|  |
| --- |
| **If you have completed CE Product Significant Change: Notification and Review: MTF-1023 form then only complete the Red Tick box** ☒ **form requirements detailed in Section 8: Significant Change Assessment.**  Ensure the NSAI completed **CE Product Significant Change: Notification and Review: MTF-1023** form is submitted with this application.  Please complete the **CE Product Significant Change: Notification and Review: MTF-1023** form if you are unsure if your proposed change is a significant change under the MDD/AIMD *or* if this proposed change will require submission of a new application under the MDR. The form can be found on the website [<here>](https://www.nsai.ie/certification/medical-devices/ce-marking-for-medical-devices/). |



**Medical Devices**

# Application Form

**Significant Change**

* **Class 2B Implantable**
* **Class 3**
* **AIMD**

**Please tick all that apply:**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Class 2B Implantable | | | | |  | |  | |
|  | Class 3 | | | | |  | |  | |
|  | AIMD | | | | |  | |  | |
|  | TSE | | | | |  | |  | |
|  | Human Blood | | | | |  | |  | |
|  | Medicinal Substance | | | | |  | |  | |
| PO Number | |  | | | | | | | |
| **Directive(s) that apply:** | | | | | **NSAI File Number** | | | | |
|  | MDD (93/42/EEC) | | | | 252.     / | | | | |
|  | AIMD (90/385/EEC) | | | | 253.     / | | | | |
|  | TSE | |  | Human Blood | | |  | | Medicinal Substances |

|  |  |
| --- | --- |
| Proposed Significant Change Reference Number as per MTF-1023, if relevant. |  |

|  |
| --- |
| Instructions |
| 1. Please complete all relevant sections of the form (excluding the NSAI Review sections). 2. Please enter as much information onto the form as possible - avoid entering “see Technical File/Design Dossier”. If the data is in the supporting documentation, please ensure that there is a clear reference to the exact location of this information. 3. Please submit an unsigned version of this Application in Word as well as a signed copy - either scanned/secured (pdf) copy. 4. All application forms and supporting data to be forwarded in soft copy via one of the following (Hard copies not required)   NSAI upload facility: see <http://www.nsaiinc.com/>   1. Supporting documents should be provided in a SEARCHABLE format. 2. Applications and supporting documentation must be in English. 3. Please send a representative sample of the device(s). This is particularly important for new/novel devices. Any video or animations of procedures/simulated use would also be helpful, if available. |

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|  |  |
| --- | --- |
| Applicants’ Submission Checklist | |
|  | Completed application form (Word format, .doc or .docx) |
|  | Application (min. Signed Declaration page(s)) scanned |
|  | QMS certificates for all sites in Table 1 |
|  | Draft Declaration of Conformity |
|  | Labelling & IFU – May be Drafts |
|  | Essential Requirements Checklist |
|  | Performance/Complaint Analysis |
|  | Risk Management documentation |
|  | Sterilisation Validation(s) – if sterile/intended to be sterilised |
|  | packaging and device stability data – if necessary |
|  | Biocompatibility data – if necessary |
|  | Electrical Safety Testing data – if necessary |
|  | Software/firmware lifecycle documents – if necessary |
|  | Bench Testing data – if necessary |
|  | Clinical Evaluation Report(s) per MEDDEV 2.7.1 |
|  | Gap analysis between MEDDEV 2.7/1 rev3 and MEDDEV 2.7/1 rev4 |
|  | Clinical Evaluation Procedure |
|  | Clinical investigation(s), plan(s), report(s) and supporting documents per MEDDEV 2.7.1 and EN ISO 14155 |
|  | if following literature review/ equivalent device route please complete and attach NSAI Equivalence form GRF-25-28 if following literature |
|  | If Post Market Clinical information is available, please complete and attach NSAI Post Market Surveillance (PMS) |
| **For Tissue of Animal Origin falling under TSE Regulation 722/2012 EU** | |
|  | Please complete Appendix 13.1 |
| **For Human Blood Derivatives** | |
|  | Please complete Appendix 13.2 |
| **For Medicinal Substances** | |
|  | Please complete Appendix 13.3 |

| **Impact to Other Applications** | |
| --- | --- |
| Do you currently have an MDR 2017/745 application scheduled or under review with NSAI? | Yes, please list the MDR File number(s): |
| No |
| If yes, does this change impact any of the MDR 2017/745 applications you have listed above | Yes |
| No, please provide detailed rationale: |

