|  |
| --- |
| **MDR 2017/745**  **Application Form: Initial Assessment** |

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**Section 1**

**Administration**

| **General Information** | | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **PO Number:** | | | | |  | | | | |
| **Manufacturer:** *(as per definition within the regulation)* | | | | |  | | | | |
| **Address:** | | | | |  | | | | |
| **Device or Device Group Name:** | | | | |  | | | | |
| **Basic UDI-DI:** | | | | |  | | | | |
| **Classification:** | | | | |  | | **Rule:** |  | |
| **Manufacturers SRN:** | | | | |  | | | | |
| **GMDN** | | | | |  | | | | |
| **EMDN** | | | | |  | | | | |
| **Model(s) #:** *(in scope of this application)* | | | | |  | | | | |
| **MDN, MDA, MDS codes:** *(refer to RFQ and MDCG 2019-14)* | | | | |  | | | | |
| **Confirm all testing and test reports has been completed and submitted. i.e., no test data pending. *Note:*** *The review cannot commence until* ***all data*** *is submitted.* | | | | |  | | | | |
| **EU Authorised Representative:** | N/A | | **Name:** | | |  | | | |
|  |  | | **Address:** | | |  | | | |
|  |  | | **Email:** | | |  | | | |
|  |  | | **Telephone:** | | |  | | | |
| **EU Authorised Representative SRN:** | N/A | |  | | | | | | |
| **Other Authorised Representative:** | N/A | | **Name:** | | |  | | | |
|  |  | | **Address:** | | |  | | | |
|  |  | | **Email:** | | |  | | | |
|  |  | | **Telephone:** | | |  | | | |
| **QMS #:** *(Format MD19.XXXX)* | | | | |  | | | | |
| **Name of Person Responsible for Regulatory Compliance (PRRC):** | | | | |  | | | | |
| **Company Liaison and Details:** | **Name:** | | | |  | | | | |
|  | **Address:** | | | |  | | | | |
|  | **Email:** | | | |  | | | | |
|  | **Telephone:** | | | |  | | | | |
| **Please Complete for Impartiality Review** | | | | | | | | | |
| **Critical Suppliers Of Products And Services as defined by your purchasing process for**  **the medical device under review**  ***Note*:** *A critical supplier is a supplier delivering materials, components, or services that may influence the safety and performance of the device \*NBOG BPG 2010-1.* | | | | | | | | | |
| **Product/Service** | | | | **Supplier Name / Address** | | | | | **Supplier Certified by** |
| *e.g., Moulded components* | | | | *e.g., MouldCo, Inc. California, USA* | | | | | *e.g., NSAI* |
|  | | | |  | | | | |  |
|  | | | |  | | | | |  |
|  | | | |  | | | | | *Add lines as required* |
| List all potential commercial competitor(s) for **the medical device under review** | | | | | | | | | |
| **Client Product to be CE Marked with NSAI** | | **Potential Commercial Competitor Name(s)** | | | | | | | |
| *e.g., Lenses by Len Inc* | | *E-Z Lenses, ACME Testing.* | | | | | | | |
|  | |  | | | | | | | |
|  | |  | | | | | | | |
|  | | *Add lines as required* | | | | | | | |

| **Signatures** | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| We, the manufacturer, declare the information in this form is correct and has been submitted as instructed. Information not provided, or provided in the wrong format, may result in prolonged review time, delays, or termination of review. | | | | | | | |
| **Signed on Behalf of the Manufacturer** | | | | | | | |
| **Signature: u** | |  | | | | | |
| **Print Name:** | |  | | | | | |
| **Position / Title:** | |  | | | | | |
| **Contact Details** | | **Email:** | |  | | | |
| **Phone:** | |  | | | |
| **Contact Person details (if different):** | | | | | | | N/A |
| **Name:** |  | | | | **Email:** |  | |
| **Position / Title:** |  | | | | **Phone:** |  | |
| **For NSAI Use Only** | | | | | | | |
| **Reviewer** | | | **Signed and Dated (DD-Mmm-YYYY)** | | | | |
| **File Manager u** | | |  | | | | |
| **Technical u** | | |  | | | | |
| **Biocompatibility u** | | |  | | | | |
| **Sterilisation u** | | |  | | | | |
| **Reusable Devices / Reprocessed Devices u** | | |  | | | | |
| **Electrical u** | | |  | | | | |
| **Software u** | | |  | | | | |
| **Clinical Reviewer u** | | |  | | | | |
| **Medicinal substances u** | | |  | | | | |
| **Tissues of Animal Origin u** | | |  | | | | |
| **Substances u** | | |  | | | | |
| **Measuring Function u** | | |  | | | | |
| **Product performance u**  *(Including functional safety)* | | |  | | | | |
| **External Expert u** | | |  | | | | |
| **Trainee u** | | |  | | | | |
| By signing this, the reviewer confirms that they have no conflict of interest with the above-named company (e.g., training, consultancy, financial, personal, or political) that would affect the integrity of the technical review process and hence the review results and that this activity is not further subcontracted. | | | | | | | |

**Section 2**

**Technical Documentation**

**Instructions**

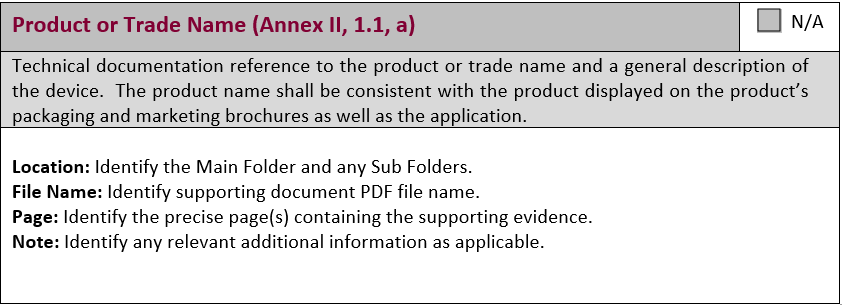
* All documentation must be in **English**.
* The completed Technical Documentation must be submitted in full. References to files from other products or previous submissions **are not accepted.**
* Ensure each relevant section is prepared by the most appropriate SME(s), the form is intended to go to those with the relevant expertise and competence to complete.
* Hard copies of Technical Documentation **are not accepted.**
* Documents must be provided in the form of **PDF files**, which are bookmarked, paginated and fully searchable.
* PDF files and attachments should not be file protected or locked.
* File names should be succinct and be accurate to the information contained within. Ensure file names are not overly long.
* Data must be presented in a coherent and logical manner, reflecting the topic and the testing conducted. Note that the duration of the review and the number of queries is dependent on the quality of the data received.

**How to Submit Technical Documentation**

* Manufacturers may submit all referenced supporting documentation in the corresponding Part or Appendix Folder within the NSAI MDR Application Folder Pack.
  + The manufacturer may use any folder architecture they wish within Part or Appendix Folder.
* Manufacturers can also submit supporting docs in their own structure (eg STED)

**How to complete this application form**

* In each section below, please provide a clear and detailed reference to signpost the reviewer to the precise folder location of the relevant supporting technical documentation and the supporting text within same.
* **Each response section includes the following to signpost to the supporting information:**
  + **Location:** Identify the Main Folder and any Sub Folders.
  + **File Name:** Identify supporting document PDF file name.
  + **Page:** Identify the precise page(s) containing the supporting evidence.
  + **Note:** Identify any relevant additional information as applicable.
* **Complete each section below by stating:**
  + The supporting document PDF file name and its precise folder location
  + The reference (page number and Section number) where the supporting information can be found within the PDF file.
  + If required, explanatory notes can accompany the reference.
  + See example below.
* Use the NA box in the header for all non-relevant sections. A detailed justification must be provided for all non-relevant sections.



# Part A – Device Description and Specification, Including Variants and Accessories

| **Annex II Preamble:** |
| --- |
| **Confirm that all Technical Documentation (including all supporting documentation submitted) has been provided in a clear, organised, unambiguous manner throughout the application and is readily searchable in an electronic format.** |
| Provide a statement confirming this and some details on how this is achieved: |

**Device description and specification**

| **Product or Trade Name (Annex II, 1.1, a)** |
| --- |
| Technical documentation reference to product or trade name and a general description of the device including its intended purpose and intended users.  It should be clear whether device under application is for single use only, multiple use, reprocessing (number of cycles) or a device without an intended medical purpose (Annex XVI). A description of all relevant packaging, sterilisation should also be indicated. |
| **Location:**  **File Name:**  **Page:**  **Note:** |

| **Basic UDI-DI (Annex II, 1.1, b)** |
| --- |
| Technical documentation reference to the Basic UDI-DI as referred to in Part C of Annex VI assigned by the manufacturer to the device in question, as soon as identification of this device becomes based on a UDI system, or otherwise a clear identification by means of product code, catalogue number or other unambiguous reference allowing traceability such as Basic-UDI-DI, EMDN code etc. |
| **Location:**  **File Name:**  **Page:**  **Note:** |

| **Intended patient population (Annex II, 1.1, c)** |
| --- |
| Technical documentation reference to the intended patient population and medical conditions to be diagnosed, treated and/or monitored and other considerations such as patient selection criteria, indications, contra-indications, warnings. |
| **Location:**  **File Name:**  **Page:**  **Note:** |

| **Description of methods and principles of operation (Annex II, 1.1, d)** |
| --- |
| Technical documentation reference to principles of operation of the device, which should include additional devices/accessories the intended user of the device, the environments of the device etc and its mode of action, scientifically demonstrated if necessary.  Evidence provided here should remain consistent throughout all Technical Documentation. |
| **Location:**  **File Name:**  **Page:**  **Note:** |

| **Qualification of the product as a device (Annex II, 1.1, e and f)** |
| --- |
| Technical documentation reference the rationale for the qualification of the product as a device (as per Article 2 (1) and a justification of the proposed Risk Class and Classification (Annex VIII Chapter III).  *For devices without an intended medical purpose as per Annex XVI, please also refer to Commission Implementing regulation (EU) 2022/2347 of 01 Dec 2022.* |
| **Location:**  **File Name:**  **Page:**  **Note:** |

| **Novel Features (Annex II, 1.1, g)** | |
| --- | --- |
| Select ‘N/A’ if section is not applicable | N/A |
| **Rationale:** | |
| Technical documentation reference to the explanation of any novel features. | |
| **Location:**  **File Name:**  **Page:**  **Note:** | |

| **Accessories to be used with the device under application (Annex II, 1.1, h)** | |
| --- | --- |
| Select ‘N/A’ if section is not applicable | N/A |
| **Rationale:** | |
| Technical documentation reference to a description of the accessories for a device, other devices and other products that are not devices, which are intended to be used in combination with it. (Article 2 point 2) | |
| **Location:**  **File Name:**  **Page:**  **Note:** | |

| **Configurations/Variants of the product under application (Annex II, 1.1, i)** |
| --- |
| Technical documentation reference to a description or complete list of the various configurations/variants of the device that are intended to be made available on the market; |
| **Location:**  **File Name:**  **Page:**  **Note:** |

| **Drawings, Pictures, Illustrations etc (Annex II, 1.1, j)** |
| --- |
| Technical documentation reference to a general description of the key functional elements, e.g., shall include labelled pictorial representations (e.g., diagrams, photographs, and drawings), clearly indicating key parts/components, including sufficient explanation to understand the drawings and diagrams.  **Note:** For active devices to also include electrical circuit drawings, diagrams, and electrical circuits. |
| **Location:**  **File Name:**  **Page:**  **Note:** |

| **Raw Materials (Annex II, 1.1, k)** |
| --- |
| Technical documentation reference to a description of the raw materials incorporated into key functional elements and those making either direct contact with the human body or indirect contact with the body, e.g., during extracorporeal circulation of body fluids.  Clearly identify all raw materials incorporated into key functional elements of the device including information on any coating materials. Identify the nature of contact with the human body (e.g., direct or indirect contact, contact with circulating body fluids etc.). Include full details of the Bill of Materials (BoM) of the device. |
| **Location:**  **File Name:**  **Page:**  **Note:** |

| **Claims from other sources (Annex II, 1.1, l)** |
| --- |
| Technical documentation reference to the technical specifications, such as features, dimensions and performance attributes, of the device and any variants/configurations and accessories that would typically appear in the product specification made available to the user, for example in brochures, catalogues, and similar publications. |
| **Location:**  **File Name:**  **Page:**  **Note:** |

**Reference to Previous and Similar Generations of the Device**

| **Previous generations (Annex II, 1.2, a)** | |
| --- | --- |
| Select ‘N/A’ if section is not applicable | N/A |
| **Rationale:** | |
| Technical documentation reference to an overview of the previous generation or generations of the device produced by the manufacturer, where such devices exist. | |
| **Location:**  **File Name:**  **Page:**  **Note:** | |

| **Similar Devices (Annex II, 1.2, b)** | |
| --- | --- |
| Select ‘N/A’ if section is not applicable | N/A |
| **Rationale:** | |
| Technical documentation reference to an overview of identified similar devices available on the Union or international markets, where such devices exist. | |
| **Location:**  **File Name:**  **Page:**  **Note:** | |

# Part B - Information to be Supplied by the Manufacturer

| **Declaration of Conformity (Annex IV, Article 19)** |
| --- |
| Declaration of Conformity in compliance with Annex IV, Article 19 |
| **Location:**  **File Name:**  **Page:**  **Note:** |

| **Labels (Annex II, 2, a)** |
| --- |
| Technical documentation reference to a representative sample set of the [English Language] label or labels on the device and on its packaging, such as single unit packaging, sales packaging, transport packaging in case of specific management conditions. |
| **Location:**  **File Name:**  **Page:**  **Note:** |

| **Instructions for Use (Annex II, 2, a)** |
| --- |
| Technical documentation reference to the instructions for use in the languages accepted in the Member States where the device is envisaged to be sold. |
| **Location:**  **File Name:**  **Page:**  **Note:** |

| **Electronic Instructions for Use (Eifu)** | |
| --- | --- |
| Select ‘N/A’ if section is not applicable | N/A |
| **Rationale:** | |
| Technical documentation shall contain a reference to the instructions for use in the languages accepted in the Member States where the device is envisaged to be sold.  The Technical Documentation shall also demonstrate compliance to Commission Implementing Regulation (EU) 2021/2226 of 14 December 2021 laying down rules for the application of Regulation (EU) 2017/745 of the European Parliament and of the Council as regards electronic instructions for use of medical devices. | |
| Provide a reference to the location in the technical file where all applicable requirements of (EU) 2021/2226 are located.  [***Note****: A compliance checklist with reference to supporting evidence in the Technical File demonstrating compliance to Regulation 2021/2226 will be accepted.*] | |
| **Location:**  **File Name:**  **Page:**  **Note:** | |

| **Article 18 Implant Card (Annex II, 2, a)** | |
| --- | --- |
| Select ‘N/A’ if section is not applicable | N/A |
| **Rationale:** | |
| Technical documentation shall provide reference to the Implant card required for all implants as per Article 18.  (*a) information allowing the identification of the device, including the device name, serial number, lot number, the UDI, the device model, as well as the name, address, and the website of the manufacturer;*  *(b) any warnings, precautions or measures to be taken by the patient or a healthcare professional with regard to reciprocal interference with reasonably foreseeable external influences, medical examinations or environmental conditions.*  *(c) any information about the expected lifetime of the device and any necessary follow-up.*  *(d) any other information to ensure safe use of the device by the patient, including the information in point (u) of Section 23.4 of Annex I.*  **Note: Only the following implantable devices are exempt from an implant card, sutures, staples, dental fillings, dental braces, tooth crowns, screws, wedges, plates, wires, pins, clips, and connectors.**  **All other implants must provide an implant card and the chosen solution to provide patient information to the patient per Article 18 clause 1.**  [***Note****: Specific guidance in relation to Implant Cards per Article 18 of the MDR is contained in MDCG 2019-8.*] | |
| **Location:**  **File Name:**  **Page:**  **Note:** | |

# Part C – Design and Manufacturing Information

This section should include information to meet the requirements of Annex II Section 3. The technical documentation and, if applicable, the summary thereof to be drawn up by the manufacturer shall be presented in a clear, organised, readily searchable and unambiguous manner.

| **Design Stages (Annex II, 3, a)** |
| --- |
| Provide the Technical documentation/reference for information to allow the design stages applied to the device to be understood.  *(This may include but is not limited to the organisation’s product/design development procedure relevant for this design and objective evidence of completed design reviews/ stage gate reviews).* |
| **Location:**  **File Name:**  **Page:**  **Note:** |

| **Manufacturing and Design information and specifications (Annex II, 3, b)** |
| --- |
| Provide the Technical documentation /references complete information and specifications, including the manufacturing processes and their validation, their adjuvants, the continuous monitoring, and the final product testing. Data shall be fully included in the technical documentation.  *This may include but is not limited to the*   * *Product Specification(s),* * *Manufacturing Process Flow including adjuvants at respective process steps (if applicable), identify the continuous monitoring steps and final product testing steps.* * *Master validation manufacturing plans/report,* * *Provide the final product release specification and a sample of final product lot /batch release testing as objective evidence of completion.* |
| **Location:**  **File Name:**  **Page:**  **Note:** |

| **Design and Manufacturing Suppliers and Subcontractors (Annex II, 3, c)** |
| --- |
| Provide Technical documentation/ references for identification of all sites, including suppliers and sub-contractors, where design and manufacturing activities are performed.  Provide a document referencing the identification of all Suppliers/ Subcontractors utilised in the outsourcing of components/assembly in the manufacturing process including sterilisation/ packaging activities, if applicable. |
| **Location:**  **File Name:**  **Page:**  **Note:** |

# Part D - General Safety and Performance Requirements

This section should include information to meet the requirements of Annex II Section 4.

The documentation shall contain information for the demonstration of conformity with the general safety and performance requirements set out in Annex I that are applicable to the device taking into account its intended purpose, and shall include a justification, validation and verification of the solutions adopted to meet those requirements.

| **Applicable and non-applicable GSPRs (Annex II, 4, a)** |
| --- |
| Technical documentation reference to solutions to the general safety and performance requirements that apply to the device and an explanation as to why others do not apply |
| **Location:**  **File Name:**  **Page:**  **Note:** |

| **Methods of conformity (Annex II, 4, b)** |
| --- |
| Technical documentation reference to the method(s) used to demonstrate conformity with each applicable general safety and performance requirement |
| **Location:**  **File Name:**  **Page:**  **Note:** |

| **Common specification, Harmonised Standards, and other Standards/ Solutions (Annex II, 4, c)** |
| --- |
| Technical documentation reference to the harmonised standards, CS and/or other solutions applied |
| **Location:**  **File Name:**  **Page:**  **Note:** |

| **Related Documentation (Annex II, 4, d)** |
| --- |
| Technical documentation reference to the precise identity of the controlled documents offering evidence of conformity with each harmonised standard, CS or other method applied to demonstrate conformity with the general safety and performance requirements.  The information referred to under this point shall incorporate a cross-reference to the location of such evidence within the full technical documentation and, if applicable, the summary technical documentation. |
| **Location:**  **File Name:**  **Page:**  **Note:** |

# Part E - Benefit-Risk Analysis and Risk Management

This section should include information to meet the requirements of Annex II Section 5 and GSPRs of Annex I Chapter 1 Sections 1 – 5, 7, 8 & 9.

| **Risk Management (Annex II, 5 (a) and (b) and Annex I Chapter 1 Sections 1 - 5, 7, 8 and 9 - GSPRs)** | | |
| --- | --- | --- |
| **Is compliance claimed to EN ISO 14971?** | Yes  No | **Year:** |
| If No, please justify and provided supporting documentation as needed: | | |
| Please list any other risk related standards or guidance’s to which compliance is being claimed: | | |

| **Benefit-risk analysis (Annex II, 5 a)** |
| --- |
| Technical documentation reference to the benefit-risk analysis referred to in **Sections 1 and 8 of Annex I** |
| **Risks associated with the intended use of the device (Annex I, Chapter 1, Section 1)** |
| Technical documentation shall illustrate that the device(s) achieves the performance intended by the manufacturer and are designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose.  Evidence that the device is safe and effective and does 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. |
| **Location:**  **File Name:**  **Page:**  **Note:** |
| **Foreseeable risks and undesired side effects (Annex I, Chapter 1, Section 8)** |
| Technical documentation reference to **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 |
| **Location:**  **File Name:**  **Page:**  **Note:** |

| **Risk Management File (Annex II, 5 b)** |
| --- |
| Technical documentation to illustrate the solutions adopted and the results of the risk management referred to in Section 3 of Annex I. |
| **Risk Management Documentation (Annex I, Chapter 1, Section 3 (a) to (f))** |
| Technical documentation reference to the establishment, implementation, documentation, and maintenance of a risk management system.  Evidence of a continuous iterative process throughout the **entire lifecycle of a device**, requiring regular systematic updating. |
| **Location:**  **File Name:**  **Page:**  **Note:** |
| **Technical documentation reference to:**   1. a risk management plan for each device |
| **Location:**  **File Name:**  **Page:**  **Note:** |
| 1. identification and analysis of the known and foreseeable hazards associated with each device |
| **Location:**  **File Name:**  **Page:**  **Note:** |
| 1. estimation and evaluation of the risks associated with, and occurring during, the intended use and during reasonably foreseeable misuse over the full lifecycle of the device |
| **Location:**  **File Name:**  **Page:**  **Note:** |
| 1. elimination or control the risks referred to in point (c) in accordance with the requirements of Annex I Section 4   Annex I Section 4: Risk Control measures in order of priority:   * Eliminate or reduce risks as far as possible through safe design and manufacture. * Where appropriate, take adequate protection measures, including alarms, if necessary, in relation to risks that cannot be eliminated; and * Provide information for safety (warnings/precautions/contra-indications) and, where appropriate, training to users.   Manufacturers shall inform users of any residual risks. |
| **Location:**  **File Name:**  **Page:**  **Note:** |
| 1. evaluation of the impact of information from the production phase and, in particular, from the post-market surveillance system, on hazards and the frequency of occurrence thereof, on estimates of their associated risks, as well as on the overall risk, benefit-risk ratio and risk acceptability |
| **Location:**  **File Name:**  **Page:**  **Note:** |
| 1. based on the evaluation of the impact of the information referred to in point (e), if necessary, amend control measures in line with the requirements of Section 4. |
| **Location:**  **File Name:**  **Page:**  **Note:** |

# Part F – Performance/Complaint Analysis

|  |  |  |
| --- | --- | --- |
| **Performance/Complaint Analysis** | | |
| **Note:** During the review of the device under evaluation the NSAI must be informed of any; recall, market withdrawal, FSN, FSCA. If any of these occur, please submit updated versions of the impacted documents e.g., CER, RMF, IFU, etc. | | |
| Is there a product history for this device? | | Yes  No |
| **Note:**   * Within the PC1 Folder there is a blank ‘PC1 Performance Complaints.xls’ which must be completed. * Devices with a previous NSAI CE Mark require 5 years of data. * Devices new to NSAI require 10 years of data.   If 5/10 years’ worth of data is not available, please provide as many years as possible. | | |
| Confirm the associated ‘PC1 Performance Complaints.xls’ has been completed. | | Yes  No |
| **Location:**  **File Name:**  **Page:**  **Note:** | | |
| Based on the completed ‘PC1 Performance Complaints.xls’ create a summary table (layout broken out by year) of individual complaints, MIRs and CAPA’s related to complaints.  Details required should include:  **Individual Complaints** – A list of all complaints and their severity, and quantity and % total sales.  **Reportable incidents** which have been submitted to the relevant competent authority – A breakdown of submitted MIR forms, stating classification type, quantity and % total sales.  **CAPA** **(only related to performance and complaints)** – Status, Root Cause Analyses, linkages to updated risk documentation if required or justification as to why risk was not impacted etc. Include any CAPAs identified during the course of post-market surveillance. | | |
| Confirm the associated summary table has been completed | Yes  No | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | |
| Provide details of any recalls, market withdrawals, FSNs, FSCAs in any jurisdiction for the device under evaluation for the time period provided. | | |
| Details: | | |
| Create a trended analysis of the data over the required time period (5/10 years) in a graphical/table format and confirm that this has been completed | | Yes  No |
| **Location:**  **File Name:**  **Page:**  **Note:** | | |
| Were any negative trends identified within the analysis?  If yes, provide a detailed justification/explanation of these trends below or upload the justification | | Yes  No |
| Trend Justification:  **Location:**  **File Name:**  **Page:**  **Note:** | | |
| Confirm if any of the complaints resulted in a CAPA and/or design change of the product.  If yes, please provide details | | Yes  No |
| **Location:**  **File Name:**  **Page:**  **Note:** | | |

