MD TECHNICAL FILE: INFORMATION TO PROVIDE IN THE FRAME OF AN INITIAL ASSESSMENT

Directives 90/385/EEC and 93/42/EEC

☐ **Annex III: EC Type-Examination**
☐ **Annex II.4: EC Design Examination**

In the case of an initial application, the technical file is subjected to a preliminary review in order to verify its content and identify items to be supplemented before starting the evaluation. Then the evaluation is planned according to the results of this review.

The manufacturer is asked to provide preferably one example of the Medical Device, or if not possible one color photo.

A recommendation on the format presentation of the technical files is available on the website of the LNE/G-MED. The manufacturer is welcome to submit the files according to this recommendation.

Part I – General information

1. Manufacturer:

Name or business name and full address of the manufacturer within the meaning of the Directive.

Note 1: The legal entity responsible for placing the medical device on the market must be explicit and consistent with the complete technical documentation and the information provided by the manufacturer (instructions for use, user's manual, labeling, etc).

2. If applicable, the name or business name of the manufacturer's authorized representative established within the European Union.

3. Identification of the medical device:

Full commercial identification *(including the accessories and the software version, if applicable, only those which are covered by the current submission)*

4. Existing certification:

✓ Quality system certification
Identification of the certificate of conformity to Annexes II.3, V or VI covering the entire medical device

Note: A conformity certificate to Annex II.3 or V or VI must have been issued by a notified body (or about to be issued), for a category of medical devices (MD) that includes the product under evaluation.

✓ Has the product been subjected to a conformity evaluation under a different status, or a different registration outside the EU territory?

5. Statements:

1) A statement from the manufacturer indicating that no other application concerning the same type of MD was made to any other notified body.
2) A statement indicating whether or not a substance derived from animal origin has been used for manufacturing the device.
3) A statement stipulating whether or not the device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product as defined in Annex 1 point 7.4, 1st paragraph of Directive 93/42/EEC or in Annex I point10, 1rst paragraph of Directive 90/385/EEC)

4) A statement stipulating whether or not the device incorporates, as an integral part, a human blood derivative (by reference to Annex I point 7.4, 3rd paragraph, of the Directive 93/42/EEC or to Annex I point 10, 3rd paragraph, of the Directive 90/385/EEC)

Part II – Technical Data

General description of the medical device

6. Formal identification of the device, subject to the application for CE marking – List of variants:

1) Identification of the variants of the device, along with their commercial references
2) If appropriate, list of accessories (only for the accessories covered by the assessment)
3) If appropriate, identification of the associated software(s)
4) Description of the commercial presentation (device within its packaging)

7. Device class and justifications/GMDN Code:

1) According to Annex IX Directive 93/42/EEC: rule applied and arguments for company's classification
2) GMDN correspondent code (http://www.gmdnagency.org/ cf. ISO 15225)

8. Description of the claimed use:

1) Intended medical use claimed
2) Indications conditions of use, related to the illness, the pathology and/or the handicap treated
3) Mode of action, including the use of accessories which are not evaluated in the frame of this assessment, if applicable
4) Clinical performances claimed for the intended use, in line of the illness, the pathology and/or the handicap treated
5) Contra-indications and side effects
6) Lifetime of the device (duration of maintenance of the clinical performances under normal conditions of use)
7) Shelf-life

Note: For joint replacement implants, please indicate the claimed performances (e.g. intended minimum and maximum relative angular movement between the skeletal parts to which the joint replacement implant is attached ; expected wear of articulating surfaces ; …)

9. In case of a medical device manufactured utilizing tissues or derivatives of animal origin:

When one (or more) material of animal origin is (are) incorporated into the medical device or used in its manufacturing process (including fermentation broth and cell banks), please provide the information listed in the document "Material of Animal Origin: Information To Provide" which are applicable, i.e:

- The elements related to viral safety are to provide whatever the animal species,
- The elements related to TSE agents transmission risk are to provide, in addition to viral safety elements, for species concerned by Regulation UE n°722/2012 (bovine, ovine and caprine species, deer, elk, mink and cats).

Note 1: A derivative product means a material or a substance obtained from an animal tissue by a manufacturing process (e.g.: collagen, gelatin, enzymes, etc)

Note 2: As an example, the reagents from biological origin used in the manufacturing process of a medical device may be peptones of bovine origin, amino acids of porcine origin, murine monoclonal antibodies, fetal calf serum (used in the cells culture media), etc

Note 3: In case of evaluation of a change in a medical device that utilizes a material from animal origin, (for example: variant of an existing product or range extension), if appropriate, the absence of impact of the change on the viral safety and the reduction of EST risk (if applicable) has to be documented.