| Declaration(S) by Applicant | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| In making this application we declare:   * The information in this form is correct. * We have not lodged an application with any other notified body to undertake conformance assessment procedures for the same product(s) / device-related quality system mentioned. * We undertake to institute and keep up to date a systematic procedure to review experience gained from devices in the post-production phase including the provisions referred to in Annex X, and to implement appropriate means to apply any necessary corrective actions and notifications, taking account of the nature and risks in relation to this product. * We agree to provide all vigilance reports to the Competent Authorities and NSAI * We agree to pay all applicable fees and understand that non-payment of fees will result in withdrawal of approval. * We undertake to fulfil the obligations imposed by the quality system approved. * We undertake to keep the approved quality system adequate and efficacious. * We agree to inform NSAI that approved the quality system of any plan for substantial changes to the quality system or the product-range covered. * We shall submit to NSAI any changes to the approved design, wherever the changes impact conformity with the essential requirements of the Directive or with the conditions prescribed for the use of the device. * We authorise NSAI to carry out all the necessary inspections at the legal manufacturer, critical sub-contractors and / or crucial supplier facilities and will supply NSAI with all relevant information to accomplish the above and in particular the following: * The documentation on the quality system * The data stipulated in the part of the quality system relating to design, such as the results of analyses, calculations, tests etc., (where relevant) * The data stipulated in the part of the quality system relating to manufacture such as inspection reports and test data, calibration data, qualification reports of the personnel concerned, etc. * We authorize and agree to allow NSAI access to all critical subcontractors and crucial suppliers, and all sites where the device or its crucial components are produced. * We agree to allow NSAI access to the Legal Manufacturer’s premises, and /or any of the above listed sites at any time for the purposes of performing unannounced audits. * As necessary we agree to provide all necessary support in acquiring the necessary travel papers, including VISA, to facilitate NSAI access to the above listed locations. * We agree to inform NSAI of the periods when the devices identified in this application will not be manufactured. * We understand that NSAI may end this contract with the Legal Manufacturer if permanent unannounced access to the above listed sites is no longer assured. * We understand that NSAI may cancel any unannounced audit at any time if the safety and security of NSAI personnel cannot be assured. | | | | | | |
| **By signing below, I accept the above declarations** | | | | | | |
| **Signed on behalf of the Manufacturer:** | |  | | **Date:** | |  |
| **Name (please print):** | |  | | | | |
| **Position / Title:** | |  | | | | |
| **Contact person** *(if different to Manufacturer)*: | |  | | | | |
| **E-mail:** |  | | **Phone:** | |  | |

|  |
| --- |
| Section 1: Manufacturer and Product Details |
| Note the “Manufacturer” as defined by the Directive(s) is “the natural or legal person with responsibility for the design, manufacture, packaging and labelling of a device before it is placed on the market under his own name, regardless of whether these operations are carried out by that person himself or on his behalf by a third party. |

| **Table 1 – Manufacturers Information and Summary Product Data** | | | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Legal Manufacturer’s Name** | | | | |  | | | | | |
| **Legal Manufacturer’s Address** | | | | |  | | | | | |
| **Design Site(s):** | | | | |  | | | | | |
| **Manufacturing Site(s):**  *(i.e., sites of actual manufacture)* | | | | |  | | | | | |
| **Assembly Site(s):** *(if applicable)* | | | | |  | | | | | |
| **Sterilisation Site(s):** *(if applicable)* | | | | |  | | | | | |
| **Scope of Site(s):**  *(i.e., as shown on the QMS cert)* | | | | |  | | | | | |
| **Name and address of EU Authorised Representative** *(if applicable)* | | | | |  | | | | | |
| **Product/Product Family Name:**  *(In compliance with NB/MED/2.5.1/*  *REC4 and NBOG’S Best Practice Guide 2006-2)* | | | | |  | | | | | |
| **GMDN Reference Number:** | | | | |  | | | | See [www.gmdnagency.com](http://www.gmdnagency.com) | |
|  | Declaration of Conformity included - Location within submission: | | | | |  | | | | |
| **MDD Only:** | | | | | | | | | | |
| **Class** | | III |  | IIb(implantable) | | | |  | Rule(s) |  |
| **Rationale** | |  | | | | | | | | |
| **Conformity Assessment** | | Annex |  | II | | |  | | III (+V) | |
| Full QA | | | | | Type testing +Production QA | | | |
| **AIMD Only:** | | | | | | | | | | |
| **Conformity Assessment** | | Annex |  | II | | |  | | | |
| Full QA | | | | |  | | | |
| **All Devices:** | | | | | | | | | | |
| **Clinical Strategy-**  **- Clinical data from:** | |  | Clinical Investigation | | | | | | | |
|  | Literature (Equivalence) | | | | | | | |
|  | Combination | | | | | | | |
| **Date of this application**  *(i.e., date of Declaration of Applicant):* | | | | | | |  | | | |

| Please complete the Table below, providing a full and up-to-date list of the current model numbers and descriptions related to this Application.  If the Declaration of Conformity is being used (instead of completing Table 2), please make sure that the WORD version is supplied. | | | |
| --- | --- | --- | --- |
| Table 2 – Product Family Information | | | |
| **Sub-Family** | **Model/Catalogue Number** | **Description** | **Class** |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |

| Section 2: Nature of Change | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| 1. | **Please provide a clear, detailed description of the change(s):** | | | | | | |
|  | | | | | | |
| **2.** | **Did the change(s) arise from a vigilance or performance issue** | | |  | **Yes** |  | **No** |
| If “Yes” please advise | | | | | | |
|  | | | | | | |
| **3.** | **Has NSAI received the Vigilance Report(s)** | | |  | **Yes** |  | **No** |
| If “Yes” please provide the relevant Unique Identifier number(s) | | | | | | |
|  | | | | | | |
| If “No” Please; | | | | | | |
|  | Justify |  | | | | |
|  | If applicable, please submit a copy of the Competent Authority report(s) along with the completed NSAI Vigilance Form located at [<http://www.nsaiinc.com/services/MedicalDevice> -“Vigilance Reporting”] to [vigilance@nsai.ie](mailto:vigilance@nsai.ie) | | | | | |
| **4.** | **Has this product been the subject of product recalls or Incident Reports in other Regulatory geographies outside EU? If yes, please summarize and provide details with supporting documentation.** | | | | | | |
|  | | | | | | |
| **5** | **For those failure modes associated with the identified Root Causes, please clarify if the Occurrence Rates outlined in the Risk Management File required an update based on the observed real-world rates.** | | | | | | |
|  | | | | | | |