# Part G - Product Verification and Validation

In this section, the applicant must declare all applicable parts relevant to meet the requirements of Annex II Section 6

| **Annex II, 6** | |
| --- | --- |
| The documentation shall contain the results and critical analyses of all verifications and validation tests and/or studies undertaken to demonstrate conformity of the device with the requirements of this Regulation and in particular the applicable general safety and performance requirements.  Provide pre-clinical and clinical data including results of tests, such as engineering, laboratory, simulated use and animal tests, and evaluation of published literature applicable to the device, taking into account its intended purpose, or to similar devices, regarding the pre-clinical safety of the device and its conformity with the specifications.  Provide detailed information regarding test design, complete test or study protocols, methods of data analysis, in addition to data summaries and test conclusions. | |
| **Select as appropriate and complete the associated form within the corresponding appendix:** | |
| **Biocompatibility** (*Annex II, 6.1 b and 6.2 d*): **Appendix 1** | Yes  N/A |
| **Rationale for N/A:** | |
| **Sterilisation** (*Annex II, 6.1 b and 6.2, e*): **Appendix 2** | Yes  N/A |
| **Rationale for N/A:** | |
| **Electrical** (*Annex II, 6.1 b*): **Appendix 3** | Yes  N/A |
| **Rationale for N/A:** | |
| **Software** (*Annex II, 6.1 b*): **Appendix 4** | Yes  N/A |
| **Rationale for N/A:** | |
| **Clinical evaluation** (*Annex II, 6.1 c, d*): **Appendix 5** | Yes  N/A |
| **Rationale for N/A:** | |
| **Ancillary medicinal substance** (*Annex II, 6.2 b*): **Appendix 6** | Yes  N/A |
| **Rationale for N/A:** | |
| **Tissue of animal origin** (*Annex II, 6.2 b*): **Appendix 7** | Yes  N/A |
| **Rationale for N/A:** | |
| **Substances** (*Annex II, 6.2 c*): **Appendix 8** | Yes  N/A |
| **Rationale for N/A:** | |
| **Measuring function** (*Annex II, 6.2 f*): **Appendix 9** | Yes  N/A |
| **Rationale for N/A:** | |
| **Mechanical product performance** (*Annex II, 6.1 b*): **Appendix 10** | Yes  N/A |
| **Rationale for N/A:** | |

# Part H – Additional Requirements

| **Usability (Annex I, Chapter 1, Section 5 (a) & (b) and Article 83 (f))** | | | |
| --- | --- | --- | --- |
| Select ‘N/A’ if section is not applicable | | | N/A |
| **Rationale:** | | | |
| Are you stating compliance to ISO 62366? | Yes  N/A | **Year:** | |
| If no, please provide rationale below. Please demonstrate through objective evidence how the chosen solution meets or exceeds the harmonized standard:  **Rationale:** | | | |
| **Location:**  **File Name:**  **Page:**  **Note:**  *If yes, a standard compliance checklist may be beneficial for the review* | | | |
| Technical documentation reference to elimination or reduction of risks related to use error:   1. Reducing as far as possible the risks related to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety) | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | |
| 1. Consideration to the technical knowledge, experience, education, training and use environment, where applicable, and the medical and physical conditions of intended users (design for lay, professional, disabled, or other users).   *Examples of documentation includes the complete Usability Engineering file & UFMEA (plan, report, etc).*  *The information provided must relate to use specification, identification of user interface characteristics related to safety and potential use errors, identification and description of hazard-related use scenarios, specific cases for lay users, etc.* | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | |

|  |  |
| --- | --- |
| **For devices without an intended medical purpose only (Annex I, Chapter I, Section 9 and Annex XVI)** | |
| Select ‘N/A’ if section is not applicable | N/A |
| **Rationale:** | |
| Technical documentation reference to consideration for when the device is used under the conditions and for the purposes intended, it does not present a risk at all or presents a risk that is no more than the maximum acceptable risk related to the product's use which is consistent with a high level of protection for the safety and health of persons. | |
| **Location:**  **File Name:**  **Page:**  **Note:** | |

| **Devices without an intended medical purpose (Article 1 (2), Annex XVI)** | |
| --- | --- |
| Select ‘N/A’ if section is not applicable | N/A |
| **Rationale:** | |
| Confirm the device type from the list of groups of products as per Annex XVI.    *Please note the following:*   * *All relevant sections of the application form must be completed (Part A – H and relevant Appendices).* * *Compliance will be assessed in relation to:*   + ***(EU) MDR 2017/745***   + *Relevant common specifications, such as Commission Implementing Regulation* ***(EU) 2022/2346***   + *Classification: MDCG 2021-21 and Commission Implementing Regulation* ***(EU) 2022/2347*** *on the reclassification of rules 9 and 10 for Annex XVI devices* | |
| |  |  |  | | --- | --- | --- | | **Annex XVI** | **Description** | **Applicable (Y/N), including rationale** | | **List 1** | Contact lenses or other items intended to be introduced into or onto the eye. | Yes  No | | **Rationale:** | | | **List 2** | Products intended to be totally or partially introduced into the human body through surgically invasive means for the purpose of modifying the anatomy or fixation of body parts with the exception of tattooing products and piercings. | Yes  No | | **Rationale:** | | | **List 3** | Substances, combinations of substances, or items intended to be used for facial or other dermal or mucous membrane filling by subcutaneous, submucous, or intradermal injection or other introduction, excluding those for tattooing. | Yes  No | | **Rationale:** | | | **List 4** | Equipment intended to be used to reduce, remove, or destroy adipose tissue, such as equipment for liposuction, lipolysis or lipoplasty. | Yes  No | | **Rationale:** | | | **List 5** | High intensity electromagnetic radiation (e.g., infra-red, visible light and ultra-violet) emitting equipment intended for use on the human body, including coherent and non-coherent sources, monochromatic and broad spectrum, such as lasers and intense pulsed light equipment, for skin resurfacing, tattoo or hair removal or other skin treatment. | Yes  No | | **Rationale:** | | | **List 6** | Equipment intended for brain stimulation that apply electrical currents or magnetic or electromagnetic fields that penetrate the cranium to modify neuronal activity in the brain. | Yes  No | | **Rationale:** | | | |

| **Reprocessed Single Use Device (EU MDR 2017/745 Article 17)** | | N/A |
| --- | --- | --- |
| **Rationale:** | | |
| Any natural of legal person who reprocesses a single-use device to make it suitable for further use within the Union shall be considered to the manufacturer of the reprocessed device and shall assume the obligations incumbent on the manufacturers laid down in EU MDR 2017/745, which include obligations relating to the traceability of the reprocessed device in accordance with Chapter III of this Regulation. The reprocessor of the device shall be considered to be a producer for the purpose of Article 3(1) of Directive 85/374/EEC. | | |
| Is this device considered to be a reprocessed single-use medical device in accordance with EU MDR 2017/745, Article 17?  **If Yes, please contact the NSAI office prior to proceeding further with this Application File Form.** | Yes  No | |
| **If No** and the device is a Reusable Device / Reprocessed Device which does not fall under EU MDR 2017/745 Article 17 complete the relevant section below. | | |

| **Devices that require processing by the User/ 3rd party to allow use or reuse (Annex I Chapter II, Sections 11.2 and 23.4 (n))** | | | | N/A |
| --- | --- | --- | --- | --- |
| **Note:** This section is **not applicable to reprocessed single use devices** as per EU MDR 2017/745 Article 17.  If ‘N/A’ has been selected, please provide a rationale:  **Rationale:** | | | | |
| **Section RD1** | | | | |
|  | Please confirm which of the following type(s) describe your product family:  i) Reusable medical devices for multiple patients or a single patient:  • Sterile, requiring reprocessing after initial use and prior to each subsequent use.  or  ii) Reusable medical devices for multiple patients or a single patient:  • Non-sterile, requiring processing prior to initial use and reprocessing prior to each subsequent use.  or  iii) Single-use medical devices:  • Non-sterile, requiring processing prior to initial use.  or  iv) Other (please clarify) | | **Product Family Type:**  *(Example: Type ii – The devices are intended for multiple patient use and provided non-sterile requiring sterilization prior to each use)*    \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | |
| Is compliance with the current version of EN ISO 17664 claimed? | | Yes  No | |
| If no, please provide a rationale and supporting documentation to support the applicable GSPR’s.  **Rationale:**  **Supporting Documentation:**  **Location:**  **File Name:**  **Page:**  **Note:** | | | |
| **Section RD2** | | | | |
|  | Please identify the **process(es)** indicated in the IFU to be followed by the user/3rd party, to allow for safe and effective use/reuse of the device(s).  **Process 1:  *(****Example: Cleaning*)  **Process 2:** *(Example: Disinfection)*  **Process 3:**  *(Example: Sterilization)* | | | |
| Please identify each applicable **stage of the process** as indicated above and in the IFU to be followed by the user/3rd party, to allow for safe and effective use/reuse of the device(s).  *Examples include but are not limited to:*  1. initial treatment of the device at point of use, 2. preparation before cleaning, 3. cleaning(manual/automated), 4. disinfection(manual/automated), 5. drying, 6. inspection/maintenance, 7. packaging, 8. sterilization, 9. storage, 10. transportation)  **Stages of the Processing presented in the IFU/alternative:** | | | |
| **Section RD3** | | | | |
|  | For each process identified in the IFU, please provide the supporting validation protocols and reports. *[Example: Cleaning Validation Protocol & Report, Disinfection Validation Protocol & Report, Sterilization Validation Protocol & Report ]*  Ensure that the necessary process parameters and tolerances defined in the IFU are addressed in the validation documents.  **Note**: Where validation studies were performed for a product family, please demonstrate commonality between the different medical devices and justify the representative device tested by defining the worst case attribute(s). | | | |
| Confirm supporting documents have been provided for review. | | Yes  No | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | |
| **Section RD4** | | | | |
|  | Please provide the **Risk Analysis** to ensure all risks associated with the use of the devices to be processed/reprocessed by the user/3rd party have been evaluated. | | | |
| Confirm supporting documents have been provided for review. | | Yes  No | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | |
| **Section RD5** | | | | |
|  | Provide the **IFU** containing information on the appropriate processes for allowing reuse, including cleaning, disinfection, packaging and, where appropriate, the validated method of re-sterilisation  **Supporting Documentation:**  **Location:**  **File Name:**  **Page:**  **Note:**  **Note:** Details of the process steps, a description of the equipment and/or accessories and specifications for process parameters and their tolerances are to be included in addition to any limitations/restrictions on processing. | | | |
|  | Please provide details of the maximum number of allowable reuses or criteria to identify when the device should no longer be reused. Note: *Per Annex I 23.4 (n), this information shall be provided in the IFU.* | | | |
| Please provide the validation documents to verify the maximum number of allowable reuses, or criteria to identify when the device should no longer be reused, so that the safety and performance of the device is not compromised. | | | |
| Confirm supporting documents have been provided for review. | | Yes  No | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | |
| **Section RD6** | | | | |
|  | Please provide evidence to demonstrate that the processes (e.g. cleaning / disinfection / sterilisation) for allowing use or reuse of the device or accessories do not impact the safety and performance of the device? *[Example: Functional testing, Biocompatibility testing, Shelf-life testing etc]* | | | |
|  | Confirm supporting documents have been provided for review. | Yes  No | | |
|  | **Supporting Documentation:**  **Location:**  **File Name:**  **Page:**  **Note:** | | | |

| **System or Procedure Pack** | N/A |
| --- | --- |
| **Rationale:** | |
| Where the device under application is determined to meet the EU MDR ‘Article 2’ definitions 10 and 11 regarding system or procedure pack, provide a statement indicating this fact.  **Note EU MDR ‘Article 2’ definitions:**  (10) ‘procedure pack’ means a combination of products packaged together and placed on the market with the purpose of being used for a specific medical purpose.  (11) ‘system’ means a combination of products, either packaged together or not, which are intended to be inter-connected or combined to achieve a specific medical purpose. | |
| **Location:**  **File Name:**  **Page:**  **Note:** | |

| **System or Procedure Pack (EU MDR Article 22, 1 a, b and c)** | N/A |
| --- | --- |
| **Rationale:** | |
| Natural or legal persons shall draw up a statement if they combine devices bearing a CE marking with the following other devices or products, in a manner that is compatible with the intended purpose of the devices or other products and within the limits of use specified by their manufacturers, in order to place them on the market as a system or procedure pack: | |
| (a) other devices bearing the CE marking; | N/A |
| **Location:**  **File Name:**  **Page:**  **Note:** | |
| (b) in vitro diagnostic medical devices bearing the CE marking in conformity with Regulation (EU) 2017/746; | N/A |
| **Location:**  **File Name:**  **Page:**  **Note:** | |
| (c) other products which are in conformity with legislation that applies to those products only where they are used within a medical procedure or their presence in the system or procedure pack is otherwise justified. | N/A |
| **Location:**  **File Name:**  **Page:**  **Note:** | |

| **System or Procedure Pack (EU MDR Article 22, 2 a, b and c)** | N/A |
| --- | --- |
| **Rationale:** | |
| In the statement made pursuant to paragraph 1 (see EU MDR Article 22, 1 a, b and c above), the natural or legal person concerned shall declare that: | |
| (a) they verified the mutual compatibility of the devices and, if applicable other products, in accordance with the manufacturers' instructions and have carried out their activities in accordance with those instructions. | N/A |
| **Location:**  **File Name:**  **Page:**  **Note:** | |
| (b) they packaged the system or procedure pack and supplied relevant information to users incorporating the information to be supplied by the manufacturers of the devices or other products which have been put together. | N/A |
| **Location:**  **File Name:**  **Page:**  **Note:** | |
| (c) the activity of combining devices and, if applicable, other products as a system or procedure pack was subject to appropriate methods of internal monitoring, verification, and validation. | N/A |
| **Location:**  **File Name:**  **Page:**  **Note:** | |

| **System or Procedure Pack (EU MDR Article 22, 3)** | N/A |
| --- | --- |
| **Rationale:** | |
| Any natural or legal person who sterilises systems or procedure packs referred to in paragraph 1 for the purpose of placing them on the market shall, at their choice, apply one of the procedures set out in Annex IX or the procedure set out in Part A of Annex XI. The application of those procedures and the involvement of the notified body shall be limited to the aspects of the procedure relating to ensuring sterility until the sterile packaging is opened or damaged. The natural or legal person shall draw up a statement declaring that sterilisation has been carried out in accordance with the manufacturer's instructions.  Please clarify how the requirement is met | |
| **Location:**  **File Name:**  **Page:**  **Note:** | |

| **System or Procedure Pack (EU MDR Article 22, 4)** | N/A |
| --- | --- |
| **Rationale:** | |
| Where the system or procedure pack incorporates devices which do not bear the CE marking or where the chosen combination of devices is not compatible in view of their original intended purpose, or where the sterilisation has not been carried out in accordance with the manufacturer's instructions, the system or procedure pack shall be treated as a device in its own right and shall be subject to the relevant conformity assessment procedure pursuant to Article 52.  The natural or legal person shall assume the obligations incumbent on manufacturers.  Please clarify how the requirement is met | |
| **Location:**  **File Name:**  **Page:**  **Note:** | |

| **System or Procedure Pack (EU MDR Article 22, 5)** | N/A |
| --- | --- |
| **Rationale:** | |
| The systems or procedure packs referred to in paragraph 1 of this Article shall not themselves bear an additional CE marking but they shall bear the name, registered trade name or registered trade mark of the person referred to in paragraphs 1 and 3 of this Article as well as the address at which that person can be contacted, so that the person's location can be established.  Systems or procedure packs shall be accompanied by the information referred to in Section 23 of Annex I. The statement referred to in paragraph 2 of this Article shall be kept at the disposal of the competent authorities, after the system or procedure pack has been put together, for the period that is applicable under Article 10(8) to the devices that have been combined. Where those periods differ, the longest period shall apply.  Please clarify how the requirement is met | |
| **Location:**  **File Name:**  **Page:**  **Note:** | |

# Appendix 1 - Biocompatibility

The section below is in support of compliance to the technical documentation requirements of Annex II sections 6.1 (a) and (b) and GSPRs of Annex I.

|  |  |
| --- | --- |
| **Equivalence** | |
| If equivalence to an existing medical device is being claimed in compliance with MDR Annex XIV, Part A, Section 3 and MDCG 2020-5, please confirm the **Biological Characteristics Section** of the **Equivalence Declaration** form (MDR-2003 or MDR-3003) has been completed. | Yes  N/A |
| If ‘N/A’ has been selected, please provide a rationale:  **Rationale:** | |
| **Location:**  **File Name:**  **Page:**  **Note:** | |

| **Biocompatibility** | | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Note:** The Biocompatibility Review will incorporate analysis of data submitted in other sections, i.e., **IFU, FMEA’s, risk documents including benefit/risk analysis, etc.** and may generate subsequent queries. | | | | | | | | | |
| Is compliance with the current revision of EN ISO 10993-1 claimed? | | | | | | | | Yes  No | |
| If no, please provide rationale:  **Rationale:** | | | | | | | | | |
| Provide a list of all ISO 10993-X standards compliance is claimed to:  **Note:** This must be in alignment with the BER and the GSPR checklist, HS section, etc. – as required. | | | | | | | | | |
| **Applicable Biocompatibility standards used** | | | | | **Year: Version** | | | | |
| *ISO 10993-5* | | | | | *2009* | | | | |
| *ISO 10993-12* | | | | | *2021* | | | | |
|  | | | | |  | | | | |
|  | | | | |  | | | | |
|  | | | | |  | | | | |
| **Biocompatibility Categorisation: Nature of Body Contact** | | | | | | | | | |
| **Surface-Contacting Devices** | | **External Communicating Devices** | | **Implant Devices** | | | | | |
|  | Intact skin |  | Blood path, indirect |  | | | Tissue/bone | | |
|  | Mucosal membrane |  | Tissue/bone/dentin |  | | | Blood | | |
|  | Breached or compromised surfaces |  | Circulating blood |  | | | | | |
| Please provide rationale for above selected Nature of Body Contact.  **Rationale:** | | | | | | | | | |
| State the identity of all supporting documentation from which the rationale for the Nature of Body Contact has been derived (for example: IFU, labelling, CER, etc.) | | | | | | | | | |
| **Document Name** | | | | **Section, page number** | | | | | |
| *CER-XXX* | | | | *Section 5, page 23* | | | | | |
|  | | | |  | | | | | |
|  | | | | Add more lines as required | | | | | |
| **Duration of Contact** | | | | | | | | | |
|  | **Limited exposure**  **(< 24hrs)** |  | **Prolonged exposure**  **(>24hrs <30 days)** |  | | **Long Term**  **(>30 days)** | | | |
| Please provide rationale for above selected Duration of Contact:  **Rationale:** | | | | | | | | | |
| State the identity of all supporting documentation from which the rationale for the Duration of Contact has been derived (for example: IFU, labelling, CER, etc.) | | | | | | | | | |
| **Document Name** | | | | **Section, page number** | | | | | |
| *CER-XXX* | | | | *Section 5, page 23* | | | | | |
|  | | | |  | | | | | |
|  | | | | *Add more lines as required* | | | | | |
| Carcinogenic, Mutagenic and *Reprotoxic* substances (CMRs) (MDR Annex II, Section 6.2 (d)) | | | | | | | | | N/A |
| Please complete the table below for devices containing CMR substances. | | | | | | | | | |
| |  |  | | --- | --- | |  | **Technical documentation reference** | | Does the device contain CMRs or Endocrine disrupting substances above 0.1% w/w?\*  Yes  No  *(Note: supporting documentation for determination of the* ***absence or presence*** *of CMRs or Endocrine disrupting substances must be provided).* | **Location:**  **File Name:**  **Page:**  **Note:** | | If yes, provide the following justification that meets the requirements of MDR Annex I 10.4.2 (a) to (d)† | **Location:**  **File Name:**  **Page:**  **Note:** | | If yes, does the device labelling/ packaging include warnings of the CMR or Endocrine disrupting substance?ǂ | **Location:**  **File Name:**  **Page:**  **Note:** | | Confirm that the DoC references CMR/ endocrine disrupting substances relevant regulations+ | **Location:**  **File Name:**  **Page:**  **Note:** |   \* Annex II, 6.2 (d) and Annex I, Chapter II, Section 10.4.1  †Annex I, Chapter II, Section 10.4.2 (a) to (d)  ǂ Annex I, Chapter II 10.4.5 & Annex I, Chapter II, Section 23.4 (s) part 6  + Annex IV point 6 | | | | | | | | | |