10. In case of a medical device incorporating a substance:

10.1 Identification of the substance incorporated to the medical device

When a medical device incorporates a substance as an integral part, fill the document "Medical device associated to a substance that may be considered as a medicine within the meaning of the directive 2001/83/CE"

If the substance is considered to be a medicine within the meaning of the directive 2001/83/CE, please refer to chapter 10.2 of this document.

10.2 Medical device incorporating a medicinal substance as an integral part

Please refer to the document "list of elements to be provided – Annex I 7.4 – Medical device incorporating a medicinal substance as an integral part".

1) Provide the necessary documents in order to pre-submit the file to the competent authority (pre-file**):**

- Introduction of the context
- For an initial application, fill the document entitled "Medical device associated to a substance that may be considered as a medicine within the meaning of the directive 2001/83/CE".
- In the case of a modification, summarize the impact of the modification on the quality, safety, usefulness and benefit/risk profile of the incorporation of medicinal substance(s) to the device.
- The application form corresponding to the competent authority consulted must be filled by the manufacturer (duly filled up to item 16 included for the ANSM application form)
- User guide and labelling
- Estimated date of submission of the QS file to the competent authority.

Note 1: The company must transmit these first elements to LNE/G-MED as soon as possible, in order to pre-submit the file to the competent authority (3 months prior submitting the file).

Note 2: In the case of a use of plants, precise which part of the plants has been used.

Note 3: In the case of vitamins and minerals, precise if the doses exceed the recommended daily intake.

2) The necessary documents for the evaluation of the Quality, Safety, Usefulness and benefit/risk profile of the incorporation of medicinal substance(s) to the medical device.

The file to provide in step 1 and step 2 must be in accordance with the document "list of elements to be provided – Annex I 7.4 – Medical device incorporating as an integral part a medicinal substance". Before evaluation of the usefulness, the CPM must carry out a preliminary review of the file.

a) **Step 1: provide 2 copies of the file for the evaluation of the usefulness by the LNE/G-MED.** This file must include at least the following items:

- Administrative file
- Abstract
- Quality file
- Non-clinical file
- Clinical file
- Usefulness file
- Full risk management report
- User's guide and labeling
- the pertinent articles that are mentioned in reference

Note 1: The results of this evaluation, as well as the file, which has been updated following on the demands of additional documents by the LNE/G-MED will be transmitted to the competent Authority in order to assess the quality and safety of the medicinal device, including the benefit/risk profile of the incorporation of the substance to the device.

b) **Step 2: after consolidating the file with the additional documents asked by the LNE/G-MED, provide the right number of copies required by the competent authority that has been consulted for the evaluation of the quality and safety (QS notice)** of the medicinal substance(s) associated with the device, this one must include at least:

- Administrative file
- Abstract
- Updated Quality file
- Updated non-clinical file
- Updated clinical file
- Updated usefulness file
- Updated full risk management file
- Updated user's guide and labeling
- Updated pertinent articles that are mentioned in reference
- Report of the evaluation of the usefulness by the LNE/G-MED

The dispositions must be adapted according to each competent authority and it is preferable to refer to the procedures of each authority (guide available on the website of each competent authority).

Note 1: The conformity can only be established after favorable evaluation of the usefulness, quality, safety and benefit/risk profile.

Note 2: In the case of an initial or complementary (modification) application, the content of the file to provide is different (see "list of elements to be provided – Annex I 7.4 – Medical device incorporating a medicinal substance as an integral part"). In the case of a modification, only the chapters affected by the modification will be filled. For the chapters that are not affected by the modification, provide an engagement and a justification that this section is not affected by the modification.

Note 3: In the case of a consultation to the ANSM, provide **6 paper AND 6 R/DVD-R/DVD (in French or in English, preferably in Word format) copies during step 2** (ANSM Guide: Notice to applicants – Medical device incorporating an ancillary medicinal substance on the ANSM website)

Note 4: Any modification of the MD having an impact on the medicinal substance will be notified to the competent Authority, which gave the initial notice. The documentation created for this purpose will be presented to the competent authority by LNE/G-MED. In case of an evaluation of the modification of a MD incorporating a medicinal subatnce (variant of an existing product or extension of the product line), if applicable, if the modification did not impact on the usefulness, the quality, and the safety of the substance, it must be documented by the manufacturer of the MD.