| Section 3: Intended Use of the Device | | | | | |
| --- | --- | --- | --- | --- | --- |
| **1.** | **Is there a change in Intended Use** |  | **Yes** |  | **No** |
| 2. | **Please enter a full description of the revised intended use and/ or indications for use of the device** | | | | |
|  | | | | |
| **3.** | **Does this change impact the classification/rule** |  | **Yes** |  | **No** |
| If “No” please justify | | | | |
|  | | | | |

| Section 4: Labelling and Instructions for Use (IFU) | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Please select NA if this section is not required for the significant change.** | | | | |  | **N/A** |
| **1.** | **Is there a change to the Labelling/IFU** | |  | **Yes** |  | **No** |
| If yes: | | | | | |
| **Please supply a sample of the revised draft labelling & IFU in English.** | | | | | |
| **2.** | **Location of the sample Label(s) & IFU in the supporting documentation** | | | | | |
|  | | | | | |
| **3.** | **Are copies of all labelling provided?** | |  | **Yes** |  | **No** |
| If ‘No’, please rationalize that the sample provided is representative of the family | | | | | |
|  | | | | | |
| **4.** | **Please clarify the exact nature of change(s) to the labelling/IFU based on the proposed change(s) under review** | | | | | |
|  | | | | | |
| **5.** | **Are the requirements of EN 980 and EN 1041 being met** | |  | **Yes** |  | **No** |
| Version of Standard |  | | | | |
| If compliance with these vertical labelling standards is not claimed, please justify - | | | | | |
|  | | | | | |

| Section 5: Solutions to Essential Requirements and Harmonised Standards | | | |
| --- | --- | --- | --- |
| **Please indicate how relevant Essential Requirements (Annex I) of the Directive are met for the proposed changes.** | | | |
| **Please select N/A if this section is not required for the significant change.** | |  | **N/A** |
| **1.** | **Location of the revised solutions to Essential Requirements in the supporting documentation** | | |
|  | | |
| **2.** | **Please list the relevant Harmonised Standards in Table 3 below** | | |
| | **Table 3 – Applicable Harmonised Standards List** | | | | | | | --- | --- | --- | --- | --- | --- | | **Standard** | **Year** | **Has the Standard been applied in full (Yes/No)** | | | | |  |  |  | **Yes** |  | **No** | |  |  |  | **Yes** |  | **No** | |  |  |  | **Yes** |  | **No** | |  |  |  | **Yes** |  | **No** | |  |  |  | **Yes** |  | **No** | |  |  |  | **Yes** |  | **No** | |  |  |  | **Yes** |  | **No** | |  |  |  | **Yes** |  | **No** | | | |

| Section 6: Risk Management | | | | | |
| --- | --- | --- | --- | --- | --- |
| **1.** | **Did the proposed change affect or change any existing risks** |  | **Yes** |  | **No** |
| If “No” please justify | | | | |
|  | | | | |
| **2.** | **Did the proposed change introduce any new risks** |  | **Yes** |  | **No** |
| If “No” please justify - | | | | |
|  | | | | |
| **3.** | **Was the Risk review documented (e.g., during change control process, update to FMEA, Memo to file etc.)** |  | **Yes** |  | **No** |
| If “No” please justify | | | | |
|  | | | | |
| **If no update to Risk Management File, please provide rationale:** | | | | | |
|  | | | | | |