| **Tests Considered/Performed for this Application** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Tests to be considered** | **ISO 10993 series**  **and Year**  ***Note:*** *A gap analysis must be provided if the current version of standard was not used* | **Test Article information** | **Location in BER where this test is discussed, or its waiving is justified** | **Test Protocol and**  **Report Number** | **Date of testing** | **Conclusion** |
| **Physical and/or Chemical**  **Characterisation** | -18: | **Test Article Model Number:**  Corresponding model number from Part A, Annex II, 1.1 (i): | **Location:**  **File Name:**  **Page:**  **Note:** |  |  |  |
| **Cytotoxicity** | -5: | **Test Article Model Number:**  Corresponding model number from Part A, Annex II, 1.1 (i): | **Location:**  **File Name:**  **Page:**  **Note:** |  |  |  |
| **Sensitisation** | -10: | **Test Article Model Number:**  Corresponding model number from Part A, Annex II, 1.1 (i): | **Location:**  **File Name:**  **Page:**  **Note:** |  |  |  |
| **Irritation (incl. intracutaneous reactivity)** | -23: | Test Article Model Number:  Corresponding model number from Part A, Annex II, 1.1 (i): | **Location:**  **File Name:**  **Page:**  **Note:** |  |  |  |
| **Material Mediated Pyrogenicity** | -11: | **Test Article Model Number:**  Corresponding model number from Part A, Annex II, 1.1 (i): | **Location:**  **File Name:**  **Page:**  **Note:** |  |  |  |
| **Acute Systemic toxicity** | -11: | **Test Article Model Number:**  Corresponding model number from Part A, Annex II, 1.1 (i): | **Location:**  **File Name:**  **Page:**  **Note:** |  |  |  |
| **Sub-Acute toxicity** | -11: | **Test Article Model Number:**  Corresponding model number from Part A, Annex II, 1.1 (i): | **Location:**  **File Name:**  **Page:**  **Note:** |  |  |  |
| **Sub-Chronic toxicity** | -11: | **Test Article Model Number:**  Corresponding model number from Part A, Annex II, 1.1 (i): | **Location:**  **File Name:**  **Page:**  **Note:** |  |  |  |
| **Chronic toxicity** | -11: | **Test Article Model Number:**  Corresponding model number from Part A, Annex II, 1.1 (i): | **Location:**  **File Name:**  **Page:**  **Note:** |  |  |  |
| **Implantation effects** | -6: | **Test Article Model Number:**  Corresponding model number from Part A, Annex II, 1.1 (i): | **Location:**  **File Name:**  **Page:**  **Note:** |  |  |  |
| **Haemocompatibility** | -4: | **Test Article Model Number:**  Corresponding model number from Part A, Annex II, 1.1 (i): | **Location:**  **File Name:**  **Page:**  **Note:** |  |  |  |
| **Genotoxicity**  **mutagenicity** | -3: | **Test Article Model Number:**  Corresponding model number from Part A, Annex II, 1.1 (i): | **Location:**  **File Name:**  **Page:**  **Note:** |  |  |  |
| **Carcinogenicity** | -3: | **Test Article Model Number:**  Corresponding model number from Part A, Annex II, 1.1 (i): | **Location:**  **File Name:**  **Page:**  **Note:** |  |  |  |
| **Reproductive and developmental toxicity** | -3: | **Test Article Model Number:**  Corresponding model number from Part A, Annex II, 1.1 (i): | **Location:**  **File Name:**  **Page:**  **Note:** |  |  |  |
| **Biodegradation** | -9: | **Test Article Model Number:**  Corresponding model number from Part A, Annex II, 1.1 (i): | **Location:**  **File Name:**  **Page:**  **Note:** |  |  |  |
| **Toxicokinetic studies** | -16: | **Test Article Model Number:**  Corresponding model number from Part A, Annex II, 1.1 (i): | **Location:**  **File Name:**  **Page:**  **Note:** |  |  |  |
| **Immunotoxicology** | -20: | **Test Article Model Number:**  Corresponding model number from Part A, Annex II, 1.1 (i): | **Location:**  **File Name:**  **Page:**  **Note:** |  |  |  |
| **Other Tests** | **Series:**  **Year:** | **Test Article Model Number:**  Corresponding model number from Part A, Annex II, 1.1 (i): | **Location:**  **File Name:**  **Page:**  **Note:** |  |  |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Please Confirm the Biological Evaluation Report (BER) and also the Biological Evaluation Plan has been provided for review.**  **Note:** This can be contained within one single document. | | | | | Yes  No | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | |
| **Please confirm the following key criteria have been documented in the BER, stating the section and page where this information is contained:** | | | | | | | |
| * **Device description** | | | | | | | |
| * + Diagrams, pictures, model numbers (consistent with those stated in Part A, Annex II, 1.1 (i) section of this form) | | | | **Location:**  **File Name:**  **Page:**  **Note:** | | | |
| * + Characterisation of the materials of construction (**direct and indirectly patient and user contacting**) including suitable alternative materials, CMR substances if present | | | | **Location:**  **File Name:**  **Page:**  **Note:** | | | |
| * + Physical characteristics | | | | **Location:**  **File Name:**  **Page:**  **Note:** | | | |
| * + Any existing toxicology and other biological safety data on product and component materials, breakdown products and metabolites | | | | **Location:**  **File Name:**  **Page:**  **Note:** | | | |
| * + Intended use | | | | **Location:**  **File Name:**  **Page:**  **Note:** | | | |
| * + List of any changes to the device over its marketed history and/ or since biological evaluation testing was initially undertaken | | | | **Location:**  **File Name:**  **Page:**  **Note:** | | | |
| * + Manufacturing information (locations, process steps, processing aids/ contaminants/ residues, additives) | | | | **Location:**  **File Name:**  **Page:**  **Note:** | | | |
| * + Packaging (pictures/ diagrams, configuration, direct/ indirect contacting materials) | | | | **Location:**  **File Name:**  **Page:**  **Note:** | | | |
| * + Leachable substances, degradation products or other components and their interactions in the final product | | | | **Location:**  **File Name:**  **Page:**  **Note:** | | | |
| * + The performance and physical characteristics of the final product (porosity, particle size, shape, surface morphology – as appropriate) | | | | **Location:**  **File Name:**  **Page:**  **Note:** | | | |
| * + Device(s) sterilisation (method, dose range, facility, cycles, re-sterilisation, justification for sterilisation parameters used for the test article used in any biological testing undertaken) | | | | **Location:**  **File Name:**  **Page:**  **Note:** | | | |
| * + Evaluation over the whole lifetime of the device (storage conditions, shelf-life, handling, duration of use, reprocessing) | | | | **Location:**  **File Name:**  **Page:**  **Note:** | | | |
| * + State the supporting document file name(s): | | | | **Location:**  **File Name:**  **Page:**  **Note:** | | | |
| **Confirm the Test Protocols and Reports, referenced in the Biological Evaluation Plan/Report, have been provided for review.**  **Note:** *Ensure Test Protocol and Report numbers have been documented in the above table ‘Tests Considered/Performed for this Application’ section and included in the submission.* | | | | | Yes  No | | |
| Provide evidence for proof of competence regarding biocompatibility (including experience with the ISO 10993 standard series) of the person(s) concluding the biocompatibility results). | | | | | Yes  No | | |
| * + State the supporting document file name(s): | | | | **Location:**  **File Name:**  **Page:**  **Note:** | | | |
| If ‘No’ has been selected for any of the above, please provide rationale:  **Rationale:** | | | | | | | |
| Confirm testing has been completed using the final medical device, or representative samples from the final medical device or materials that have been processed in the same manner as the final medical device. | | | | | Yes  No | | |
| If ‘No’ has been selected for any of the above, please provide rationale:  **Rationale:** | | | | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | |
| A comprehensive description of traceability between the model numbers applied for in this submission (Part A, Annex II, 1.1 (i)) and the test articles used in any biological testing presented must be provided in the BER.  State the section and page where this is documented. | | | | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | |
| If applicable where the test article / model is not identical to a model stated in section Part A, Annex II, 1.1 (i), a rationale must be provided. | | | | | | N/A | |
| Where N/A is selected please provide a rationale  **Rationale:** | | | | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | |
| Where only one model variant (e.g., one size) was tested, justification why it is representative of all the application models listed in Part A, Annex II, Section 1.1 (i). | | | | | | | N/A |
| Where N/A is selected please provide a rationale  **Rationale:** | | | | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | |
| Where any testing has been undertaken, confirm that this has been performed using an ISO 17025 accredited testing facility and please ensure the corresponding certificate has been provided for review. | | | | | Yes  No | | |
| If no, provide rationale:  **Rationale:** | | | | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | |
| Where any testing has been undertaken, confirm that conformity with the provisions of Directive 2004/10/EC of the European Parliament and of the Council (GLP) is demonstrated. (Annex II, Section 6.1 (b)) | | | | | Yes  No | | |
| If no, provide rationale:  **Rationale:** | | | | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | |
| Where the final medical device is sterilised, please complete the table below. Confirm that the relevant supporting sterilisation documentation/ evidence for the test article(s) has been provided for review. | | | | | Yes  No | | |
| If no, provide rationale:  **Rationale:** | | | | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | |
| **Test Article ID (aligned with ‘Test Article information’ provided in ‘Tests Considered/ Performed for this Application’ table)** | **Sterilisation type** | **Sterilisation dose** | **Number of cycles** | | **Supporting Documentation file Name** | | |
| *BIC-XXX-001* | *Gamma Irradiation* | *25kGy* | *2* | | *STER-XXX, Section 4, page 60* | | |
|  |  |  |  | |  | | |
|  |  |  |  | |  | | |
| Please provide rationale for the chosen sterilisation dose for each test article listed | | | | | | | |
| **Rationale:**  Please upload all supporting documentation. | | | | | | | |

# Appendix 2

## Sterilisation

| **Sterilisation (Annex II sections 6.1 (b), 6.2 (e) and GSPRs of Annex I, Chapter II, Section 11.5).** | | | | | | | | | | | | | | | | | | N/A |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| If ‘N/A’ has been selected, please provide a rationale:  **Rationale:** | | | | | | | | | | | | | | | | | | |
| **Section S1** | | | | | | | | | | | | | | | | | | |
|  | Please be aware that the Sterilisation Review will incorporate analysis of data submitted in other sections, i.e., IFU and labels, and Risk documents etc. and may generate subsequent queries. | | | | | | | | | | | | | | | | | |
| **Section S2** | | | | | | | | | | | | | | | | | | |
|  | **Sterilisation Information Summary** | | | | | | | | | | | | | | | | | |
| |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | | **Product Family** | **Model/ Part No** | **Ster Method** | **Mfg Site & Address** | **Sterilisation Site & Address** | **Site Responsible for Release** | **Protocol & Report No** | **Is Parametric release used?** | | |  |  |  |  |  |  |  | Yes | No | |  |  |  |  |  |  |  | Yes | No | |  |  |  |  |  |  |  | Yes | No | |  |  |  |  |  |  |  | Yes | No | |  |  |  |  |  |  |  | Yes | No |   *Add lines as required.*  Provide a history of the sterilisation of the device(s) in scope of application, including how the product was initially validated, information on any revalidations, changes that impacted the sterilisation validation etc.    Any further detail: | | | | | | | | | | | | | | | | | |
| Confirm that all relevant QMS certificates for the sterilisation providers have been provided for review. | | | | | | | | | | | | | | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
| Confirm the Proof of competence of Sterilisation expert (e.g., author/approver) has been provided for review. | | | | | | | | | | | | | | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
| **Section S3** | | | | | | | | | | | | | | | | | | |
|  | **Ethylene Oxide (EO): (**Note: If **EO is not** **used** select N/A and do not complete this section). | | | | | | | | | | | | | | | N/A | | |
| Is compliance with the current version of EN ISO 11135 claimed? | | | | | | | | | | | | | Yes  No | | | | |
| If no, please provide a rationale and supporting documentation to support the applicable GSPR’s.  **Rationale:** | | | | | | | | | | | | | | | | | |
| Please provide the following information regarding the sterilisation of the product(s) in scope of application  Sterilisation Chamber(s) used  Sterilisation Cycle number used  Validation method used e.g. Annex B Overkill/Half Cycle, Annex A Fraction Negative | | | | | | | | | | | | | | | | | |
| Provide the Initial validation information *(For all devices under the scope of this application)* | | | | **Protocol#** | | | |  | | | | | | | | | |
| **Year:** | | | |  | | | | | | | | | |
| **Report#** | | | |  | | | | | | | | | |
| **Year:** | | | |  | | | | | | | | | |
| Please provide evidence that the IQ and OQ has been completed and approved. | | | | | | | | | | | | | Yes  No | | | | |
| Has a full PQ validation been performed? | | | | | | | | | | | | | Yes  No | | | | |
| In the instance where a full validation was not performed, has adoption into an existing product family or processing category, or equivalence to a validated product been used? | | | | | | | | | | | | | Yes  No | | | | |
| If the sterilisation validation of the product is by adoption into an existing product family or processing category, or equivalence to a validated product, please provide the appropriate rationale along with all supporting documentation (e.g., the initial validation protocol and report referenced in the adoption report).  **Rationale:** | | | | | | | | | | | | | | | | | |
| List the supporting document titles and references: | | | | | | | | | | | | | | | | | |
| Confirm that the documents have been provided for review. | | | | | | | | | | | | | Yes  No | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
| If the Initial Validation is greater than 1 year old, please also provide the latest revalidation/ requalification *(For all device types under the scope of this application)* | | | | **Protocol#** | | | | |  | | | | | | | | |
| **Year:** | | | | |  | | | | | | | | |
| **Report#** | | | | |  | | | | | | | | |
| **Year:** | | | | |  | | | | | | | | |
| Please define the frequency of the requalification and how it was justified | | | | | | | | | | | | | | | | | |
| If internal or external process devices (EPCDs or IPCDs) are used, please describe these in detail. | | | | | | | | | | | | | | | | | |
| If the PCD’s are different to those used in the initial validation, please provide a rationale.  **Rationale:** | | | | | | | | | | | | | | | | | |
| Provide supporting documentation to show the appropriateness of the PCD used for Process definition, validation or routine monitoring and control. The PCD shall present a challenge to the sterilisation process that is equivalent to or greater than the challenge presented by the natural product bioburden, at the most difficult to sterilise location within the product. Confirm supporting documentation has been provided for review | | | | | | | | | | | | | Yes  No | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
| **EO Residuals**  Categorize the device according to the duration of contact: | | | | | | | | | | | | | | | | | |
| A – Limited Exposure | | |  | | | |  | | | | | | | | | | |
| B – Prolonged Exposure | | |  | | | |
| C – Permanent Contact | | |  | | | |
| Is compliance with the current version of EN ISO 10993-7 claimed? | | | | | | | | | | | | | Yes  No | | | | |
| If no, please provide a rationale and supporting documentation to support the applicable GSPR’s.  **Rationale:** | | | | | | | | | | | | | | | | | |
| If the device is a surface contacting device or an implant as defined in ISO 10993-7, please either submit (under this section of the Application File) the necessary **Tolerable Contact Limit (TCL) testing** in accordance with ISO 10993-7 or confirm that the necessary irritation testing to the biocompatibility standard ISO 10993-10 has been completed and meets the acceptance criteria.  **Rationale:** | | | | | | | | | | | | | | | | | |
| Is the device intended for use by neonates and infants? | | | | | | | | | | | | | Yes  No | | | | |
| If Yes, is compliance with the current version of EN ISO 10993-7/Amendment 1 claimed. | | | | | | | | | | | | | Yes  No | | | | |
| Provide the relevant EO residual protocols and reports.  Confirm that the supporting documents have been provided for review | | | | | | | | | | | | | Yes  No | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
|  | Is the device placed on the market in a “defined microbiological condition” per Annex II, 6.2 e) of MDR (2017/745); e.g., non-pyrogenic. | | | | | | | | | | | | | Yes  No | | | | |
| If **Yes**, please state the microbiological condition, and provide evidence to support this microbiological condition.   * Test method used. * Test method qualification protocol and report. * Requirements for routine monitoring (sample size and frequency). * Acceptance criteria. * Results of two recent tests. | | | | | | | | | | | | | | | | | |
|  | If **No,** please provide a rationale.  **Rationale:** | | | | | | | | | | | | | | | | | |
| Confirm that the supporting documents have been provided for review. | | | | | | | | | | | | | Yes  No | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
| Please provide product Bioburden data for the last 12 months. | | | | | | | | | | | | | | | | | |
| Confirm that the supporting documents have been provided for review. | | | | | | | | | | | | | Yes  No | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
| Please provide an approved copy of the Process Specification used for routine sterilisation of the product.  For each Process specification, show how compliance is shown with each clause of the ‘Review and Approval of Validation’ section of EN ISO 11135 section 9.5 .  Identify the location of the supporting evidence for each part of the standard in the table below:  **Note: Please replicate this Table as required** | | | | | | | | | | | | | | | | | |
| |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | | **Product Family** | **Process Specification #** | **Clause of standard** | ***Protocol &/or Report Docume*nt#** | **Page #** | **Paragraph #** | | *e.g., Acme* | *e.g., ABC Doc* | *e.g., ISO11135 9.5 a)* | *e.g., PP 123* | *e.g.,*  *Page 23* | *e.g., 6.2* | |  |  |  |  |  |  | |  |  |  |  |  |  |   *Add lines as required.* | | | | | | | | | | | | | | | | | |
|  | Confirm that the supporting documents have been provided for review. | | | | | | | | | | | | | Yes  No | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
| **Section S4** | | | | | | | | | | | | | | | | | | |
|  | **Irradiation:**  **(**If **Irradiation is not used** select N/A and do not complete this section). | | | | | | | | | | | | | | | | | N/A |
| Is compliance with the current version of EN ISO 11137 claimed? | | | | | | | | | | | | | Yes  No | | | | |
| If no, please provide rationale and any supporting documentation to support the applicable GSPR’s. | | | | | | | | | | | | | | | | | |
| Select the irradiation process used: |  | | | | | E – Beam | | | | |  | | | | | | |
|  | | | | | Gamma | | | | |
|  | | | | | X-Ray | | | | |
|  | | | | | Other | | | | |
| If **Other** selected, please state process: | | | | | | | | | | | | | | | | |
| What dose setting method(s) is used: |  | | | | | VDMAX25 | | | | |  | | | | | | |
|  | | | | | Other VDMAX:  Please provide VDMAX method used | | | | |
|  | | | | | Method 1 | | | | |
|  | | | | | Method 2 | | | | |
| Confirm that the full validation(s) has been provided for review.  This must include:   * Initial dose establishment with protocol, report and supporting data. * Dose mapping and load configuration for the sterilisation facility(-ies) used. * Product family definition and last annual product family review per EN ISO 11137-2, Section 4. | | | | | | | | | | | | | Yes  No | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
| Please provide evidence that the IQ and OQ has been completed and approved. | | | | | | | | | | | | | | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
| Has a full PQ validation been performed? | | | | | | | | | | | | | Yes  No | | | | |
| In the instance where a full validation has not been performed, has adoption into an existing product family or processing category, or equivalence to a validated product been used? | | | | | | | | | | | | | Yes  No | | | | |
| If the sterilisation validation of the product is by adoption into an existing product family or processing category, or equivalence to a validated product, please provide the appropriate rationale along with all supporting documentation (e.g., the initial validation protocol and report referenced in the adoption report).  **Rationale:** | | | | | | | | | | | | | | | | | |
| List the supporting document titles and references: | | | | | | | | | | | | | | | | | |
| Confirm that the documents have been provided for review. | | | | | | | | | | | | | Yes  No | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
| Confirm that the last year’s dose audit reports (If the initial dose establishment is greater than 12 months) have been provided for review. | | | | | | | | | | | | | Yes  No | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
|  | Is the device placed on the market in a “defined microbiological condition” per Annex II, 6.2 e) of MDR (2017/745); e.g., non-pyrogenic. | | | | | | | | | | | | | Yes  No | | | | |
| If **Yes**, please state the microbiological condition, and provide evidence to support this microbiological condition.   * Test method used. * Test method qualification protocol and report. * Requirements for routine monitoring (sample size and frequency). * Acceptance criteria. * Results of two recent tests. | | | | | | | | | | | | | | | | | |
| If **No,** please provide a rationale.  **Rationale:** | | | | | | | | | | | | | | | | | |
|  | Confirm that the supporting documents have been provided for review. | | | | | | | | | | | | | Yes  No | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
| Please provide product Bioburden data for the last 12 months. | | | | | | | | | | | | | | | | | |
|  | | | | | | | | | | | | | | | | | |
| Confirm that the supporting documents have been provided for review. | | | | | | | | | | | | | Yes  No | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
| Please provide an approved copy of the Process Specification used for routine sterilisation of the product.  For each Process specification, show how compliance is shown with each clause of the ‘Review and Approval of Validation’ section of EN ISO 11137-1 section 9.4.3 (Gamma) or 9.4.4 (E beam/X Ray).  Identify the location of the supporting evidence for each part of the standard in the table below:  **Note: Please replicate this Table as required** | | | | | | | | | | | | | | | | | |
| |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | | **Product Family** | **Process Specification #** | **Clause of standard** | ***Protocol &/or Report Docume*nt#** | **Page #** | **Paragraph #** | | *e.g., Acme* | *e.g., ABC Doc* | *e.g., ISO11137-1 9.4.3 a)* | *e.g., PP 123* | *e.g.,*  *Page 23* | *e.g., 6.2* | |  |  |  |  |  |  | |  |  |  |  |  |  |   *Add lines as required.* | | | | | | | | | | | | | | | | | |
| Confirm that the supporting documents have been provided for review. | | | | | | | | | | | | | Yes  No | | | | |
| **Section S5** | | | | | | | | | | | | | | | | | | |
|  | **Moist Heat: (**If **Moist Heat is not used** select ‘N/A’ and do not complete this section). | | | | | | | | | | | | | | | | N/A | |
| Is compliance with the current version of EN ISO 17665 claimed? | | | | | | | | | | | | | Yes  No | | | | |
| If No, please provide rationale and any supporting documentation to support the applicable GSPR’s.  **Rationale:** | | | | | | | | | | | | | | | | | |
| What type of cycle is used? | |  | | | Pre-Vac | | |  | | | | | | | | | |
|  | | | Gravity | | |
|  | | | Other | | |
| If Other selected, please add details: | | | | | | | | | | | | | | | |
| Provide the Initial validation information *(For all devices under the scope of this application)* | | **Protocol#** | | | | | | | |  | | | | | | | |
| **Year:** | | | | | | | |  | | | | | | | |
| **Report#** | | | | | | | |  | | | | | | | |
| **Year:** | | | | | | | |  | | | | | | | |
| Please provide evidence that the IQ and OQ has been completed and approved. | | | | | | | | | | | | | | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
| Has a full PQ validation been performed? | | | | | | | | | | | | Yes  No | | | | | |
| In the instance where a full validation has not been performed, has adoption into an existing product family or processing category, or equivalence to a validated product been used?  **Rationale:** | | | | | | | | | | | | | | | | | |
| If the sterilisation validation of the product is by adoption into an existing product family or processing category, or equivalence to a validated product, please provide the appropriate rationale along with all supporting documentation (e.g., the initial validation protocol and report referenced in the adoption report).  **Rationale:** | | | | | | | | | | | | | | | | | |
| List the supporting document titles and references: | | | | | | | | | | | | | | | | | |
| Confirm that the supporting documents has been provided for review. | | | | | | | | | | | | | Yes  No | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
|  | If the Initial Validation is greater than 1 year old, please also provide the latest revalidation/ requalification *(For all device types under the scope of this application)* | | | | **Protocol#** | | | | |  | | | | | | | | |
| **Year:** | | | | |  | | | | | | | | |
| **Report#** | | | | |  | | | | | | | | |
| **Year:** | | | | |  | | | | | | | | |
| Please define the frequency of the requalification and how it was justified | | | | | | | | | | | | | | | | | |
| Is the device placed on the market in a “defined microbiological condition” per Annex II, 6.2 e) of MDR (2017/745); e.g., non-pyrogenic. | | | | | | | | | | | | | Yes  No | | | | |
| If **Yes**, please state the microbiological condition, and provide evidence to support this microbiological condition.   * Test method used. * Test method qualification protocol and report. * Requirements for routine monitoring (sample size and frequency). * Acceptance criteria. * Results of two recent tests. | | | | | | | | | | | | | | | | | |
| If **No,** please provide a rationale.  **Rationale:** | | | | | | | | | | | | | | | | | |
| Confirm that the supporting documents have been provided for review. | | | | | | | | | | | | | Yes  No | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
| Please provide product Bioburden data for the last 12 months. | | | | | | | | | | | | | | | | | |
| Confirm that the supporting documents have been provided for review. | | | | | | | | | | | | | Yes  No | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
|  | Please provide an approved copy of the Process Specification used for routine sterilisation of the product.  For each Process specification, show how compliance is shown with each clause of the ‘Review and Approval of Validation’ section of the relevant standard, i.e.   * EN ISO 17665-1 section 9.5.2 (Moist heat).   Identify the location of the supporting evidence for each part of the standard in the table below:  **Note: Please replicate this Table as required** | | | | | | | | | | | | | | | | | |
| |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | | **Product Family** | **Process Specification #** | **Clause of standard** | ***Protocol &/or Report Docume*nt#** | **Page #** | **Paragraph #** | | *e.g., Acme* | *e.g., ABC Doc* | *e.g., ISO17665-1 9.5.2 a)* | *e.g., PP 123* | *e.g.,*  *Page 23* | *e.g., 6.2* | |  |  |  |  |  |  | |  |  |  |  |  |  |   *Add lines as required.* | | | | | | | | | | | | | | | | | |
| Confirm that the supporting documents have been provided for review. | | | | | | | | | | | | | | Yes  No | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | |  | | | |
| **Section S6** | | | | | | | | | | | | | | | | | | |
|  | **Aseptic processing: (**If **Aseptic Processing is not performed** select N/A and do not complete this section). | | | | | | | | | | | | | | | | | N/A |
| Is compliance with the current version of the applicable EN ISO 13408 series claimed? | | | | | | | | | | | | | Yes  No | | | | |
| If no, please explain and provide rationale and any supporting documentation to support the applicable GSPR’s.  **Rationale:** | | | | | | | | | | | | | | | | | |
| Confirm that the Protocol/Report for the initial media fill for each fill line has been provided for review. | | | | | | | | | | | | | Yes  No | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
| Confirm that the Protocol/Report for the latest requalification of the media fill(s), for each fill line has been provided for review. | | | | | | | | | | | | | Yes  No | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
| Confirm that the Protocol/Report for the full sterilisation validation for the sterilisation of all components (bottles, caps, etc.) has been provided for review.   |  |  |  |  |  | | --- | --- | --- | --- | --- | | Model numbers/  sizes | Components | Sterilisation method | Sterilisation completed by | Evidence of successful sterilisation | |  | *e.g. lid/cap* |  |  | *e.g. sterilisation validation report* | |  |  |  |  |  | | | | | | | | | | | | | | Yes  No | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
|  | Please provide a list of all the ancillary filling equipment, which also require sterilisation. For each item provide the associated validation protocol/reports and latest requalifications by filling out the table below.   |  |  |  |  | | --- | --- | --- | --- | | Ancillary filling equipment | Initial Sterilisation Validation  Protocol ref #/Report ref # | Latest requalification  Protocol ref #/Report ref # | Sterilisation Requalification  Date | |  |  |  |  | |  |  |  |  | |  |  |  |  |   *Add lines as required.* | | | | | | | | | | | | | | | | | |
| **Section S7** | | | | | | | | | | | | | | | | | | |
|  | **Other Sterilisation Method: (**If this **section is not required**, please confirm by selecting N/A and do not complete). | | | | | | | | | | | | | | | | | N/A |
| If one of the above methods is not used, please describe the method, list the standards applied and provide associated validation(s) (e.g., dry heat, liquid chemical, Hydrogen Peroxide, etc.). | | | | | | | | | | | | | | | | | |
| Please provide details:    List the supporting document titles and references: | | | | | | | | | | | | | | | | | |
| Confirm that the documents have been provided for review: | | | | | | | | | | | | | Yes  No | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
| Provide the Initial validation information *(For all devices under the scope of this application)* | | | | **Protocol#** | | | | |  | | | | | | | | |
| **Year:** | | | | |  | | | | | | | | |
| **Report#** | | | | |  | | | | | | | | |
| **Year:** | | | | |  | | | | | | | | |
| **Rationale:** | | | | | | | | | | | | | | | | | |
| Please provide evidence that the IQ and OQ has been completed and approved. | | | | | | | | | | | | | | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
| Has a full PQ validation been performed? | | | | | | | | | | | | Yes  No | | | | | |
| In the instance where a full validation has not been performed, has adoption into an existing product family or processing category, or equivalence to a validated product been used?  **Rationale:** | | | | | | | | | | | | | | | | | |
|  | If the sterilisation validation of the product is by adoption into an existing product family or processing category, or equivalence to a validated product, please provide the appropriate rationale along with all supporting documentation (e.g., the initial validation protocol and report referenced in the adoption report).  **Rationale:** | | | | | | | | | | | | | | | | | |
| Confirm that the supporting documents has been provided for review. | | | | | | | | | | | | | Yes  No | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
| If the Initial Validation is greater than 1 year old, please also provide the latest revalidation/ requalification *(For all device types under the scope of this application)* | | | | **Protocol#** | | | | |  | | | | | | | | |
| **Year:** | | | | |  | | | | | | | | |
| **Report#** | | | | |  | | | | | | | | |
| **Year:** | | | | |  | | | | | | | | |
| Please define the frequency of the requalification and how it was justified | | | | | | | | | | | | | | | | | |
| Is the device placed on the market in a “defined microbiological condition” per Annex II, 6.2 e) of MDR (2017/745); e.g., non-pyrogenic. | | | | | | | | | | | | | Yes  No | | | | |
| If **Yes**, please state the microbiological condition, and provide evidence to support this microbiological condition.   * Test method used. * Test method qualification protocol and report. * Requirements for routine monitoring (sample size and frequency). * Acceptance criteria. * Results of two recent tests. | | | | | | | | | | | | | | | | | |
| If **No,** please provide a rationale.  **Rationale:** | | | | | | | | | | | | | | | | | |
| Confirm that the supporting documents have been provided for review. | | | | | | | | | | | | | Yes  No | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
| Please provide product Bioburden data for the last 12 months. | | | | | | | | | | | | | | | | | |
|  | | | | | | | | | | | | | | | | | |
| Confirm that the supporting documents have been provided for review. | | | | | | | | | | | | | Yes  No | | | | |
| **Location:**  **File Name:**  **Page:**  **Note:** | | | | | | | | | | | | | | | | | |
| Please provide an approved copy of the Process Specification used for routine sterilisation of the product. | | | | | | | | | | | | | | | | | |
| Please provide an approved copy of the Process Specification used for routine sterilisation of the product.  For each Process specification, show how compliance is shown with each clause of the ‘Review and Approval of Validation’ section of the relevant standard.  Identify the location of the supporting evidence for each part of the standard in the table below:  **Note: Please replicate this Table as required** | | | | | | | | | | | | | | | | | |
| |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | | **Product Family** | **Process Specification #** | **Clause of standard** | ***Protocol &/or Report Docume*nt#** | **Page #** | **Paragraph #** | | *e.g., Acme* | *e.g., ABC Doc* | *e.g., ISO17665-1 9.5.2 a)* | *e.g., PP 123* | *e.g.,*  *Page 23* | *e.g., 6.2* | |  |  |  |  |  |  | |  |  |  |  |  |  |   *Add lines as required.* | | | | | | | | | | | | | | | | | |

