|  |
| --- |
| **MDR 2017/745**  **Product Submission Form** |

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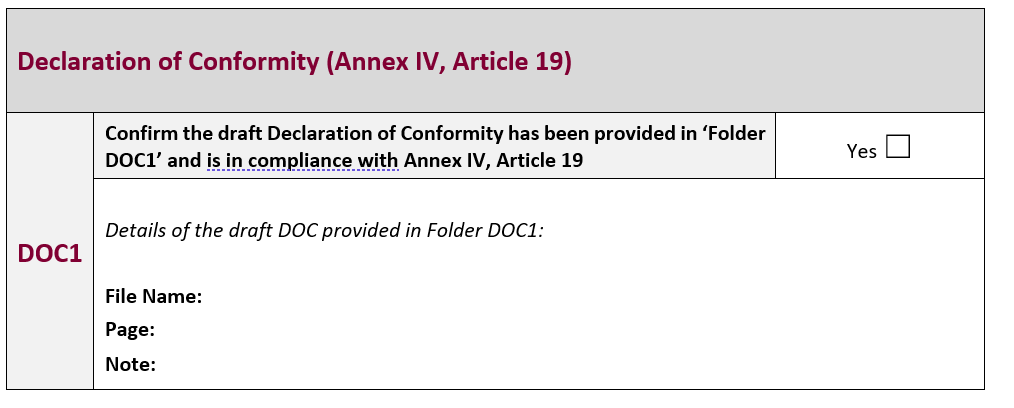
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| **Manufacturer Declaration** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| We, the manufacturer, declare the information in this form is correct and has been submitted as instructed. Information not provided, or provided in the wrong 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:** |  | |

**Instructions on how to complete this submission form**

* 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 section is prepared by the most appropriate SME(s), with the relevant expertise and competence to complete the form.
* Hard copies of Technical Documentation **are not accepted.**
* Documents must be provided in **PDF format** 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.
* All sections of the form must be filled in with the requested information in a clear and detailed format
* Where supporting documentation is requested, the following must be filled in to signpost to the information:
  + **File Name:** Identify supporting document PDF file name.
  + **Page:** Identify the precise page(s) and section containing the supporting evidence within the PDF file.
  + **Note:** Add inany additional information/explanatory notes, if applicable.

See example below.



* For **Class Is** submissions, complete **Sections 1, 2 (Parts A,B,D and E)** and **Appendix 2a/2b**
* For **Class Im** submissions, complete **Sections 1, 2 (Parts A,B,D and E)** and **Appendix 9**
* For **Class Ir** submissions, complete **Sections 1, 2 (Parts A,B,D and E)** and **Appendix 11**
* For **Class** **IIa – Class III** submissions, complete **Sections 1, 2 and 3** and **all applicable Appendices**
* Use the **N/A** box in the header for all non-relevant sections. A detailed justification must be provided for all sections identified as not applicable.

# Section 1 - General Information

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| General Information: Administrative | | | | | | | | | | |
| **G0** | **NSAI File #** | | | | 745. ✱✱✱ | | | | | |
| **Manufacturer:** *(as per definition within the regulation)* | | | |  | | | | | |
| **Manufacturer Address:** | | | |  | | | | | |
| **Manufacturers SRN:** | | | |  | | | | | |
| **Conformity Assessment Scope**  (*i.e. the device range covered. This is the scope that will appear on certificate*) | | | |  | | | | | |
| **Conformity Assessment Route** | | | | **Annex IX**   Chapter I  Chapter II  Chapter III  *For Annex IX indicate both the Annex and chapter(s) used*  **Annex XI, Part A** | | | | | |
| **Provide details of any existing approvals (e.g., MDD/FDA/TGA)?** | | | |  | | | | | |
| **Confirm all testing and test reports have been completed and submitted. i.e., no test data pending.**  ***Note:*** *The review cannot commence until* ***all supporting data*** *is submitted.* | | | | Yes | | | | | |
| **Name of Person Responsible for Regulatory Compliance (PRRC):** | | | |  | | | | | |
| **Company Liaison and Details:** | | | | **Name:** |  | | | | |
| **Address:** |  | | | | |
| **Email:** |  | | | | |
|  | **Telephone:** |  | | | | |
| General Information: Product | | | | | | | | | | |
| **G1** | **Product or Product trade name:** | | | |  | | | | | |
| **Classification:** | | | |  | | | **Classification rule as per MDR 2017/745** | |  |
| **Provide rationale for Classification Rule:** | | | |  | | | | | |
| **Model Number** *(in scope of this submission)* | | | | **Basic UDI-DI:** | | | | **Intended Purpose** | |
|  | | | |  | | | |  | |
|  | | | |  | | | |  | |
|  | | | |  | | | |  | |
| *Add more lines as required* | | | | | | | | | |
| **Product MDA/MDN, MDS codes:** *(refer to NSAI Contract Review Sheet and MDCG 2019-14)* | | | |  | | | | | |
| **Are the models part of a System or Procedure Pack** | | | | Yes  No  If Yes, complete Appendix 10  If No, please provide a justification as to why it is not considered a System or procedure pack  Justification: | | | | | |
| **System or procedure Pack Number** *(if applicable)* | | | | Description: | | | | | |
| **Duration of use** | | | |  | | | | | |
| **Rationale for Duration of use** | | | |  | | | | | |
| **Proposed Shelf Life** | | | |  | | | | | |
| **EMDN** | | | |  | | | | | |
| **EU Authorised Representative:** | | N/A | | **Name:** | |  | | | |
| **Address:** | |  | | | |
| **Email:** | |  | | | |
| **Telephone:** | |  | | | |
| **EU Authorised Representative SRN:** | | N/A | |  | | | | | |
| General Information: Sites | | | | | | | | | | |
| **G2** | Provide below the details of any site(s) related to this submission (including sites where design and manufacturing activities are performed (including Distribution, packaging, Sterilisation etc) and details of relevant CRITICAL suppliers and sub-contractors sites.  **Note:** please add additional lines for additional sites as necessary. | | | | | | | | | |
| **Site 1** | | | | | | | | | |
| **Company/Division/Business Unit:** | | | |  | | | | | |
| **Address:** | | | |  | | | | | |
| **Device type/Generic Device Group** | | | |  | | | | | |
| **Details of activities performed on site.** | | | |  | | | | | |
| **Confirm a copy of the valid ISO13485 QMS Cert for this site has been provided in Folder G2** | | | | Yes | | | | | |
| **File Name:**  **Page:**  **Note:** | | | | | |
| **Site 2** | | | | | | | | | |
| **Company/Division/Business Unit:** | | | |  | | | | | |
| **Address:** | | | |  | | | | | |
| **Device type/Generic Device Group** | | | |  | | | | | |
| **Details of activities performed on site.** | | | |  | | | | | |
| **Confirm a copy of the valid ISO13485 QMS Cert for this site has been provided in the Folder G2** | | | | Yes | | | | | |
| **File Name:**  **Page:**  **Note:** | | | | | |
| **Site 3** | | | | | | | | | |
| **Company/Division/Business Unit:** | | | |  | | | | | |
| **Address:** | | | |  | | | | | |
| **Device type/Generic Device Group** | | | |  | | | | | |
| **Details of activities performed on site.** | | | |  | | | | | |
| **Confirm a copy of the valid ISO13485 QMS Cert for this site has been provided in Folder G2** | | | | Yes | | | | | |
| **File Name:**  **Page:**  **Note:** | | | | | |
| **Site 4** | | | | | | | | | |
| **Company/Division/Business Unit:** | | | |  | | | | | |
| **Address:** | | | |  | | | | | |
| **Device type/Generic Device Group** | | | |  | | | | | |
| **Details of activities performed on site.** | | | |  | | | | | |
| **Confirm a copy of the valid ISO13485 QMS Cert for this site has been provided in Folder G2** | | | | Yes | | | | | |
| **File Name:**  **Page:**  **Note:** | | | | | |
| General Information: Critical Suppliers and potential commercial competitor(s) | | | | | | | | | | |
| **G3** | **List below all 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** | | | | | **File name and location** |
| *e.g., Moulded components* | | | *e.g., MouldCo, Inc. California, USA* | *e.g., NSAI* | | | | | *Ensure valid copy of certificate is provided in* ***Folder G3*** |
|  | | |  |  | | | | |  |
| *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* |  | | | | | | | | |

| Declaration of Conformity **(Annex IV, Article 19)** | | |
| --- | --- | --- |
| **DOC1** | **Confirm the draft Declaration of Conformity has been provided in ‘Folder DOC1’ and is in compliance with Annex IV, Article 19** | Yes |
| *Details of the draft DOC provided in Folder DOC1:*  **File Name:**  **Page:**  **Note:** | |

|  |  |
| --- | --- |
| Device Overview: Device Description and Intended Purpose | |
| **Provide a general description of the device.**  *If applicable, ensure all devices/components/accessories which comprise the system or procedure pack are considered.* | |
| **General Device Description:** | |
| **Provide annotated image(s) of the device and all levels of packaging** | |
| **Annotated Image(s) of the device and all levels of packaging:** | |
| State the intended purpose of the device.  Ensure that the intended purpose is consistent across all technical documentation | |
| **Intended Purpose:** | |
| **Confirm that the intended purpose statement matches the intended purpose statement in all other supporting document.** | **Yes** |
| State the indications for use for the device. | |
| **Indications for use:** | |
| **Provide a general overview of the principles of operation of the device, mode of action. Include any links to online demonstration videos to aid understanding.** | |
| **Details:** | |
| **Provide description of all accessories for the device, other devices and other products that are not devices which can be used in combination with it, including complete list of various configurations/variants of the device intended to be made available on the market.** | N/A |
| **Description or Rationale for selecting N/A:** | |
| **Are there any novel features in the device.** | Yes  No |
| **Provide an explanation of any/all novel features, if applicable.** | |
| **Explanation:** | |
| **Have previous generations of the device been produced.** | Yes  No |
| **If yes, provide details:** | |

| Labelling and IFU | | |
| --- | --- | --- |
| **LIFU1** | Confirm a copy of the Product Labels, IFU (if applicable), and relevant instruction manuals (if applicable), have been uploaded to **Folder LIFU1**  ***Note****:*  *Include all levels of labelling (device, packaging, carton, etc.).*  *Ensure labels are life size or provide a scale.*  *Labelling in draft format is acceptable* | Yes |
| *Details of all supporting documentation provided in Folder LIFU1:*  **File Name:**  **Page:**  **Note:** | |
| Confirm the product complies with the relevant requirement for **ANNEX I Chapter III, 23.1-4** | Yes |
| Provide the website address/page where this information (IFU) is made available and kept up to date: | |
| Provide a link to the website: | |
| Confirm labelling standard and year used: | EN ISO 15223-1  Year: 20XX \_\_\_\_\_\_\_  Other Standards detail below |
| If other labelling standards are used, please provide details: | |
| **LIFU2** | Confirm UDI labelling applied to product(s) with full details (as per MDR 2017/745, Article 27) have been uploaded to **Folder LIFU2** | Yes |
| *Details of all supporting documentation provided in Folder LIFU2:*  **File Name:**  **Page:**  **Note:** | |
| 1. If N/A, please provide rationale: | |

| Importer (per Articles 13, 14, 16, 30, 31 and Annex III/VI of EU MDR) | | | |
| --- | --- | --- | --- |
| **IMP1** | **Declare whether or not the device(s) under evaluation are placed on the market by an importer(s) per Articles 13, 14, 16, 30, 31 and Annex III/VI of EU MDR.** | Yes | No |
| If yes is selected above, provide in ***Folder IMP1***, details on the Importer’s name, registered trade name or registered trade mark, registered place of business and address at which it can be contacted, so that its location can be established.’  **File Name:**  **Page:**  **Note:** | | |

|  |  |  |  |
| --- | --- | --- | --- |
| Distributor (per Articles 14, 16, 25, 30, 31 and Annex III/VI of EU MDR) | | | |
| **DIST1** | **Declare whether or not the device(s) under evaluation are placed on the market by a distributor(s) per Articles 14, 16, 25, 30, 31 and Annex III/VI of EU MDR.** | Yes | No |
| If yes is selected above, provide in ***Folder DIST1***, details on the Distributor’s name, registered trade name or registered trade mark, registered place of business and address at which it can be contacted, so that its location can be established.’  **File Name:**  **Page:**  **Note:** | | |

| Refurbished Medical Devices (per Article 1 and Annex VI of EU MDR) | | | |
| --- | --- | --- | --- |
| **REF1** | **Declare whether or not the device(s) under evaluation are fully refurbished between patient uses per Articles 1 and Annex VI of EU MDR** | Yes | No |
| If yes is selected above, provide in ***Folder REF1***, verification of refurbishment activities by the manufacturer that bring the used medical device ‘into conformity with this Regulation, combined with the assignment of a new lifetime to the refurbished device.’  **File Name:**  **Page:**  **Note:** | | |

# Section 2 - Technical

### 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 submissionand is readily searchable in an electronic format.** |
| Provide a statement confirming this and how it has been achieved: |