| **Section 7: Sterilisation** | | | | | | | | | | | | | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Please select NA if this section is not required for the significant change.** | | | | | | | | | | | | | | | | |  | | **N/A** | |
| 1. Sterilisation Validation | | | | | | | | | | | | | | | | | | | | |
| **For devices provided sterile** | | | | | | | | | | | | | | | | | | | | |
| **1.** | | **Does the proposed change affect sterilisation** | | | | | | | | | | |  | | **Yes** | |  | | | **No** |
| If “No” please justify | | | | | | | | | | | | | | | | | | |
|  | | | | | | | | | | | | | | | | | | |
| **2.** | | **Is a full validation/revalidation required** | | | | | | | | | | |  | | **Yes** | |  | | | **No** |
| **3.** | | If a full validation/revalidation not completed, please provide an Adoption justification/rationale report | | | | | | | | | | | | | | | | | | |
|  | | | | | | | | | | | | | | | | | | |
| **4.** | | | **Table 4 – Sterilisation Information Summary** | | | | | | | --- | --- | --- | --- | --- | --- | | **Device**  **sub-family** | **Cat.**  **Number** | **Sterilisation Method** | **Sterilisation Location** | **Protocol / Report No.** | **Site Resp for Release** | |  |  |  |  |  |  | |  |  |  |  |  |  | |  |  |  |  |  |  | |  |  |  |  |  |  | |  |  |  |  |  |  | |  |  |  |  |  |  | | | | | | | | | | | | | | | | | | | |
| **4.1.** | **Is EtO used for Sterilisation of the device(s):** *If “No” please go to Question 4.2 below.* | | | | | | | | | |  | | **Yes** | |  | | | **No** |
| **Is compliance with EN ISO 10993-7 latest version claimed** | | | | | | | | | |  | | **Yes** | |  | | | **No** |
| If “No” please explain | | | | |  | | | | | | | | | | | | |
| Is compliance with EN ISO 11135 latest version claimed | | | | | | | | | |  | | **Yes** | |  | | | **No** |
| If “No” please explain | | | | |  | | | | | | | | | | | | |
| Please categorise the device according to the duration of contact | | | | | | | | | | | | | | | | | |
|  | A – Limited Exposure | | | | | | | | | | | | | | | | |
|  | B – Prolonged Exposure | | | | | | | | | | | | | | | | |
|  | C – Permanent Contact | | | | | | | | | | | | | | | | |
| **4.2.** | **Is irradiation used for Sterilisation of the device(s):** *If “No” please go to Question #3 below.* | | | | | | | | | |  | | **Yes** | |  | | | **No** |
| **a.** | Is compliance with EN ISO 11137 latest version claimed | | | | | | | | |  | | **Yes** | |  | | | **No** |
| If “No” please explain: | | | |  | | | | | | | | | | | | |
|  | **Gamma** | | | |  | | **E-Beam** | | | | | | | | | |
| **b.** | What Dose setting method(s) are used | | | | | | | | | | | | | | | | |
|  | **VDMAX25** | |  | **Method 1** | | | | |  | | **Method 2** | | | | | |
| **4.3** | **Is moist heat used for Sterilisation of the device(s):** *If “No” please go to Question #4 below.* | | | | | | | | | |  | | **Yes** | |  | | | **No** |
| **Is compliance with EN ISO 11138 latest version claimed** | | | | | | | | | |  | | **Yes** | |  | | | **No** |
| If “No” please explain | | | |  | | | | | | | | | | | | | |
| **What cycle type used** | | | |  | **Pre-vac** | | | |  | **Gravity** | | |  | | **Other** | | |
| Details if “Other” | | | |  | | | | | | | | | | | | | |
| **4.4** | If one of the above methods is not used, please describe the method – (e.g., Dry heat, Aseptic Fill, Liquid Chemical, etc.) and list the standard(s) applied | | | | | | | | |  | | | | | | | | |
| 1. Maintenance of Sterility over shelf life | | | | | | | | | | | | | | | | | | | | |
| **Does the change affect the products shelf life** | | | | | | | | | | | | |  | | **Yes** | |  | | | **No** |
| If “no” please justify: | | | | | | | | | | | | | | | | | | | | |
|  | | | | | | | | | | | | | | | | | | | | |
| **1.** | **Please define the shelf life/expiry date** | | | | | | | | | | | | | **Years** | | | | | | |
| **2.** | **Please confirm the number of sterilisation cycles that the device and packaging were subjected to prior to stability testing -** | | | | | | | | | | | | |  | | | | | | |
| **3.** | **Please describe the preconditioning applied (eg. Ageing, transport etc):** | | | | | | | | | | | | |  | | | | | | |
| **4.** | **Is compliance with EN ISO 11607 latest version claimed** | | | | | | | | | | | |  | | **Yes** | |  | | | **No** |
| If “no” please justify: | | | | |  | | | | | | | | | | | | | | |
| **5.** | **If submitting Accelerated Aging data to support Shelf life, please confirm start date and expected completion date for real time Packaging studies** | | | | | | | | | | | | | | | | | | | |
|  | | | | | | | | |  | | | | | | | | | | |
| **6.** | **Please list and supply all relevant reports which substantiate Packaging shelf life** | | | | | | | | | | | | | | | | | | | |
|  | | | | | | | | | | | | | | | | | | | |

| Section 8: Biocompatibility | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Please select NA if this section is not required for the significant change.** | | | | | | |  | **N/A** |
| **1.** | **Is the biocompatibility status of the device affected by this change** | | | |  | **Yes** |  | **No** |
| If “No” please explain |  | | | | | | |
| **2.** | **Is compliance with EN ISO 10993-1 latest version claimed** | | | |  | **Yes** |  | **No** |
| If “No” please explain |  | | | | | | |
| **3.** | **Please identify additional testing requirements in Table 5 (section 4 below)** | | | | | | | |
| **4.** | | Table 5 – Tests considered/done | | | | | | | --- | --- | --- | --- | --- | --- | | Tests to be considered | ISO 10993 series  Year | Test completed by | Report number | Date | Conclusion | | Cytotoxicity | -5 : |  |  |  |  | | Sensitisation  (Delayed type hypersensitivity) | -10 : |  |  |  |  | | Irritation or intra-cutaneous reactivity | -10 : |  |  |  |  | | Systemic toxicity (Acute)  pyrogenicity | -11 : |  |  |  |  | | Sub-chronic toxicity (sub acute toxicity) | -11 : |  |  |  |  | | Genotoxicity  mutagenicity | -3 : |  |  |  |  | | Implantation | -6 : |  |  |  |  | | Haemo-compatibility | -4 : |  |  |  |  | | Chronic toxicity | -11 : |  |  |  |  | | Carcinogenicity | -3 : |  |  |  |  | | Reproductive and developmental toxicity | -3 : |  |  |  |  | | Biodegradation | -9 : |  |  |  |  | | Toxicokinetic studies | -16 : |  |  |  |  | | Immunotoxicology | -20 : |  |  |  |  | | Other Tests |  |  |  |  |  | | | | | | | | |
| **5.** | **Has testing been done on finished/sterilized device(s), or on materials that have been processed in the same manner, including sterilization** | | |  | | **Yes** |  | **No** |
| If “no” please justify: | |  | | | | | |
| **6.** | **Have biocompatibility test results been assessed and deemed acceptable by a competent individual?** | | | | | | | |
|  | | | | | | | |