**Appendix 2**

## Maintenance of Sterile Barrier Systems / Sterile Fluid Path

| **Maintenance of Sterile Barrier Systems / Sterile Fluid Path (Annex II sections 6.2 (e) and Annex I Chapter I, Section 7, 11.3, 11.4, 11.7, 14.2a)** | | | | | | | N/A |
| --- | --- | --- | --- | --- | --- | --- | --- |
| If ‘N/A’ has been selected, please provide a rationale:  **Rationale:** | | | | | | | |
| **Section S8** | | | | | | | |
|  | 1. Please provide a description of the packaging [Part #’s] (Primary, Secondary, Tertiary Packaging) including the relevant Packaging Specification(s). 2. Define the sterile barrier system or sterile fluid path. 3. Please provide information of any specified storage conditions. | | | | | | |
| 1. Description:      1. Definition:      1. Storage Conditions:     List the supporting document titles and References: | | | | | | |
| Confirm that the documents have been provided for review: | | | | | Yes  No | |
| **Location:**  **File name:**  **Reference:**        **Note:** | | | | | | |
| Is compliance with the current versions of the EN ISO 11607 series claimed? | | | | | Yes  No | |
| If no, please provide rationale and supporting documentation to support the applicable GSPR’s.  **Rationale:** | | | | | | |
| Define the shelf life (in years). | | |  | | | |
| Shelf-life data based on | | |  | Accelerated Aging | | |
|  | Real Time Aging | | |
| **Section S9** | | | | | | | |
|  | If submitting **Accelerated Aging (AA) data** to support shelf life, confirm start and completion date for accelerated aging Packaging studies. | | | | | | N/A |
| **Start Date:**  *(DD/Mmm/YYYY)* | **Completion Date:**  *(DD/Mmm/YYYY)* | | | | | |
| Provide a summary (*by filling out the table below*) of the AA shelf-life testing conducted on the packaging / packaged device.   |  |  |  |  |  | | --- | --- | --- | --- | --- | | **Test Performed** | **Acceptance Criteria** | **Test Protocol #/**  **Report #** | **Page #** | **Paragraph #** | |  |  |  |  |  | |  |  |  |  | *Add lines as required* | | | | | | | |
| Confirm that the documents have been provided for review. | | | | | Yes  No | |
| **Location:**  **File name:**  **Reference:**  **Note:** | | | | | | |
| Please confirm the sterilisation conditions that the packaging/sterile fluid path received prior to Accelerated Aging testing, i.e., number of EO sterilisation cycles or the maximum acceptable dose. | | | | | | |
| Please provide evidence (i.e. certs of irradiation or batch records) of the worst case sterilisation condition received prior to Accelerated Aging testing e.g. above maximum acceptable dose, 2 x ster etc. | | | | | | |
| If submitting **Real Time data** to support shelf life, confirm start date and expected or completion date for real time Packaging studies. | | | | | | N/A |
| **Start Date:**    *(DD/Mmm/YYYY)* | | **Expected Completion Date**    *(DD/Mmm/YYYY)*  or  **Completion Date:**    *(DD/Mmm/YYYY)* | | | | |
| Provide a summary *(by filling out the table below)* of the Real Time shelf-life testing conducted on the packaging / packaged device.   |  |  |  |  |  | | --- | --- | --- | --- | --- | | **Test Performed** | **Acceptance Criteria** | **Test Protocol #/**  **Report #** | **Page #** | **Paragraph #** | |  |  |  |  |  | |  |  |  |  | *Add lines as required* | | | | | | | |
| Confirm that the documents have been provided for review. | | | | | Yes  No | |
| **Location:**  **File name:**  **Reference:**  **Note:** | | | | | | |
| Please confirm the sterilisation conditions that the packaging/sterile fluid path received prior to Real Time testing, i.e., number of EO sterilisation cycles or the maximum acceptable dose. | | | | | | |
|  | Please provide evidence (i.e. certs of irradiation or batch records) of the worst case sterilisation condition received prior to Real time Aging testing e.g. above maximum acceptable dose, 2 x ster etc. | | | | | | |
| **Section S10** | | | | | | | |
|  | In accordance with MDR Annex I, GSPR 7, provide an overview of the testing conducted on the packaging to ensure that the characteristics and performance during its intended use, are not adversely affected during **transport and storage**, for example, through fluctuations of temperature and humidity, taking account of the instructions and information provided by the manufacturer.   |  |  |  |  |  | | --- | --- | --- | --- | --- | | **Test Performed** | **Acceptance Criteria** | **Test Protocol #/**  **Report #** | **Page #** | **Paragraph #** | |  |  |  |  |  | |  |  |  |  | *Add lines as required* | | | | | | | |
| Confirm that the documents have been provided for review. | | | | | Yes  No | |
| **Location:**  **File name:**  **Reference:**  **Note:** | | | | | | |
| Please confirm the sterilisation conditions that the packaging/sterile fluid path received prior to Distribution/Transport simulation testing, i.e., number of EO sterilisation cycles or the maximum acceptable dose. | | | | | | |
|  | Please provide evidence (i.e. certs of irradiation or batch records) of the worst case sterilisation conditions for the distribution and simulation testing e.g. above maximum acceptable dose , 2 x ster etc. | | | | | | |

# Appendix 3 – Electrical

| **Equivalence (Electrical)** | | |
| --- | --- | --- |
| If equivalence to an existing medical device is being claimed in compliance with MDR Annex XIV, Part A, Section 3 & MDCG 2020-5, please confirm the **Technical Characteristics (Electrical) Section** of the **Equivalence Declaration form** (MDR-2003 or MDR-3003) has been completed. | | Yes  No |
| If ‘N/A’ has been selected, please provide a rationale:  **Rationale:** | | |
| **Description of the medical electrical equipment / system including description of accessories** | | |
| Is the product Medical Electrical Equipment? | | Yes  No |
| Is the product a Medical Electrical Equipment System?  *i.e.,* *Is the product a combination of devices or pieces of equipment (with at least one being medical electrical equipment) that are interconnected and work together for a specific medical application?* | | Yes  No |
| Provide evidence in the technical file that describes the extent of the medical electrical equipment / system. This should include a description of all accessories, clearly indicating if they form part of this submission. Also, if relevant the evidence should include details of any other devices intended to be used in combination with this device: | | |
| **Location:**  **File name:**  **Reference:**  **Note:** | | |
| **Essential Performance of the medical electrical equipment** | |
| Provide evidence in the technical file that outlines the Essential Performance of the device (Note: if *no Essential Performance* is claimed, there can be no performance of a **clinical** function by the device other than that related to basic safety, where loss or degradation beyond limits specified by the manufacturer results in an unacceptable risk – NSAI will also compare to clinical performance claims elsewhere in the submission (such as device labelling) as well as if applicable EN 60601-2-xx standards specify Essential Performance for the device type/intended use): | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| **General Standard (60601-1): General requirements for basic safety and essential performance of medical electrical equipment and systems** | |
| Have the applicable requirements of EN 60601-1 latest version, including the mandatory risk assessment to EN 14971 been applied? | Yes  No |
| Provide the reference and location of the evidence that supports this, i.e., EN 60601-1 test plans and reports: | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| **EMC (60601-1-2): Medical electrical equipment - Part 1-2: General requirements for basic safety and essential performance - Collateral Standard: Electromagnetic disturbances - Requirements and tests.** | |
| Have the applicable requirements of EN 60601-1-2 latest version, including the corresponding EMC Declaration included in Instructions for use been submitted? | Yes  No |
| Provide the reference and location of the evidence that supports this, i.e., EN 60601-1-2 test plans and reports, EMC declaration etc: | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| **Other Collateral Standards** | |
| Have other relevant collateral standards been identified as applicable to the device under review for example: usability, alarms, radiation protection, home healthcare etc? | Yes  No |
| Provide a list of the relevant collateral standards identified and the location of the evidence that demonstrates conformity to the standards cited: | |
| **Collateral Standard 1:**  **Location:**  **File name:**  **Reference:**  **Note:**      **Collateral Standard 2:**  **Location:**  **File name:**  **Reference:**  **Note:**  Manufacturer to continue above as necessary for **all** relevant collateral standards identified. | |
| **Particular Standards** | |
| Have any particular standards been identified as applicable to the device under review for example: high frequency surgical equipment, endoscopy equipment, ECG, BP monitoring equipment etc? | Yes  No |
| Provide a list of the relevant particular standards identified and the location of the evidence that demonstrates conformity to the standards cited: | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| **Medical electrical equipment incorporating software / firmware** | |
| Does either the medical electrical equipment or any of its accessories incorporate software or firmware? | Yes  No |
| Provide evidence in the technical file that describes the software / firmware aspects of the medical electrical equipment or accessories. If yes is selected above the manufacturer should also complete the following **Appendix 4 (Software)**. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

# Appendix 4 – Software

| **Equivalence (Software)** | |
| --- | --- |
| If equivalence to an existing medical device is being claimed in compliance with MDR Annex XIV, Part A, Section 3 & MDCG 2020-5, please confirm the **Technical Characteristics (Software) Section** of the **Equivalence Declaration** form (MDR-2003 or MDR-3003) has been completed. | Yes  No |
| If ‘No’ has been selected, please provide a rationale:  **Rationale:** | |

| **Software (Annex II, 6.1 (a))**  **This section relates to the software of the device and is relevant to the Software in the device or if the device is medical device software, of software as a medical device including apps.** | N/A |
| --- | --- |
| If ‘N/A’ has been selected, please provide a rationale:  **Rationale:** | |
| Technical documentation reference to all relevant pre-clinical and clinical data. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| The manufacturer shall demonstrate the results of tests, such as engineering, laboratory, simulated use and animal tests. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Software (Annex II, 6.1 (b1))**  **This section relates to the software aspect of the device. This section is relevant to the Software in the device or if the device is medical device software, or software as a medical device including apps.** | N/A |
| --- | --- |
| If ‘N/A’ has been selected, please provide a rationale:  **Rationale:** | |
| The manufacturer shall demonstrate in the technical file detailed information regarding test design, complete test or study protocols, methods of data analysis, in addition to data summaries and test conclusions regarding in particular:   * Software verification and validation (describing the software design and development process and evidence of the validation of the software, as used in the finished device.   This information shall typically include the summary results of all verification, validation and testing performed both in-house and in a simulated or actual user environment prior to final release. It shall also address all of the different hardware configurations and, where applicable, operating systems identified in the information supplied by the manufacturer); | |
| This section should provide evidence from the chosen methods of meeting all the relevant GSPRS including but not limited to GSPR 17.  **Note:** it is beneficial to include a 62304/82304 checklist and the clause-by-clause outputs in a folder named after that clause.  The Documentation should also have the following:   * Evidence of Lifecycle design per EN 62304/82304, clause by clause. * Standard compliance checklist (62304/82304 etc). The supporting documentation should be included create a folder structure or the standard and folders to each clause. * Description of software architectural design, identifying the modules/functional units of the software and their interfaces, * A document detailing the software safety classification and a clear demonstration/ rationale via risk assessment as to how the software does not contribute to a hazardous situation relating to the level of injury that the software can contribute to. Risk control measures external to the software to support a risk classification should be clearly referenced/ documented. * Software requirements trace matrix clearly demonstrating sources from (MDR, 62304, 82304, 14971 13485, regulatory requirements, user documentation, maintenance, and inter-operability requirements etc). * Clear distinction between functional and non-functional requirements (timing, stress, etc) * Annex 17.4 requirements relating to hardware, it networks characteristics, Security measures including protection against unauthorised access and security requirements. | |
| **Software Version under application**: Provide the version(s) of the device software here. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Software (Annex II, 6.1 (b2))**  **This section relates to the software of the device and is relevant to the Software in the device or if the device is medical device software, of software as a medical device including apps.** | N/A |
| --- | --- |
| If ‘N/A’ has been selected, please provide a rationale:  **Rationale:** | |
| Technical documentation reference to all relevant pre-clinical and clinical data. | |
| This section is a continuation of above but more precise information relating to validation and verification evidence is required. Reference the documentation for Annex II b requirements are found and include the documentation in the technical file.  The following is required note the documentation should be reflected of the GSPRs and Standards chosen to demonstrate conformance, and should have conclusions that support the GSPRs (direct reference to the GSPRs should be evident in the conclusions)   * Software Verification & Validation Plan (62304/82304 or other etc). * Description of the software design and development process. * Evidence of validation of the version of the software used in the device. * Results of validation /verification. * Description of device testing environment and justification | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Cyber Security Software (Annex II, 6.1 (b))**  **This section relates to the software of the device and is relevant to the Software in the device or if the device is medical device software, of software as a medical device including apps.** | N/A |
| --- | --- |
| If ‘N/A’ has been selected, please provide a rationale:  **Rationale:** | |
| Technical documentation reference to all Cyber security related data  Copy and paste the file name reference below for each of the following and upload in a logical structured folder architecture the evidence. An example below is using Appendix 4 6.1 Cyber 1, 6.1 Cyber 2.... 6.1 cyber N  **Appendix 4 6.1 Cyber 1 should contain:**  A clear analysis via system diagram(s) that clearly demonstrate all the following:   * All interfaces/Assets used for risk section above between medical and non-medical devices. * All interface type ie BLE, Wi-Fi Ethernet, * For the interfaces above detail the protocols used e.g... HTTPS, API, etc. * A clear indication of what data type is being transferred (remote interface, Personal information etc) * Demonstrate the human machine inputs (Touch screen, Keyboard, mouse click etc).   **Appendix 4 Folder 6.1 Cyber 2 should contain:**  The Complete security risk assessment file (Plan, Risk analysis matrix and report), The analysis should also detail the treat modelling technique used and demonstrate the assessment of vulnerabilities and threats for all identified assets for threats/Hazardous situations including soup and their evidence of control and mitigation.  **Appendix 4 Folder 6.1 Cyber 3 should contain:**  A list of the security controls used within the device to mitigate security risks.  **Appendix 4 Folder 6.1 Cyber 4 should contain:**  The security specific Verification and Validation reports and any penetration test reports.  **Appendix 4 Folder 6.1 Cyber 5 should contain:**  A cybersecurity bill of materials and or a list of Soup components.  **Appendix 4 Folder 6.1 Cyber 6 should contain:**  The official instructions for use and a copy highlighting/ indicating the appropriate cybersecurity related GSPRs and standards relating to information relating to security measures.  Any integrator specific manuals for the installation of the device. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

# Appendix 5 – Clinical evaluation

**Important notes to the applicant:**

* All clinical reviewers attempt to perform their review in a harmonised manner; however, there could be differences based on the perspective of the specific clinical reviewer for your file and that could lead to variances in the queries as every file is reviewed independent of the other.
* Please note that here are **two clinical review application forms** [one form for for **Class IIa and IIb Non-Implantable Devices** and the other for **Class III (implantable and Non-Implantable Devices) and Class IIA Implantable and IIB Implantable Devices**]. Ensure that you complete the correct clinical form for your device classification, as the wrong form will be rejected.
* Upload any supporting documentation in the respective subfolder within appendix 5 (for example – CER is uploaded to Appendix 5, Subfolder C4).
* All uploaded documents must be provided in a pdf searchable format.
* Devices that are required to undergo the Clinical Evaluation Consultation Procedure as per article 54, will take a longer overall review time, allowing time for expert panel review.
* Devices that may require external clinical expert review may require additional review time.

