis of clinical risks (i.e., device problems and patient problems) identified in **Section 3.4.3**. The analysis will conclude on the acceptability of known and foreseeable risks including undesirable side-effects when weighed against the evaluated benefits to the patient and/or user, and consequently when weighed against the current state of the art of similar devices and/or therapeutic alternatives.

The examination of [device short name] safety will consist of the quantification of clinical risks as reported in the clinical data available for [device short name] and equivalent device. As it is recognized that the quality of clinical data is not equivalent per the type of clinical evidence analyzed, the result of quantitative data may differ from a source to another and could not be comparable. For instance, quantitative data reported in the publicly available databases of vigilance is generally not aligned with the quantitative data obtained via the internal complaints handling. However, the data will be as much as possible quantified in a way to be easily interpreted and compared to data coming from the state of the art. The following table provides examples of quantification methods applied according to the type of clinical data analyzed.

Table 17: Quantitative methods to evaluate the safety

| **Type of clinical evidence** | **Examples of quantitative methods of safety evaluation** |
| --- | --- |
| Internal vigilance data | * % of clinical risk / number of sales
* % of clinical risk / number of sales / years
* % of clinical risk / number of uses
* % of clinical risk / number of uses / years
 |
| Vigilance in publicly available database | * Occurrence of clinical risk
* Occurrence of clinical risk / reporting period
 |
| Literature articles | * % of clinical risks reported / number of patients
* % of clinical risks reported / number of patients / years
 |
| Clinical or PMCF investigation | * % of adverse event reported / number of patients
* % of adverse event reported / number of patients / years
 |

*Note: clinical risk represents each device/patient problem that are residual risks and side-effects*

The acceptability of known and foreseeable risks will be based on quantitative data of clinical risks applicable to [device short name] (including clinical risks reported for equivalent devices), as compared to the available quantitative data for similar devices and/or therapeutic alternatives as reported in the current state of the art.

Any discrepancies with the acceptable limits recognized in the state of the art will be further justified and, when applicable, discussed regarding the [device short name] benefits and overall benefit/risk profile.

### Performance evaluation (GSPR 1,6)

To be customized as necessary if Article 61(10) route is used, if the device is a WET and depending on the device classification and data available.

[Device short name] shall achieve the performance intended and claimed by [manufacturer short name].

Based on pre-clinical evidence, the evaluation of performance will confirm [device short name] meets the technical state of the art recognized in Europe by compliance to applicable harmonized or international standards or common specifications.

In addition, [manufacturer short name] will substantiate the claims of clinical performances and safety with a sufficient level of clinical evidence for the medical condition(s) to be treated/diagnosed and the targeted population.

Any clinical claims of safety or performance will need to be substantiated with clinical data on [device short name] or equivalent devices using recognized clinical outcome parameters representative of the corresponding claims. The clinical evaluation report will make a difference between key safety and performance outcome parameters that will have been justified as relevant regarding the state of the art and the other outcome parameters that are not representative or are considered less representative than the key parameters.

The analysis of clinical data available will describe the quantitative results for all clinical outcome parameters with an emphasis on the key safety and performance outcome parameters. The results will be compared to the acceptance criteria defined based on the data obtained from similar devices or therapeutic alternative treatments.

### Benefit / risk (B/R) profile (GSPR 8)

Using the favorable and unfavorable clinical data collected throughout the clinical evaluation process, the CER will weigh the benefits brought with [device short name] against the device safety taking into account the generally acknowledged state of the art.

The corresponding section of the CER can be considered as a standalone rationale emphasizing all supportive information already discussed and analyzed in the CER to position the B/R of [device short name] in the landscape of therapeutic alternatives and similar devices. As a result, the B/R discussion will include a summary of the following information when applicable:

* clinical experience as reported in [manufacturer short name]’s QMS,
* trends observed via the review of PMS data,
* pre-clinical data that support the compliance to technical state of the art,
* pivotal clinical evidence of safety and performance (e.g., clinical investigation, literature articles)
* device performance analysis regarding the [manufacturer short name] claims,
* device safety analysis in relation to the risk management file, information to users,
* acceptability of clinical risks including undesirable side-effects,
* analysis of systematic misuses or off-label uses,

In addition, the CER will discuss the qualitative and/or quantitative data that support how the clinical benefit(s) of [device short name] is achieved.