| Section 9: Medical Electrical (ME) Equipment and Systems, plus Software | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Please select NA if this section is not required for the significant change.** | | | | | | |  | **N/A** |
| **1.** | **Is the product ME Equipment or System** | | | |  | **Yes** |  | **No** |
| **2.** | **Please answer all questions below and complete Tables 6,7 & 8**  **Please provide all relevant Test Reports, and EN 62304 Software Development Process & Validation Report, as well as Software Risk Assessment** | | | | | | | |
| **3.** | **Have the applicable requirements of EN 60601-1 latest version, including the mandatory risk assessment to EN 14971 been applied** | | | |  | **Yes** |  | **No** |
| **a.** | If “Yes” – please list all applicable “Part 2’s” in Table 8 below | | | | | | |
| **b.** | (i) | If “No”, is a particular standard (60601-2-xx) applicable that refers to a prior 60601-1 (ex. 2nd edition)? | |  | **Yes** |  | **No** |
| (ii) | If “No” – please provide rationale for not applying the latest version of EN 60601-1 | | | | | |
|  | | | | | | |
| **4.** | **Please list the document(s) submitted substantiating conformance to the edition of EN 60601-1 claimed –** | | | | | | | |
|  | | | | | | | |
| **Note** – the electrical review will include a review of the document(s) in which conformance with all applicable EN 60601-1 requirements as well as EN 60601-2-x if applicable are tested. Please ensure the tester understands and is familiar with a comprehensive test report/checklist format addressing each applicable requirement. Abbreviated reports and summaries are NOT acceptable. | | | | | | | |
| **5.** | **What is the expected Service Life of the device** | | | | | years | | |
| **6.** | **What is the Essential Performance of the device -** | | | | |  | | |
| **8.** | **Does the product incorporate Software/Firmware or meets the Definition of Standalone Software per MEDDEV 2.1/6?** | | | |  | **Yes** |  | **No** |
| **If “Yes” Have the requirements of EN 62304, including the mandatory risk assessment to EN 14971 been applied in submitted software documents?** | | | |  | **Yes** |  | **No** |
| **Version of Standard:** | | |  | | | | |
| If not the latest version, please explain - | | |  | | | | |
| **9.** | **Please provide the safety classification (A, B, C) and rationale for each software or firmware unit.** | | | | | | | |
| **Please also provide all documentation to demonstrate compliance with EN 62304: as shown below** | | | | | | | |
| |  |  |  |  | | --- | --- | --- | --- | | **Table 6 – EN 62304 Compliance** | | | | | **EN 62304 requirement** | **Class A** | **Class B** | **Class C** | | **4.3 Software safety classification** | X | X | X | | **5.1 Software development plan** | X | X | X | | **5.2 Software**  **requirements** | X | X  (incl. RISK CONTROL measures) | X  (incl. RISK CONTROL measures) | | **5.3 Software**  **ARCHITECTURAL design** | N/A | X | X  (incl. segregation for RISK CONTROL) | | **5.4 Software detailed design** | N/A | X | X  (incl. detailed design of SOFTWARE UNIT & interfaces) | | **5.5 SOFTWARE UNIT**  **implementation** | X | X  (incl. verification & acceptance criteria) | X  (incl. verification & acceptance criteria) | | **5.6 Software integration**  **& integration testing** | N/A | X | X | | **5.7 SOFTWARE SYSTEM**  **testing** | N/A | X | X | | **5.8 Software release (VERSION)** | X | X  (incl. ANOMALIES, how created, archive, repeatability) | X  (incl. ANOMALIES, how created, archive, repeatability) | | **6.1 Software**  **maintenance plan** | X | X | X | | **6.2 Problem &**  **modification analysis** | X | X  (incl. analysis of CHANGE REQUESTS) | X  (incl. analysis of CHANGE REQUESTS) | | **6.3 Modification**  **implementation** | X | X | X | | **7.1 Analysis of software**  **contributing to hazardous**  **situations** | N/A | X | X | | **7.2 RISK CONTROL**  **measures** | N/A | X | X | | **7.3 VERIFICATION of RISK CONTROL measures** | N/A | X | X | | **7.4 RISK MANAGEMENT of software changes** | X | X  (incl. impact on existing RISK CONTROL measures) | X  (incl. impact on existing RISK CONTROL measures) | | **8 Software configuration**  **Management PROCESS** | X | X | X | | **9 Software problem**  **resolution PROCESS** | X | X | X | | | | | | | | |
| **10.** | |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | | Table 7 – Collateral Standards | | | | | | | | | **EN 60601-1-X** | **Year** | **Title** | | **Applied/ Report** | | | | | **EN 60601-1-2** |  | Medical electrical equipment - Part 1-2: General requirements for basic safety and essential performance - Collateral standard: Electromagnetic compatibility - Requirements and tests | |  | **Yes** |  | **No** | | Report: | | | | | **EN 60601-1-3** |  | Medical electrical equipment - Part 1-3: General requirements for basic safety and essential performance - Collateral Standard: Radiation protection in diagnostic X-ray equipment | |  | **Yes** |  | **No** | | Report: | | | | | **EN 60601-1-6** |  | Medical electrical equipment - Part 1-6: General requirements for safety - Collateral standard: Usability | |  | **Yes** |  | **No** | | Report: | | | | | **EN 60601-1-8** |  | Medical electrical equipment - Part 1-8: General requirements for basic safety and essential performance - Collateral Standard: General requirements, tests and guidance for alarm systems in medical electrical equipment and medical electrical systems | |  | **Yes** |  | **No** | | Report: | | | | | **EN 60601-1-10** |  | Medical electrical equipment - Part 1-10: General requirements for basic safety and essential performance - Collateral Standard: Requirements for the development of physiologic closed-loop controllers | |  | **Yes** |  | **No** | | Report: | | | | | **EN 60601-1-11** |  | Medical electrical equipment -- Part 1-11: General requirements for basic safety and essential performance - Collateral standard: Requirements for medical electrical equipment and medical electrical systems used in the home healthcare environment | |  | **Yes** |  | **No** | | Report: | | | | | For Collateral Standards not applied, please explain - | | |  | | | | | | | | | | | | |
| **11.** | |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | | **Table 8 – Particular Standards** | | | | | | | | | | **EN 60601-2-X\*** | **Year** | **Title** | | | **Report** | | | | |  |  |  | | |  | | | | |  |  |  | | |  | | | | |  |  |  | | |  | | | | |  |  |  | | |  | | | | |  |  |  | | |  | | | | |  |  |  | | |  | | | | | \*Also includes EN 80601-2-x. For Particular Standards not applied, please explain - | | | | | | | | | |  | | | | | | | | | | **Does the product incorporate SaMD or COTS** | | | |  | | **Yes** |  | **No** | | If “Yes” Have the requirements of FDA Guidance on cybersecurity been applied | | | |  | | **Yes** |  | **No** | | **Version of Guidance:** | | |  | | | | | | | | | | | | | |