Note 5: when modifications are made on the medicinal substance, particularly when related to its manufacturing process, or when modifications made to the device have an impact on the medicinal substance, the competent authority must be consulted to confirm the quality and safety level of the substance. The utility of incorporating ancillary medicinal substance into the device is to be assessed by the LNE/G-MED (external expert) prior consulting the AC.

Note 6: the decision of certification or no certification is subject to a data at the consulted AC.

Note 7: When the CA gives its opinion on the potential impact of new data on the benefit-risk ratio related to the addition of a substance into the device, a new evaluation of the device conformity must be planned.

11.A. In case of a device put on another market than Europe, the history of changes occurred on the medical device since its placing on the market (date of placing on the market to be specified).

Design data: Medical device characteristics, safety and performance

12. Design concept

The design concept of the medical device should be defined:
- Evolution of a device already CE marked by the manufacturer
- Development on the basis of a similar device of a competitor
- Totally new medical device

In case of a totally new medical device, it should be mentioned and exposed in details if needed whether the device is innovative or not. To do so, the innovation degree of the device should be defined taking into account the criteria given in ANSM "Degrees of novelty card" whose link is given below:

http://ansm.sante.fr/var/ansm_site/storage/original/application/569e94a19945e1f0eb6e6d0d0fff8c21.pdf

13.1 In case of a CE-Design evaluation examination according to Annex II. 4, provide the following design quality records:

1) Planning the design project (final version)
2) Identification of the output data of the design verification
3) Records of the results and conclusions of the transfer of R&D
4) Minutes of all the design review performed during the realization of the project

13.2 In case of EC type examination in accordance with Annex III:

The sampling method selected is to be specified:
- reference to the reports included in the technical file,
- a specific on site visit to perform a test,
- sample taking for testing in a laboratory.

The reports included in the file may be taken into account if evidence is given that the tests have been performed on devices that are representative of the whole production.

14. Standards and documents applied by the manufacturer:

List of the standards, preferably harmonized **(1)**, and other documents (e.g.: European Pharmacopoeia monographs) applied by the manufacturer as design input data.
(1) See the last list of applicable European harmonized standards, published in the Official Journal of European Union.

When the harmonized standards are not used, the solutions implemented must be equivalent and the equivalence documented.

15. Characteristics of components and finished product (device):

1) Specifications of the main components (raw materials) (**note 1** of § 20**:** physical, chemical, biological specifications, etc… the manufacturer has to specify detailed specification included references, revision number, date of the revision of these specifications.
2) Specifications of manufacturing additives (**note 1** of § 20)**:** physical, chemical, biological specifications, etc… the manufacturer has to specify detailed specification included references, revision number, date of the revision of these specifications.
3) Specifications of the primary packaging (the one in direct contact with the MD, note 1 of § 20), its reference, number of revision and date of revision
4) Identification of the materials in contact with the patient (implanted or not) and/or the user
5) Specifications of the finished product: physical, chemical, biological, microbiological cleanliness
6) If applicable, specifications of the accessories : physical, chemical, biological, microbiological cleanness
7) *Where applicable*, plans, diagrams: the manufacturer has to specify plans and diagrams references, revision number and date of revision.

Note 1 : For medical devices using particles with at least one dimension below 100 nm, documentation provided by the manufacturer contains further characteristics as agglomeration state / aggregation, composition (e.g., chemical composition and structure), particle size / size distribution, purity/impurity, shape, solubility (hydrophobicity, liposolubility, water solubility), stability, surface area, surface chemistry, surface charge, coating characteristics.

Note 2 : Adjuvant : any solvent, lubricant or aid of manufacture that is necessary to the manufacture of the MD, that is not planned to be part of the composition, but is potentially present. To be distinguished from an additive (e.g. : antioxidant, stabilizer, dye-stuff…), that is part of the MD.