## Clinical Performance for Class IIa and IIb Non-Implantable Devices.

**Note:** Have you confirmed that as per above, that this is appropriate form for the device class? Yes

| **Clinical Performance for Class IIa and IIb Non-Implantable Devices.**  NOTE: You must only use this section if your device falls under the above classification | | | | | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Section C1** | | | | | | | | | | | | |
|  | **Note:** The Clinical Review will incorporate analysis of other documents in the technical file data submitted in other sections and may generate subsequent queries. | | | | | | | | | | | |
| **Section C2** | | | | | | | | | | | | |
|  | Please identify the individual(s) who performed the clinical evaluation, as stated in the submitted CER: | | | | | | | | | | | |
| **Name** | | **Role** | | | **Qualification** | | | | | | |
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| Please list the Clinical Expert(s) and End User(s) who reviewed and approved the CER and all Clinically related Risks:  **Note:** ***All clinical experts must be appropriate for the device. For high-risk devices clinical experts should be in active clinical practice.*** | | | | | | | | | | | |
| **Clinical Expert/ End User** | | | | | | | | | **Speciality** | | |
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| Confirm that all CVs of listed evaluators including that of the Clinical expert(s) have been uploaded to the **C2 Folder**. | | | | | | | | | | | Yes  No |
| Confirm that separate declarations of interest (as per MEDDEV 2.7.1 rev 4) for each of the evaluators including that of the Clinical expert(s) have been uploaded to the **C2 Folder**. | | | | | | | | | | | Yes  No |
| Provide justification of the choice of evaluator(s): Taking into consideration   * the device technology and its application. * research methodology (clinical investigation design and biostatistics). * diagnosis and management of the conditions intended to be treated or diagnosed by the device. | | | | | | | | | | | |
| Evaluator Justifications:    Supporting documents can be uploaded to the **C2 Folder.** | | | | | | | | | | | |
| **Section C3** | | | | | | | | | | | | |
|  | Confirm a copy of the **Clinical Evaluation Plan** compliant to the MDR 2017/745 Chapter VI and ANNEX XIV, Part A has been uploaded to the **C3 Folder**. | | | | | | | | | | | Yes  No |
| **Within the CEP & CER, reference where each of the following can be found** | | | | | | | | | | | |
| **Request** | | | | | | | | | | **CEP Reference** | **CER Reference** |
| GSPR that require support from Clinical Data | | | | | | | | | |  |  |
| Intended Purpose of the Device | | | | | | | | | |  |  |
| Specification of intended target groups with clear indications and contra-indications | | | | | | | | | |  |  |
| Clinical benefits to patients with relevant and specified clinical outcome parameters | | | | | | | | | |  |  |
| 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 acceptability of the benefit-risk ratio for the various indications and for the intended purpose or purposes of the device (based on the state of the art) | | | | | | | | | |  |  |
| Benefit-risk issues relating to specific components such as use of pharmaceutical, non- viable animal or human tissues, are to be addressed.  **Note:** *If using special components e.g., TOAO, human tissue etc. a justification must be provided within the documents.* | | | | | | | | | |  |  |
| Clinical Development Plan | | | | | | | | | |  |  |
| Confirm what studies were performed for the clinical development plan of the device under evaluation e.g., Animal studies, First in man studies, pilot studies, usability studies, confirmatory studies, PMCF studies, etc. | | | | | | | | | | | |
| Specify Details:    Supporting documents can be uploaded to the **C3 Folder.** | | | | | | | | | | | |
| CLINICAL EVALUATION ROUTE TABLE([Refer to Clinical Evaluation Pathway document on NSAI website](https://www.nsai.ie/certification/medical-devices/ce-marking-for-medical-devices/))**Important – Notes must be read and considered where applicable.** **‘Legacy devices’**: this is considered to include all devices previously CE marked under the European Medical Devices Directive 93/42/EEC (MDD) or Active Implantable Medical Devices Directive 90/385/EEC (AIMDD) | | | | | | | | | | | |
| **Note 1:** **As per MDCG 2020-6,** all legacy devices which have been placed on the market have been subjected to conformity assessment and therefore are presumed to have been supported by clinical data at the time of conformity assessment. Post market clinical data together with the clinical data generated for the conformity assessment under the MDD/AIMDD will be the basis of the clinical evaluation process for legacy devices under the MDR, hence manufacturers must state what the clinical evaluation route (equivalence and/or clinical investigation) was during the initial conformity assessment**.**  **Note 2:** If your **device is a legacy device** which claimedequivalence as the clinical evaluation route during the initial conformity assessment (when the device was first CE marked), and you have not presented an equivalent device/argument to meet the MDR requirements, or no clinical investigation(s) have been performed for this MDR submission, the below statements shall apply during the review of your file –  As per MDCG 2020-6 Section 5, page 9 of 22, and the European Commission guidance MEDDEV 2.12/2 regarding PMCF, where a clinical evaluation was based exclusively on clinical data from equivalent devices for initial conformity assessment, the certifying notified body shall **verify that PMCF studies** have been conducted**.**  **Note 3:** For **Legacy devices**, if equivalence was claimed in the initial conformity assessment a completed PMCF study(-ies) **must** be provided for review as per MEDDEV 2.12/2.  **Note 4:** For **new devices under the MDR** (not legacy devices) claiming equivalence, a PMCF study plan(s) must be provided for review as per MEDDEV 2.12/2. | | | | | | | | | | | |
| Is your device a legacy device? | | | | | | | | | | | Yes  No |
| If your device is a legacy device (as defined by MDCG 2020-6), state what your clinical evaluation route was **during your initial conformity assessment** (when the device was first CE marked):  Equivalence, clinical investigation, or both equivalence and clinical investigation. | | | | Equivalence  Clinical Investigation  Both  N/A | | | | | | | |
| **For Legacy devices**, if equivalence was claimed in the initial conformity assessment a completed PMCF Activity(-ies) **must** be provided as per MEDDEV 2.12/2. Please confirm that a PMCF plan and PMCF report has been submitted in the **C9** folder. | | | | | | | | | | | Yes  No |
| For **new devices under the MDR** (not legacy devices) claiming equivalence, a PMCF study plan(s) must be provided as per MEDDEV 2.12/2. Please confirm that PMCF study plan has been submitted in the **C9** folder**.** | | | | | | | | | | | Yes  No |
| Tick the appropriate box in each case.  **Note 1**: Specify your chosen clinical evaluation methodology for this MDR application as per MDR 2017/745 and MDCG 2020-6.  **Note 2**: For each option, NSAI clinical decision will be based on the review and verification that the manufacturer has met each condition for the specific article claimed. | | | | | | | | | | | |
| **Article 61(3)** | | | Equivalence  Clinical Investigation  **And**  Alternative treatment options **(cannot claim only option c)** | | | | | | | | |
| **Article 61(9)** | | | **Note 1:** MDR requirement for devices with no medical purpose (annex XVI devices)  **Conditions:**   * The requirement to demonstrate a clinical benefit in accordance with chapter VI, Annexes XIV and XV shall be understood as a requirement to demonstrate the performance of the device. * Clinical evaluations of these products shall be based on relevant data concerning safety, including data from post-market surveillance, PMCF, and, where applicable, specific clinical investigation. * Clinical investigations shall be performed for these products unless reliance on existing clinical data from an analogous medical device is duly justified.   **NOTE 2:** As per MDR article 61(9), a manufacturer may either perform a clinical investigation for these Annex XVI devices or rely on an analogous medical device. | | | | | | | | |
| **Article 61(10)** | | | **NOTE 1:** Where the demonstration of conformity with general safety and performance requirements based on **clinical data is not deemed appropriate,**  **Conditions:**   * This will be considered only for low risk devices (not for class III and Implantable devices), **with no clinical benefit** hence the device does not have a  positive impact on the health of an individual, expressed in terms of a meaningful, measurable, patient-relevant clinical outcome(s), including outcome(s) related to diagnosis, or a positive impact on patient management or public health,  Examples of devices that may be considered under this article are a lab fridge, a lab scale for weighing or measuring blood products, etc. * The Manufacturers shall provide adequate justification which is based on the results of the manufacturer's risk management and on consideration of the specifics of the interaction between the device and the human body, the clinical performance intended and the claims of the manufacturer. * The Manufacturers shall duly substantiate in the technical documentation, and why it considers a demonstration of conformity with general safety and performance requirements that is based on the results of non-clinical testing methods alone, including performance evaluation, bench testing and pre-clinical evaluation, to be adequate. | | | | | | | | |
| If claiming Article 61(10), provide a detailed justification for reliance on this article.  **NOTE:** This justification must be based on the output of the risk management process. It should include an evaluation of clinical STATE-OF-THE-ART, including alternative diagnostic and treatment options, including those identified from literature, and an appraisal of their relevance to the device under evaluation. | | | | | | | | | | | |
| **Justification:** | | | | | | | | | | | |
| Tick from the below list what type of evidence your claim to article 61(10) is reliant on:  Ensure that the Evidence has been uploaded to the **C3 Folder.** | | | | | | | | | | | |
|  | Performance Evaluation | | | | | | | | | | |
|  | Bench Testing | | | | | | | | | | |
|  | Preclinical Evaluation | | | | | | | | | | |
| Confirm that the available clinical data for the device or an equivalent device has been searched for in the literature, identified and this data has been integrated in the clinical evaluation. | | | | | | | | | | | Yes  No |
| Specify what document, including section of same document, where this can be reviewed: | | | | | | | |  | | | |
| Confirm that the results of your risk management are supportive of the use of non-clinical testing methods.  Provide evidence of this and specify sections in the risk management documents where this can be reviewed. | | | | | | | | | | | Yes  No |
| Specify section in the Risk Management where this can be reviewed: | | | | | | | | | | | |
| Confirm the CER has been updated with information on the non-clinical data, regarding the interaction between the device and the human body.  Provide evidence of this and specify sections in the CER where this can be reviewed. | | | | | | | | | | | Yes  No |
| Specify section in the CER where this can be reviewed: | | | | | | | | | | | |
| Confirm the CER includes a discussion on the justification why the intended clinical performance of the device can rely on non-clinical data.  Provide evidence of this and specify sections in the CER where this can be reviewed. | | | | | | | | | | | Yes  No |
| Specify section in the CER where this can be reviewed: | | | | | | | | | | | |
| **MDCG 2020-6**  **Appendix III** | | **NOTE 1:** For manufacturers of legacy devices choosing clinical evaluation route based on **Sufficient Clinical Evidence as per MDCG 2020-6,** reference is made in Appendix III of MDCG 2020-6: Suggested hierarchy of clinical evidence for confirmation of conformity with relevant GSPRs under MDR.  **NOTE** **2**: If claiming sufficient clinical evidence as per MDCG 2020-6, ensure that you have provided adequate objective evidence/ appropriate level of evidence to support your device class and type. | | | | | | | | | | |
| **MDCG 2020-6 Section 1.2** | | **NOTE 1:** Legacy devices claiming WET must fulfil the following criteria below, by providing detailed rationale why the device fulfils these criteria and must provide supporting documents to justify the rationale given for each criterion (all 4 criteria must be fulfilled). The common features of the devices which are well-established technologies are that they all have:   * Relatively simple, common, and stable designs with little evolution. * Their generic device group has well-known safety and has not been associated with safety issues in the past. * Well-known clinical performance characteristics and their generic device group are standard of care devices where there is little evolution in indications and the state of the art. * A long history on the market.   **NOTE 2:** A manufacturer that claims that a device qualifies as a WET device must specify what level of evidence have provided based on MDCG 2020-6, appendix III table ([MDCG website](https://health.ec.europa.eu/medical-devices-sector/new-regulations/guidance-mdcg-endorsed-documents-and-other-guidance_en)).  **Reliance solely on complaints and vigilance is not sufficient**. | | | | | | | | | | |
| **Section C4** | | | | | | | | | | | | |
|  | Ensure all PMS data submitted in the CER is not older than 3 months from the date of file submission.  **Note: *if the length of review exceeds 2 years there may be a request that the CER be updated with current data.*** | | | | | | | | | | | |
| Confirm a copy of the **Clinical Evaluation Report** compliant to the MDR 2017/745 Chapter VI and ANNEX XIV has been uploaded to the **C4 Folder.** | | | | | | | | | | | Yes  No |
| Please indicate specific sections where each of the following can be found in the CER.  **Note: Multiple sections cannot be referenced below.** | | | | | | | | | | | |
| **Requirements** | | | | | | | | | **CER Reference** | | |
| Summary | | | | | | | | |  | | |
| Scope of the clinical evaluation | | | | | | | | |  | | |
| Clinical background, current knowledge,  state of the art | | | | | | | | |  | | |
| Device under evaluation | | | | | | | | |  | | |
| Type of evaluation | | | | | | | | |  | | |
| Demonstration of equivalence (only when equivalence is claimed)  **Note:** *The information on equivalence in the CER should be exactly the same as in the completed NSAI equivalence declaration form*. | | | | | | | | |  | | |
| Clinical data generated and held by the manufacturer | | | | | | | | |  | | |
| Clinical data from literature | | | | | | | | |  | | |
| Summary and appraisal of clinical data | | | | | | | | |  | | |
| Analysis of the clinical data | | | | | | | | |  | | |
| Conclusions | | | | | | | | |  | | |
| Statement that the evaluators agree with the contents of the report. | | | | | | | | |  | | |
| Dates and signatures | | | | | | | | |  | | |
| Qualification of the responsible evaluators and justification of the choice of evaluators. | | | | | | | | |  | | |
| References | | | | | | | | |  | | |
| Specify section where analysis and results of the PMCFER have been documented. | | | | | | | | |  | | |
| Confirm how often the CER is updated and provide rationale: | | | | | | | | | Update Frequency: | | |
| **Rationale:**  Supporting documents can be uploaded to the **C4 Folder**. | | | | | | | | | | | |
| **Section C5** | | | | | | | | | | | | |
|  | List which premarket investigations have been performed for the device. Specify which are exploratory or confirmatory investigations and provide supporting documentation in the **C5 Folder.** | | | | | | | | | | | |
|  | | | | | | | | | | | |
| List which post-market investigations have been performed for the device and provide supporting documentation in the **C5 Folder.** | | | | | | | | | | | |
|  | | | | | | | | | | | |
| Confirm if clinical investigation(s) have been performed, as per Articles 62-82, with this device. | | | | | | | | | | | Yes  No |
| If No, please provide rationale as per MDR 2017/745, Article 61, 4-6:  **Rationale:** | | | | | | | | | | | |
| If yes, is this study a confirmatory investigation?  **Note:** *A pivotal study is the only accepted study confirmatory study; all other studies (First in Man, Pilot Studies, feasibility studies, Bench Testing etc.) will be treated as supportive data.*  If yes, documents can be uploaded to the **C5 Folder.** | | | | | | | | | | | Yes  No |
| Confirm the clinical investigation(s) been publicly registered in a domain **other than EUDAMED.** | | | | | | | | | | | Yes  No |
| If yes, provide location of registration: | | | | | | | | | | | |
| Confirm the clinical investigation(s) been publicly registered on EUDAMED? | | | | | | | | | | | Yes  No |
| If no, provide a rationale:  **Rationale:** | | | | | | | | | | | |
| State the EUDAMED single registration number(s) for the clinical investigation(s). | | | | | | | | | | |  |
| Did the clinical investigation(s) result in a publication in a scientific journal? If yes, upload the full text of the publication to the C5 Folder. | | | | | | | | | | | Yes  No |
| Confirm EN ISO 14155 version used: | | | | EN ISO 14155 Version (e,g., 2023): | | | | | | | |
| Confirm a statement of compliance to the Declaration of Helsinki is included in the CIP and CIR. | | | | | | | | | | | Yes  No |
| Confirm a clinical investigation plan (CIP) has been uploaded to **the C5 Folder**. | | | | | | | | | | | Yes  No |
| Have there been any updates to the CIP. | | | | | | | | | | | Yes  No |
| If yes, please list all versions/revisions and rational for the changes in the CIP:    Supporting documents can be uploaded to the **C5 Folder.** | | | | | | | | | | | |
| Confirm a Clinical Investigation Report (CIR) has been uploaded to **the C5 Folder**. | | | | | | | | | | | Yes  No |
| Have there been any updates to the CIR. | | | | | | | | | | | Yes  No |
| Is the CIR signed and dated by the principal investigator and sponsor? | | | | | | | | | | | Yes  No |
| If yes, please list all versions/revisions and rational for the changes in the CIR:    Supporting documents can be uploaded to the **C5 Folder.** | | | | | | | | | | | |
| Confirm letter of ethics approval has been uploaded to the **C5 Folder.** | | | | | | | | | | | Yes  No |
| Confirm evidence of no objection from competent authority has been uploaded to the **C5 Folder.** | | | | | | | | | | | Yes  No |
| Confirm the investigator’s brochure(s) has been uploaded to the **C5 Folder.** | | | | | | | | | | | Yes  No |
| Confirm a sample of the informed consent for the investigation has been uploaded to the **C5 Folder** | | | | | | | | | | | Yes  No |
| **Section C6** | | | | | | | | | | | | |
|  | Confirm a standalone copy of the literature search protocol has been uploaded to the **C6 Folder.**  **Note: *Data should be current within 3 months at the time of application*.** | | | | | | | | | | | Yes  No |
| Confirm a standalone copy of the literature search report has been uploaded to the **C6 Folder.** | | | | | | | | | | | Yes  No |
| Confirm that multiple sources have been used to complete literature search. | | | | | | | | | | | Yes  No |
| Please supply a list of literature search databases used. | | | | | | | | | | | |
| Database:    **Note: *Multiple data bases must be used for the literature search.*** | | | | | | | | | | | |
| Will the device be used in any of the special populations listed below? Tick any that apply. | | | | | | | | | | | |
| Elderly population | | | | | | | | | | | Yes  No |
| Pediatric population | | | | | | | | | | | Yes  No |
| Pregnant or lactating women | | | | | | | | | | | Yes  No |
| Patients with hepatic and/or renal impairment | | | | | | | | | | | Yes  No |
| Patients with other relevant co-morbidity | | | | | | | | | | | Yes  No |
| Patients with disease severity different from that studied in clinical trials | | | | | | | | | | | Yes  No |
| Population with specific racial and/or ethnic origins | | | | | | | | | | | Yes  No |
| Other Please specify: | | | | | | | | | | | |
| Please reference sections in the CER where evidence which supports the use of the device in these populations has been discussed including justification/rationale for use special population: | | | | | | | | | | | |
| **Section C7** | | | | | | | | | | | | |
|  | **Labelling and IFU:** confirm that there is traceability of information between the clinical evaluation and the labels and IFU.  Supporting documents can be uploaded to the **C7 Folder.** | | | | | | | | | | | Yes  No |
| Please discuss how the information between the Clinical Evaluation, IFU and Risk is traceable with specific references. | | | | | | | | | | | |
| Provide a traceability matrix in tabular format showing traceability between CER, IFU and Risk and upload to C7 folder | | | | | | | | | | | |
| **Section C8** | | | | | | | | | | | | |
|  | **Risk:** confirm that there is traceability of information between the clinical evaluation and the Risk documentation.  Supporting documents can be uploaded to the **C8 Folder.** | | | | | | | | | | | Yes  No |
| **Section C9** | | | | | | | | | | | | |
|  | **PMS and PMCF Plan (PMCF plan and report must align with templates provided in MDCG 2020-7 and MDCG 2020-8 respectively)**  **Note: PMCF Plan and report that do not align with these templates will not be accepted.** | | | | | | | | | | | |
| Confirm a PMS Plan has been uploaded to the **C9 Folder.** | | | | | | | | | | | Yes  No |
| Confirm a PMCF Plan has been uploaded to the **C9 Folder.** | | | | | | | | | | | Yes  No |
| Confirm a PMCF Evaluation Report (if applicable) has been uploaded to the **C9 Folder.** | | | | | | | | | | | Yes  No |
| Please indicate where each of the following can be found in the PMCF plan as per MDR 2017/745, Annex XIV, B. | | | | | | | | | | | |
| **Requirements** | | | | | | | **Reference section within PMCF Plan** | | | | |
| Methods and procedures used in proactively collecting and evaluating clinical data. | | | | | | |  | | | | |
| Rationale for the appropriateness for the methods and procedures. | | | | | | |  | | | | |
| References relevant parts of the CER and Risk management document related. | | | | | | |  | | | | |
| The specific objectives to be addressed by the PMCF | | | | | | |  | | | | |
| An evaluation of the clinical data relating to equivalent or similar devices | | | | | | |  | | | | |
| Reference to any relevant CS, harmonised standards when used by the manufacturer, and relevant guidance on PMCF | | | | | | |  | | | | |
| A detailed and adequately justified time schedule for PMCF activities (e.g., analysis of PMCF data and reporting) to be undertaken by the manufacturer. | | | | | | |  | | | | |
| **PMCF Evaluation Report** | | | | | | | | | | | |
| Confirm a PMCF Evaluation Report (if applicable) has been uploaded to the **C9 Folder.** | | | | | | | | | | | Yes  No |
| **Requirements** | | | | | | **Reference section within PMCFER** | | | | | |
| Analysis of the PMCF findings | | | | | |  | | | | | |
| All results of the PMCF findings. | | | | | |  | | | | | |
| Have the conclusions of the PMCFER been considered for the clinical evaluation? | | | | | | | | | | | Yes  No |
| Please state in which section evidence to support this can be found in the CER: | | | | | | | | | | | |
| Have the conclusions of the PMCFER been considered for the Risk Management process? | | | | | | | | | | | Yes  No |
| Please state in which section evidence to support this can be found in the Risk Management documents:    If No, please provide rationale: | | | | | | | | | | | |
| Based on the conclusions of the PMCFER is there a need for preventative and/or corrective action to be taken. | | | | | | | | | | | Yes  No |
| If yes, please provide all details including implementation of Preventative Action/Corrective Action:    If No, please provide rationale: | | | | | | | | | | | |
| Confirm PMCFER details as per MDR 2017/745, Chapter 6, Article 61, 11. | | | | | | | | | Last Update: **DD-Mmm-YYYY**    Update Frequency: | | |
| **Section C10** | | | | | | | | | | | | |
|  | **Periodic Safety Update Report**  **Note:** As per MDCG 2022-21, if this the first conformity assessment for a new device under the MDR (not previously marketed or put into service under AIMDD 90/385/EEC & MDD 90/42/EEC), there is no obligation to submit the PSUR with this application. | | | | | | | | | | | |
| Confirm a PSUR has been uploaded to the **C10** Folder. | | | | | | | | | | | Yes  No |
| Confirm when the PSUR was last updated [DD-Mmm-YYYY] | | | | | | | | | | |  |
| Confirm the data from the PSUR has been incorporated in Risk, IFU and clinical evaluation. | | | | | | | | | | | Yes  No |
| If No, please provide rationale:  **Rationale:** | | | | | | | | | | | |
| Confirm the conclusions of the benefit-risk determination is set out by the PSUR. | | | | | | | | | | | Yes  No |
| Confirm the main findings of the PMCF is set out by the PSUR. | | | | | | | | | | | Yes  No |
| Confirm the volume of sales of the device and an estimate evaluation of the size and other characteristics of the population using the device and, where practicable, the usage frequency of the device is set out by the PSUR. | | | | | | | | | | | Yes  No |
| If No, to any of the above, please provide rationale:  **Rationale:** | | | | | | | | | | | |

## Clinical Performance for: Class III (Implantable and Non-Implantable Devices) and Class IIa Implantable and IIb Implantable Devices