| Section 10: Device Testing | | | | | | | | | | | | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Please select NA if this section is not required for the significant change.** | | | | | | | | | | | | | | | |  | | **N/A** | |
| 1. Device Design Testing | | | | | | | | | | | | | | | | | | | |
| **1.** | | **Do the changes require additional bench testing** | | | | | | | | | | | |  | **Yes** |  | | **No** | |
| If “No” please justify: | | | |  | | | | | | | | | | | | | |
| **2.** | | **Do the changes require repeat bench testing at current product shelf life** *e.g., material change requiring bench testing to verify device functionality at shelf life* | | | | | | | | | | | |  | **Yes** |  | | | **No** |
| If “No” please justify: | | | |  | | | | | | | | | | | | | |
| **3.** | | **For the proposed change(s), please supply a Design Traceability Matrix or Design Input/ Output document and verify that the following have been included:** | | | | | | | | | | | | | | | | | |
| * 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), internally validated specification with clinical feedback, etc.) | | | | | | | | | | | | | | | |  | |
| * Design Output/ Documented Evidence | | | | | | | | | | | | | | | |  | |
| * Comment on whether D/I was met or not | | | | | | | | | | | | | | | |  | |
| **4.** | | **Depending on the type of the device, “bench testing” can include, but is not limited to:** | | | | | | | | | | | | | | | | | |
| * Static and dynamic accelerated durability | | | | | | | | | | | | | | | | | |
| * Bond strength | | | | | | | | | | | | | | | | | |
| * Coating integrity | | | | | | | | | | | | | | | | | |
| * Coating durability | | | | | | | | | | | | | | | | | |
| * Corrosion testing | | | | | | | | | | | | | | | | | |
| * Simulated use testing | | | | | | | | | | | | | | | | | |
| **Note: NSAI shall not accept “For Information Only” data (FIO); all attributes tested shall have clinically relevant specifications.**  **Note: If safety and performance of the proposed device is being demonstrated via equivalence to a predicate device, please supply side-by-side bench data of the devices in question.** | | | | | | | | | | | | | | | | | | | |
| **5.** | | **Please verify that the following has been supplied:** | | | | | | | | | | | | | | | | | |
|  | Representative sample of the device | | | | | | | | | | | | | | | | |
|  | Video of procedures/simulated use, (if available) | | | | | | | | | | | | | | | | |
|  | Computer modelling reports- Finite Element Analysis (FEA), Computational Fluid Dynamics (CFD), etc. (if applicable.) | | | | | | | | | | | | | | | | |
|  | All relevant bench test protocols and reports. | | | | | | | | | | | | | | | | |
| **6.** | | **Please verify that the protocols and reports include:** | | | | | | | | | | | | | | | | | |
|  | Justified test parameters per relevant standards | | | | | | | | | | | | | | | | |
|  | Acceptance Criteria | | | | | | | | | | | | | | | | |
|  | Sample size methods, justification and documented source | | | | | | | | | | | | | | | | |
|  | Justified deviations (if applicable) | | | | | | | | | | | | | | | | |
| If not, please justify: | | | | | | | | | | | | | | | | | |
|  | | | | | | | | | | | | | | | | | |
| **7.** | | **Materials of Construction:** | | | | | | | | | | | | | | | | | |
| **7.1** | Please supply relevant Material Safety Data Sheets (MSDS) | | | | | | | | | | | | | | | | |
| **7.2** | Please summarize all applicable components and materials as follows: | | | | | | | | | | | | | | | | |
| | **Table 9 Materials of Construction:** | | | | | | | | --- | --- | --- | --- | --- | --- | --- | | **Device Component** | **Component number** | **Material Trade Name** | **Material Grade** | **Certified for Medical Use** | **Supplier** | **Supplier approved via internal AVL** | | ***(Catheter Shaft)*** | ***(Part Number)***  ***(RM0325)*** | ***(Pebax)*** | ***(7233 SA01 MED)*** | ***Yes/No and Evidence*** | ***Materials Inc*** | ***Yes/No*** | |  |  |  |  |  |  |  | |  |  |  |  |  |  |  | |  |  |  |  |  |  |  | | **Note: Please supply this table as an attachment to the submission** | | | | | | | | | | | | | | | | | | | | | | | | |
| **7.3** | Please describe the design characteristics that address the interaction of the device surface and its environment of use. | | | | | | | | | | | | | | | | |
|  | | | | | | | | | | | | | | | | |
| 1. Device Stability | | | | | | | | | | | | | | | | | | | |
| **1.** | **Is there a change in the product shelf life** | | | | | | | | | | |  | | **Yes** | |  | **No** | | |
| **2.** | **Current shelf life**: | | |  | | | | | | **Proposed shelf life:** | | | | | |  | | | |
| **3.** | **Is the aging based on** | | | | |  | **Accelerated** | | | | | |  | **Real Time data** | | | | | |
| **4.** | **Confirm start date of real time studies** | | | | | | | |  | | | | | | | | | | |
| **5.** | **Please supply the relevant report(s) which substantiate device shelf life** | | | | | | | | | | | | | | | | | | |
| **Protocol #** | | | |  | | | **Report #** | | | | | | | |  | | | |
| **6.** | **Please confirm the number of sterilisation cycles that the devices have undergone prior to testing** | | | | | | | | | | | | | | | | | | |
|  | | | | | | | | | | | | | | | | | | |
| **7.** | **Please note the conditioning applied (e.g., Ageing, transport etc)** | | | | | | | | | | | | | | | | | | |
|  | | | | | | | | | | | | | | | | | | |
| **8.** | **Were all device attributes assessed at the proposed shelf life?** | | | | | | | | | |  | | | **Yes** | |  | **No** | | |
| If “No” please justify reason for omitting other attributes- | | | | | | | | | | | | | | | | | | |
|  | | | | | | | | | | | | | | | | | | |