16. Pre-clinical evaluation: demonstration of compliance of the characteristics of the medical device, in line with the standards, documents and/or applied state of the art:

1) Biological evaluation: Structured biological assessment program based on risk management process (according to ISO 14971)
2) Mechanical, physical, chemical, electrical evaluation, etc : reports related with the testing performed, along with the certificate of the laboratory which performed the testing (e.g.: ISO/CEI 17025 accreditation), and rational in case of absence of preclinical testing. Besides, when an assessment refers to a report or a document of the manufacturer which is older than 5 years, the corresponding data must be provided along with a rational for its applicability
3) Demonstration that characteristics are maintained :
    - within the framework of the stability study, so as to justify the shelf life (linked with § 21-A-2)
    - during the expected lifetime of devices
4) Conclusion regarding the demonstration and maintenance of the characteristics

Note 1: When the device is designed to be used in a sterile state, the tests should be performed on the sterile device.

Note 2: In case the tests were not performed in conformity to the provisions stated in the applicable standards or regulations, the manufacturer shall document the demonstration of equivalence of the solutions adopted.

Note 3: The biological assessment program will contain all the data (biological tests, bibliographic data, chemical tests) used by the manufacturer and that justify the methodology implemented. These data should be the basis for the justification of the manufacturer's decisions. The results of the evaluation program and the data used must be provided. LNE/G-MED put at your disposal a guidance document related to the presentation of the control of biological risk.

Note 4: The calculations (including finite element calculations) and the simulations cannot demonstrate the achievement of the performances assigned by the manufacturer and then, where applicable, the device conformity to the applicable standards and regulations. Manufacturer must consider the need to confirm these simulations and calculations through tests.

Note 5: The absence of preclinical data is to be justified in a document. Whenever an evaluation makes reference to an evaluation report or any document of the company that dates back from more than 5 years, the corresponding date are to be sent as well along with a rational of its applicability.

Note 6: For radiation emitting devices and electrical devices, safety pertaining to those properties and characteristics are to be taken into account.

Note 7: When studies have been conducted using animal models, detailed information are to be provided regarding i.e. study objectives, methodology, results, analysis, and conclusions including rational and limitations for selection of the model(s).

Note 8: When simulated use testing has been performed, detailed information are to be provided by the manufacturer.

Note 9 : In the case where the manufacturer would perform the preclinical testing internally or in a laboratory which is not accredited 17025, LNE/G-MED could ask for the corresponding validation of the testing method used.

Note 10 : The presentation of the results is preferably done using a table.

Standard / Document / State of the art	Characteristic	Specification	Requirement	Demonstration method of conformity to the requirement (Testing, rational)	Accreditation number of the laboratory, expire date of the accreditation
Examples :					
Standard ISO 7198 § 8.7.2.1	Permeability	-Porosity -Water permeability	-Physical criteria for porosity -Physical criteria for water	XXX	XXX

			permeability		
Standard ISO 868-5 § 4.5	Sterile sealing	Seal strength	1.2 N for 15 mm	XXX	XXX

Definitions :

- Characteristic : inherent property of the MD
- Specification : document stating requirements related to a characteristic
- Requirement : stated expectation, implied or mandatory
- Conformity : fulfilment of a requirement

17. Usability file

Provision of the usability file, which includes or refers the following items:

1) Specifications of use
2) Identification of the interface characteristics, related to the safety and potential user errors
3) Identification of the hazards and hazardous situations, as well as the elements of associated risk control
4) Description of the use scenarios and identification of those which will be tested
5) Specifications of the user interface (including the accompanying documents), which integrate the technical requirements subject to testing
6) Planning of interface evaluation which mentions and justifies the objectives and the methods used. For the usability testing, the representative user profiles and the testing environment are to be précised and justified
7) Results of evaluation, analysis of the results and conclusion on the acceptability of the usability of the device

18. If applicable, validation of software (reference standard: EN/IEC 62304: 2006):

Description and validation report

Note: For the software validation, refer to "the LNE/G-MED guide for the elements to be provided in the assessment for the software".

19. Clinical evaluation

Reference documents:, MEDDEV 2.7.1 rev 4
(http://ec.europa.eu/health/medical-devices/files/meddev/2_7_1rev_4_en.pdf) "Clinical Evaluation Report – Presentation Guide": LNE/G-MED guideline for presentation of clinical evaluation; Directive 2001/20/EC

19.A.1 Initial evaluation

Clinical evaluation of the device should be provided in the form of a summary report confirming compliance with the essential requirements regarding the characteristics and performances assigned to the medical device as well as the evaluation of the side-effects and the acceptability of the benefit/risk ratio.