**Device description and specification**

In order to show compliance to Annex II of MDR 2017/745 the Technical documentation shall include reference to:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Product or Trade Name (Annex II, 1.1, a)** | | | | |
| **PtA1** | | **Provide in Folder PtA1, supporting evidence where the technical documentation makes 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 submission n 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.* | | |
| *Details of all supporting documentation provided in* ***Folder PtA1****:*  **File Name:**  **Page:**  **Note:** | | |
| **Basic UDI-DI (Annex II, 1.1, b)** | | | | |
| **PtA2** | | **Provide in Folder PtA2, supporting evidence where the technical documentation makes 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.* | | |
| *Details of all supporting documentation provided in* ***Folder PtA2****:*  **File Name:**  **Page:**  **Note:** | | |
| **Intended patient population (Annex II, 1.1, c)** | | | | |
| **PtA3** | | **Provide in Folder PtA3, supporting evidence where the technical documentation makes 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.* | | |
| *Details of all supporting documentation provided in* ***Folder PtA3****:*  **File Name:**  **Page:**  **Note:** | | |
| **Description of methods and principles of operation (Annex II, 1.1, d)** | | | | |
| **PtA4** | | | **Provide in Folder PtA4, supporting evidence where the technical documentation makes reference to:** *Principles of operation of the device and its mode of action, scientifically demonstrated if necessary.*  *Evidence provided here should remain consistent throughout all Technical Documentation.* | |
| *Details of all supporting documentation provided in* ***Folder PtA4****:*  **File Name:**  **Page:**  **Note:** | |
| **Qualification of the product as a device (Annex II, 1.1, e and f)** | | | | |
| **PtA5** | | **Provide in Folder PtA5, supporting evidence where the technical documentation makes reference to:** *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.* | | |
| *Details of all supporting documentation provided in* ***Folder PtA5****:*  **File Name:**  **Page:**  **Note:** | | |
| **Novel Features (Annex II, 1.1, g)** | | | | |
| **PtA6** | | Select ‘N/A’ if section is not applicable and provide rationale | | N/A |
| *Details of all supporting documentation provided in* ***Folder PtA6****:*  **File Name:**  **Page:**  **Note:** | | |
| **Rationale:** | | |
| **Provide in Folder PtA6, supporting evidence where the technical documentation makes reference to:** An explanation of any novel features. | | |
| *Details of all supporting documentation provided in* ***Folder PtA6****:*  **File Name:**  **Page:**  **Note:** | | |
| **Accessories to be used with the device under submission (Annex II, 1.1, h)** | | | | |
| **PtA7** | | Select ‘N/A’ if section is not applicable and provide rationale | | N/A |
| **Rationale:** | | |
| **Provide in Folder PtA7, supporting evidence where the technical documentation makes 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)* | | |
| *Details of all supporting documentation provided in* ***Folder PtA7****:*  **File Name:**  **Page:**  **Note:** | | |
| **Configurations/Variants of the product under submission (Annex II, 1.1, i)** | | | | |
| **PtA8** | | | **Provide in Folder PtA8, supporting evidence where the technical documentation makes 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;* | |
| *Details of all supporting documentation provided in* ***Folder PtA8****:*  **File Name:**  **Page:**  **Note:** | |
| **Drawings, Pictures, Illustrations etc (Annex II, 1.1, j)** | | | | |
| **PtA9** | | **Provide in Folder PtA9, supporting evidence where the technical documentation makes reference to:** *A general description of the key functional elements, e.g. its parts/components (including software if appropriate), its formulation, its composition, its functionality and, where relevant, its qualitative and quantitative composition.*  *Where appropriate this 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.* | | |
| *Details of all supporting documentation provided in* ***Folder PtA9****:*  **File Name:**  **Page:**  **Note:** | | |
| **Raw Materials (Annex II, 1.1, k)** | | | | |
| **PtA10** | | **Provide in Folder PtA10, supporting evidence where the technical documentation makes 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.* | | |
| *Details of all supporting documentation provided in* ***Folder PtA10****:*  **File Name:**  **Page:**  **Note:** | | |
| **Claims from other sources (Annex II, 1.1, l)** | | | | |
| **PtA11** | **Provide in Folder PtA11, supporting evidence where the technical documentation makes reference to:** *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.* | | | |
| Provide a list of Technical specifications that have been deemed relevant to communicate to the user.   * Provide a list of all information available to the user (example in brochures, catalogues, and similar publications) that contains said Technical specifications | | | |
| *Details of all supporting documentation provided in* ***Folder PtA11****:*  **File Name:**  **Page:**  **Note:** | | | |

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

In order to show compliance to Annex II of MDR 2017/745 the Technical documentation shall include reference to:

| **Previous generations (Annex II, 1.2, a)** | | | | |
| --- | --- | --- | --- | --- |
| **PtA12** | | Select ‘N/A’ if section is not applicable and provide rationale | N/A | |
| **Rationale:** | | |
| **Provide in Folder PtA12, supporting evidence where the technical documentation makes reference to:** *an overview of the previous generation or generations of the device produced by the manufacturer, where such devices exist.* | | |
| *Details of all supporting documentation provided in* ***Folder PtA12****:*  **File Name:**  **Page:**  **Note:** | | |
| **Similar Devices (Annex II, 1.2, b)** | | | | |
| **PtA13** | Select ‘N/A’ if section is not applicable and provide rationale | | | N/A |
| **Rationale:** | | | |
| **Provide in Folder PtA13, supporting evidence where the technical documentation makes reference to:** *an overview of identified similar devices available on the Union or international markets, where such devices exist.* | | | |
| *Details of all supporting documentation provided in* ***Folder PtA13****:*  **File Name:**  **Page:**  **Note:** | | | |

### Part B - Information to be Supplied by the Manufacturer

In order to show compliance to Annex II of MDR 2017/745 the manufacturer shall supply:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Labels (Annex II, 2, a)** | | | | |
| **PtB1** | **Provide in Folder PtB1,** *a complete set of 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 in the languages accepted in the Member States where the device is envisaged to be sold.* | | | |
| *Details of all supporting documentation provided in* ***Folder PtB1****:*  **File Name:**  **Page:**  **Note:** | | | |
| **Instructions for Use (Annex II, 2, a)** | | | | |
| **PtB2** | **Provide in Folder PtB2,** *supporting evidence where the technical documentation makes reference to: a reference to the instructions for use in the languages accepted in the Member States where the device is envisaged to be sold.* | | | |
| *Details of all supporting documentation provided in* ***Folder PtB2****:*  **File Name:**  **Page:**  **Note:** | | | |
| **Electronic Instructions for Use (Eifu)** | | | | |
| **PtB3** | Select ‘N/A’ if Eifu section is not applicable and provide rationale | | | N/A |
| Rationale: | | | |
| **Provide in Folder PtB3, if applicable,** *supporting evidence to 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 in Folder PtB3,** *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.]* | | | |
| *Details of all supporting documentation provided in* ***Folder PtB3****:*  **File Name:**  **Page:**  **Note:** | | | |
| **Implant Card Article 18** | | | | |
|  | Select ‘N/A’ if section is not applicable and provide rationale | | N/A | |
| **PtB4** | | Rationale: | | |
| **Provide in Folder PtB4,** *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.*  *Specific guidance in relation to Implant Cards per Article 18 of the MDR is contained in MDCG 2019-8.* | | |
| *Details of all supporting documentation provided in* ***Folder PtB4****:*  **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.

In order to show compliance to Annex II of MDR 2017/745 the Technical documentation shall include reference to :

|  |  |  |  |
| --- | --- | --- | --- |
| **Design Stages (Annex II, 3, a)** | | | |
| **PtC1** | | **Provide in Folder PtC1,** *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).* | |
| *Details of all supporting documentation provided in* ***Folder PtC1****:*  **File Name:**  **Page:**  **Note:** | |
| **Manufacturing and Design information and specifications (Annex II, 3, b)** | | | |
| **PtC2** | | | **Provide in Folder PtC2,** *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;* |
| *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.* * *Manufacturing processes and their validation.* * *Master validation manufacturing plans/report.* * *Provide the final product/batch release specification and a sample of final product lot /batch release testing as objective evidence of completion.* |
| *Details of all supporting documentation provided in* ***Folder PtC2****:*  **File Name:**  **Page:**  **Note:** |
| **Design and Manufacturing Suppliers and Subcontractors (Annex II, 3, c)** | | | |
| **PtC3** | **Provide in Folder PtC3,** *identification of all sites, including suppliers and sub-contractors, where design and manufacturing activities are performed.* | | |
| *Details of all supporting documentation provided in* ***Folder PtC3****:*  **File Name:**  **Page:**  **Note:** | | |

### Part D - General Safety and Performance Requirements

| **PtD1** | **Applicable and non-applicable GSPRs (Annex II, 4, a)** |
| --- | --- |
| **Provide in Folder PtD1,** *solutions to the general safety and performance requirements that apply to the device and an explanation as to why others do not apply* |
| *Details of all supporting documentation provided in* ***Folder PtD1****:*  **File Name:**  **Page:**  **Note:** |
| **Methods of conformity (Annex II, 4, b)** |
| **Provide in Folder PtD1,** *the method or methods used to demonstrate conformity with each applicable general safety and performance requirement* |
| *Details of all supporting documentation provided in* ***Folder PtD1****:*  **File Name:**  **Page:**  **Note:** |
| **PtD1** | **Harmonised Standards, Common specification or other Standards/ Solutions (Annex II, 4, c)** |
| **Provide in Folder PtD1,** *the harmonised standards, CS or other solutions applied* |
| *Details of all supporting documentation provided in* ***Folder PtD1****:*  **File Name:**  **Page:**  **Note:** |
| **Related Documentation (Annex II, 4, d)** |
| **Provide in Folder PtD1,** *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.* |
| *Details of all supporting documentation provided in* ***Folder PtD1****:*  **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** |
| --- |
| List all of the main hazards associated with the device: |

| **Risk Management** | |
| --- | --- |
| Is compliance to the current revision of ISO 14971 claimed? | Yes  No |
| If no, please provide a rationale  **Rationale:** | |

|  |  |
| --- | --- |
| **Benefit-risk analysis (Annex II, 5 a)** | |
| **PtE1** | **Provide in Folder PtE1,** *Technical documentation illustrating 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.* |
| **Provide in Folder PtE1,** *technical documentation* ***referencing 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* |
| *Details of all supporting documentation provided in* ***Folder PtE1****:*  **File Name:**  **Page:**  **Note:** |

|  |  |
| --- | --- |
| **Risk Management File (Annex II, 5 b)** | |
| **PtE2** | *Manufacturers shall establish, implement, document and maintain a risk management system. Risk management shall be understood as a continuous iterative process throughout the entire lifecycle of a device, requiring regular systematic updating. In carrying out risk management manufacturers shall:* |
| **Provide in Folder PtE2,** *technical documentation reference to:*   1. *a risk management plan for each device* |
| *Details of all supporting documentation provided in* ***Folder PtE2****:*  **File Name:**  **Page:**  **Note:** |
| **Provide in Folder PtE2,** *technical documentation reference to:*   1. *identification and analysis of the known and foreseeable hazards associated with each device* |
| *Details of all supporting documentation provided in* ***Folder PtE2****:*  **File Name:**  **Page:**  **Note:** |
| **Provide in Folder PtE2,** *technical documentation reference to:*   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* |
| *Details of all supporting documentation provided in* ***Folder PtE2****:*  **File Name:**  **Page:**  **Note:** |
| **Provide in Folder PtE2,** *technical documentation reference to:*   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.* |
| *Details of all supporting documentation provided in* ***Folder PtE2****:*  **File Name:**  **Page:**  **Note:** |
| **Provide in Folder PtE2,** *technical documentation reference to:*   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* |
|  | *Details of all supporting documentation provided in* ***Folder PtE2****:*  **File Name:**  **Page:**  **Note:** |
| **Provide in Folder PtE2,** *technical documentation reference to:*   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.* |
| *Details of all supporting documentation provided in* ***Folder PtE2****:*  **File Name:**  **Page:**  **Note:** |

### Part F - Product Verification and Validation

| **Evaluation of published literature (Pre-Clinical) (Annex II, 6.1 a)** | |
| --- | --- |
| **PtF1** | **Provide in Folder PtF1,** *an 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* |
| *Details of all supporting documentation provided in* ***Folder PtF1****:*  **File Name:**  **Page:**  **Note:** |

**In this following 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.** | |
| **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:** | |

# Section 3 - Additional Requirements

In this section, the applicant must complete all sections that are relevant to the device(s)