| Section 11: Clinical Testing (Animal Model) | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Please select NA if this section is not required for the significant change.** | | | |  | | **N/A** | |
| **1.** | **Have acute/chronic animal studies been completed to substantiate the *in vivo* safety and/or effectiveness of the device design** |  | **Yes** |  | | **No** | |
| If “No” please explain | | | | | | |
|  | | | | | | |
| **2.** | **Does the data provide detailed information on all studies in animal models which substantiate the stated intended use, i.e.:** | | | | | | |
| * Study objectives | | | |  | | |
| * Methodology | | | |  | | |
| * Results, Analysis and Conclusions | | | |  | | |
| * Rationale for selection of the model(s) | | | |  | | |
| If “No” please explain | | | | | | |
|  | | | | | | |
| **3.** | **Please provide summary data of acute in vivo device performance and indicate the document number(s) of all studies in animal models** | | | | | | |
|  | | | | | | |
| **4.** | **Please provide summary data of acute in vivo device performance against pre-defined requirements, and/or clearly define the location of the relevant data within each animal report** | | | | | | |
|  | | | | | | |
| **5.** | **Was the product design assessed in the animal studies equivalent to the device design of this submission design** |  | **Yes** |  | | | **No** |
| If “No” please explain - | | | | | | |
|  | | | | | | |

| Section 12 – Clinical Performance (Human) | | | | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Please select NA if this section is not required for the significant change.** | | | | | | | | | |  | **N/A** |
| 1. Clinical Evaluation | | | | | | | | | | | |
| **1.** | **Do the changes require additional clinical data** | | | |  | | | | **Yes** |  | **No** |
| If “No” please justify - | | | | | | | | | | |
|  | | | | | | | | | | |
| **Revisions to the MDD 93/42/EC by 2007/47/EC have implications for the clinical data & the evaluation of the data to be provided by Manufacturers to the Notified Body, to demonstrate the clinical safety & performance of the medical device.**  **Clinical data must always be documented for all medical device classifications, as per Annex X OF The MDD 93/42/EEC.**  **MedDev 2.7.1 latest version provides guidance on the procedure to be adopted by the Manufacturer to evaluate clinical data.**  **Please supply a Clinical Evaluation Report to support the safe use of the device as per MedDev 2.7.1.**  **Please supply a clinical investigation plan(s)/Report(s) per EN ISO 14155 latest revision.** | | | | | | | | | | | |
| **2.** | **Please provide the document number and location of the Clinical Evaluation Report (CER) -** | | | |  | | | | | | |
| **3.** | **Does the supporting documentation submitted to NSAI include:** | | | | | | | | | | |
|  | Literature search protocol | | | | | | | | | |
|  | Full text of articles referenced in the CER. | | | | | | | | | |
| If not please explain: | | | | | | | | | | |
|  | | | | | | | | | | |
| **4.** | **Does the CER comply with MedDev 2.7.1** | | | |  | | | | **Yes** |  | **No** |
| **Version of MedDev used:** | | |  | | | | | | | |
| Has a gap analysis between MEDDEV 2.7.1 rev 3 and MEDDEV 2.7.1 rev 4 been submitted? Please provide location of gap analysis | | |  | | | | | | | |
| If “No” please justify - | | | | | | | | | | |
|  | | | | | | | | | | |
| **5.** | a. | **Does the CER address the relevant risks of predicate device** | | | |  | | | **Yes** |  | **No** |
| If “No” please justify - | | | | | | | | | |
|  | | | | | | | | | |
| b. | **Does the CER address Post market surveillance and or PMCF** *i.e., Registry or study (reference MED DEV 2.12 /2)* | | | | |  | | **Yes** |  | **No** |
| c. | **How often is the CER updated with data from the post market surveillance (reference Annex X 93/42/EEC** | | | | | | | | | |
|  | | | | | | | | | |
| **How often is the CER updated?** |  | | | | | | | | |
| **Please provide justification for the frequency of update** |  | | | | | | | | |
| **6.** | **Please identify the individual(s) who performed the clinical evaluation** - | | | | | | | | | | |
|  | | | | | | | | | | |
| **Is their CV included?** | | | | | | |  | **Yes** |  | **No** |
| **Is a declaration of interest of the evaluators included?** | | | | | | |  | **Yes** |  | **No** |
| If “No” please justify - | | | | | | | | | | |
|  | | | | | | | | | | |
| **7.** | **Please provide justification of the choice of evaluator(s)** | | | | | | | | | | |
|  | | | | | | | | | | |
| **8.** | **Was a clinical investigation completed to demonstrate the safety and performance of the device?** | | | | | | |  | **Yes** |  | **No** |
| **Version of MedDev used:** | | |  | | | | | | | |
| If “No” please justify - | | | | | | | | | | |
|  | | | | | | | | | | |
| **9.** | a. | Are any clinical investigations planned | | | | | |  | **Yes** |  | **No** |
| b. | Are any clinical investigations on-going | | | | | |  | **Yes** |  | **No** |
| c. | Are any clinical investigations completed | | | | | |  | **Yes** |  | **No** |
| If “Yes” please provide additional information and status – | | | | | | | | | | |
|  | | | | | | | | | | |
| **10.** | **For clinical investigations, does the supporting documentation submitted to NSAI include** | | | | | | | | | | |
|  | Letter of no objection from Competent Authority/-ies (CAs) or other regulatory agency/-ies as appropriate | | | | | | | | | |
|  | Clinical investigation plan and amendments for which no grounds for objection were raised | | | | | | | | | |
|  | Ethics committee opinion(s) and comments arising from their review | | | | | | | | | |
|  | Signed and dated final report (signed by the sponsor, the co-coordinating clinical investigator – if appointed – and principal investigator at each site). | | | | | | | | | |
| If not please explain: | | | | | | | | | | |