**Note:** Have you confirmed that as per above, that this is appropriate form for the device class? Yes

| **B. Clinical Performance for: Class III (implantable and Non-Implantable Devices) and Class IIA Implantable and IIB Implantable Devices**  **NOTE 1: You must only use this section if your device falls under the above classifications.**  **NOTE 2: For some class III implantable devices and IIB active devices that administer or remove medicinal substances, the file review will be extended if an Expert Panel is required.** | | | | | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Section C1** | | | | | | | | | | | | |
|  | **Note:** The Clinical Review will incorporate analysis of other documents in the technical file data submitted in other sections and may generate subsequent queries. | | | | | | | | | | | |
| **Section C2** | | | | | | | | | | | | |
|  | Please identify the individual(s) who performed the clinical evaluation, as stated in the submitted CER: | | | | | | | | | | | |
| **Name** | **Role** | | | **Qualification** | | | | | | | |
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| Please list the Clinical Expert(s) and End User(s) who reviewed and approved the CER and all Clinically related Risks:  ***Note: All clinical experts must be appropriate for the device. For high-risk devices clinical experts should be in active clinical practice.*** | | | | | | | | | | | |
| **Clinical Expert/ End User** | | | | | | | **Speciality** | | | | |
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| Confirm that all CVs of listed evaluators including that of the Clinical expert(s) have been uploaded to the **C2 Folder**. | | | | | | | | | | | Yes  No |
| Confirm that separate declarations of interest (as per MEDDEV 2.7.1 Rev 4) for each of the evaluators including that of the Clinical expert(s) have been uploaded to the **C2 Folder**. | | | | | | | | | | | Yes  No |
| Provide justification of the choice of evaluator(s): Taking into consideration   * the device technology and its application. * research methodology (clinical investigation design and biostatistics). * diagnosis and management of the conditions intended to be treated or diagnosed by the device. | | | | | | | | | | | |
| Evaluator Justifications:    Supporting documents can be uploaded to the **C2 Folder.** | | | | | | | | | | | |
| **Section C3** | | | | | | | | | | | | |
|  | Confirm a copy of the **Clinical Evaluation Plan** compliant to the MDR 2017/745 Chapter VI and ANNEX XIV, Part A has been uploaded to the **C3 Folder**. | | | | | | | | | | | Yes  No |
| **Within the CEP and CER, reference where each of the following can be found:** | | | | | | | | | | | |
| **Request** | | | | | **CEP Reference** | | | | | **CER Reference** | |
| GSPR that require support from Clinical Data | | | | |  | | | | |  | |
| Intended Purpose of the Device | | | | |  | | | | |  | |
| Specification of intended target groups with clear indications and contra-indications | | | | |  | | | | |  | |
| Clinical benefits to patients with relevant and specified clinical outcome parameters | | | | |  | | | | |  | |
| 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 acceptability of the benefit-risk ratio for the various indications and for the intended purpose or purposes of the device (based on the state of the art) | | | | |  | | | | |  | |
| Benefit-risk issues relating to specific components such as use of pharmaceutical, non- viable animal or human tissues, are to be addressed | | | | |  | | | | |  | |
| Clinical Development Plan | | | | |  | | | | |  | |
| Confirm what studies were performed for the clinical development plan of the device under evaluation e.g., Animal studies, First in man studies, pilot studies, usability studies, confirmatory studies, PMCF studies, etc. | | | | | | | | | | | |
| Specify Details:    Supporting documents can be uploaded to the **C3 Folder.** | | | | | | | | | | | |
| CLINICAL EVALUATION ROUTE([Refer to Clinical Evaluation Pathway document on NSAI website](https://www.nsai.ie/certification/medical-devices/ce-marking-for-medical-devices/)) **Important – Notes must be read and considered where applicable.**  **‘Legacy devices’**: this is considered to include all devices previously CE marked under the European Medical Devices Directive 93/42/EEC (MDD) or Active Implantable Medical Devices Directive 90/385/EEC (AIMDD) | | | | | | | | | | | |
| **Note 1:** **As per MDCG 2020-6,** all legacy devices which have been placed on the market have been subjected to conformity assessment and therefore are presumed to have been supported by clinical data at the time of conformity assessment. Post market clinical data together with the clinical data generated for the conformity assessment under the MDD/AIMDD will be the basis of the clinical evaluation process for legacy devices under the MDR, hence manufacturers must state what the clinical evaluation route (equivalence and/or clinical investigation) was during the initial conformity assessment.  **Note 2:** If your **device is a legacy device** which claimedequivalence as the clinical evaluation route during the initial conformity assessment (when the device was first CE marked), and you have not presented an equivalent device/argument to meet the MDR requirements, or no clinical investigation(s) have been performed for this MDR submission, the below statements shall apply during the review of your file –  As per MDCG 2020-6 Section 5, page 9 of 22, and the European Commission guidance MEDDEV 2.12/2 regarding PMCF, where a clinical evaluation was based exclusively on clinical data from equivalent devices for initial conformity assessment, the certifying notified body shall **verify that PMCF studies** have been conducted.  **Note 3:** For **Legacy devices**, if equivalence was claimed in the initial conformity assessment a completed PMCF study(-ies) **must** be provided for review as per MEDDEV 2.12/2.  **Note 4:** For **new devices under the MDR** (not legacy devices) claiming equivalence, a PMCF study plan(s) must be provided for review as per MEDDEV 2.12/2. | | | | | | | | | | | |
| Is your device a legacy device? | | | | | | | | | | | Yes  No |
| If your device is a legacy device (as defined by MDCG 2020-6), state what your clinical evaluation route was **during your initial conformity assessment** (when the device was first CE marked):  Equivalence, clinical investigation, or both equivalence and clinical investigation. | | | | | | | | Equivalence  Clinical Investigation  Both  NA | | | |
| For Legacy devices, if equivalence was claimed in the initial conformity assessment a completed PMCF Activity(-ies) must be provided as per MEDDEV 2.12/2.  Please confirm that a PMCF study plan and PMCF report has been submitted in the **C9** folder. | | | | | | | | | | | Yes  No |
| For **new devices** under the MDR (not legacy devices) claiming equivalence, a PMCF study plan(s) must be provided as per MEDDEV 2.12/2.  Please confirm that PMCF study plan has been submitted in folder **C9.** | | | | | | | | | | | Yes  No |
| Tick the appropriate box in each case.  **Note 1**: Specify your chosen clinical evaluation methodology for this MDR application as per MDR 2017/745 and MDCG 2020-6.  **Note 2**: For each option, NSAI clinical decision will be based on the review and verification that the manufacturer has met each condition for the specific article claimed. | | | | | | | | | | | |
| **Article 61(3)** | | Equivalence  Clinical Investigation  **And**  Alternative treatment options **(cannot claim only option c)** | | | | | | | | | |
| **Article 61(4)** | | **Note**- MDR exception for manufacturers of Implantable and class III devices that choose not to perform a clinical investigation:  **Conditions:**   * Manufacturer has made modifications to a device already marketed (under the directives or regulation) by themselves. * Can claim equivalence to a device marketed by same Manufacturers. * NB agrees with equivalence claim. * Clinical evaluation of the marketed device is sufficient to demonstrate conformity to the GSPRs (CER of the marketed MDR compliant). * Manufacturers must perform a PMCF study and show us the plan (which should include a study) to demonstrate safety and performance of the device to be certified. | | | | | | | | | |
| **Article 61(5)** | | **Note:** MDR exception for manufacturers of Implantable and class III devices that choose not to perform a clinical investigation:  **Conditions:**  **Manufacturers can claim equivalence to a diff device that you don’t manufacture (different device must** be CE- Marked under the MDR)   * Provide a contract in place that explicitly allows the Manufacturers of the 2nd device full access to the technical documentation of the equivalent device on an ongoing basis. * The original clinical evaluation must be performed in accordance with the requirements of the MDR (CER of the equivalent device must be MDR compliant).   Manufacturer needs to Provide clear evidence of this to NSAI | | | | | | | | | |
| **Article 61(6a)** | | **Note 1:** MDR exception for manufacturers of Legacy Implantable and class III devices who choose not to perform a clinical investigation:  **Conditions:**   * Need to base their clinical evaluation on sufficient clinical data (as per MDCG 2020-6). * Compliant to the relevant product specific CS where such a CS is available (In the absence of CS, Manufacturers will need to prove sufficient clinical evidence).   **Note 2:** If a Manufacturers claims Article 61 (6a & 6b) & no CS exists at the time of certification, when the relevant CS becomes available or released post certification, the manufacturer must update their technical documentation to comply with the relevant common specifications or run the risk of losing your certification. | | | | | | | | | |
| **Article 61(6b)** | | **Note:** Applies to sutures, staples, dental fillings, dental braces, tooth crowns, screws, wedges, plates, wires, pins, clips, connectors.  **Conditions:**   * Manufacturers must base their clinical evaluation on sufficient clinical data (as per MDCG 2020-6) * Manufacturers must be compliant with the relevant common specs.   **NOTE 2:** In the absence of CS, manufacturers must prove sufficient clinical evidence | | | | | | | | | |
| **Article 61(9)** | | **Note 1:** MDR requirement for devices with no medical purpose (annex XVI devices)  **Conditions:**   * The requirement to demonstrate a clinical benefit in accordance with chapter VI, Annexes XIV and XV shall be understood as a requirement to demonstrate the performance of the device. * Clinical evaluations of these products shall be based on relevant data concerning safety, including data from post-market surveillance, PMCF, and, where applicable, specific clinical investigation. * Clinical investigations shall be performed for these products unless reliance on existing clinical data from an analogous medical device is duly justified.   **NOTE 2:** As per MDR article 61(9), a manufacturer may either perform a clinical investigation for these Annex XVI devices or rely on an analogous medical device. | | | | | | | | | |
| **NOTE 1:** **Article 61(10)** cannot be applied to Class III or implantable devices. | | | | | | | | | | | |
| **MDCG 2020-6**  **Appendix III** | | **NOTE 1:** For manufacturers of legacy devices choosing clinical evaluation route based on **Sufficient Clinical Evidence as per MDCG 2020-6,** reference is made in Appendix III of MDCG 2020-6: Suggested hierarchy of clinical evidence for confirmation of conformity with relevant GSPRs under MDR.  NOTE 2: If claiming sufficient clinical evidence as per MDCG 2020-6, ensure that you have provided adequate objective evidence/ appropriate level of evidence to support your device class and type. | | | | | | | | | |
| **MDCG 2020-6 Section 1.2** | | **Note 1:** Legacy devices claiming WET must fulfil the following criteria below, by providing detailed rationale why the device fulfils these criteria and must provide supporting documents to justify the rationale given for each criterion (all 4 criteria must be fulfilled). The common features of the devices which are well-established technologies are that they all have:   * Relatively simple, common, and stable designs with little evolution. * Their generic device group has well-known safety and has not been associated with safety issues in the past. * Well-known clinical performance characteristics and their generic device group are standard of care devices where there is little evolution in indications and the state of the art. * A long history on the market.   **Note 2:** A manufacturer that claims that a device qualifies as a WET device must specify what level of evidence have provided based on MDCG 2020-6, appendix III table ([MDCG website](https://health.ec.europa.eu/medical-devices-sector/new-regulations/guidance-mdcg-endorsed-documents-and-other-guidance_en)). Reliance solely on complaints and vigilance is not sufficient. | | | | | | | | | |
| Have other currently available alternative treatment options been considered? | | | | | | | | | | | Yes  No |
| **Section C4** | | | | | | | | | | | | |
|  | Ensure all PMS data submitted in the CER is not older than 3 months from the date of file submission.  **Note: *if the length of review exceeds 12 months there may be a request that the CER be updated with current data.*** | | | | | | | | | | | |
| Confirm a copy of the **Clinical Evaluation Report** compliant to the MDR 2017/745 Chapter VI and ANNEX XIV has been uploaded to the **C4 Folder.** | | | | | | | | | | | Yes  No |
| Please indicate specific sections where each of the following can be found in the CER.  **Note:** Multiple sections cannot be referenced below. | | | | | | | | | | | |
| **Requirements** | | | | | | | **CER Reference** | | | | |
| Summary | | | | | | |  | | | | |
| Scope of the clinical evaluation | | | | | | |  | | | | |
| Clinical background, current knowledge,  state of the art | | | | | | |  | | | | |
| Device under evaluation | | | | | | |  | | | | |
| Type of evaluation | | | | | | |  | | | | |
| Demonstration of equivalence (only when  equivalence is claimed).  **Note:** The information on equivalence in the CER should be exactly the same as in the completed NSAI equivalence declaration form | | | | | | |  | | | | |
| Clinical data generated and held by the manufacturer | | | | | | |  | | | | |
| Clinical data from literature | | | | | | |  | | | | |
| Summary and appraisal of clinical data | | | | | | |  | | | | |
| Analysis of the clinical data | | | | | | |  | | | | |
| Conclusions | | | | | | |  | | | | |
| Statement that the evaluators agree with the contents of the report. | | | | | | |  | | | | |
| Dates and signatures | | | | | | |  | | | | |
| Qualification of the responsible evaluators and justification of the choice of evaluators. | | | | | | |  | | | | |
| References | | | | | | |  | | | | |
| Specify section where analysis and results of the PMCFER have been documented. | | | | | | |  | | | | |
| Confirm how often the CER is updated and provide rationale: | | | | | | | Update Frequency: | | | | |
| **Rationale:**  Supporting documents can be uploaded to the **C4 Folder.** | | | | | | | | | | | |
| Was an expert panel engaged regarding the planning of the clinical evaluation (intended clinical development strategy and/or proposals for clinical investigation) as per MDR 2017/745, Chapter VI, Article 61, 2. | | | | | | | | | | | Yes  No |
| If yes, confirm correspondence with expert panel(s) has been uploaded to **the C4 Folder**. | | | | | | | | | | | Yes  No |
| State reference within the CER where the views expressed by the expert panel have been considered. | | | | | | | | | | | |
| Reference specific section within CER: | | | | | | | | | | | |
| **Section C5** | | | | | | | | | | | | |
|  | List which premarket investigations have been performed for the device. Specify which are exploratory or confirmatory investigations and provide supporting documentation in **the C5 Folder**. | | | | | | | | | | | |
|  | | | | | | | | | | | |
| List which post-market investigations have been performed for the device and provide supporting documentation in the **C5 Folder.** | | | | | | | | | | | |
|  | | | | | | | | | | | |
| Confirm if clinical investigation(s) have been performed, as per Articles 62-82, with this device. | | | | | | | | | | | Yes  No |
| If No, please provide rationale as per MDR 2017/745, Article 61, 4-6:  **Rationale:** | | | | | | | | | | | |
| If yes, is this study a confirmatory investigation?  **Note:** ***A pivotal study is the only accepted study confirmatory study; all other studies (First in Man, Pilot Studies, feasibility studies, Bench Testing etc.) will be treated as supportive data.***  If yes, **documents** can be uploaded to the **C5 Folder.** | | | | | | | | | | | Yes  No |
| If No, please provide rationale:  **Rationale:** | | | | | | | | | | | |
| Confirm the clinical investigation(s) been publicly registered in a domain **other** than **EUDAMED.** | | | | | | | | | | | Yes  No |
| If yes, provide location of registration: | | | | | | | | | | | |
| Confirm the clinical investigation(s) been publicly registered on EUDAMED? | | | | | | | | | | | Yes  No |
| If no, provide a rationale:  **Rationale:** | | | | | | | | | | | |
| State the EUDAMED single registration number(s) for the clinical investigation(s). | | | | | |  | | | | | |
| Did the clinical investigation(s) result in a publication in a scientific journal? If yes, upload the full text of the publication to **the C5 Folder**. | | | | | | | | | | | Yes  No |
| Confirm EN ISO 14155 version used: | | | EN ISO 14155 Version (e.g., 2023) | | | | | | | | |
| Confirm a statement of compliance to the Declaration of Helsinki is included in the CIP and CIR. | | | | | | | | | | | Yes  No |
| Confirm a clinical investigation plan (CIP) has been uploaded to **the C5 Folder**. | | | | | | | | | | | Yes  No |
| Have there been any updates to the CIP? | | | | | | | | | | | Yes  No |
| If yes, please list all versions/revisions and rational for the changes in the CIP:    Supporting documents can be uploaded to the **C5 Folder.** | | | | | | | | | | | |
| Confirm a Clinical Investigation Report (CIR) has been uploaded to **the C5 Folder**. | | | | | | | | | | | Yes  No |
| Have there been any updates to the CIR. | | | | | | | | | | | Yes  No |
| If yes, please list all versions/revisions and rational for the changes in the CIR:    Supporting documents can be uploaded to the **C5 Folder.** | | | | | | | | | | | |
| Confirm letter of ethics approval has been uploaded to **the C5 Folder**. | | | | | | | | | | | Yes  No |
| Confirm if the expert panel was consulted regarding the Clinical Investigation. | | | | | | | | | | | Yes  No |
| If yes, confirm correspondence has been uploaded to **the C5 Folder**. | | | | | | | | | | | Yes  No |
| Confirm evidence of no objection from competent authority has been uploaded to **the C5 Folder**. | | | | | | | | | | | Yes  No |
| Confirm the investigator’s brochure(s) has been uploaded to **the C5 Folder**. | | | | | | | | | | | Yes  No |
| Confirm a sample of the informed consent for the investigation has been uploaded to the C5 Folder | | | | | | | | | | | Yes  No |
| Confirm if the clinical investigations result in a publication in a scientific journal.  If yes, upload the full text of the publication in **the C5 Folder**. | | | | | | | | | | | Yes  No |
| **Section C6** | | | | | | | | | | | | |
|  | Confirm a standalone copy of the literature search protocol has been uploaded to the **C6 Folder.**  ***Note: Data should be current within 3 months at the time of application.*** | | | | | | | | | | | Yes  No |
| Confirm a standalone copy of the literature search report has been uploaded to the **C6 Folder.** | | | | | | | | | | | Yes  No |
| Confirm that multiple sources have been used to complete literature search. | | | | | | | | | | | Yes  No |
| Please supply a list of literature search databases used. | | | | | | | | | | | |
| Database    **Note: *Multiple data bases must be used for the literature search.*** | | | | | | | | | | | |
| Will the device be used in any of the special populations listed below? Tick any that apply. | | | | | | | | | | | |
| Elderly population; | | | | | | | | | | | Yes  No |
| Pediatric population; | | | | | | | | | | | Yes  No |
| Pregnant or lactating women; | | | | | | | | | | | Yes  No |
| Patients with hepatic and/or renal impairment; | | | | | | | | | | | Yes  No |
| Patients with other relevant co-morbidity; | | | | | | | | | | | Yes  No |
| Patients with disease severity different from that studied in clinical trials; | | | | | | | | | | | Yes  No |
| Population with specific racial and/or ethnic origins | | | | | | | | | | | Yes  No |
| Other Please specify: | | | | | | | | | | | |
| Please reference sections in the CER where evidence which supports the use of the device in these populations has been discussed including justification/rationale for use special population: | | | | | | | | | | | |
| **Section C7** | | | | | | | | | | | | |
|  | **Labelling and IFU:** confirm that there is traceability of information between the clinical evaluation and the labels and IFU. | | | | | | | | | | | Yes  No |
| Please discuss how the information between the Clinical Evaluation, IFU and Risk is traceable with specific references. | | | | | | | | | | | |
| Provide a traceability matrix in tabular format showing traceability between CER, IFU and Risk and upload to C7 folder.  Supporting documents can be uploaded to the **C7 Folder.** | | | | | | | | | | | |
| **Section C8** | | | | | | | | | | | | |
|  | **Risk:** confirm that there is traceability of information between the clinical evaluation and the Risk documentation.  Supporting documents can be uploaded to the **C8 Folder.** | | | | | | | | | | | Yes  No |
| **Section C9** | | | | | | | | | | | | |
|  | **PMS and PMCF Plan:**  **(PMCF plan must align with templates provided in MDCG 2020-7)** | | | | | | | | | | | |
| Confirm a PMS Plan has been uploaded to the **C9 Folder.** | | | | | | | | | | | Yes  No |
| Confirm a PMCF Plan has been uploaded to the **C9 Folder.** | | | | | | | | | | | Yes  No |
| Confirm a PMCF Evaluation Report (if applicable) has been uploaded to the **C9 Folder.** | | | | | | | | | | | Yes  No |
| Please indicate where each of the following can be found in the PMCF plan as per MDR 2017/745, Annex XIV, B. | | | | | | | | | | | |
| **Requirements** | | | | | **Reference section within PMCF Plan** | | | | | | |
| Methods and procedures used in proactively collecting and evaluating clinical data. | | | | |  | | | | | | |
| Rationale for the appropriateness for the methods and procedures. | | | | |  | | | | | | |
| References relevant parts of the CER and Risk management document related. | | | | |  | | | | | | |
| The specific objectives to be addressed by the PMCF | | | | |  | | | | | | |
| An evaluation of the clinical data relating to equivalent or similar devices | | | | |  | | | | | | |
| Reference to any relevant CS, harmonised standards when used by the manufacturer, and relevant guidance on PMCF | | | | |  | | | | | | |
| A detailed and adequately justified time schedule for PMCF activities (e.g., analysis of PMCF data and reporting) to be undertaken by the manufacturer. | | | | |  | | | | | | |
| **PMS and PMCF Plan (PMCF plan and report must align with templates provided in MDCG 2020-7 & MDCG 2020-8 respectively)**  **Note: PMCF Plan and report that do not align with these templates will not be accepted.** | | | | | | | | | | | |
| Confirm a PMCF Evaluation Report (if applicable) has been uploaded to the **C9 Folder.** | | | | | | | | | | | Yes  No |
| **Requirements** | | | | | **Reference section within PMCFER** | | | | | | |
| Analysis of the PMCF findings | | | | |  | | | | | | |
| All results of the PMCF findings. | | | | |  | | | | | | |
| Have the conclusions of the PMCFER been considered for the clinical evaluation? | | | | | | | | | | | Yes  No |
| Please state in which section evidence to support this can be found in the CER: | | | | | | | | | | | |
| Have the conclusions of the PMCFER been considered for the Risk Management process? | | | | | | | | | | | Yes  No |
| Please state in which section evidence to support this can be found in the Risk Management documents: | | | | | | | | | | | |
| Based on the conclusions of the PMCFER is there a need for preventative and/or corrective action to be taken. | | | | | | | | | | | Yes  No |
| If yes, please provide all details including implementation of Preventative Action/Corrective Action:    If ‘No’, please provide rationale: | | | | | | | | | | | |
| Confirm PMCFER details as per MDR 2017/745, Chapter 6, Article 61, 11. | | | | | Last Update: [DD-Mmm-YYYY].    Update Frequency: | | | | | | |
| **Section C10** | | | | | | | | | | | | |
|  | **Periodic Safety Update Report**  **Note: As per** MDCG 2022-21, **if this the first conformity assessment for a new device under the MDR** (not previously marketed or put into service under AIMDD 90/385/EEC & MDD 90/42/EEC), **there is no obligation to submit the PSUR with this application.** | | | | | | | | | | | |
| Confirm a PSUR has been uploaded to the C10 Folder. | | | | | | | | | | | Yes  No |
| Confirm when the PSUR was last updated [DD-Mmm-YYYY]. | | | | | | | | | | |  |
| Confirm the data from the PSUR has been incorporated in Risk, IFU and clinical evaluation. | | | | | | | | | | | Yes  No |
| If No, please provide rationale:  Rationale: | | | | | | | | | | | |
| Confirm the conclusions of the benefit-risk determination is set out by the PSUR. | | | | | | | | | | | Yes  No |
| Confirm the main findings of the PMCF is set out by the PSUR. | | | | | | | | | | | Yes  No |
| Confirm the volume of sales of the device and an estimate evaluation of the size and other characteristics of the population using the device and, where practicable, the usage frequency of the device is set out by the PSUR. | | | | | | | | | | | Yes  No |
| If No, to any of the above, provide rationale:  Rationale: | | | | | | | | | | | |
| **Section C11** | | | | | | | | | | | | |
|  | **Summary of Safety and Clinical Performance** | | | | | | | | | | | |
| Confirm an SSCP as per MDR, article 32 and MDCG Guidance document 2019-9, Appendix: Template for the SSCP  has been uploaded to the C11 Folder. | | | | | | | | | | | Yes  No |
| Confirm when the SSCP was last updated [DD-Mmm-YYYY].  Note: SSCPs should be updated annually as per MDR article 32. | | | | | | | | | | |  |
| Confirm the SSCP has been updated to coincide with the PSUR and PMCF Report updates as per MDCG Guidance document 2019-9. | | | | | | | | | | | Yes  No |
| Confirm a traceability matrix or evidence of alignment has been uploaded to the C11 Folder. | | | | | | | | | | | Yes  No |
| If No, provide rationale:  Rationale: | | | | | | | | | | | |
| Confirm the information in the SSCP is traceable with information seen in the relevant documents of the technical file (intended use, intended patient groups, contraindications, device description, risks, warnings and precautions, training for users). | | | | | | | | | | | Yes  No |
| Does the IFU have a direct link to find SSCP on EUDAMED. | | | | | | | | | | | Yes  No |
| State the supporting document file name and page reference: | |  | | | | | | | | | |
| Confirm the SSCP includes the ‘General Information Texts’ for users and for patients (if applicable) as per MDCG Guidance document 2019-9 rev 1, Appendix: Template for the SSCP. | | | | | | | | | | | Yes  No |
| State the supporting document file name and page reference: | |  | | | | | | | | | |
| **SSCP References** | | | | | | | | | | | |
| MDR article 32 and MDCG 2019-9 Rev 1 Guidance document provides instructions and a template for a compliant SSCP. Please reference sections or page numbers where the below headings and their subsequent subheadings can be found in the submitted SSCP. | | | | | | | | | | | |
| Headings | | | | | Reference | | | | | | |
| Device Identification and General Information | | | | |  | | | | | | |
| Intended use of the device | | | | |  | | | | | | |
| Device description | | | | |  | | | | | | |
| Risks and warnings | | | | | | | | |  | | |
| Summary of clinical evaluation and post-market clinical follow-up (PMCF) | | | | | | | | |  | | |
| Possible diagnostic or therapeutic alternatives | | | | | | | | |  | | |
| Suggested intended users and training for users | | | | | | | | |  | | |
| Reference to relevant harmonised standards and CS applied | | | | | | | | |  | | |
| Revision history | | | | | | | | |  | | |
| Confirm the SSCP includes a patient specific/lay person’s section as per MDR article 32 and MDCG Guidance document 2019-9, Appendix: Template for the SSCP. | | | | | | | | | | | Yes  No |
| If No, please provide rationale:  **Rationale:** | | | | | | | | | | | |
| **Section C12** | | | | | | | | | | | | |
|  | **Clinical Evaluation Consultation Procedure (Article 54)**  **(For Class III implantable and Class IIB Active devices that administer or remove medicinal substances)** | | | | | | | | | | | |
| Is your device a Class III implantable and Class IIB Active devices that administer or remove medicinal substances? | | | | | | | | | | | Yes  No |
| Did you consult an expert panel prior to your clinical evaluation and/or clinical investigation as per article 61(2), with the aim of reviewing your intended clinical development strategy and proposals for clinical investigation? | | | | | | | | | | | Yes  No |
| Provide document(s) showing the views expressed by the expert panel and upload to C12 folder. | | | | | | | | | | | |
| Have the views expressed by the expert panel been documented in the clinical evaluation report? | | | | | | | | | | | Yes  No |
| Specify section in the CER where the expert panel views have been expressed. | | | | | | | | | | | |
| CER Reference: | | | | | | | | | | | |
| Is the procedure required by Article 54(1) [*Clinical Evaluation Consultation Procedure as specified in Section 5.1 of Annex IX or as referred to in Section 6 of Annex X*] to be applied? | | | | | | | | | | | Yes  No |
| ***Note: NSAI will consider application of article 54, If your device is a Class III implantable or Class IIB Active devices that administer or remove medicinal substances.*** | | | | | | | | | | | |
| Specify if your device falls under the following criteria:  (a) renewal of a certificate issued under the MDR;  (b) the device has been designed by modifying a device already marketed by the same manufacturer for the same intended purpose, and the manufacturer has demonstrated to the satisfaction of the notified body that the modifications do not adversely affect the benefit-risk ratio of the device;  (c) the principles of the clinical evaluation of the device type or category have been addressed in a CS | | | | | | | | | | | |
| If option (a) has been selected above, please provide NSAI file number for the previously issued NSAI certificate. | | | | | | | | | | | |
| File number: | | | | | | | | | | | |
| If option (b) has been selected above, the following documents must be provided:   * A pdf document which includes the following- * A detailed list of the modification(s) that have been made to the device since the last certification, and * Rationale demonstrating that each of the modification(s) do not affect the benefit-risk ratio of the device.   Confirm that this document has been included in the C12 folder | | | | | | | | | | | |
| If option (c) has been selected above, specify what common specification has been applied? | | | | | | | | | | | |
| Common Specification: | | | | | | | | | | | |
| Does your device have any Novel aspects? | | | | | | | | | | | Yes  No |
| Provide a pdf document which describes in detail the novel aspects of your device | | | | | | | | | | | |
| Novel aspects:    Upload supporting documents regarding novelty in C12 folder | | | | | | | | | | | |

# Appendix 6 – Medical devices incorporating an ancillary medicinal substance.

**Important notes to the applicant:**

* This section applies to medical devices incorporating an ancillary medicinal substance according to EU MDR Annex I, 12.1 and Annex II, 6.2 (a) and Annex IX, 5.2.
* If the medical device includes more than one ancillary medicinal substances, only one file covering the combination is required, however the requested information for each ancillary medicinal substance must be unambiguously provided.
* Per EU MDR Annex IX, 5.2, NSAI must seek a scientific opinion from either an EU Member State competent authority or the EMA on the quality and safety of the ancillary medicinal substance.
* Per EU MDR Annex IX, 5.2, where the ancillary medicinal substance is derived from human blood or plasma, NSAI must seek a scientific opinion from the EMA on the quality and safety of the ancillary medicinal substance.
* In any event, where NSAI must seek a scientific opinion from the EMA or a competent authority, it is the responsibility of the applicant to ensure either:
  + the EMA compliant eCTD submission package is assembled and validated (per EMA guidance, including generation of any XML delivery files) ready for NSAI to submit via EMA’s ‘eSubmission Gateway Syncplicity Web Client’, *or*
  + the competent authority submission package is assembled per the requirements of that competent authority (chosen by the applicant) ready for NSAI to submit to that chosen competent authority. Please note that competent authorities may have different requirements, therefore the applicant is encouraged to view the competent authority’s website to ensure specific submission package requirements are fulfilled.
  + For all EMA or competent authority submissions, NSAI will work with the applicant to provide any specifically requested Notified Body documents (e.g. cover letter, statement that the usefulness of the ancillary medicinal substances has been verified by the notified body etc.)