### Product Performance and Stability

This section should include information to meet the requirements of Annex II Section 6.1. (a) & (b) and relevant GSPR’s for product performance and stability 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 performance requirements and in turn the verification of effectiveness of additional risk control mitigations.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Product Performance and Stability (Annex II, 3(b) & 6.1)** | | | | | N/A |
| **PPS1** | **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. | | | Yes  No | |
| If ‘No’ is ticked, please provide details/differences and rationale that submitted design verification testing remains valid: | | | | |
| **Device Version:**  Provide an overview of the design history of the device if the design verification data of the current design under submission is supported by data generated for previous generations/iterations of the design. | | | N/A | |
| **Device Version Change Summary Table** | | | | |
| **Change 1** | **Date of the Change:** | | | |
| **Technical Details of the Change:** | | | |
| **Rationale for the Change:** | | | |
| **Details of the executed DV testing:** *e.g., fully executed design verification – design attributes* | | | |
| **Change 2** | **Date of the Change:** | | | |
| **Technical Details of the Change:** | | | |
| **Rationale for the Change:** | | | |
| **Details of the executed DV testing:** *e.g., fully executed design verification – design attributes* | | | |
| *Additional lines can be added here for more changes* | | | | |
| **PPS2** | Provide, in ***Folder PPS2***, the Design Traceability Matrix or Design Input/ Output document and Product Specification.  The Design Traceability Matrix or Design Input/ Output document should 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 MPP1), provide details on device version/change, with specific protocol and report section which shows compliance to the GSPR’s. | | | | |
| *Details of all supporting documentation provided in* ***Folder PPS2****:*  **File Name:**  **Page:**  **Note:** | | | | |
| **PPS3** | **Design Verification Testing** | | | | |
| Provide, in ***Folder PPS3*** the relevant Design Verification Testing (protocols and reports), substantiating the Design Outputs meet the Design Inputs in the PPS3 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 do not require “For Information Only” data (FIO); all attributes tested shall have clinically relevant specifications with appropriate acceptance criteria. | | | | |
| *Details of all supporting documentation provided in* ***Folder PPS3****:*  **File Name:**  **Page:**  **Note:** | | | | |
| **PPS4** | Confirm if bench top models for ‘Simulated Use’ were used during pre-clinical testing. If yes, provide, in ***Folder PPS4***, evidence that such models have been clinically approved as anatomically correct. | | | Yes  No | |
| Provide Rationale is ‘No’ is ticked: | | | | |
| *Details of all supporting documentation provided in* ***Folder PPS4****:*  **File Name:**  **Page:**  **Note:** | | | | |
| **PPS5** | **Product Lifetime** | | | | |
| State the product lifetime (per GSPR 6) : | |  | | |
| Provide, in ***Folder PPS5***, the characteristics and the testing to demonstrate the performance of the device at the proposed product lifetime. | | | | |
| *Details of all supporting documentation provided in* ***Folder PPS5****:*  **File Name:**  **Page:**  **Note:** | | | | |
| **PPS6** | **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). Supporting information may be provided in ***Folder PPS6*** | | | Yes  No | |
| **Outline of objective/purpose :** | | | | |
| If Yes, outline has computer modelling been completed on the full device design? Supporting information may be provided in ***Folder PPS6*** | | | Yes  No | |
| **Outline:** | | | | |
| Outline the source of the computer modelling inputs e.g., scan data, anatomical physiology etc. Supporting information may be provided in ***Folder PPS6*** | | | | |
| **Outline:** | | | | |
| In relation to Computer modelling, confirm the device tested is the same generation/ version for which CE mark approval is being sought. Supporting information may be provided in ***Folder PPS6*** | | | Yes  No | |
| *Details of all supporting documentation provided in* ***Folder PPS6****:*  **File Name:**  **Page:**  **Note:** | | | | |
| **PPS7** | **Device Verification Stability/Shelf Life** | | | | |
| Confirm you have provided, in ***Folder PPS7***, the supporting document file names for the device stability protocols and reports contain reference to device testing i.e., not just packaging testing: Ensure that the device stability protocols and reports contain reference to device testing i.e., not just packaging testing:  Provide all the necessary protocols and reports for the Accelerated and Realtime 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) | | | Yes  No | |
| **Rationale if ‘No’ is ticked:** | | | | |
| *Details of all supporting documentation provided in* ***Folder PPS7****:*  **File Name:**  **Page:**  **Note:** | | | | |
| Define the shelf life/expiry date. | | | | |
| **Years:** | | | | |
| Confirm the sterilisation conditions that the product and packaging received prior to Accelerated and or Real-Time Aging testing, i.e., number of EO sterilisation cycles or the maximum acceptable dose | | | | |
| **Cycles or Max dose:** | | | | |
| Confirm that the following has been provided in ***Folder PPS7:*** design verification protocols and reports of the specific transportation and conditioning applied to the devices substantiating device stability. | | | Yes  No | |
| Were all device attributes/design outputs assessed at the proposed shelf-life?  If ‘No’ is ticked, please provide, in Folder PPS7, a supporting rationale/details including, if applicable, the justification for omitting other attributes | | | Yes  No | |
| Have Real time aging studies been completed? | | | Yes  No | |
| **Rationale if ‘No’ is ticked:** | | | | |
| If submitting Accelerated Aging data only to support shelf life, please **confirm start date and expected completion date for real time studies.** | | | | |
| **Real Time Stability dates**  **Start Date:** *DD-MM-YYYY*  **Completion Date** *DD-MMM-YYYY* | | | | |

### 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 ☐ |
| **PC1** | **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 ☐ |
| *Provide rationale here if ‘No’ is ticked:* | |
| *Details of all supporting documentation provided in* ***Folder PC1****:*  **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. Ensure this table is then provided in Folder PC1.  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 ☐ |
| *Provide rationale here if ‘No’ is ticked:* | |
| *Details of all supporting documentation provided in* ***Folder PC1****:*  **File Name:**  **Page:**  **Note:** | |
| **PC2** | Provide details of any recalls, market withdrawals, FSNs, FSCAs in any jurisdiction for the device under evaluation for the time period provided. | |
| Details:  *Provide summary details here and any supplementary documentation may be provided in* ***Folder PC2:*** | |
| *Details of all supporting documentation provided in* ***Folder PC2****:*  **File Name:**  **Page:**  **Note:** | |
| **PC3** | 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 provided in **Folder PC3** | Yes☐ No ☐ |
| *Provide rationale here if ‘No’ is ticked:* | |
| *Details of all supporting documentation provided in* ***Folder PC3****:*  **File Name:**  **Page:**  **Note:** | |
| **PC4** | Were any negative trends identified within the analysis?  If yes, provide a summary below and ensure a detailed justification/explanation of these trends is provided in **Folder PC4** | Yes☐ No ☐ |
| Summary of negative trends identified: | |
| Confirm if any of the complaints resulted in a CAPA and/or design change of the product.  If yes, please provide details | Yes☐ No ☐ |
| *Details of all supporting documentation provided in* ***Folder PC4****:*  **File Name:**  **Page:**  **Note:** | |

### Usability

|  |  |  |  |
| --- | --- | --- | --- |
| **Usability (Annex I, Chapter 1, Section 5 (a) & (b) and Article 83 (f))** | | | |
| Select ‘N/A’ if section is not applicable | | | N/A |
| **Rationale:** | | | |
| **US1** | Is compliance to ISO 62366 claimed? | Yes  No | **Year:** |
| If no, please provide rationale below. Please demonstrate through objective evidence how the chosen solution meets or exceeds the harmonized standard:  **Rationale:** | | |
| *Details of all supporting documentation provided in* ***Folder US1****:*  **File Name:**  **Page:**  **Note:** | | |
| **US2** | **Provide in Folder US2,** technical documentation demonstrating that the following has been considered:  *in eliminating or reducing risks related to use error the manufacturer shall:*   1. *Reduce 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)* | | |
| *Details of all supporting documentation provided in* ***Folder US2****:*  **File Name:**  **Page:**  **Note:** | | |
| **Provide in Folder US2,** technical documentation demonstrating that the following has been considered:  *in eliminating or reducing risks related to use error the manufacturer shall:*   1. *Give 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 include 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. | | |
| *Details of all supporting documentation provided in* ***Folder US2****:*  **File Name:**  **Page:**  **Note:** | | |

### Devices without an intended medical purpose

|  |  |  |
| --- | --- | --- |
| **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:** | | |
| **DWIP1** | **Provide in Folder DWIP1,** technical documentation demonstrating that the following has been considered:  *In eliminating or reducing risks related to use error the manufacturer shall:*  *for the devices referred to in Annex XVI, the general safety requirements set out in Sections 1 and 8 shall be understood to mean that the device, when 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.* | |
| *Details of all supporting documentation provided in* ***Folder DWIP1****:*  **File Name:**  **Page:**  **Note:** | |
| **Devices without an intended medical purpose (Article 1 (2), Annex XVI)** | | |

|  |  |  |  |
| --- | --- | --- | --- |
| **DWIP2** | Confirm the device type from the list of groups of products as per Annex XVI.    Please note the following:   * All relevant sections of the submission form must be completed (Section 1-Section 3 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:** | |
| *Details of all supporting documentation provided in* ***Folder DWIP2****:*  **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.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **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. | | | | | | | | |
| **BC1** | **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 with:**  **Note: This must be in alignment with the BER and the GSPR checklist, HS section, etc. – as required.** | | | | | | | |
| **Applicable Biocompatibility standards used** | | | | **Year: Version** | | | |
| *For example ISO 10993-5* | | | | *2009* | | | |
| *For example 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 | |  | | |
| 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.) and provide, *in Folder BC1*, a copy of each stated document** | | | | | | | |
| **Document Name** | | | | | **Section, page number** | | |
| *For example, IFU-XXX* | | | | | *Section 1, page 1* | | |
| *For example, CER-XXX* | | | | | *Section 1, page 2* | | |
| *Add more lines as required* | | | | |  | | |
| **Biocompatibility Categorisation: 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.) and provide, in *Folder BC1*, a copy of the stated document** | | | | | | | |
| **Document Name** | | | | | **Section, page number** | | |
| *For example, IFU-XXX* | | | | | *Section 1, page 1* | | |
| *For example, CER-XXX* | | | | | *Section 1, page 2* | | |
|  | *Add more lines as required* | | | | |  | | |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Carcinogenic, Mutagenic and Reprotoxic substances (CMRs)** | | | | |
| **Carcinogenic, Mutagenic and *Reprotoxic* substances (CMRs) (MDR Annex II, Section 6.2 (d))** | | | | |
| **BC2** | **Does the device contain CMRs or Endocrine disrupting substances above 0.1% w/w?**  **Ref. Annex II, 6.2 (d) and Annex I, Chapter II, Section 10.4.1**  **Note: Supporting documentation for determination of the absence or presence of CMRs or Endocrine disrupting substances must be provided in *Folder BC2*** | Yes | No | |
| **Rationale** if ‘No’ is ticked: | | | |
| **If yes has been ticked, confirm the required justification that meets the requirements of MDR Annex I 10.4.2 (a) to (d) has been provided in *Folder BC2*.**  **Ref. Annex I, Chapter II, Section 10.4.2 (a) to (d)** | Yes | | No |
| **Rationale** if ‘No’ is ticked: | | | |
| **If yes has been ticked, confirm the device labelling/ packaging include warnings of the CMR or Endocrine disrupting substance**  **Ref. Annex I, Chapter II 10.4.5 & Annex I, Chapter II, Section 23.4 (s) part 6** | Yes | | No |
| **Rationale** if ‘No’ is ticked: | | | |
| **Confirm that the DoC references CMR/ endocrine disrupting substances relevant regulations**  **Ref. Annex IV point 6** | Yes | | No |
| *Details of all supporting documentation provided in* ***Folder BC2****:*  **File Name:**  **Page:**  **Note:** | | | |

| **Tests Considered/Performed for this Submission** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Tests to be considered** | **ISO 10993 series**  **and Year** | **Test Article information**  (including corresponding model number from Section G1 of this Submission Form) | **Location in provided BEP/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:** | **BEP/BER:** *ref ID*  **Page:** *exact page* |  |  |  |
| **Cytotoxicity** | -5: | **Test Article Model Number:** | **BEP/BER:** *ref ID*  **Page:** *exact page* |  |  |  |
| **Sensitisation** | -10: | **Test Article Model Number:** | **BEP/BER:** *ref ID*  **Page:** *exact page* |  |  |  |
| **Irritation (incl. intracutaneous reactivity)** | -23: | **Test Article Model Number:** | **BEP/BER:** *ref ID*  **Page:** *exact page* |  |  |  |
| **Material Mediated Pyrogenicity** | -11: | **Test Article Model Number:** | **BEP/BER:** *ref ID*  **Page:** *exact page* |  |  |  |
| **Acute Systemic toxicity** | -11: | **Test Article Model Number:** | **BEP/BER:** *ref ID*  **Page:** *exact page* |  |  |  |
| **Sub-Acute toxicity** | -11: | **Test Article Model Number:** | **BEP/BER:** *ref ID*  **Page:** *exact page* |  |  |  |
| **Sub-Chronic toxicity** | -11: | **Test Article Model Number:** | **BEP/BER:** *ref ID*  **Page:** *exact page* |  |  |  |
| **Chronic toxicity** | -11: | **Test Article Model Number:** | **BEP/BER:** *ref ID*  **Page:** *exact page* |  |  |  |
| **Implantation effects** | -6: | **Test Article Model Number:** | **BEP/BER:** *ref ID*  **Page:** *exact page* |  |  |  |
| **Haemocompatibility** | -4: | **Test Article Model Number:** | **BEP/BER:** *ref ID*  **Page:** *exact page* |  |  |  |
| **Genotoxicity**  **mutagenicity** | -3: | **Test Article Model Number:** | **BEP/BER:** *ref ID*  **Page:** *exact page* |  |  |  |
| **Carcinogenicity** | -3: | **Test Article Model Number:** | **BEP/BER:** *ref ID*  **Page:** *exact page* |  |  |  |
| **Reproductive and developmental toxicity** | -3: | **Test Article Model Number:** | **BEP/BER:** *ref ID*  **Page:** *exact page* |  |  |  |
| **Biodegradation** | -9: | **Test Article Model Number:** | **BEP/BER:** *ref ID*  **Page:** *exact page* |  |  |  |
| **Toxicokinetic studies** | -16: | **Test Article Model Number:** | **BEP/BER:** *ref ID*  **Page:** *exact page* |  |  |  |
| **Immunotoxicology** | -20: | **Test Article Model Number:** | **BEP/BER:** *ref ID*  **Page:** *exact page* |  |  |  |
| **Other Tests** | **Series:**  **Year:** | **Test Article Model Number:** | **BEP/BER:** *ref ID*  **Page:** *exact page* |  |  |  |