| Section 13 – Appendices | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Please select NA if this section is not required for the significant change.** | | | | | |  | **N/A** |
| 1. Regulation 722/2012: TSE | | | | | | | |
| **1.** | **Does the product contain tissue of animal origin covered by Regulation 722/2012** |  | | **Yes** |  | | **No** |
| **2.** | **Do the changes impact the tissue of animal origin** |  | | **Yes** |  | | **No** |
| If “No” please justify - | | | | | | |
|  | | | | | | |
| **If “No” please go to Section 13.2** | | | | | | |
| Human Blood Derivative(s) | | | | | | | |
| **1.** | **Does the product contain human blood derivative(s) covered by Directive 2000/70/EC** |  | | **Yes** |  | | **No** |
| **Do the changes impact the human blood derivative(s)** |  | | **Yes** |  | | **No** |
| If “No” please justify - | | | | | | |
|  | | | | | | |
| **If “No” please go to Section 13.3** | | | | | | |
| 1. Devices incorporating Medicinal Substances | | | | | | | |
| **1.** | **Does the product incorporate a medicinal substance liable to act on the body with ancillary action** |  | | **Yes** |  | | **No** |
| Please confirm if the proposed change impacts the sections in **Table 13.3** below: | | | | | | |
| |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | | **Table 10** | | | | | | | |  | **Section** | **Yes** | **No** | **Agreed by NSAI** | **Reviewer** | **Date** | | **Medicinal substance**  **Requirements** | **Qualitative and quantitative particulars of the constituents** |  |  |  |  |  | | **Drug Master File** |  |  |  |  |  | | **E.Ph. monographs or methods** |  |  |  |  |  | | **E.D.Q.M. certificate** |  |  |  |  |  | | **Description of method of manufacture** |  |  |  |  |  | | **Control of starting materials** |  |  |  |  |  | | **Control of tests carried out at intermediate stages of the manufacturing process of the medical device** |  |  |  |  |  | | **Control tests on finished product** |  |  |  |  |  | | **Toxicity** |  |  |  |  |  | | **Reproductive Function** |  |  |  |  |  | | **Embryo/foetal and perinatal Toxicity** |  |  |  |  |  | | **Mutagenic Potential** |  |  |  |  |  | | **Carcinogenicity Potential** |  |  |  |  |  | | **Pharmacodynamics** |  |  |  |  |  | | **Pharmacokinetics** |  |  |  |  |  | | **Local tolerance** |  |  |  |  |  | | **Risk Analysis – additional** |  |  |  |  |  | | **Stability – additional** |  |  |  |  |  | | | | | | | |
| **2.** | **Do the changes require a supplementary Competent Authority review per MDD ER 7.4 paragraph 3** | |  | **Yes** |  | | **No** |
| If “No” please justify - | | | | | | |
|  | | | | | | |
| **If “No” – no additional sections required.** | | | | | | |
| Changes to the ancillary substance incorporated in a device, in particular related to its manufacturing process, need to be reviewed by the relevant Competent Authority to confirm that the Quality and Safety of the ancillary substance are maintained.  Please, highlighting the change(s) from the originally approved data | | | | | | |

| Section 14 – Design dossier | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Please select NA if this section is not required for the significant change.** | | | |  | **N/A** |
| **1.** | **Does the product use particles with at least one dimension below 100nm** |  | **Yes** |  | **No** |

| Section 15 – Critical Process Changes | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Please select NA if this section is not required for the significant change.** | | | |  | **N/A** |
| **1.** | **Has there been a change to manufacturing processes** |  | **Yes** |  | **No** |
| If No, please justify - | | | | |
|  | | | | |
| **2.** | **Has there been a change in critical processes and/or materials** |  | **Yes** |  | **No** |
| If Yes, please supply a detailed overview - | | | | |
|  | | | | |
| If No, please justify - | | | | |
|  | | | | |
| **Note For devices containing medicinal substances, human blood derivatives or using tissue of animal origin, additional information may be requested in the appropriate Appendix/Appendices.** | | | | | |
| **3.** | **Have there been any changes in key laboratory studies and testing –** |  | **Yes** |  | **No** |
| If Yes, please supply a summary of changes - | | | | |
|  | | | | |
| If No, please justify - | | | | |
|  | | | | |