**General Information - Medical devices incorporating an ancillary medicinal substance.**

|  |  |
| --- | --- |
| **Ancillary medicinal substance (EU MDR Annex II, 6.2, a)** | N/A |
| **Rationale**: | |
| Where a device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product within the meaning of point 2 of Article 1 of Directive 2001/83/EC, including a medicinal product derived from human blood or human plasma, as referred to in the first subparagraph of Article 1(8), provide a statement indicating this fact. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Information regarding the ancillary medicinal substance** | | | | N/A |
| **Rationale**: | | | | |
| Name of the ancillary medicinal substance. |  | | | |
| Is the medicinal product derived from human blood or human plasma | | | Yes  No | |
| Name and address of ancillary medicinal substance manufacturer. |  | | | |
| Name and location address of ancillary medicinal substance supplier(s). |  | | | |
| Contact name and email address of ancillary medicinal substance supplier(s) |  | | | |
| Confirm that NSAI has the applicant’s authorisation to directly contact the ancillary medicinal substance supplier(s) in relation to client’s device | | Yes  No | | |
| Is a European Directorate for the Quality of Medicines & HealthCare (EDQM) Pharmacopoeia Eur. Certificate of Suitability provided for the ancillary medicinal substance? If yes, provide document reference. | | Yes  No | | |
| **Location:**  **File name:**  **Reference:**  **Note:** | | | | |

|  |  |  |
| --- | --- | --- |
| **Principal intended action of the device and action of the medicinal substance (ancillary to the device (medicinal substance plus device)** | | N/A |
| **Rationale**: | | |
| **Provide description and method by which the principal intended action of the medical device is achieved.** | **Provide description and method by which the medicinal substance imparts ancillary action to the medical device.** | |
|  |  | |

|  |  |
| --- | --- |
| **Usefulness of the ancillary medicinal substance as part of the medical device** | N/A |
| **Rationale**: | |
| Provide a comprehensive rationale and justification for using the medicinal substance in relation to the specific intended purpose of the device. The suitability of the ancillary medicinal substance to achieve its intended action and whether the potential inherent risks (aspect of “safety”) due to the medicinal substance must justified in relation to the benefit to be obtained within the intended purpose of the device. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

|  |  |
| --- | --- |
| **Ancillary medicinal substance data submission package** | |
| Confirm that the ancillary medicinal substance data submission package has been prepared (per the EMA or competent authority guidance, as appropriate) and has been provided to NSAI. | Yes  N/A |
| **Rationale**: | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

# Appendix 7 – Medical devices incorporating tissues or cells of animal origin.

**Important notes to the applicant:**

* This section applies to medical devices utilising tissue or cells of animal origin or their derivatives according to MDR Annex I, GSPR 13.2.
* If the device is a system and includes multiple components, then identify the components which incorporate these animals’ derived materials.
* Manufacturing subcontractors should be consulted, if appropriate, to establish if any such animal derived materials are used during manufacture, even if they do not feature in the final device. The manufacturer should request evidence of compliance to ISO 22442 or EU 722/2012 or for any applicable exclusions (e.g., tallow species and processing method utilised) from the subcontractor.
* Devices which incorporate animal-derived substances may be subject to requirements of additional European Directives / Regulations. Additional review resources may be required, including external independent reviewers and/or Competent Authority consultation and/or a European Agency for the Evaluation of Medicinal Products (EMA).
* Sections (A), (B) and (C) must be completed for all medical devices utilising animal tissues and their derivatives.
* Sections (D) and (E) must be completed for medical devices utilising animal tissues and their derivatives originating from bovine, ovine and caprine species, deer, elk, mink, and cats.

**Section (A): General information for medical devices utilising animal tissues and their derivatives.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Tissues or cells of animal origin (EU MDR Annex II, 6.2, b)** | | | | N/A |
| **Rationale**: | | | | |
| Where a device is manufactured utilising tissues or cells of animal origin, or their derivatives, provide a statement indicating this fact. In such a case, the documentation shall identify all materials of human or animal origin used and provide detailed information concerning the conformity with Sections 13.1. or 13.2., respectively, of Annex I. | | | | |
| **Location:**  **File name:**  **Reference:**  **Note:** | | | | |
| Where a device is manufactured utilising tissues or cells of animal origin, or their derivatives, has the ISO 22442-series been used? | | | | |
| **ISO 22442-1** | Yes  No | **Year:** |  | |
| **ISO 22442-2** | Yes  No | **Year:** |
| **ISO 22442-3** | Yes  No | **Year:** |

|  |  |
| --- | --- |
| **Tissues of animal origin relevant to COMMISSION REGULATION (EU) No 722/2012 (EU MDR Annex I, 13.2, c)** | N/A |
| **Rationale**: | |
| Where a device is manufactured utilising tissues of animal origin relevant to COMMISSION REGULATION (EU) No 722/2012 (animal tissues, as well as their derivatives, originating from bovine, ovine and caprine species, deer, elk, mink, and cats), provide a statement indicating this fact. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Information regarding the tissue of animal origin starting material** | | | | N/A |
| --- | --- | --- | --- | --- |
| **Rationale**: | | | | |
| Is there an EDQM (European Directorate for the Quality of Medicines) certificate available? | | | Yes  No | |
| **Copy provided as File Name:** | | | | |
| Starting tissue used: |  | | | |
| Species Used: |  | | | |
| Geographical sourcing: |  | | | |
| Name and address of ‘TOAO material supplier’ to the medical device manufacture: | |  | | |
| Name and address of any raw material supplier to the ‘TOAO material supplier’ e.g., slaughterhouses, hide suppliers etc: | |  | | |

**Section (B): ISO 22442-1 aligned requirements.**

|  |  |
| --- | --- |
| **Risk management: Justification for the use of animal tissues or derivatives** | N/A |
| **Rationale**: | |
| Provide a justification for the use of animal material (including the choice of animal species and tissues) based on the residual risk acceptability, taking into account the balance of residual risk and expected medical benefit, as compared to available alternatives. | |
| **Location:**  **File name:**  **Reference:**  **Note:**      **Note:** | |

|  |  |
| --- | --- |
| **Risk analysis: Device contact with the patient or other persons** | N/A |
| **Rationale**: | |
| The quantity of material, the contact surface area and the type(s) of material coming into contact with body tissues or fluids as well as the type of body tissue or fluid it comes into contact with, shall be addressed in the risk analysis. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Risk analysis: Materials and/or components incorporated in the medical device or are used with, or are in contact with, the medical device.** | N/A |
| --- | --- |
| **Rationale**: | |
| If viable animal materials are utilized in the manufacture of the medical device, verification that the final medical device contains no viable animal material. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on the intended use of any animal tissue or derivative. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on the geographical source, species, age and feeding (including use of animal-derived protein) of animals. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on veterinary control, conditions under which the animal materials are recovered, potential for cross-contamination. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on the type and anatomical source of tissue. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on the production process, particularly if it uses materials pooled from more than one animal. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on the nature of material utilised in the medical device (e.g., intact tissue, highly purified derivative). | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on the method of utilization or incorporation into the medical device. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

|  |  |
| --- | --- |
| **Risk analysis: Devices supplied sterile or intended to be sterilised by the user or are other microbiological controls applicable** | N/A |
| **Rationale**: | |
| Given the biological nature of animal tissues or derivatives, variations in the bioburden of bacteria, mould and yeast of the animal material shall be estimated. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

|  |  |
| --- | --- |
| **Risk analysis: Unwanted outputs of substances** | N/A |
| **Rationale**: | |
| The possible presence of toxic residue related to the manufacturing process utilized or degradation by-products shall be addressed taking into account the physical characteristics (e.g., porosity, heterogeneity) and chemical composition of animal tissues or derivatives. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Risk analysis: Identification of hazards and hazardous situations** | N/A |
| --- | --- |
| **Rationale**: | |
| Provide comprehensive information on the possible hazards associated with animal tissues or derivatives. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on the hazards posed by animal tissues or derivatives with regard to potential contamination by transmissible agents and their susceptibility to elimination and/or inactivation during processing. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on the hazards posed by animal tissues or derivatives with regard to potential for contaminants on the finished material which can cause an undesired pyrogenic, immunological or toxicological reaction. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on the hazards posed by animal tissues or derivatives with regard to potential for the finished material itself to cause an undesired pyrogenic, immunological or toxicological reaction. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Risk control: Risk control options** | N/A |
| --- | --- |
| **Rationale**: | |
| Provide the documented and justified risk control options for risk related to parasites and  unclassified pathogenic entities. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide the documented and justified risk control options for risk related to risk related to:   * bacteria * moulds * yeasts | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide the documented and justified risk control options for risk related to risk related to viruses. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide the documented and justified risk control options for risk related to risk related to  TSE agents. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide the documented and justified risk control options for risk related to undesired, pyrogenic reaction, immunological reaction, and toxicological reaction. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide the documented risk reduction measures identified. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide the documented assessment as to the balance between medical benefit and residual risk being determined as acceptable. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

**Section (C): ISO 22442-2 aligned requirements.**

| **General requirements:** | |
| --- | --- |
| **Quality system elements** | N/A |
| **Rationale**: | |
| Provide comprehensive information on how a documented system has been established and maintained to control the quality of materials of animal origin and is verified by the medical device manufacturer. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the Quality System has considered documented the specification of the age. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the Quality System has considered the geographical origin (such as country or region) of the animal material. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the Quality System has considered the state of health of the animals. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the Quality System has considered acceptance criteria for the animals taking into account the source-species. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the Quality System has considered and documented the acceptance criteria for animals taking into account the perceived risk from pathogens. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the Quality System has considered and documented the ability to obtain appropriate assurances, including full traceability to the slaughterhouse. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the Quality System has considered and documented hygiene and quality assurance requirements to be met by the slaughterer including the provisions in the slaughterhouse to prevent cross-contamination within and between animals. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the Quality System has considered and documented procedures for the collection, preservation, handling, storage, and transport of materials of animal origin. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Personnel** | N/A |
| --- | --- |
| **Rationale**: | |
| Provide comprehensive information on how the Quality System has considered and documented procedures for assignment of qualified personnel with Responsibility for the collection, handling, and storage of materials. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Sourcing:** | |
| --- | --- |
| **General** | |
| Provide comprehensive information on how the risk management has considered and documented that the animal material shall not be compromised by cross-contamination before, during, or after slaughter and that animals shall be confirmed as having been declared fit for human consumption. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented a justification for choice of animal material sourced from species that are not intended for human consumption (including missing inspection and certification). Relevant quality criteria for this type of material are to be defined by the manufacturer. | N/A |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented where animal by-products not intended for human consumption are sourced, these have to be ‘Category 3 (i.e., safe) materials or equivalent. | N/A |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Species and strain** | N/A |
| --- | --- |
| **Rationale**: | |
| Provide comprehensive information on how the risk management has considered and documented the risk of certain diseases dependent on the animal species and possibly strain as part of the establishment of control measures. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Geography** | N/A |
| --- | --- |
| **Rationale**: | |
| Provide comprehensive information on how the risk management has considered and documented the risk of certain diseases dependent on geographical origin as part of the establishment of control measures. | |

| **Inspection** | N/A |
| --- | --- |
| **Rationale**: | |
| Provide comprehensive information on how the risk management has considered and documented that sourcing of animal material is subject to control and individual inspection by a veterinarian. If individual animals cannot be inspected, the justification for this shall be documented and a relevant sampling plan provided. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented that bovine, caprine, equine, ovine, and porcine species shall be subject to ante-mortem veterinary inspection. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented that bovine, caprine, equine, ovine, and porcine species shall be subject to ante-mortem veterinary inspection and that prior to certification, a post-mortem inspection of bovine, caprine, cervid, equine, ovine, and porcine species shall be performed by a veterinarian immediately after slaughter according to local custom and practice. The inspection shall include at least the following:  a) visual inspection.  b) palpation of specified organs.  c) incision of organs and lymph nodes.  d) investigation of anomalies (e.g., inconsistency, colour, and smell);  e) if necessary, laboratory tests. | N/A |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented that Animals showing locomotive system abnormalities or neurological disorders shall not be used for the production of medical devices; Tallow derivatives, animal charcoal, and amino acids `Category 3 materials or equivalent’ | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented that for materials (including pooled blood supplies) for direct use in medical devices and that are not subject to a validated process to reduce TSE risk in line with ISO 22442-3, consideration is be given to the application of a validated biochemical test for the presence of TSE in the source animal. | N/A |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Certification** | N/A |
| --- | --- |
| **Rationale**: | |
| Provide comprehensive information on how the risk management has considered and documented that material of animal origin intended for utilization in medical devices originates from animals confirmed by a veterinarian as being fit for human consumption. Records to demonstrate conformance with veterinary inspection criteria at the abattoir, certificate details, and source should be provided. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented that for species where such certification by a veterinarian cannot be obtained, a status equivalent to “fit for human consumption” is present such as a confirmation of apparent good health. | N/A |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

|  |  |
| --- | --- |
| **Traceability** | N/A |
| **Rationale**: | |
| Provide comprehensive information on how the risk management has considered and documented the established traceability system. Traceability to the slaughterhouse should  be assured, as well as traceability by suppliers of processed animal materials. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Collection:** | N/A |
| --- | --- |
| **Rationale:** | |
| Provide comprehensive information on how the risk management has considered and documented that between the manufacturer of the medical device and the supplier of material of animal origin, there shall be a technical agreement defining the following:   * the limits of responsibilities. * specifications of the material. * documentation provided by the supplier allowing the manufacturer to meet the requirements of this document. * inspection criteria. * procedures (including specific measures to prevent cross-contamination). * audits. * procedures for ensuring that all deliveries have traceability of relevant certificates. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented that materials derived from TSE susceptible species (including pooled blood supplies) intended for direct use in medical devices and that are not subject to a validated process in line with ISO 22442-3 to reduce TSE risks to an acceptable level determined by the risk management process are harvested from slaughterhouses designated by the medical device manufacturer. | N/A |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented that the collection of the material is conducted in accordance with the documented procedures. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented that the systems for certification and traceability are specified when tissues of animal origin are pooled at the place of slaughter or subsequently. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented the limits of pooling permitted and how this limit is justified. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Handling:** | N/A |
| --- | --- |
| **Rationale**: | |
| Provide comprehensive information on how the risk management has considered and documented that any material of animal origin that requires further dissection or trimming is removed as soon as possible to an area separate from that used for slaughtering and collection. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented that areas for handling material of animal origin is suitably equipped and maintained at an appropriate level of cleanliness and environmental protection and that implements for dissection and trimming are kept clean to minimize risk of cross-contamination. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Storage, transport, and labelling:** | N/A |
| --- | --- |
| **Rationale:** | |
| Provide comprehensive information on how the risk management has considered and documented that collected material is stored and transported in closed or other appropriate containers. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented that the conditions for storage and transport do not compromise compliance with the relevant qualities of the animal material, in particular, by environmental or enzymatic degradation or microbial proliferation. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented that the storage, transport and labelling of the material is conducted in accordance with the documented procedures. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented that the primary container of the collected material is labelled appropriately to avoid cross contamination and mix up during the transport and storage. The label shall at least contain details of the material, collection date and the location for traceability. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

**Section (D): ISO 22442-1 aligned Risk control for viruses and TSE agents.**

|  |  |
| --- | --- |
| **Risk control for viruses and TSE agents** | N/A |
| **Rationale:** | |
| Risk control shall be implemented by separately addressing the risks related to different categories of viruses and TSE agents. After defining the characteristics of the product, the medical device manufacturer shall comply with the relevant requirements of both ISO 22442-2 and ISO 22442-3. If exceptions to ISO 22442-2 and ISO 22442-3 are made, these exceptions shall be documented and justified. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide a copy of the technical agreement between the medical device manufacturer and the animal material/derivative supplier to demonstrate compliance with the requirements of this document (see ISO 22442-2:2020, Clause 6). | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Collagen tissues of animal origin** | N/A |
| --- | --- |
| **Rationale:** | |
| Provide comprehensive information on how the risk management has considered for collagen produced from bone, the bone shall be sourced from countries with minimal exposure to bovine spongiform encephalopathy (BSE). Sourcing bone from countries with limited exposure to BSE shall be justified by reference to other applicable risk control measures (see ISO 22442-2:2020, Annex A). Bone shall not be sourced from countries where infection with the BSE agent is undetermined (s. OIE classification), unless from a low-risk herd as defined in ISO 22442-2. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered for collagen produced from bones, the manufacturing conditions specified for gelatine are applicable. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Collagen produced from hides and skins does not usually present a significant TSE risk, provided that cross-contamination with potentially infected materials, for example central nervous tissues, is avoided during their procurement. Provide comprehensive information on how the risk management has considered measures to prevent cross-contamination (see ISO 22442-2) and measures that are adopted in the technical agreement between the collagen supplier and the medical device manufacturer to prevent such cross-contamination. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the Collagen is obtained from animals declared as fit for human consumption (see ISO 22442-2). | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Gelatine derived from hides and bones** | N/A |
| --- | --- |
| **Rationale:** | |
| Provide comprehensive information on how the Gelatine is obtained from animals declared as fit for human consumption. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Hides as the starting material: Gelatine produced from hides does not usually present a significant TSE risk provided that cross- contamination with potentially infected materials, for example central nervous tissues, is avoided during their procurement. Provide comprehensive information on how the risk management has considered measures to prevent cross-contamination (see ISO 22442-2) and measures that are adopted to prevent such cross-contamination in the technical agreement between the gelatine supplier and the medical device manufacturer. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Bones as the starting material: Provide comprehensive information on how the risk management has considered bone shall be sourced from countries with minimal or limited exposure to BSE. Bone shall not be sourced from countries where infection with the BSE agent is classified as undetermined by OIE, unless from a low-risk herd as defined in ISO 22442-2. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Bones as the starting material: Provide comprehensive information on how the risk management has considered skulls and spinal cords shall be removed from the collected bones (raw/starting material) from cattle of a specific age as defined. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Bones as the starting material: Provide comprehensive information on how the risk management has considered vertebrae shall be removed from the raw/starting materials from cattle of all ages from countries with limited exposure to BSE. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Bovine blood derivatives** | N/A |
| --- | --- |
| **Rationale:** | |
| General: Provide comprehensive information on how the risk management has considered foetal bovine serum should be obtained from foetuses harvested in abattoirs from healthy dams fit for human consumption and the womb should be completely removed. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| **General:** Provide comprehensive information on how the risk management has considered the foetal blood shall be harvested in a dedicated space or area by cardiac puncture into a closed collection system using an aseptic technique. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| **General:** Provide comprehensive information on how the risk management has considered in the case of donor bovine serum, given that it can be derived from animals less than 36 months old, the BSE status of the donor herd shall be well defined and documented. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| **General:** Provide comprehensive information on how the risk management has considered serum shall be collected according to specified protocols by personnel trained in these procedures and the precautions necessary to avoid cross-contamination with higher risk tissues. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| **General:** Provide comprehensive information on how the risk management has considered for bovine blood derivatives, documentation to demonstrate compliance with this document shall be provided, taking into account the relevant requirements listed in ISO 22442-1 Annex C. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| **Traceability:** Provide comprehensive information on how the risk management has considered traceability to the slaughterhouse shall be ensured for each batch of serum or plasma. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| **Traceability:** Provide comprehensive information on how the risk management has considered slaughterhouses shall have available lists of farms from which the animals are sourced. If serum is produced from living animals, records shall be available for each serum batch to ensure traceability to the farms and to the individual animal. When traceability to the individual animal is not possible, this shall be justified in the risk management file. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| **Geographical origin:** Provide comprehensive information on how the risk management has considered bovine blood shall be sourced from countries with minimal exposure to BSE unless otherwise justified and authorized. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| **Stunning methods:** Provide comprehensive information on how the risk management has considered the stunning methods shall be described for the bovine blood collection process unless the material is sourced from a country of negligible geographical BSE risk (see ISO 22442-2:2020, A.3.1). | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| **Stunning methods:** Provide comprehensive information on how the risk management has considered where sourcing of blood is from countries with limited exposure to BSE, a non-penetrative stunner or electro-narcosis shall be used for slaughter of animals over 12 months of age. The use of non-penetrative stunning shall be justified on the basis of an estimate of the risk of dissemination of brain particles into the blood. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Tallow derivatives** | N/A |
| --- | --- |
| **Rationale:** | |
| Provide comprehensive information on how the risk management has considered materials manufactured under the conditions at least as rigorous as those given below shall be considered as presenting an acceptable TSE risk, irrespective of the geographical origin and the nature of the tissues from which tallow derivatives are derived. The following are examples of rigorous processes:   1. trans-esterification or hydrolysis at not less than 200 °C for not less than 20 min under pressure (glycerol, fatty acids and fatty acid esters production). 2. saponification with sodium hydroxide solution, at a concentration of 12 mol/l (glycerol and soap production):    1. batch process: at not less than 95 °C for not less than 3 h.    2. continuous process: at not less than 140 °C, under pressure for not less than 8 min or equivalent. 3. Distillation at 200oC | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Animal charcoal** | N/A |
| --- | --- |
| **Rationale:** | |
| Provide comprehensive information on how the risk management has considered animal charcoal is prepared by carbonization of animal tissues, such as bones, using a temperature ≥800 °C (animal charcoal prepared under these conditions shall be considered as presenting an acceptable TSE risk). | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Milk and milk derivatives** | N/A |
| --- | --- |
| **Rationale:** | |
| Provide comprehensive information on how the risk management has considered milk derivatives manufactured according to the conditions below are considered as presenting an acceptable TSE risk:   * the milk is sourced from healthy animals under the same conditions as milk collected for human consumption. * no other ruminant-derived materials, with the exception of calf rennet, are used in the preparation of such derivatives (e.g., pancreatic enzyme digests of casein). | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Wool and its derivatives** | N/A |
| --- | --- |
| **Rationale:** | |
| Provide comprehensive information on how the risk management has considered wool is sourced from live healthy animals and its derivatives, such as lanolin and wool alcohols, are in compliance with ISO 22442-1. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered wool derivatives is produced from wool that is sourced from slaughtered animals declared "fit for human consumption". | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered the manufacturing process in relation to pH, temperature and duration of treatment meets at least one of the stipulated processing conditions listed below:   * treatment at pH ≥ 13 (initial; corresponding to concentrations of sodium hydroxide ≥0,1 mol/l) at ≥60 °C for at least 1 h; this normally occurs during the reflux stage of the organic-alkaline treatment. * molecular distillation at ≥220 °C under reduced pressure. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

|  |  |
| --- | --- |
| **Amino acids** | N/A |
| **Rationale:** | |
| Provide comprehensive information on how the risk management has considered amino acids prepared using the following processing conditions are considered as presenting an acceptable TSE risk:   * amino acids produced from hides and skins by a process which involves exposure of the material to a pH of 1 to 2, followed by a pH ≥ 11, followed by heat treatment at 140 °C for 30 min at 3 bar. * the resulting amino acids or peptides shall be filtered after production. * analysis shall be performed using a validated and sensitive method to control any residual intact macromolecules with a justified limit set. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Peptones** | N/A |
| --- | --- |
| **Rationale:** | |
| Provide comprehensive information on how the risk management has considered, where tissue of TSE-relevant animal species is the protein source material, the tissue must be sourced from animals fit for consumption with a maximum age of 30 months old for cattle from countries with a controlled BSE risk (Category B). The age of animals is of minimal concern for animals from countries with a negligible BSE risk (Category A). | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