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| **BC3** | | **Confirm the Biological Evaluation Report (BER) and also the Biological Evaluation Plan has been provided for review in *Folder BC3*.**  **Note:** This can be contained within one single document. | | | | Yes  No | | | | | |
| If ‘No’ is ticked, provide a rationale: | | | | | | | | | |
| *Details of all supporting documentation provided in* ***Folder BC3****:*  **File Name:**  **Page:**  **Note:** | | | | | | | | | |
| **Confirm the following key criteria have been documented in the BER, stating the section and page where this information is contained:** | | | | | | | | | | | |
| **BC3** | | * + Diagrams, pictures, model numbers (consistent with those stated in Part A, Annex II, 1.1 (i) section of this form) | | | | | **BEP/BER:** *ref ID*  **Page:** *exact page* | | | | |
| * + Characterisation of the materials of construction (**direct and indirectly patient and user contacting**) including suitable alternative materials, CMR substances if present | | | | | **BEP/BER:** *ref ID*  **Page:** *exact page* | | | | |
| * + Physical characteristics | | | | | **BEP/BER:** *ref ID*  **Page:** *exact page* | | | | |
| * + Any existing toxicology and other biological safety data on product and component materials, breakdown products and metabolites | | | | | **BEP/BER:** *ref ID*  **Page:** *exact page* | | | | |
| * + Intended use | | | | | **BEP/BER:** *ref ID*  **Page:** *exact page* | | | | |
| * + List of any changes to the device over its marketed history and/ or since biological evaluation testing was initially undertaken | | | | | **BEP/BER:** *ref ID*  **Page:** *exact page* | | | | |
| * + Manufacturing information (locations, process steps, processing aids/ contaminants/ residues, additives) | | | | | **BEP/BER:** *ref ID*  **Page:** *exact page* | | | | |
| * + Packaging (pictures/ diagrams, configuration, direct/ indirect contacting materials) | | | | | **BEP/BER:** *ref ID*  **Page:** *exact page* | | | | |
| * + Leachable substances, degradation products or other components and their interactions in the final product | | | | | **BEP/BER:** *ref ID*  **Page:** *exact page* | | | | |
| * + The performance and physical characteristics of the final product (porosity, particle size, shape, surface morphology – as appropriate) | | | | | **BEP/BER:** *ref ID*  **Page:** *exact page* | | | | |
| * + 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) | | | | | **BEP/BER:** *ref ID*  **Page:** *exact page* | | | | |
| * + Evaluation over the whole lifetime of the device (storage conditions, shelf-life, handling, duration of use, reprocessing) | | | | | **BEP/BER:** *ref ID*  **Page:** *exact page* | | | | |
| **BC4** | **Confirm a gap analysis has been conducted and provided in *Folder BC4* for any non-current standards used to perform any biological/physicochemical testing or analysis.** | | | | | | | Yes  No | | | |
| If ‘No’ is ticked, provide a rationale: | | | | | | | | | | |
| *Details of all supporting documentation provided in* ***Folder BC4****:*  **File Name:**  **Page:**  **Note:** | | | | | | | | | | |
| **BC5** | **Confirm the Test Protocols and Reports, referenced in the Biological Evaluation Plan/Report, have been provided for review in *Folder BC5***  **Note:** *Ensure Test Protocol and Report numbers have been documented in the above table ‘Tests Considered/Performed for this Submission’ section and included in the submission.* | | | | | | | Yes  No | | | |
| If ‘No’ is ticked, provide a rationale: | | | | | | | | | | |
| *Details of all supporting documentation provided in* ***Folder BC5****:*  **File Name:**  **Page:**  **Note:** | | | | | | | | | | |
| **BC6** | **Confirm that evidence has been provided in *Folder BC6* supporting competence of the person(s) concluding the biocompatibility results and assessment** | | | | | | | | Yes  No | | |
| If ‘No’ is ticked, provide a rationale: | | | | | | | | | | |
| *Details of all supporting documentation provided in* ***Folder BC6****:*  **File Name:**  **Page:**  **Note:** | | | | | | | | | | |
| **BC7** | **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’ is ticked, provide a rationale: | | | | | | | | | | |
| **A comprehensive description of traceability between the model numbers applied for in this submission (*Section G1 of this Submission Form*) and the test articles used in any biological testing presented must be provided in the BEP/BER.**  **State the exact page where this is documented.** | | | | | | | | | | |
| **BEP/BER:** *ref ID*  **Page:** *exact page* | | | | | | | | | | |
| **If applicable where the test article / model is not identical to a model stated in *Section G1 of this Submission Form*, a rationale must be provided.** | | | | | | | | | N/A | |
| Rationale: | | | | | | | | | | |
| **Where only one model variant (e.g., one size) was tested, justification why it is representative of all the submission models listed in *Section G1 of this Submission Form*** | | | | | | | | | N/A | |
|  | Justification: | | | | | | | | | | |
|  | **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 in *Folder BC7.*** | | | | | | | | Yes No | | |
| If ‘No’ is ticked, provide a rationale: | | | | | | | | | | |
| *Details of all supporting documentation provided in* ***Folder BC7****:*  **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’ is ticked, provide a rationale: | | | | | | | | | | |
| **BC8** | **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 in *Folder BC8*** | | | | | | | | Yes No | | |
| If ‘No’ is ticked, provide a rationale: | | | | | | | | | | |
| **Test Article ID (aligned with ‘Test Article information’ provided in ‘Tests Considered/ Performed for this Submission’ table)** | | **Sterilisation type** | **Sterilisation dose** | **Number of cycles** | | | | | | **Supporting Documentation file Name**  ***(provided in Folder BC8)*** |
| *TESTARTICLE-XXX-001* | | *Gamma Irradiation* | *25kGy* | *2* | | | | | | *File Name:*  *Page:* |
|  | |  |  |  | | | | | |  |
|  | |  |  |  | | | | | |  |
| Please provide rationale for the chosen sterilisation dose for each test article listed | | | | | | | | | | |
| **Rationale:** | | | | | | | | | | |
| *Details of all supporting documentation provided in* ***Folder BC8****:*  **File Name:**  **Page:**  **Note:** | | | | | | | | | | |