In conclusion, [manufacturer short name] will state whether or not the risks associated with [device short name]’s use, constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art. Any gaps identified with the clinical data available, any significant, specific or emerging risks to be monitored, or any needs to confirm the device safety or performance throughout the expected lifetime of [device short name], will require a specific attention and will be emphasized for consideration in the PMCF activities.

# Clinical Development Plan

A clinical development plan is always required and shall at least include a summary of data from the PMCF plan.

The following table summarizes the clinical development plan for [device short name].

Table 18: Clinical development plan

| **Clinical development activities** | **Type of clinical development activities** | **Objectives** | **Description** | **Acceptance criteria** | **Milestones** |
| --- | --- | --- | --- | --- | --- |
| ***Pre-market studies*** |
| Exploratory investigation | [study type] | e.g., first in man study, feasibility study | Include a short description of the study with the current status | Include the primary acceptance criteria | Include the schedule for important milestones (e.g., Q1/YYYY – recruitmentQ1/ZZZZ – end of recruitmentQ1-Q3/ZZZZ – Data analysis ) |
| Clinical investigation | [study type] (e.g., randomized controlled clinical trial) | Pivotal study to evaluate the safety performance of [device short name] |  |  |  |
| ***Post-market studies*** |
| PMCF investigation | [study type] | Alignment with PMCF plan (e.g., confirm the device safety and performance until the end of the expected lifetime) |  |  |  |
| PMCF registry | [study type] | Alignment with PMCF plan (e.g., identifying previously unknown side-effects) |  |  |  |
| PMCF survey | [study type] | Alignment with PMCF plan (e.g., identifying and analyzing emergent risks on the basis of factual evidence) |  |  |  |
| PMCF general procedures | Literature review | Alignment with PMCF plan |  |  |  |
| Vigilance / recall review | Alignment with PMCF plan |  |  |  |
| Clinical investigation | Pivotal study | (e.g., extension of the initial indications) |  |  |  |

If deemed necessary, the clinical development plan can be further described in detail in the next sections

## Premarket Studies

### [Activity 1]

#### Type of clinical development activity

XXX

#### Objectives

XXX

#### Description

XXX

#### Acceptance criteria

XXX

#### Milestones and schedules

XXX

### [Activity 2]

#### Type of clinical development activity

XXX

#### Objectives

XXX

#### Description

XXX

#### Acceptance criteria

XXX

#### Milestones and schedules

XXX

## Post-market Studies

### [Activity 3]

#### Type of clinical development activity

XXX

#### Objectives

XXX

#### Description

XXX

#### Acceptance criteria

XXX

#### Milestones and schedules

XXX

### [Activity 4]

#### Type of clinical development activity

XXX

#### Objectives

XXX

#### Description

XXX

#### Acceptance criteria

XXX

#### Milestones and schedules

XXX

# Reference

Include the citations of any articles used in the CEP

1. XXX
2. XXX
3. XXX

# Appendix I – Appraisal plan

Document available under another specific Lex form: LEX-FORM-EU-010 - Appraisal Plan

# Appendix II – Clinical data search protocol (only for first CEP)

Document available under another specific Lex form: LEX-FORM-EU-004 - Clinical data search protocol

# Appendix III – Literature search report for SoA (only for first CEP)

Document available under another specific Lex form: LEX-FORM-EU-006 - Literature search report for SoA

# Appendix IV – Literature search report for AC (only for first CEP)

Document available under another specific Lex form: LEX-FORM-EU-007 - Literature search report for AC