**Section (E): ISO 22442-2 Additional requirements relating to the application of this document to bovine-sourced materials and other TSE relevant animal species.**

|  |  |  |
| --- | --- | --- |
| **TSE relevant animal species** | | N/A |
| **Rationale:** | | |
| Is the material of animal origin sourced TSE relevant animal species including bovine, ovine and caprine species, deer, elk, mink and cats. If no is selected, the remainder of this section does not need to be completed. | Yes  No | |

|  |  |
| --- | --- |
| **General aspects** | N/A |
| **Rationale:** | |
| Provide comprehensive information on how the risk management has considered and documented that when animal material sourced from more than one animal is pooled, and one is identified as high risk, this risk applies to the whole pool. | N/A |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Likelihood of infectivity in the source animals** | N/A |
| --- | --- |
| **Rationale:** | |
| Provide comprehensive information on how the risk management has considered and documented that the likelihood of the BSE agent being present in the source cattle is estimated by reference to published assessments and other relevant data where applicable (To address the risk for transmission of the extremely rare, atypical BSE the age of the source cattle should considered as the important parameter). | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented that where a low probability of infectivity in the source animals is a significant factor in the BSE risk estimate, the procurement and manufacturing processes incorporates measures to prevent cross-contamination from animals or materials of higher BSE risk. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented that when assessing the BSE status, consideration is given to each of the countries in which an animal has lived from birth through rearing to slaughter. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented that the BSE risk estimate relating to geographical sourcing has taken into account the prevalence of BSE infection in domestic cattle in the countries or regions, historical data on the importation of the BSE agent, and an assessment of the effectiveness of the surveillance programme. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented that the incidence of BSE has been assessed (including the trend, using at least the last eight years’ data). Classification of countries or regions according to their BSE risk verification should be based primarily on the classification by the World Organisation for Animal Health (OIE). | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented that published assessments relating to BSE risks associated with specific countries have been taken into account. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented precautions taken to avoid cross-contamination during slaughter, collection, handling, storage, and transport of animal material. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented the methods of stunning and a justification for the method of stunning used and whether the tissues are to be derived from single animals or are to be pooled. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented procedures to prevent cross-contamination from other animals or from higher risk tissues during transport, storage, and any subsequent manufacturing operations. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented the age of the donor animals. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented the feeding history of the donor animals. For all TSE relevant animal species sourced materials, the manufacturer provides published evidence of the procedures that have been implemented in the country of origin of the source TSE relevant animal species to ensure that the potential for transmission of a causative agent of BSE is minimized. The following evidence shall be addressed in the risk assessment:  a) whether or not protein derived from ruminants, produced locally, or imported has been fed to ruminants and the date of effective implementation of any statutory ban on such feeding.  b) where materials are derived from cattle fed with ruminant-derived protein during the preceding eight years, verification that protein has not been obtained from countries where there is a high incidence of BSE, scrapie, or CWD.  c) whether or not cattle over the age of six months or cattle under the age of six months which are retained beyond that age and/or progeny of affected females are or have been imported from countries with a high incidence of BSE, such cattle may increase the risk of introducing the BSE agent if their tissues are rendered and subsequently fed to ruminants. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented the likelihood that the BSE agent would be present in the particular tissue used. This shall be estimated by reference to a published assessment (see ISO 22442-1:2020, D.3.4). Since the data upon which studies of tissue infectivity are based may be incomplete, take into account an estimate of uncertainty based on an evaluation of the quality and quantity of the underlying data. The most up to date information shall be used. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

|  |  |
| --- | --- |
| **Measures to prevent cross-contamination** | N/A |
| **Rationale**: | |
| Provide comprehensive information on how the risk management has considered and documented all precautions taken to avoid cross-contamination during slaughter of the source animal. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented that for collection and handling, the following practices were adopted:  a) for all materials, the potential for extraneous contamination shall be minimized, especially in countries with known cases of BSE. For materials which are not pooled at collection, single use or suitably decontaminated containers (suitably closed to prevent cross-contamination and labelled) may be placed in one large container for transit.  b) whenever possible, materials from animals from different geographical sources shall not be pooled unless they are obtained from countries of low geographical BSE risk or from closed herds.  c) documented procedures shall be established and maintained to prevent cross-contamination from other animals or from higher risk tissues. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented all precautions taken to avoid cross-contamination during storage and transport of the source animal. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

**Section (F): Additional requirements relating to COMMISSION REGULATION (EU) No 722/2012**

**Article 1 (2)**

|  |  |
| --- | --- |
| Confirm that the medical device under application has utilised animal tissues, as well as their derivatives, originating from bovine, ovine and caprine species, deer, elk, mink, and cats | Yes  No |

**Article 1 (3)**

|  |  |
| --- | --- |
| Confirm that the medical device under application has utilised collagen, gelatine or tallow that meets at least the requirements as fit for human consumption laid down in Regulation (EC) No 1069/2009. If yes or N/A are selected, it is not necessary to complete the remaining parts of this section. | Yes  N/A |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

**Article 5 (2)**

|  |
| --- |
| (a) Provide comprehensive information on the risk analysis and risk management process aligned to the utilisation of the animal tissue in the medical device under application. See also Annex I, 1.2 |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| (b) Provide comprehensive information on how the risk management has considered and documented the justification for the use of animal tissues or derivatives, taking into consideration lower risk tissues or synthetic alternatives. See also Annex I, 1.1 |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| (c) Provide comprehensive information on how the risk management has considered and documented the results of elimination and inactivation studies or results of the analysis of relevant literature. |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| (d) Provide comprehensive information on how the risk management has considered and documented the manufacturer’s control of the sources of raw materials, finished products, production process, testing, and subcontractors. |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| (e) Provide comprehensive information on how the risk management has considered and documented the need to audit matters related to the sourcing and processing of animal tissues and derivatives, processes to eliminate or inactivate pathogens, including those activities carried out by suppliers. |
| **Location:**  **File name:**  **Reference:**  **Note:** |

**Annex I (1.2)**

|  |
| --- |
| Provide comprehensive information on how the risk management has considered and documented the hazards and evaluate the risks associated with those tissues or derivatives, establish documentation on measures taken to minimise the risk of transmission and demonstrate the acceptability of the residual risk associated with the device utilising such tissues or derivatives, taking into account the intended use and the benefit of the device. |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| Provide comprehensive information on how the risk management has considered and documented the selecting starting materials (tissues or derivatives) considered appropriate regarding their potential contamination with TSE infectious agents taking into account further collection, handling, transport, storage and processing. |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| Provide comprehensive information on how the risk management has considered and documented applying a production process to remove or inactivate TSE infectious agents on controlled sourced tissues or derivatives. |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| Provide comprehensive information on how the risk management has considered and documented maintaining a system to collect and evaluate production and post-production information regarding changes. |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| Provide comprehensive information on how the risk management has considered and documented taking into account the characteristics of the device and its intended use. |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| Provide comprehensive information on how the risk management has considered and documented in performing the risk analysis and risk management strategy, due consideration is given to the relevant published opinions adopted by the relevant European or international scientific committees or bodies, such as the Scientific Steering Committee (SSC), the European Food Safety Agency (EFSA), the European Medicines Agency (EMA), the World Organisation for Animal Health (OIE) and the World Health Organisation (WHO). |
| **Location:**  **File name:**  **Reference:**  **Note:** |

**Annex I (1.2.1)**

|  |
| --- |
| Provide comprehensive information on how the risk management has considered and documented that risk animals such as fallen stock, emergency slaughtered, and TSE suspected animals are excluded as a source of material. |
| **Location:**  **File name:**  **Reference:**  **Note:** |

**Annex I (1.2.2)**

|  |
| --- |
| Provide comprehensive information on how the risk management has considered and documented that when assessing the risk of the source country, Commission Decision 2007/453/EC (current version) establishing the BSE status of Member States or third countries or regions thereof according to their BSE risk has been taken into account. |
| **Location:**  **File name:**  **Reference:**  **Note:** |

**Annex I (1.2.3)**

|  |
| --- |
| Provide comprehensive information on how the risk management has considered and documented that the classification of the risks relating to different types of starting tissue as defined in the WHO Guidelines on Tissue Infectivity Distribution in Transmissible Spongiform Encephalopathies (2006), as amended, is taken into account. |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| Provide comprehensive information on how the risk management has considered and documented that sourcing of animal tissue has been performed in such a manner as to maintain control over the traceability and integrity of source tissue. |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| Provide comprehensive information on how the risk management has considered and documented that the animals have been subjected to veterinary ante- and post-mortem inspection. |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| Provide comprehensive information on how the risk management has considered and documented that Regulation (EC) No 1069/2009 has been applied and that only category 3 material in accordance with Article 10 of Regulation (EC) No 1069/2009 has been used. |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| Provide comprehensive information on how the risk management has considered and documented that for bovine, ovine and caprine animals, the list of specified risk material (SRM) laid down in Annex V to Regulation (EC) No 999/2001 is to be considered as being potentially of high TSE infectivity. |
| **Location:**  **File name:**  **Reference:**  **Note:** |

**Annex I (1.2.4)**

|  |
| --- |
| Provide comprehensive information on how the risk management has considered and documented that the risk of cross-contamination during slaughtering, collection, processing, handling, storage and transport is minimised. |
| **Location:**  **File name:**  **Reference:**  **Note:** |

**Annex I (1.2.5.1)**

|  |  |
| --- | --- |
| Provide comprehensive information on how the risk management has considered and documented that for devices which cannot withstand an inactivation or elimination process without undergoing unacceptable degradation, the manufacturer must rely principally on the control of sourcing. | N/A |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

**Annex I (1.2.5.2)**

|  |  |
| --- | --- |
| Provide comprehensive information on how the risk management has considered and documented that for devices, if claims are made by the manufacturer for the ability of manufacturing processes to remove or inactivate TSE infectious agents, these must be substantiated by appropriate documentation | N/A |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented relevant information from an analysis of appropriate scientific literature that can be used to support inactivation and elimination factors, where the specific processes referred to in the literature are comparable to those used for the device. | N/A |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented if the literature search fails to substantiate the claims, the manufacturer must set up a specific inactivation or elimination study. | N/A |
| **Location:**  **File name:**  **Reference:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented procedures to ensure that the validated processing parameters are applied during routine manufacture. A final report must identify manufacturing parameters and limits that are critical to the effectiveness of the inactivation or elimination process. | N/A |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

**Annex I (1.2.6)**

|  |
| --- |
| Provide comprehensive information on how the risk management has considered and documented the quantity of raw tissues or derivatives of animal origin required to produce a single unit of the medical device. |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| Provide comprehensive information on how the risk management has considered and documented an assessment as to whether the production process has the potential to concentrate levels of TSE infectious agents present in the animal starting tissues or derivatives |
| **Location:**  **File name:**  **Reference:**  **Note:** |

**Annex I (1.2.7)**

|  |
| --- |
| Provide comprehensive information on how the risk management has considered and documented the maximum quantity of animal tissues or derivatives coming into contact with the patient or user when using a single medical device. |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| Provide comprehensive information on how the risk management has considered and documented the contact area: its surface, type (e.g., skin, mucous tissue, brain) and condition (e.g., healthy or damaged). |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| Provide comprehensive information on how the risk management has considered and documented the type of the tissues or derivatives coming into contact with the patients or users. |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| Provide comprehensive information on how the risk management has considered and documented the period of time the device is intended to remain in contact with the body (including bioresorption effect). |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| Provide comprehensive information on how the risk management has considered and documented the number of medical devices that could be used in a given procedure or, if possible, over the lifetime of a patient or user. |
| **Location:**  **File name:**  **Reference:**  **Note:** |

**Annex I (1.2.8)**

|  |
| --- |
| Provide comprehensive information on how the risk management has considered and documented taking into account of the route of administration as indicated in the product information. |
| **Location:**  **File name:**  **Reference:**  **Note:** |

**Annex I (1.3)**

|  |
| --- |
| Provide comprehensive information on how the risk management has considered and documented the establishment and maintenance of a systematic procedure to review information gained about the medical device or similar devices in the post-production phase. The information must be evaluated for possible relevance to safety. |
| **Location:**  **File name:**  **Reference:**  **Note:** |

# Appendix 8 – Substances intended to be introduced into the human body and that are absorbed by or locally dispersed in the human body

**Important notes to the applicant:**

* This section applies to medical devices that are composed of substances or combinations of substances that are intended to be introduced into the human body and that are absorbed by or locally dispersed in the human body according to EU MDR ‘*Annex I, 12.2, 23.2 (r), 23.4 (t)*’ and ‘*Annex II, 6.2 (c)*’ and ‘*Annex IX, 5.4*’.
* Devices that are composed of such substances may be subject to requirements of additional European Directives / Regulations. Additional review resources may be required, including external independent reviewers and/or competent authority consultation and/or a European Medicines Agency.
* Where a medical device, or its products of metabolism, are systemically absorbed by the human body in order to achieve their intended purpose (per EU MDR Annex IX, 5.4 b), NSAI must seek a scientific opinion from a competent authority on the compliance of the device with the relevant requirements laid down in Annex I to Directive 2001/83/EC.

| **Medical device composed of substances absorbed by or locally dispersed in the human body, meeting definition per EU MDR Annex I, 12.2** | N/A |
| --- | --- |
| Where a medical device is composed of substances or combinations of substances that are intended to be introduced into the human body and that are absorbed by or locally dispersed in the human body according to **EU MDR ‘Annex I, 12.2**, [and by association **EU MDR Annex I 23.2 (r)** and **23.4 (t)**’ and **‘Annex II, 6.2 (c)’**], provide a statement indicating this fact. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Medical device composed of substances absorbed by or locally dispersed in the human body, meeting definition per EU MDR Annex IX, 5.4 a.** | N/A |
| --- | --- |
| Where a medical device is composed of substances or combinations of substances that are intended to be introduced into the human body (via a body orifice or applied to the skin ) and that are absorbed by or locally dispersed in the human body according to E**U MDR ‘Annex IX, 5.4 (a)’** [and by association **EU MDR ‘Annex I, 12.2’** and **‘Annex II, 6.2 (c)**], provide a statement indicating this fact. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

| **Medical device composed of substances absorbed by or locally dispersed in the human body, meeting definition per EU MDR Annex IX, 5.4 b.** | N/A |
| --- | --- |
| Where the device substances, or its products of metabolism, are systemically absorbed by the human body in order to achieve their intended purpose, according to **EU MDR ‘Annex IX, 5.4 (b)’** [and by association **EU MDR ‘Annex I, 12.2’** and **‘Annex II, 6.2 (c)**], provide a statement indicating this fact. | |
| **Location:**  **File name:**  **Reference:**  **Note:** | |

**Information regarding the substance(s)**

|  |  |  |  |
| --- | --- | --- | --- |
| Identity of the substance(s) |  | | |
| Is the substance derived from human blood or human plasma? | | Yes  No | |
| Is the substance derived from animals? | | Yes  No | |
| Is the substance supplied as ‘medical grade’?  If yes, provide reference to evidence of this fact | | Yes  No | |
| **Location:**  **File name:**  **Reference:**  **Note:** | | | |
| For medical devices to which ‘EU MDR Annex VIII Rule 21’ applies, provide information (including any tests for product characterisation) on the determined qualification as a medical device (based on mechanism of action) and for establishing the right classification according to Rule 21. | | | N/A |
| **Location:**  **File name:**  **Reference:**  **Note:** | | | |

**Quality and safety of absorbable substance(s)**

| **Annex II 6.2 (c)** |
| --- |
| Provide detailed information, including test design, complete test or study protocols, methods of data analysis, and data summaries and test conclusions, regarding studies in relation to:   * absorption * distribution * metabolism * excretion   In the absence of such studies, a justification shall be provided. |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| Provide detailed information, including test design, complete test or study protocols, methods of data analysis, and data summaries and test conclusions, regarding studies in relation to:   * possible interactions of those substances, or of their products of metabolism in the human body, with other devices, medicinal products, or other substances, considering the target population, and its associated medical conditions.   In the absence of such studies, a justification shall be provided. |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| Provide detailed information, including test design, complete test or study protocols, methods of data analysis, and data summaries and test conclusions, regarding studies in relation to:   * local tolerance   In the absence of such studies, a justification shall be provided. |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| Provide detailed information, including test design, complete test or study protocols, methods of data analysis, and data summaries and test conclusions, regarding studies in relation to:   * toxicity, including single-dose toxicity, repeat-dose toxicity, genotoxicity, carcinogenicity, and reproductive and developmental toxicity, as applicable depending on the level and nature of exposure to the device.   In the absence of such studies, a justification shall be provided. |

*Note: If evidence is based on published literature, manufacturers should rationalise the applicability of such literature data to their own device considering the nature of their device, intended purpose, contact with various body tissues and other substances, the target population, and its associated medical conditions etc.*

# Appendix 9 – Medical device with a measuring function

|  |  |
| --- | --- |
| **Section MF1** | |
|  | Provide evidence associated with:   * Diagnostic devices and devices with a measuring function, shall be designed and manufactured in such a way as to provide sufficient accuracy, precision, and stability for their intended purpose, based on appropriate scientific and technical methods. The limits of accuracy shall be indicated by the manufacturer. * The measurements made by devices with a measuring function shall be expressed in legal units conforming to the provisions of Council Directive 80/181/EEC.   (Annex I Section 15.1 and 15.2) |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| **Section MF2** | |
|  | Provide the technical specification associated with accuracy including its tolerance and range. (Annex II Section 1.1) |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| **Section MF3** | |
|  | Provide the results and critical analyses of verification and validation tests and /or studies undertaken to establish the performance requirements of the measurement function of the device. (Annex II Section 6) |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| **Section MF4** | |
|  | Provide a description of the methods used in order to ensure the accuracy as given in the specifications. (Annex II Section 6.2(f) |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| **Section MF5** | |
|  | Provide references to where risk is considered, and the design is controlled with respect to (i)The ergonomic features of the measurement features/design (Annex I Section 5(a) and 14(a).  (ii)Risks associated with loss of accuracy of any measuring mechanism from aging of materials used (Annex I Section 14.2(g)  (iii) Risks associated with loss of accuracy during the lifetime of the device (Annex I Section 6)  If these risks were not deemed appropriate to the measurement function of the device Justify why not. |
| **Location:**  **File name:**  **Reference:**  **Note:** |
| **Section MF6** | |
|  | Provide the Information in the Instructions for use containing specifications the user requires to use the device appropriately, e.g., if the device has a measuring function, the degree of accuracy claimed for it;(Annex I Section 23.4) |
| **Location:**  **File name:**  **Reference:**  **Note:** |

# Appendix 10 –Mechanical Product Performance

This section should include information to meet the requirements of Annex II Section 6.1. (a) & (b) and relevant GSPR’s for mechanical aspects of the device. This section includes the performance and safety requirements of Annex II part 6.1(b), more specifically the verification of the mechanical performance requirements and in turn the verification of effectiveness of additional risk control mitigations.

**Note:** The Mechanical Product Performance will incorporate analysis of data submitted in other sections, i.e., Design and Manufacturing, Labelling and IFU, FMEA’s, risk documents including benefit/risk analysis, and may generate subsequent queries

|  |  |
| --- | --- |
| **Equivalence** | |
| If equivalence to an existing medical device is being claimed in compliance with MDR Annex XIV, Part A, Section 3 & MDCG 2020-5, please confirm the **Technical Characteristics (Mechanical) Section** of the **Equivalence Declaration** form (MDR-2003 or MDR-3003) has been completed. | Yes  No |
| If ‘N/A’ has been selected, please provide a rationale:  **Rationale:** | |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Mechanical Product Performance (Annex II, 3(b) & 6.1)** | | | | N/A |
| **MPP1** | **Device Design** | | | |
| In relation to Device Design, confirm the device tested for design verification is the same version for which CE mark approval is being sought. If not, please provide details/differences and rationale that submitted design verification testing remains valid: | | Yes  No | |
| **Device Version:**  Provide an overview of the design history of the device if the design verification data of the current design under application is supported by data generated for previous generations.   |  |  |  |  | | --- | --- | --- | --- | | **Date of the Change** | **Technical Details of the Change** | **Rationale for the Change** | **Details of the executed DV testing** | | e.g., *01-Jan-2023* | *Enter technical change details here* | *Discuss rationale for change here* | *e.g., fully executed design verification – design attributes* | |  |  |  |  | |  |  |  |  | | | | |
| **MPP2** | Provide the design drawings/functional drawings/exploded drawings in the MPP2. For example, all relevant 2D/3D/exploded/animated drawings/illustrations include details to illustrate all components, their material composition, and technical dimensions. | | | |
| **Location:**  **File name:**  **Reference:**  **Note:** | | | |
| **MPP3** | Provide the Design Traceability Matrix or Design Input/ Output document and Product Specification to MPP3 Folder.  The Design Traceability Matrix or Design Input/ Output document shall make specific reference to:   * Design Input / User Need * Specification for each Input * Source of each specification * Justification of the source (via use of a standard: Harmonised, Non-Harmonised ASTM, AAMI), predicate device testing, internally validated specification with clinical feedback, etc.) * Design Output/ Documented Evidence * Comment on whether D/I was met or not. * references multiple documents due to changes or updates (as described in Device design history PP1), provide details on device version/change, with specific protocol and report section which shows compliance to the GSPR’s. | | | |
| **Location:**  **File name:**  **Reference:**  **Note:** | | | |
| **MPP4** | **Design Verification Testing** | | | |
| Provide the relevant Design Verification Testing (protocols and reports), substantiating the Design Outputs meet the Design Inputs in the MPP4 Folder.  Ensure that the protocols and reports supplied include the following:   * Description of test methods and Justified test parameters per relevant standards. * Clearly stated acceptance criteria * Results and raw data, analysis, conclusions, and discussions of results * Sample size methods, justification, and documented source * Justified deviations (if applicable)   **Note:** NSAI shall not accept “For Information Only” data (FIO); all attributes tested shall have clinically relevant specifications. | | | |
| **Location:**  **File name:**  **Reference:**  **Note:** | | | |
| **MPP5** | Confirm if bench top models for ‘Simulated Use’ were used during pre-clinical testing. If yes, provide evidence that such models have been clinically approved as anatomically correct. | | Yes  No | |
| **Location:**  **File name:**  **Reference:**  **Note:** | | | |
| **MPP6** | **Product Lifetime** | | | |
| State the product lifetime: |  | | |
| Provide the characteristics and the testing to demonstrate the performance of the device at the proposed product lifetime. | | | |
| **Location:**  **File name:**  **Reference:**  **Note:** | | | |
| **MPP7** | **Computer Modelling** | | | |
| Confirm if computer modelling has been used during pre-clinical testing.  If Yes Outline the objective/purpose of the computer modelling (i.e., if relevant, indicate what design output or GSPR the computer modelling data is being used to support). | | Yes  No | |
| **Location:**  **File name:**  **Reference:**  **Note:** | | | |
| If Yes Has computer modelling been completed on the full device design? | | Yes  No | |
| **Location:**  **File name:**  **Reference:**  **Note:** | | | |
| Outline the source of the computer modelling inputs e.g., scan data, anatomical physiology etc | | | |
| **Location:**  **File name:**  **Reference:**  **Note:** | | | |
| In relation to Computer modelling, confirm the device tested is the same generation/ version for which CE mark approval is being sought. | | Yes  No | |
| **Version:**  **Location:**  **File name:**  **Reference:**  **Note:** | | | |
| **MPP8** | **Device Verification Stability/Shelf Life** | | | |
| In relation to device stability, confirm the device tested is the same version for which CE mark approval is being sought:  Please provide rationale/details including details, if applicable, of changes/differences that demonstrate the submitted design stability testing remains valid. | | Yes  No | |
| **Device Version tested in Stability Study**:  **Location:**  **File name:**  **Reference:**  **Note:** | | | |
| State the supporting document file name:  Confirm that the device stability protocols and reports contain reference to device testing i.e., not just packaging testing: | | Yes  No | |
| **Location:**  **File name:**  **Reference:**  **Note:** | | | |
| Define the shelf life/expiry date. | | | |
| **Years:**  **Location:**  **File name:**  **Reference:**  **Note:** | | | |
| Confirm the number of sterilisation cycles that the device and packaging were subjected to prior to stability testing: | | | |
| **Cycles:**  **Location:**  **File name:**  **Reference:**  **Note:** | | | |
| Provide evidence of the specific transportation and conditioning applied to the devices substantiating device stability. | | | |
| **Location:**  **File name:**  **Reference:**  **Note:** | | | |
| Were all device attributes/design outputs assessed at the proposed shelf-life? | | Yes  No | |
| If no, please provide rationale/details including, if applicable, the justification for omitting other attributes: | | | |
| **Location:**  **File name:**  **Reference:**  **Note:** | | | |
| Confirm all the necessary protocols and reports for the Accelerated aging studies have been provided. | | Yes  No | |
| Provide all the necessary protocols and reports for the Accelerated aging studies. Please ensure that the protocols and reports supplied include the following:   * Description of test methods and Justified test parameters per relevant standards. * Clearly stated acceptance criteria * Results and raw data, analysis, conclusions, and discussions of results * Sample size methods, justification, and documented source * Justified deviations (if applicable)   ***Note: NSAI shall not accept “For Information Only” data (FIO); all attributes tested shall have clinically relevant specifications.*** | | | |
| **Location:**  **File name:**  **Reference:**  **Note:** | | | |
| Have Real time aging studies been completed?  If yes, provide all the necessary protocols and reports for real time studies.  If no, proceed to next question. | | Yes  No | |
| **Location:**  **File name:**  **Reference:**  **Note:** | | | |
| If submitting Accelerated Aging data to support shelf life, please **confirm start date and expected completion date for real time studies.** | | | |
| **Real Time Stability:**  **Start Date** DD-Mmm-YYYY:  **Completion Date** DD-Mmm-YYYY**:** | | | |
| **MPP9** | **Manufacturing Processes** | | | |
| Confirm a documented overview, of manufacturing process(es) (i.e., process flow) including any activities performed by, or products/components obtained from, suppliers have been uploaded to the MPP 10.  Manufacturing processes should contain the following:   * Assembly * Special processes * Critical materials, components | | | |
| **Location:**  **File name:**  **Reference:**  **Note:** | | | |
| Provide evidence of completed process validations to support the manufacturing processes and their validation, (This evidence may be in the form of a completed validation master plan/report or similar with pass/fail status of each validation) upload to the MPP 10 **Folder.** | | | |
| **Location:**  **File name:**  **Reference:**  **Note:** | | | |