# Appendix 2a - Sterilisation

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| --- | --- | --- | --- | --- | --- | --- |
| **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: | | | | | | |
| **S1** | Please be aware that the Sterilisation Review will incorporate analysis of data submitted in other sections, i.e., IFU and labels, Performance and Risk documents etc. and may generate subsequent queries. | | | | | |
| **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, in Folder S2*,* a history of the sterilisation of the device(s) in scope of submission, 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 in **Folder S2***.* | | | | | |
| *Details of all supporting documentation provided in* ***Folder S2****:*  **File Name:**  **Page:**  **Note:** | | | | | |
| Provide the Proof of competence of Sterilisation expert (e.g., author/approver) for review in **Folder S2**. | | | | | |
| *Details of all supporting documentation provided in* ***Folder S2****:*  **File Name:**  **Page:**  **Note:** | | | | | |
| **Ethylene Oxide** | | | | | | |
| **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 submission  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 submission)* | | **Protocol#** | | |  |
| **Year:** | | |  |
| **Report#** | | |  |
| **Year:** | | |  |
| Please provide evidence that the IQ and OQ has been completed and approved in **Folder S3**. | | | | | 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 |
| *Details of all supporting documentation provided in* ***Folder S3****:*  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 submission)* | | **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.  **Description:** | | | | | |
| If the PCD’s are different to those used in the initial validation, please provide a rationale.  **Rationale:** | | | | | |
| Provide supporting documentation in **Folder S3** 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 |
| *Details of all supporting documentation provided in* ***Folder S3****:*  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 Submission 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 in neonates and infants? | | | | | Yes No |
| If Yes, is compliance with the current version of EN ISO 10993-7/Amendment 1 claimed. | | | | | Yes No |
| If No, is device contraindicated for use in neonates and infants | | | | | Yes No |
| Provide the relevant EO residual protocols and reports.  Confirm that the supporting documents have been provided for review | | | | | Yes No |
| *Details of all supporting documentation provided in* ***Folder S3****:*  **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 in **Folder S3** 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 |
| *Details of all supporting documentation provided in* ***Folder S3****:*  **File Name:**  **Page:**  **Note:** | | | | | |
| Please provide product Bioburden data for the last 12 months in **Folder S3**. | | | | | |
| Confirm that the supporting documents have been provided for review in **Folder S3**. | | | | | Yes No |
| *Details of all supporting documentation provided in* ***Folder S3****:*  **File Name:**  **Page:**  **Note:** | | | | | |
| Please provide an approved copy in **Folder S3**of the Process Specification used for routine sterilisation of the product.  For each Process specification, show how compliance is shown to EN ISO 11135, Section 9.5.6 (‘Review and Approval of Validation’ section)  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 9.5.6* | *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 |
| *Details of all supporting documentation provided in* ***Folder S3:***  **File Name:**  **Page:**  **Note:** | | | | | |
| **Irradiation** | | | | | | |
| **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.  Rationale: | | | | | |
| 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 in **Folder S4.**  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 |
| *Details of all supporting documentation provided in* ***Folder S4:***  **File Name:**  **Page:**  **Note:** | | | | | |
| Please provide evidence that the IQ and OQ has been completed and approved. | | | | | |
|  | *Details of all supporting documentation provided in* ***Folder S4:***  **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 in **Folder S4.** | | | | | Yes No |
| *Details of all supporting documentation provided in* ***Folder S4:***  **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 in **Folder S4**. | | | | | Yes No |
| *Details of all supporting documentation provided in* ***Folder S4****:*  **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 in **Folder S4**. | | | | | Yes No |
| *Details of all supporting documentation provided in* ***Folder S4:***  **File Name:**  **Page:**  **Note:** | | | | | |
| Please provide product Bioburden data for the last 12 months in **Folder S4**. | | | | | |
|  | Confirm that the supporting documents have been provided for review in **Folder S4**. | | | | | Yes No |
| *Details of all supporting documentation provided in* ***Folder S4:***  **File Name:**  **Page:**  **Note:** | | | | | |
| Please provide an approved copy of the Process Specification used for routine sterilisation of the product in **Folder S4.**  For each Process specification, show how compliance is shown with each clause of EN ISO 11137-1 section 9.4.3 (Gamma) or 9.4.4 (E beam/X Ray), (‘Review and Approval of Validation’ section)  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 in **Folder S4.** | | | | | Yes No |
| Moist Heat | | | | | | |
| **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 submission)* | **Protocol#** | | |  | |
| **Year:** | | |  | |
| **Report#** | | |  | |
| **Year:** | | |  | |
| Please provide evidence that the IQ and OQ has been completed and approved. | | | | | |
| *Details of all supporting documentation provided in* ***Folder S5:***  **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 in **Folder S5.** | | | | | Yes No |
| *Details of all supporting documentation provided in* ***Folder S5:***  **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 submission)* | | **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 in **Folder S5.** | | | | | Yes No |
| *Details of all supporting documentation provided* ***in Folder S5:***  **File Name:**  **Page:**  **Note:** | | | | | |
| Please provide product Bioburden data for the last 12 months in **Folder S5**. | | | | | |
| Confirm that the supporting documents have been provided for review in **Folder S5**. | | | | | Yes No |
| *Details of all supporting documentation provided in* ***Folder S5:***  **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 relevant clause of the ‘Review and Approval of Validation’ section 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 in **Folder S5**. | | | | | Yes No |
| *Details of all supporting documentation provided in* ***Folder S5:***  **File Name:**  **Page:**  **Note:** | | | | | |
| **Aseptic processing** | | | | | | |
| **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 in **Folder S6.** | | | | | Yes No |
| *Details of all supporting documentation provided in* ***Folder S6:***  **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 in **Folder S6.** | | | | | Yes No |
| *Details of all supporting documentation provided in* ***Folder S6:***  **File Name:**  **Page:**  **Note:** | | | | | |
| Confirm that the Protocol/Report for the full sterilisation validation of all components (bottles, caps, etc.) has been provided for review.  and that the validations comply with the applicable sterilization standard; i.e. ISO 11135, ISO 11137-1 ISO 11137-2, ISO 22587, etc | | | | | Yes No |
| Complete table providing required information for the sterilisation of all components (bottles, caps, etc.)   |  |  |  |  |  | | --- | --- | --- | --- | --- | | **Model numbers/**  **sizes** | **Components** | **Sterilisation method** | **Sterilisation completed by** | **Evidence of successful sterilisation** | |  | *e.g. lid/cap* |  |  | *e.g. sterilisation validation report* | |  |  |  |  |  |   *Add lines as required.* | | | | | |
| *Details of all supporting documentation provided in* ***Folder S6****:*  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.* | | | | | |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Dry Heat** | | | | | | | | |
| **S7** | **Dry Heat: (If Dry Heat is not used select ‘N/A’ and do not complete this section).** | | | | | | | N/A |
| Is compliance with the current version of EN ISO 20857 claimed? | | | | | Yes No | | |
| If No, please provide rationale and any supporting documentation to support the applicable GSPR’s.  Rationale: | | | | | | | |
| Is the dry heat process used outside the range of conditions that are widely recognized? | | | | | Yes No | | |
| If Yes, please provide rationale and any supporting documentation to demonstrate the microbicidal effectiveness.  Rationale:  *Details of all supporting documentation provided in* ***Folder S7****:*  **File Name:**  **Page:**  **Note:** | | | | | | | |
| Provide the Initial validation information *(For all devices under the scope of this submission)* | | **Protocol#** | |  | | | |
| **Year:** | |  | | | |
| **Report#** | |  | | | |
| **Year:** | |  | | | |
| **Rationale:** | | | | | | | |
| Please provide evidence that the IQ and OQ has been completed and approved. | | | | | | | |
| *Details of all supporting documentation provided in* ***Folder S7****:*  **File Name:**  **Page:**  **Note:** | | | | | | | |
| Has a full PQ validation been performed? | | | | | Yes No | | |
| Does the PQ cover depyrogenation in addition to sterilization? | | | | | Yes No | | |
| *Details of all supporting documentation provided in* ***Folder S7****:*  **File Name:**  **Page:**  **Note:** | | | | | | | |
| 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 | | |
| *Details of all supporting documentation provided in* ***Folder S7****:*  **File Name:**  **Page:**  **Note:** | | | | | | | |
| If the Initial Validation is greater than the company defined interval, please also provide the latest revalidation/ requalification *(For all device types under the scope of this submission)* | | **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 in **Folder S7**. | | | | | Yes No | | |
| *Details of all supporting documentation provided in* ***Folder S7****:*  **File Name:**  **Page:**  **Note:** | | | | | | | |
| Please provide validation data for the product Bioburden method and routine monitoring data for the last 12 months. | | | | | | | |
| Confirm that the supporting documents have been provided for review. | | | | | Yes No | | |
| *Details of all supporting documentation provided in* ***Folder S7****:*  **File Name:**  **Page:**  **Note:** | | | | | | | |
| Do the biological indicator certificates used comply to EN ISO 11138-4? | | | | | | Yes No | |
| Confirm that the supporting documents have been provided for review. | | | | | | Yes No | |
| *Details of all supporting documentation provided in* ***Folder S7****:*  **File Name:**  **Page:**  **Note:** | | | | | | | |
| If product sterility testing is or was performed, does it comply with EN ISO 11737-2 | | | | | | Yes No | |
| Confirm that the supporting documents have been provided for review. | | | | | | Yes No | |
| *Details of all supporting documentation provided in* ***Folder S7****:*  **File Name:**  **Page:**  **Note:** | | | | | | | |
| Please provide an approved copy of the Process Specification used for routine sterilisation of the product in **Folder S7**. | | | | | | | |
| 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 EN ISO 20857 Section 9.6.2 (‘Review and Approval of Validation’ section)  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., EN ISO 20857 9.6.2)* | *e.g., PP 123* | *e.g.,*  *Page 23* | *e.g., 6.2* | |  |  |  |  |  |  | |  |  |  |  |  |  |   *Add lines as required.* | | | | | | | |
| **Liquid Chemical** | | | | | | | | |
| **S8** | **Liquid Chemical: (If Liquid Chemical is not used select ‘N/A’ and do not complete this section).** | | | | | N/A | | |
| Is compliance with the current version of EN ISO 14160 claimed? | | | | | Yes No | | |
| If No, please provide rationale and any supporting documentation to support the applicable GSPR’s.  **Rationale:** | | | | | | | |
| Is a full description provided for the Sterilizing agent characterization? | | | | | Yes No | | |
| If Yes, please provide   * The name and formulation of the liquid chemical sterilizing agent, including concentration(s) of the active agent(s) and pH. * Statement that the sterilizing agent is not reused. * The liquid chemical sterilizing agent storage conditions. * The means of ensuring that the liquid chemical sterilizing agent is free from viable microorganisms before use. * The method for neutralization of the liquid chemical sterilizing agent prior to culturing for recovery of survivors has been validated. | | | | | | | |
| *Details of all supporting documentation provided in* ***Folder S8****:*  **File Name:**  **Page:**  **Note:** | | | | | | | |
|  | *Have microbial studies been done to demonstrate the lethal action of the liquid chemical sterilizing agent against a range of representative microorganisms* | | | | | Yes No | | |
| If Yes please provide:   * Data to demonstrate the lethal action of the liquid chemical sterilizing agent against a range of representative microorganisms. * Data to identify the process variables that affect the lethal action of the liquid chemical sterilizing agent, e.g. time, temperature, liquid chemical sterilizing agent concentration and pH. * Data to assess the microbicidal effectiveness of the liquid chemical sterilizing agent at the tolerance limits for the combination of process variables that results in the lowest microbicidal activity. * Confirmation the microbicidal effectiveness studies included screening test to identify microorganisms with a high resistance to the process. This included organisms from the product bioburden and the environment, as well as a reference organism(s) known to be innately resistant to the liquid chemical sterilizing agent. * Documentation to address the inactivation kinetics and how the sterilization process applicable to the defined product(s). | | | | | | | |
| *Details of all supporting documentation provided in* ***Folder S8****:*  **File Name:**  **Page:**  **Note:** | | | | | | | |
| Provide the Initial validation information *(For all devices under the scope of this submission)* | **Protocol#** | | | |  | | |
| **Year:** | | | |  | | |
| **Report#** | | | |  | | |
| **Year:** | | | |  | | |
| **Rationale:** | | | | | | | |
| Provide evidence that the IQ and OQ has been completed and approved. | | | | | | | |
| *Details of all supporting documentation provided in* ***Folder S8****:*  **File Name:**  **Page:**  **Note:** | | | | | | | |
| Has a full PQ validation been performed? | | | | | Yes No | | |
| If Parametric Release is used are the requirements of EN ISO 14160 section 1.4 met? | | | | | Yes No | | |
| Is the concentration and pH of the chemical sterililant recorded before and after each cycle? | | | | | Yes No | | |
| Are any aseptic manipulations (e.g. aseptic transfer of the medical device, aseptic transfer of solutions to/from the medical device final container), conducted following completion of the sterilization process and that the procedures after exposure to the liquid chemical sterilizing agent validated in accordance with the applicable part(s) of ISO 13408? | | | | | Yes No | | |
|  | *Details of all supporting documentation provided in* ***Folder S8****:*  **File Name:**  **Page:**  **Note:** | | | | | | | |
| 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 | | |
| *Details of all supporting documentation provided in* ***Folder S8****:*  **File Name:**  **Page:**  **Note:** | | | | | | | |
| If the Initial Validation is greater than the company defined interval, please also provide the latest revalidation/ requalification *(For all device types under the scope of this submission)* | | | **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 in **Folder S8**. | | | | | Yes No | | |
| *Details of all supporting documentation provided in* ***Folder S8****:*  **File Name:**  **Page:**  **Note:** | | | | | | | |
| Please provide validation data for the product Bioburden method and routine monitoring data for the last 12 months. | | | | | | | |
| Confirm that the supporting documents have been provided for review. | | | | | Yes No | | |
| *Details of all supporting documentation provided in* ***Folder S8****:*  **File Name:**  **Page:**  **Note:** | | | | | | | |
| Are biological indicators used and do they comply to the applicable EN ISO 11138 series standard? | | | | | Yes No | | |
| Confirm that the supporting documents have been provided for review. | | | | | Yes No | | |
| *Details of all supporting documentation provided in* ***Folder S8****:*  **File Name:**  **Page:**  **Note:** | | | | | | | |
|  | If product sterility testing is or was performed, does it comply with EN ISO 11737-2 | | | | | Yes No | | |
| Confirm that the supporting documents have been provided for review. | | | | | Yes No | | |
| *Details of all supporting documentation provided in* ***Folder S8****:*  **File Name:**  **Page:**  **Note:** | | | | | | | |
| Please provide an approved copy of the Process Specification used for routine sterilisation of the product in **Folder S8**. | | | | | | | |
| 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 EN ISO 14160 Section 9.5.3 (‘Review and Approval of Validation’ section).  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., EN ISO 14160 9.5.3* | *e.g., PP 123* | *e.g.,*  *Page 23* | *e.g., 6.2* | |  |  |  |  |  |  | |  |  |  |  |  |  |   *Add lines as required.* | | | | | | | |

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| --- | --- | --- | --- | --- | --- |
| **Other Sterilisation Methods** | | | | | |
| **S9** | **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 in Folder **S9**: | | | Yes No | |
| *Details of all supporting documentation provided in* ***Folder S9****:*  **File Name:**  **Page:**  **Note:** | | | | |
| Provide the Initial validation information *(For all devices under the scope of this submission)* | **Protocol#** |  | | |
| **Year:** |  | | |
| **Report#** |  | | |
| **Year:** |  | | |
| **Rationale:** | | | | |
| Please provide evidence that the IQ and OQ has been completed and approved. | | | | |
| *Details of all supporting documentation provided in* ***Folder S9****:*  **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 | |
| *Details of all supporting documentation provided in* ***Folder S9****:*  **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 submission)* | **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 in **Folder S9**. | | | Yes No | |
| *Details of all supporting documentation provided in* ***Folder S9****:*  **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 | |
| *Details of all supporting documentation provided in* ***Folder S9****:*  **File Name:**  **Page:**  **Note:** | | | | |
| Please provide an approved copy of the Process Specification used for routine sterilisation of the product in **Folder S9**. | | | | |
| 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 relevant 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 2b - 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:** | | | | | | | |
| **S10** | 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: 2. Definition: 3. Storage Conditions:   List the supporting document titles and References: | | | | | | |
| Confirm that the documents have been provided for review: | | | | | Yes No | |
| *Details of all supporting documentation provided in* ***Folder S10****:*  **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 | | |
| **Stability testing (Aging)** | | | | | | | |
| **S10** | 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 in **Folder S10.** | | | | | Yes  No | |
| *Details of all supporting documentation provided in* ***Folder S10****:*  **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 in **Folder S10**. | | | | | Yes  No | |
| *Details of all supporting documentation provided in* ***Folder S10****:*  **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. | | | | | | |
| **Packaging system performance testing** | | | | | | | |
| **S11** | 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 in **Folder S11.** | | | | | Yes  No | |
| *Details of all supporting documentation provided in* ***Folder S11****:*  **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

|  |  |  |
| --- | --- | --- |
| **Description of the medical electrical equipment / system including description of accessories** | | |
| **ELEC1** | 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***Folder ELEC1*** 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: | |
| *Details of all supporting documentation provided in* ***Folder ELEC1****:*  **File Name:**  **Page:**  **Note:** | |
| **Essential Performance of the medical electrical equipment** | | |
| **ELEC2** | Provide evidence in***Folder ELEC2*** 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): | |
| *Details of all supporting documentation provided in* ***Folder ELEC2****:*  **File Name:**  **Page:**  **Note:** | |
| **General Standard (60601-1): General requirements for basic safety and essential performance of medical electrical equipment and systems** | | |
| **ELEC3** | Have the applicable requirements of EN 60601-1 latest version, including the mandatory risk assessment to EN 14971 been applied? | Yes  No |
| Provide in***Folder ELEC3,*** evidence that supports this, i.e., EN 60601-1 test plans and reports: | |
| *Details of all supporting documentation provided in* ***Folder ELEC3****:*  **File Name:**  **Page:**  **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.** | | |
| **ELEC4** | 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 in ***Folder ELEC4,*** evidence that supports this, i.e., EN 60601-1-2 test plans and reports, EMC declaration etc: | |
| *Details of all supporting documentation provided in* ***Folder ELEC4****:*  **File Name:**  **Page:**  **Note:** | |
| **Other Collateral Standards** | | |
| **ELEC5** | 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 provide *in* ***Folder ELEC5*** evidence that demonstrates conformity to the standards cited: | |
| **List:** | |
| *Details of all supporting documentation provided in* ***Folder ELEC5****:*  **File Name:**  **Page:**  **Note:** | |
| **Particular Standards** | | |
| **ELEC6** | 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 provide in ***Folder ELEC6*** evidence that demonstrates conformity to the standards cited: | |
| **List:** | |
| *Details of all supporting documentation provided in* ***Folder ELEC6****:*  **File Name:**  **Page:**  **Note:** | |
| **Medical electrical equipment incorporating software / firmware** | | |
| **ELEC7** | Does either the medical electrical equipment or any of its accessories incorporate software or firmware? | Yes  No |
| Provide evidence in ***Folder ELEC7*** 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)**. | |
| *Details of all supporting documentation provided in* ***Folder ELEC7****:*  **File Name:**  **Page:**  **Note:** | |

# Appendix 4 – Software

| **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 |
| --- | --- | --- |
| **SOFT1** | If ‘N/A’ has been selected, please provide a rationale:  **Rationale:** | |
| Provide in ***Folder SOFT1*** technical documentation referencing to all relevant pre-clinical and clinical data. | |
| Provide in ***Folder SOFT1*** supporting evidence to meet the requirement that the manufacturer shall demonstrate the results of tests, such as engineering, laboratory, simulated use and animal tests. | |
| *Details of all supporting documentation provided in* ***Folder SOFT1****:*  **File Name:**  **Page:**  **Note:** | |

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| **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 |
| **SOFT2** | If ‘N/A’ has been selected, please provide a rationale:  **Rationale:** | |
| Provide in ***Folder SOFT2,*** supporting evidence that the requirement is met that 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 provided in ***Folder SOFT2,*** 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 submission**: Provide the version(s) of the device software here: | |
| *Details of all supporting documentation provided in* ***Folder SOFT2****:*  **File Name:**  **Page:**  **Note:** | |

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| **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 |
| **SOFT3** | 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 documentation is required to be provided in ***Folder SOFT3*** and 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 | |
| *Details of all supporting documentation provided in* ***Folder SOFT3****:*  **File Name:**  **Page:**  **Note:** | |

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| --- | --- | --- |
| **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 |
| **SOFT4** | 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. | |
| *Details of all supporting documentation provided in* ***Folder SOFT4****:*  **File Name:**  **Page:**  **Note:** | |

# Appendix 5 – Clinical evaluation

**Important notes to the applicant:**

* Please note that here are **2 separate clinical review submission forms;**
* **Form A**: Low-Risk Non-Implantable Devices (Class IIa & IIb devices)
* **Form B:** High-Risk & All Implantable Devices (Class III, & ALL Implantable Devices)
* Ensure that you complete the correct clinical form for your device classification
* Upload any supporting documentation in the respective subfolder within appendix 5 (for example – CER is uploaded to Appendix 5, Subfolder Clinical Evaluation).
* Where multiple Clinical Investigations are provided to support the device, please upload supporting documentation for each investigation in an organised way, with sub-folders dedicated to each investigation, as seen in the Clinical Investigations folder.
* All uploaded documents must be provided in a pdf searchable format.
* 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 minor variances in the queries as every file is reviewed independent of the other.

**Other Considerations:**

* Where transferring from another NB, **10 years of PMS & Literature search data is required** for the initial conformity assessment.
* Devices that are required to undergo the Clinical Evaluation Consultation Procedure per article 54, will take a longer overall review time, allowing time for expert panel review.
* Devices that may require external clinical expert review will require additional review time.

## Clinical Performance for Low-Risk Non-Implantable Devices

(Class IIa & IIb devices)

**Note:** Confirm, per above, that this form is appropriate 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 1 – Clinical Review

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| **Section 1** | |
| **1** | **Note:** The Clinical Review will incorporate scrutiny of clinically relevant aspects from other documents in the technical file submission and may generate relevant queries. |

### Section 2 – Clinical Evaluation Team

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| --- | --- | --- | --- | --- |
| **Section 2 – Clinical Evaluation Team** | | | | |
| **2** | 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.*** | | | |
| **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 **Clinical Evaluation Team 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 **Clinical Evaluation Team 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 **Clinical Evaluation Team Folder**.**.** | | | |

### Section 3 – Clinical Evaluation Plan

|  |  |  |  |  |
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| **Section 3 – Clinical Evaluation Plan** | | | | |
| **3** | 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 **Clinical Evaluation 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 **Clinical Investigations 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:** **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 | | |
| **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 Clinical Characteristics Section of the Equivalence Declaration form (MDR-2003) has been completed and provided in the **Clinical Evaluation Folder.** | | | Yes  No |
| **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 **Post Market** 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 **Post Market** folder**.** | | | Yes  No |
| Tick the appropriate box in each case.  **Note 1**: Specify your chosen clinical evaluation methodology for this MDR submission 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)** | | |
| **MDCG 2020-6**  **Sufficient Clinical Evidence** per MDCG 2020-6, Appendix III | For manufacturers of legacy devices choosing this route of assessment**,** reference is made to *Appendix III of MDCG 2020-6: Suggested hierarchy of clinical evidence for confirmation of conformity with relevant GSPRs under MDR*.  **NOTE:** Where 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. * Rationale for why that level of evidence (quality & quantity) can be considered sufficient for the device | | |
| **MDCG 2020-6 Section 1.2**  **Legacy devices claiming WET** | **Note:** Applicable devices must fulfil the following criteria below;   * 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.   Detailed rationale as to how the device fulfils these criteria, and evidence for same in supporting documents will be sought during the review.  The level of evidence (per MDCG 2020-6, Appendix III) provided must be specified and justified as to how it can be considered sufficient. *Reliance solely on complaints and vigilance data is not considered sufficient.* | | |
| **Article 61(9)** 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:** 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 *(see MDCG 2023-6)* | | |
| **Article 61(10)** 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 **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 **Clinical Evaluation 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: | | | |

### Section 4 – Clinical Evaluation Report

|  |  |  |  |
| --- | --- | --- | --- |
| **Section 4 – Clinical Evaluation Report** | | | |
| **4** | Ensure all PMS data submitted in the CER is not older than 12 months from the date of file submission.  **Note: *PMS data must remain current per EU MDR 2017/745 regulations throughout the review process. This may require submission of new PSUR data, and its integration to the CER where applicable (Art 86 requirements)*** | | |
| Confirm a copy of the **Clinical Evaluation Report** compliant to the MDR 2017/745 Chapter VI and ANNEX XIV has been uploaded to the **Clinical Evaluation 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 **Clinical Evaluation Folder**. | | |

### Section 5 – Literature Search

|  |  |  |
| --- | --- | --- |
| **Section 5 – Literature Search** | | |
| **5** | Confirm a copy of the literature search protocol has been uploaded to the **Literature Search Folder.**  **Note: *Data should be current within 12 months at the time of submission*.** | Yes  No |
| Confirm a copy of the literature search report has been uploaded to the **Literature Search 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 |
| Paediatric 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 6 – Clinical Investigations

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| --- | --- | --- | --- |
| **Section 6 – Clinical Investigations** | | | |
| **6** | List which premarket investigations have been performed for the device. Specify which are exploratory or confirmatory investigations and provide supporting documentation in the **Clinical Investigations Folder.**  **Please provide a folder for each investigation, with supporting documents enclosed in each folder**  **NOTE:** Where Equivalence is being claimed, please upload clinical investigations & supporting documents for the equivalent device to the **Clinical Investigations Folder**;  *These will be assessed to MDR & ISO 14155 standards* | | |
|  | | |
| List which post-market investigations have been performed for the device and provide supporting documentation in the **Clinical Investigations 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 **Clinical Investigations 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 **Clinical Investigations 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 **Clinical Investigations Folder.** | | |
| Confirm a Clinical Investigation Report (CIR) has been uploaded to the **Clinical Investigations 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 **Clinical Investigations Folder.** | | |
| Confirm letter of ethics approval has been uploaded to the **Clinical Investigations Folder.** | | Yes  No |
| Confirm evidence of no objection from competent authority has been uploaded to the **Clinical Investigations Folder.** | | Yes  No |
| Confirm the investigator’s brochure(s) has been uploaded to the **Clinical Investigations Folder.** | | Yes  No |
| Confirm a sample of the informed consent for the investigation has been uploaded to the **Clinical Investigations Folder.** | | Yes  No |

### Section 7 - Labelling & Information provided by Manufacturer

|  |  |  |
| --- | --- | --- |
| **Section 7 – Labelling & Information provide by the Manufacturer** | | |
| **7** | **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 **Labelling 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 **Labelling Folder** | |

### Section 8 – Clinical Aspects of Risk

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| **Section 8 – Clinical Aspects of Risk** | | |
| **8** | **Risk:** confirm that there is traceability of information between the clinical evaluation and the Risk documentation.  Supporting documents can be uploaded to the **Clinical Risk Folder** | Yes  No |

### Section 9 – Post Market

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| **Section 9 – Post Market** |

#### PMS & PMCF Plans

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| --- | --- | --- | --- |
| **9** | **PMS and PMCF Plan:**  PMCF plan must align with template provided in MDCG 2020-7 | | |
| Confirm a PMS Plan has been uploaded to the **Post Market Folder** | | Yes  No |
| Confirm an MDCG 2020-7 compliant PMCF Plan has been uploaded to the **Post Market Folder.** | | Yes  No |
| Confirm an MDCG 2020-8 compliant PMCF Evaluation Report (if applicable) has been uploaded to the **Post Market 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

|  |  |  |  |
| --- | --- | --- | --- |
| **9** | **PMCF Evaluation Report** | | |
| **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: | |

#### PSUR

|  |  |  |
| --- | --- | --- |
| **10** | **Periodic Safety Update Report (PSUR)**  **New devices: 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)*, **a PSUR is not expected for the conformity assessment**  **For legacy devices, a current PSUR is required** | |
| Confirm a PSUR has been uploaded to the **Post Market** Folder. | Yes  No |
| Confirm when the PSUR was last updated [DD-Mmm-YYYY] | [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 High-Risk & ALL Implantable Devices

(Class III, & ALL Implantable Devices)

**Note:** Confirm, per above, that this form is appropriate for the device class? Yes

### Section 1 – Clinical Review

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| **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 1** | |
| **1** | **Note:** The Clinical Review will incorporate scrutiny of clinically relevant aspects from other documents in the technical file submission and may generate relevant queries. |

### Section 2 - Clinical Evaluation Team

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Section 2 – Clinical Evaluation Team** | | | | |
| **2** | 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 **Clinical Evaluation Team 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 **Clinical Evaluation Team 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 **Clinical Evaluation Team Folder**. | | | |

### Section 3 - Clinical Evaluation Plan

|  |  |  |  |  |  |
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| **Section 3 – Clinical Evaluation Plan** | | | | | |
| **3** | 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 **Clinical Evaluation 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 **Clinical Evaluation 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:** **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 | |
| **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 Clinical Characteristics Section of the Equivalence Declaration form (MDR-3003) has been completed and provided in the **Clinical Evaluation Folder.** | | | | Yes  No |
| **For Legacy devices**, if equivalence was claimed in the initial MDD 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 **Post Market 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 **Post Market folder** | | | | Yes  No |
| Tick the appropriate box in each case.  **Note 1**: Specify your chosen clinical evaluation methodology for this MDR submission per MDR 2017/745 and/or 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)** 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 MDD or MDR) by themselves. * Clinical evaluation of the marketed device is sufficient to demonstrate conformity to the GSPRs *(CER of the marketed MDR compliant)*. * **Manufacturers must provide a PMCF plan** *(which includes a study designed to demonstrate safety and performance of the device to be certified)*. * **NB must endorse equivalence claim** based on evidence provided to substantiate same *(see MDCG 2020-5)* | | | |
| **Article 61(5)** 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 device made by another manufacturer *(different device must be CE- Marked under the MDR)*   * Provide a **contract in place** that explicitly allows the Manufacturers of the 2nd device full & ongoing access to the technical documentation of the equivalent device. * The original clinical evaluation must be performed in accordance with the requirements of the MDR (CER of the equivalent device must be MDR compliant).   ***It remains the responsibility of the Applicant to demonstrate all features to the Notified Body.*** | | | |
| **Article 61(6a)** MDR exception for manufacturers of **Legacy Implantable and class III** devices who choose not to perform a clinical investigation: | **Conditions:**   * Need to base clinical evaluation on sufficient clinical data (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) *Listed* WET** devices per Art 61(6)b | **Conditions:**   * Manufacturers must base their clinical evaluation on sufficient clinical data *(see 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)** 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:** 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 *(see MDCG 2023-6)* | | | |
| **NOTE 1:** **Article 61(10)** cannot be applied to Class III or implantable devices. | | | | |
| **MDCG 2020-6**  **Sufficient Clinical Evidence** per MDCG 2020-6, Appendix III | For manufacturers of legacy devices choosing this route of assessment**,** reference is made to *Appendix III of MDCG 2020-6: Suggested hierarchy of clinical evidence for confirmation of conformity with relevant GSPRs under MDR*.  **NOTE 1:** Where 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. * Rationale for why that level of evidence (quality & quantity) can be considered sufficient for the device | | | |
| **MDCG 2020-6 Section 1.2**  **Legacy devices claiming WET** | **Note:** Applicable devices must fulfil the following criteria below;   * 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.   Detailed rationale as to how the device fulfils these criteria, and evidence for same in supporting documents will be sought during the review.  The level of evidence (per MDCG 2020-6, Appendix III) provided must be specified and justified as to how it can be considered sufficient. *Reliance solely on complaints and vigilance data is not considered sufficient.* | | | |
| Have other currently available alternative treatment options been considered? | | | | Yes  No |

### Section 4 - Clinical Evaluation Report

|  |  |  |  |
| --- | --- | --- | --- |
| **Section 4 – Clinical Evaluation Report** | | | |
| **4** | Ensure all PMS data submitted in the CER is not older than 12 months from the date of file submission.  **Note: *PMS data must remain current per EU MDR 2017/745 regulations throughout the review process. This may require submission of new PSUR data, and its integration to the CER where applicable (Art 86 requirements)*** | | |
| Confirm a copy of the **Clinical Evaluation Report** compliant to the MDR 2017/745 Chapter VI and ANNEX XIV has been uploaded to the **Clinical Evaluation 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 & 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 **Clinical Evaluation 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 **Clinical Evaluation 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 5 – Literature Search

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| **Section 5 – Literature Search** | | |
| **5** | Confirm a standalone copy of the literature search protocol has been uploaded to the **Literature Search Folder.**  ***Note: Data should be current within 12 months at the time of submission.*** | Yes  No |
| Confirm a standalone copy of the literature search report has been uploaded to the **Literature Search 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 |
| Paediatric 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 6 – Clinical Investigations

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| **Section 6– Clinical Investigations** | | | | |
| **6** | List which premarket investigations have been performed for the device. Specify which are exploratory or confirmatory investigations and provide supporting documentation in the **Clinical Investigations Folder**.  **Please provide a folder for each investigation, with supporting documents enclosed in each folder**  **NOTE:** Where Equivalence is being claimed, please upload clinical investigations & supporting documents for the equivalent device to the **Clinical Investigations Folder**;  *These will be assessed to MDR & ISO 14155 standards* | | | |
|  | | | |
| List which post-market investigations have been performed for the device and provide supporting documentation in the **Clinical Investigations 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 confirmatory study;*  *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 **Clinical Investigations 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 **Clinical Investigations 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 **Clinical Investigations 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 **Clinical Investigations Folder**. | | | |
| Confirm a Clinical Investigation Report (CIR) has been uploaded to the **Clinical Investigations 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 **Clinical Investigations Folder**. | | | |
| Confirm letter of ethics approval has been uploaded to the **Clinical Investigations Folder**. | | | Yes  No |
| Confirm if the expert panel was consulted regarding the Clinical Investigation. | | | Yes  No |
| If yes, confirm correspondence has been uploaded to **t**he **Clinical Investigations Folder**. | | | Yes  No |
| Confirm evidence of no objection from competent authority has been uploaded to the **Clinical Investigations Folder**. | | | Yes  No |
| Confirm the investigator’s brochure(s) has been uploaded to the **Clinical Investigations Folder**. | | | Yes  No |
| Confirm a sample of the informed consent for the investigation has been uploaded to the **Clinical Investigations 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 **Clinical Investigations Folder**. | | | Yes  No |

### Section 7 – Labelling & Information provided by Manufacturer

|  |  |  |
| --- | --- | --- |
| **Section 7 – Labelling & Information provided by Manufacturer** | | |
| **7** | **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 **Labelling folder.**  Supporting documents can be uploaded to the **Labelling folder.** | |

#### SSCP

|  |  |  |  |
| --- | --- | --- | --- |
| **SSCP** | | | |
| **Summary of Safety and Clinical Performance**  ***Applicable to all Class III & Implantable devices*** | | | |
| Confirm an SSCP as per MDR, article 32 and MDCG Guidance document 2019-9, Appendix: Template for the SSCP  has been uploaded to the **Labelling 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 **Labelling 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 8 – Clinical Aspects of Risk

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| --- | --- | --- |
| **Section 8 – Clinical Aspects of Risk** | | |
| **8** | **Risk:** confirm that there is traceability of information between the clinical evaluation and the Risk documentation.  Supporting documents can be uploaded to the **Clinical Risk Folder.** | Yes  No |

### Section 9 – Post-Market

#### PMS & PMCF Plans

|  |  |  |
| --- | --- | --- |
| **Section 9 – Post Market** | | |
| **9** | **PMS and PMCF Plan:**  **PMCF plan must align with template provided in MDCG 2020-7** | |
| Confirm a PMS Plan has been uploaded to the **Post Market Folder.** | Yes  No |
| Confirm an MDCG 2020-7 compliant PMCF Plan has been uploaded to the **Post Market Folder.** | Yes  No |
| Confirm an MDCG 2020-8 compliant PMCF Evaluation Report (if applicable) has been uploaded to the **Post Market 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

|  |  |  |
| --- | --- | --- |
| **PMCF Evaluation Report** | | |
| **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: | |

#### PSUR

|  |  |  |
| --- | --- | --- |
| **PSUR** | | |
|  | **Periodic Safety Update Report**  **New devices: 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)*, **a PSUR is not expected for the conformity assessment**  **For legacy devices, a current PSUR is required** | |
| Confirm a PSUR has been uploaded to the **Post Market** 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 10 – CECP

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| **Section 10 - CECP** | | |
| **10** | **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 or 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 **Clinical Evaluation** **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:   1. renewal of a certificate issued under the MDR; 2. 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; 3. 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 **Clinical Evaluation 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 **Clinical Evaluation 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 if N/A**: | | |
| **AMS1** | 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 in ***Folder AMS1***. | |
| *Details of all supporting documentation provided in* ***Folder AMS1****:*  **File Name:**  **Page:**  **Note:** | |

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| --- | --- | --- |
| **Information regarding the ancillary medicinal substance** | | |
| **AMS2** | 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.If yes, provide authorisation document in ***Folder AMS2*** | 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 in ***Folder AMS2*** | Yes  No |
| *Details of all supporting documentation provided in* ***Folder AMS2****:*  **File Name:**  **Page:**  **Note:** | |

|  |  |
| --- | --- |
| **Principal intended action of the device and action of the medicinal substance (ancillary to the device (medicinal substance plus device)** | |
| **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.** |
|  |  |

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| **Usefulness of the ancillary medicinal substance as part of the medical device** | |
| **AMS3** | Provide, in ***Folder AMS3***, 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. |
| *Details of all supporting documentation provided in* ***Folder AMS3****:*  **File Name:**  **Page:**  **Note:** |

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| **Ancillary medicinal substance data submission package** | | |
| **AMS4** | 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 in ***Folder AMS4***. | Yes  No |
| **Rationale if ‘No’:** | |
| *Details of all supporting documentation provided in* ***Folder AMS4****:*  **File Name:**  **Page:**  **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.**

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| --- | --- | --- | --- | --- |
| **Tissues or cells of animal origin (EU MDR Annex II, 6.2, b)** | | | | N/A |
| **Rationale if N/A**: | | | | |
| **TOAO1** | Where a device is manufactured utilising tissues or cells of animal origin, or their derivatives, provide, in ***Folder TOAO1***, 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. | | | |
| *Details of all supporting documentation provided in* ***Folder TOAO1****:*  **File Name:**  **Page:**  **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 if N/A**: | | |
| **TOAO2** | 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. | |
| *Details of all supporting documentation provided in* ***Folder TOAO2****:*  **File Name:**  **Page:**  **Note:** | |

| **Information regarding the tissue of animal origin starting material** | | | |
| --- | --- | --- | --- |
| **TOAO3** | Is there an EDQM (European Directorate for the Quality of Medicines) certificate available?  If ‘Yes’, a copy must be provided in **Folder TOAO3**  If ‘No’, a rationale must be provided below | | Yes  No |
| **Rationale for ticking ‘No’**: | | |
| 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: |  | |
| *Details of all supporting documentation provided in* ***Folder TOAO3****:*  **File Name:**  **Page:**  **Note:** | | |

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

**Important Note:** Supporting evidence must be provided in ***Folder TOAO4*** for **all requirements** listed below. The **file name** and the **exact page** must be referenced in the field below each requirement.

|  |
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| **Risk management: Justification for the use of animal tissues or derivatives** |
| Provide, in ***Folder TOAO4***, 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. |
| *Details of all supporting documentation provided in* ***Folder TOAO4****:*  **File Name:**  **Page:**  **Note:** |

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| **Risk analysis: Device contact with the patient or other persons** |
| 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. |
| *Details of all supporting documentation provided in* ***Folder TOAO4****:*  **File Name:**  **Page:**  **Note:** |

| **Risk analysis: Materials and/or components incorporated in the medical device or are used with, or are in contact with, the medical device.** |
| --- |
| If viable animal materials are utilized in the manufacture of the medical device, verification that the final medical device contains no viable animal material. |
| *Details of all supporting documentation provided in* ***Folder TOAO4****:*  **File Name:**  **Page:**  **Note:** |
| Provide comprehensive information on the intended use of any animal tissue or derivative. |
| *Details of all supporting documentation provided in* ***Folder TOAO4****:*  **File Name:**  **Page:**  **Note:** |
| Provide comprehensive information on the geographical source, species, age and feeding (including use of animal-derived protein) of animals. |
| *Details of all supporting documentation provided in* ***Folder TOAO4****:*  **File Name:**  **Page:**  **Note:** |
| Provide comprehensive information on veterinary control, conditions under which the animal materials are recovered, potential for cross-contamination. |
| *Details of all supporting documentation provided in* ***Folder TOAO4****:*  **File Name:**  **Page:**  **Note:** |
| Provide comprehensive information on the type and anatomical source of tissue. |
| *Details of all supporting documentation provided in* ***Folder TOAO4****:*  **File Name:**  **Page:**  **Note:** |
| Provide comprehensive information on the production process, particularly if it uses materials pooled from more than one animal. |
| *Details of all supporting documentation provided in* ***Folder TOAO4****:*  **File Name:**  **Page:**  **Note:** |
| Provide comprehensive information on the nature of material utilised in the medical device (e.g., intact tissue, highly purified derivative). |
| *Details of all supporting documentation provided in* ***Folder TOAO4****:*  **File Name:**  **Page:**  **Note:** |
| Provide comprehensive information on the method of utilization or incorporation into the medical device. |
| *Details of all supporting documentation provided in* ***Folder TOAO4****:*  **File Name:**  **Page:**  **Note:** |

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| **Risk analysis: Devices supplied sterile or intended to be sterilised by the user or are other microbiological controls applicable** |
| 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. |
| *Details of all supporting documentation provided in* ***Folder TOAO4****:*  **File Name:**  **Page:**  **Note:** |

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| **Risk analysis: Unwanted outputs of substances** |
| 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. |
| *Details of all supporting documentation provided in* ***Folder TOAO4****:*  **File Name:**  **Page:**  **Note:** |

| **Risk analysis: Identification of hazards and hazardous situations** |
| --- |
| Provide comprehensive information on the possible hazards associated with animal tissues or derivatives. |
| *Details of all supporting documentation provided in* ***Folder TOAO4****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO4****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO4****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO4****:*  **File Name:**  **Page:**  **Note:** |

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| **Risk control: Risk control options** |
| Provide the documented and justified risk control options for risk related to parasites and  unclassified pathogenic entities. |
| *Details of all supporting documentation provided in* ***Folder TOAO4****:*  **File Name:**  **Page:**  **Note:** |
| Provide the documented and justified risk control options for risk related to risk related to:   * bacteria * moulds * yeasts |
| *Details of all supporting documentation provided in* ***Folder TOAO4****:*  **File Name:**  **Page:**  **Note:** |
| Provide the documented and justified risk control options for risk related to risk related to viruses. |
| *Details of all supporting documentation provided in* ***Folder TOAO4****:*  **File Name:**  **Page:**  **Note:** |
| Provide the documented and justified risk control options for risk related to risk related to  TSE agents. |
| *Details of all supporting documentation provided in* ***Folder TOAO4****:*  **File Name:**  **Page:**  **Note:** |
| Provide the documented and justified risk control options for risk related to undesired, pyrogenic reaction, immunological reaction, and toxicological reaction. |
| *Details of all supporting documentation provided in* ***Folder TOAO4****:*  **File Name:**  **Page:**  **Note:** |
| Provide the documented risk reduction measures identified. |
| *Details of all supporting documentation provided in* ***Folder TOAO4****:*  **File Name:**  **Page:**  **Note:** |
| Provide the documented assessment as to the balance between medical benefit and residual risk being determined as acceptable. |
| *Details of all supporting documentation provided in* ***Folder TOAO4****:*  **File Name:**  **Page:**  **Note:** |

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

**Important Note:** Supporting evidence must be provided in ***Folder TOAO5*** for **all requirements** listed below. The **file name** and the **exact page** must be referenced in the field below each requirement.

|  |
| --- |
| **General requirements:** |
| **Quality system elements** |
| 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. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **Note:** |
| Provide comprehensive information on how the Quality System has considered documented the specification of the age. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **Note:** |
| Provide comprehensive information on how the Quality System has considered the geographical origin (such as country or region) of the animal material. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **Note:** |
| Provide comprehensive information on how the Quality System has considered the state of health of the animals. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **Note:** |
| Provide comprehensive information on how the Quality System has considered acceptance criteria for the animals taking into account the source-species. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **Note:** |

| **Personnel** |
| --- |
| 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. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **Note:** |

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| **Species and strain** |
| 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. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **Note:** |

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| **Geography** |
| 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. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **Note:** |

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| **Inspection** |
| 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. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **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’ |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **Note:** |

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| **Certification** |
| 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. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **Note:** |

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| **Traceability** |
| 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. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **Note:** |

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| **Collection:** | |
| 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. | |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **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 |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **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. | |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **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. | |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered and documented the limits of pooling permitted and how this limit is justified. | |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **Note:** | |

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| **Handling:** |
| 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. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **Note:** |

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| **Storage, transport, and labelling:** |
| 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. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO5****:*  **File Name:**  **Page:**  **Note:** |

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

**Important Note:** Supporting evidence must be provided in ***Folder TOAO6*** for **all applicable requirements** listed below. The **file name** and the **exact page** must be referenced in the field below each requirement.

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| **Risk control for viruses and TSE agents** |
| 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. |
| *Details of all supporting documentation provided in* ***Folder TOAO6****:*  **File Name:**  **Page:**  **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). |
| *Details of all supporting documentation provided in* ***Folder TOAO6****:*  **File Name:**  **Page:**  **Note:** |

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| **Collagen tissues of animal origin** | N/A |
| **Rationale if N/A is ticked:** | |
| 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. | |
| *Details of all supporting documentation provided in* ***Folder TOAO6****:*  **File Name:**  **Page:**  **Note:** | |
| Provide comprehensive information on how the risk management has considered for collagen produced from bones, the manufacturing conditions specified for gelatine are applicable. | |
| *Details of all supporting documentation provided in* ***Folder TOAO6****:*  **File Name:**  **Page:**  **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. | |
| *Details of all supporting documentation provided in* ***Folder TOAO6****:*  **File Name:**  **Page:**  **Note:** | |
| Provide comprehensive information on how the Collagen is obtained from animals declared as fit for human consumption (see ISO 22442-2). | |
| *Details of all supporting documentation provided in* ***Folder TOAO6****:*  **File Name:**  **Page:**  **Note:** | |

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| **Gelatine derived from hides and bones** | N/A |
| **Rationale if N/A is ticked:** | |
| Provide comprehensive information on how the Gelatine is obtained from animals declared as fit for human consumption. | |
| *Details of all supporting documentation provided in* ***Folder TOAO6****:*  **File Name:**  **Page:**  **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. | |
| *Details of all supporting documentation provided in* ***Folder TOAO6****:*  **File Name:**  **Page:**  **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. | |
| *Details of all supporting documentation provided in* ***Folder TOAO6****:*  **File Name:**  **Page:**  **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. | |
| *Details of all supporting documentation provided in* ***Folder TOAO6****:*  **File Name:**  **Page:**  **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. | |
| *Details of all supporting documentation provided in* ***Folder TOAO6****:*  **File Name:**  **Page:**  **Note:** | |

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| **Bovine blood derivatives** | N/A |
| **Rationale if N/A ticked:** | |
| 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. | |
| *Details of all supporting documentation provided in* ***Folder TOAO6****:*  **File Name:**  **Page:**  **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. | |
| *Details of all supporting documentation provided in* ***Folder TOAO6****:*  **File Name:**  **Page:**  **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. | |
| *Details of all supporting documentation provided in* ***Folder TOAO6****:*  **File Name:**  **Page:**  **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. | |
| *Details of all supporting documentation provided in* ***Folder TOAO6****:*  **File Name:**  **Page:**  **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. | |
| **File Name:**  **Page:**  **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. | |
| **File Name:**  **Page:**  **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. | |
| **File Name:**  **Page:**  **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. | |
| **File Name:**  **Page:**  **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). | |
| **File Name:**  **Page:**  **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. | |
| **File Name:**  **Page:**  **Note:** | |

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| **Tallow derivatives** | N/A |
| **Rationale if N/A ticked:** | |
| 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 | |
| *Details of all supporting documentation provided in* ***Folder TOAO6****:*  **File Name:**  **Page:**  **Note:** | |

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| **Animal charcoal** | N/A |
| **Rationale if N/A ticked:** | |
| 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 u3swznder these conditions shall be considered as presenting an acceptable TSE risk). | |
| *Details of all supporting documentation provided in* ***Folder TOAO6****:*  **File Name:**  **Page:**  **Note:** | |

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| **Milk and milk derivatives** | N/A |
| **Rationale if N/A is ticked:** | |
| 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). | |
| *Details of all supporting documentation provided in* ***Folder TOAO6****:*  **File Name:**  **Page:**  **Note:** | |

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| **Wool and its derivatives** | N/A |
| **Rationale if N/A is ticked:** | |
| 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. | |
| *Details of all supporting documentation provided in* ***Folder TOAO6****:*  **File Name:**  **Page:**  **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". | |
| *Details of all supporting documentation provided in* ***Folder TOAO6****:*  **File Name:**  **Page:**  **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. | |
| *Details of all supporting documentation provided in* ***Folder TOAO6****:*  **File Name:**  **Page:**  **Note:** | |

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| **Amino acids** | N/A |
| **Rationale if N/A is ticked:** | |
| 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. | |
| *Details of all supporting documentation provided in* ***Folder TOAO6****:*  **File Name:**  **Page:**  **Note:** | |

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| **Peptones** | N/A |
| **Rationale if N/A is ticked:** | |
| 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). | |
| *Details of all supporting documentation provided in* ***Folder TOAO6****:*  **File Name:**  **Page:**  **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.**

**Important Note:** Supporting evidence must be provided in ***Folder TOAO7*** for **all requirements** listed below. The **file name** and the **exact page** must be referenced in the field below each requirement.

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| **TSE relevant animal species** | | N/A |
| **Rationale if N/A ticked:** | | |
| Is the material of animal origin sourced from 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 | |

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| **General aspects** |
| 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. |
| *Details of all supporting documentation provided in* ***Folder TOAO7****:*  **File Name:**  **Page:**  **Note:** |

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| **Likelihood of infectivity in the source animals** |
| 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). |
| *Details of all supporting documentation provided in* ***Folder TOAO7****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO7****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO7****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO7****:*  **File Name:**  **Page:**  **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). |
| *Details of all supporting documentation provided in* ***Folder TOAO7****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO7****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO7****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO7****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO7****:*  **File Name:**  **Page:**  **Note:** |
| Provide comprehensive information on how the risk management has considered and documented the age of the donor animals. |
| *Details of all supporting documentation provided in* ***Folder TOAO7****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO7****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO7****:*  **File Name:**  **Page:**  **Note:** |

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| **Measures to prevent cross-contamination** |
| 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. |
| *Details of all supporting documentation provided in* ***Folder TOAO7****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO7****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO7****:*  **File Name:**  **Page:**  **Note:** |

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

**Important Note:** Supporting evidence must be provided in ***Folder TOAO8*** for **all requirements** listed below. The **file name** and the **exact page** must be referenced in the field below each requirement.

**Article 1 (2)**

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| Confirm that the medical device under submission 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)**

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| Confirm that the medical device under submission 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 is selected, it is not necessary to complete the remaining parts of this section.  If N/A is selected, please complete remainder of this section. | Yes N/A |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **Note:** | |

**Article 5 (2)**

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| (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 submission. See also Annex I, 1.2 |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **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 |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **Note:** |

**Annex I (1.2)**

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| 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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **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). |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **Note:** |

**Annex I (1.2.1)**

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| 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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **Note:** |

**Annex I (1.2.2)**

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| 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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **Note:** |

**Annex I (1.2.3)**

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| 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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **Note:** |

**Annex I (1.2.4)**

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| 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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **Note:** |

**Annex I (1.2.5.1)**

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| 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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **Note:** |

**Annex I (1.2.5.2)**

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| 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 |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **Note:** |

**Annex I (1.2.6)**

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| 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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **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 |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **Note:** |

**Annex I (1.2.7)**

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| 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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **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). |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **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). |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **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. |
| *Details of all supporting documentation provided in* ***Folder TOAO8****:*  **File Name:**  **Page:**  **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 |
| --- | --- | --- |
| **Rationale if N/A is ticked:** | | |
| **SUB1** | 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. | |
| *Details of all supporting documentation provided in* ***Folder SUB1****:*  **File Name:**  **Page:**  **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 |
| --- | --- | --- |
| **Rationale if N/A is ticked:** | | |
| **SUB2** | 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. | |
| *Details of all supporting documentation provided in* ***Folder SUB2****:*  **File Name:**  **Page:**  **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 |
| --- | --- | --- |
| **Rationale if N/A is ticked:** | | |
| **SUB3** | 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. | |
| *Details of all supporting documentation provided in* ***Folder SUB3****:*  **File Name:**  **Page:**  **Note:** | |

**Information regarding the substance(s)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **SUB4** | 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 in ***Folder SUB4*** | | Yes  No | |
| *Details of all supporting documentation provided in* ***Folder SUB4****:*  **File Name:**  **Page:**  **Note:** | | | |
| For medical devices to which ‘EU MDR Annex VIII Rule 21’ applies, provide information in ***Folder SUB4*** (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 |
| *Details of all supporting documentation provided in* ***Folder SUB4****:*  **File Name:**  **Page:**  **Note:** | | | |

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

| **Annex II 6.2 (c)** | |
| --- | --- |
| **SUB5** | Provide detailed information in ***Folder SUB5***, 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. |
| *Details of all supporting documentation provided in* ***Folder SUB5****:*  **File Name:**  **Page:**  **Note:** |
| Provide detailed information in ***Folder SUB5***, 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. |
| *Details of all supporting documentation provided in* ***Folder SUB5****:*  **File Name:**  **Page:**  **Note:** |
| Provide detailed information in ***Folder SUB5***, 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. |
| *Details of all supporting documentation provided in* ***Folder SUB5****:*  **File Name:**  **Page:**  **Note:** |
| Provide detailed information in ***Folder SUB5***, 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. |
| *Details of all supporting documentation provided in* ***Folder SUB5****:*  **File Name:**  **Page:**  **Note:** |

*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** | |
| **MF1** | Provide evidence in ***Folder MF1*** 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) |
| *Details of all supporting documentation provided in* ***Folder MF1****:*  **File Name:**  **Page:**  **Note:** |
| **Section MF2** | |
| **MF2** | Provide in ***Folder MF2*** the technical specification associated with accuracy including its tolerance and range. (Annex II Section 1.1) |
| *Details of all supporting documentation provided in* ***Folder MF2****:*  **File Name:**  **Page:**  **Note:** |
| **Section MF3** | |
| **MF3** | Provide in ***Folder MF3*** 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) |
| *Details of all supporting documentation provided in* ***Folder MF3****:*  **File Name:**  **Page:**  **Note:** |
| **Section MF4** | |
| **MF4** | Provide in ***Folder MF4*** a description of the methods used in order to ensure the accuracy as given in the specifications. (Annex II Section 6.2(f) |
| *Details of all supporting documentation provided in* ***Folder MF4****:*  **File Name:**  **Page:**  **Note:** |
| **Section MF5** | |
| **MF5** | Provide in ***Folder MF5*** 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. |
| *Details of all supporting documentation provided in* ***Folder MF5****:*  **File Name:**  **Page:**  **Note:** |
| **Section MF6** | |
| **MF6** | Provide in ***Folder MF6*** 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) |
| *Details of all supporting documentation provided in* ***Folder MF6****:*  **File Name:**  **Page:**  **Note:** |

# Appendix 10: Devices in Systems or Procedure Packs

|  |  |  |  |
| --- | --- | --- | --- |
| **System or Procedure Pack** | | | |
| Select ‘N/A’ if section is not applicable | | N/A | |
| **Rationale:** | | | |
| **SPP1** | Where the device under submission 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. | | |
| **Statement:** | | |
| *Details of all supporting documentation provided in* ***Folder SPP1****:*  **File Name:**  **Page:**  **Note:** | | |
| **EU MDR Article 22, 1 a, b and c** | | | |
| **SPP2** | 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 |
| *Details of all supporting documentation provided in* ***Folder SPP2****:*  **File Name:**  **Page:**  **Note:** | | |
| **(b) in vitro diagnostic medical devices bearing the CE marking in conformity with Regulation (EU) 2017/746;** | | N/A |
| *Details of all supporting documentation provided in* ***Folder SPP2****:*  **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 |
| *Details of all supporting documentation provided in* ***Folder SPP2****:*  **File Name:**  **Page:**  **Note:** | | |
| **EU MDR Article 22, 2 a, b and c** | | | ☐ N/A |
| **Rationale:** | | | |
| **SPP3** | 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 (*please select following as appropriate*): | | |
| **(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 |
| *Details of all supporting documentation provided in* ***Folder SPP3****:*  **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 |
| *Details of all supporting documentation provided in* ***Folder SPP3****:*  **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 |
| *Details of all supporting documentation provided in* ***Folder SPP3****:*  **File Name:**  **Page:**  **Note:** | | |
| **EU MDR Article 22, 3** | | | N/A |
| **Rationale:** | | | |
| **SPP4** | 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 provide a statement on how the requirement is met. | | |
| **Statement:** | | |
| *Details of all supporting documentation provided in* ***Folder SPP4****:*  **File Name:**  **Page:**  **Note:** | | |
| **EU MDR Article 22, 4** | | | ☐N/A |
| **Rationale:** | | | |
| **SPP5** | 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 provide a statement on how the requirement is met. | | |
| **Statement:** | | |
| *Details of all supporting documentation provided in* ***Folder SPP5****:*  **File Name:**  **Page:**  **Note:** | | |
| **EU MDR Article 22, 5** | | | ☐N/A |
| **Rationale:** | | | |
| **SPP6** | 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 provide a statement on how the requirement is met. | | |
| **Statement:** | | |
| *Details of all supporting documentation provided in* ***Folder SPP6****:*  **File Name:**  **Page:**  **Note:** | | |

# Appendix 11: ‘Reprocessed Single Use Devices’ and ‘Devices that require processing by the user/3rd party to allow use or reuse’

| **Reprocessed Single Use Device (EU MDR 2017/745 Article 17)** | | |
| --- | --- | --- |
| Select ‘N/A’ if section is not applicable | 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 Submission 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))**  **Note:** This section is **not applicable to reprocessed single use devices** as per EU MDR 2017/745 Article 17. | | | | |
| --- | --- | --- | --- | --- |
| Select ‘N/A’ if section is not applicable and provide rationale | | N/A | | |
| **Rationale:** | | | | |
| **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:** | | | |
| *Details of all supporting documentation provided in* ***Folder RD1****:*  **File Name:**  **Page:**  **Note:** | | | |
| **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:** | | | |
| *Details of all supporting documentation provided in* ***Folder RD2****:*  **File Name:**  **Page:**  **Note:** | | | |
| **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 in **Folder RD3** | | Yes  No | |
| *Details of all supporting documentation provided in* ***Folder RD3****:*  **File Name:**  **Page:**  **Note:** | | | |
| **RD4** | Please provide in **Folder RD4** the **Risk Analysis** that demonstrates 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 in **Folder RD4**? | | Yes No | |
| *Details of all supporting documentation provided in* ***Folder RD4****:*  **File Name:**  **Page:**  **Note:** | | | |
| **RD5** | Provide in **Folder RD5**, the **IFU** containing information on the appropriate processes for allowing reuse, including cleaning, disinfection, packaging and, where appropriate, the validated method of re-sterilisation  **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. | | | |
| Confirm supporting documents have been provided for review in **Folder RD5** | | Yes No | |
| *Details of all supporting documentation provided in* ***Folder RD5****:*  **File Name:**  **Page:**  **Note:** | | | |
| 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.* | | | |
| **Details:** | | | |
| Please provide**, in Folder RD5,** 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 in **Folder RD5** | | | Yes No |
| *Details of all supporting documentation provided in* ***Folder RD5****:*  **File Name:**  **Page:**  **Note:** | | | |
| **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 in **Folder RD6** | | Yes No | |
| *Details of all supporting documentation provided in* ***Folder RD6****:*  **File Name:**  **Page:**  **Note:** | | | |

**END OF FORM**