This summary report consists of:

- Either a critical evaluation of the data from the compilation of the relevant scientific literature regarding the performances, safety, design characteristics and intended purpose of the medical device when there is demonstration of equivalence of the device to the device to which data are related (cf. Annex 1 of MEDDEV 2.12-2 and § 5.1b of MEDDEV 2.7.1 rev. 4 for the equivalence criteria), and in this case a specific post-market clinical follow up is required.
- Or a critical evaluation of the results of all clinical investigations carried out (EN ISO 14155–1 and –2).
- Or a critical evaluation of both combined.

The path followed must be indicated and the data on which the clinical evaluation is based (reference articles, clinical investigation reports, etc) must be sent together with the elements justifying the conformity of the clinical investigations to the applicable requirements (clinical investigation plan, opinion of the ethical committee, authorization from the supervisory authorities, informed consent form, etc).

The methodology which should be applied for collecting, selecting and analyzing data and for demonstrating that the performance and safety level of the device complies with the manufacturer's claims and with essential requirements is described in the specific LNE/G-MED guideline "Clinical Evaluation Report – Presentation Guide".

Clinical data presented by the manufacturer will be subjected to a specific evaluation report entitled "Review and evaluation of the clinical evaluation report", which will be attached to the general report.

The level of innovation of the device (see § 12 above) should be taken into account if applicable, particularly with regards to the justification of the path used for demonstrating the clinical evidence.

Note 1: Clinical investigations must be carried out for the implantable devices and the Class III devices, unless the use of existing clinical data can be duly justified. In the event there is no clinical investigation, this should be justified by the manufacturer and a specific post market clinical follow up is required.

Note 2: When the demonstration of conformity to the essential requirements based on the clinical data is not considered appropriate, a documented justification has to be given based on risk management output and under consideration of the specifics of the device/body interaction**,** the clinical performances intended and the claims of the manufacturer.
When demonstration of conformity with the essential requirements is based on performance evaluation, bench testing and pre-clinical evaluation alone, adequacy of the demonstration has to be duly substantiated.

Note 3: If necessary, clinical data will be transmitted to an expert from the medical discipline, designated by the Medical and Scientific Committee of LNE/G-MED.

19.A.2 Description of post-market surveillance program, including the clinical follow-up, put in place for the medical device

Data generated from PMS program comprise safety reports including adverse event reports, materiovigilance notices, results of databases and literature analyses, etc …and data from formal post-market clinical follow up conducted in accordance with one or several of the following methods:

- Post market follow up of patients included in a pre-EC marking investigation.
- Implementation of a new prospective investigation (register, cohort study, etc.).
- Implementation of a retrospective study (analysis of previous registers, retrospective cohort).

The following situations require a specific clinical follow up (post market clinical study):

- Innovation, for instance when the design of the device, the materials, substances, operating principles, technology or medical indications are new.
- Significant changes in the product or its use claims for which a pre-market clinical evaluation and a new evaluation were conducted.
- High risk product, for instance risk related to the design, materials, components, invasivity and clinical procedures.
- High risk anatomical localizations.
- High risk target patients, for example children and elderly people.
- Seriousness of the disease / treatment complications.
- Ability to generalize clinical investigation results.
- No sufficient information on long-term performance and safety.
- Results of any previous clinical investigation, including adverse events or post market follow up activities.
- Identification of sub-populations that were not previously studied and which could reveal a different benefits / risk ratio, for instance hip implants in various ethnic populations.
- Continuous validation in case of a difference between the reasonable time scale for pre market follow up and the expected shelf life of the product.
- Risks identified that result from the literature or other sources for similar marketed devices.
- Interaction with other medical devices or treatments.
- Verification of the device safety and performance when it is used on a broader and more varied population of clinical users.
- Emergence of new information on safety and performance.
- If EC marking is based on equivalence.

see MEDDEV 2.12/2 rev2 (Guidelines on Post-Market Clinical Follow-up Studies)
http://ec.europa.eu/health/medical-devices/files/meddev/2_12_2_ol_en.pdf

Note: In the absence of a formal post-market clinical follow-up for the medical device, a documented justification is required.

Product manufacturing

20. Production

Raw materials, additives, primary packaging (note 1)	Supplier / Address	Distributeur / Address

Manufacturing stages	Company (Quality Certificates) (note 3)	Address
Design		
Manufacturing **(note 2 and 4)** **Describe the main steps of the manufacturing process**		
Cleaning of the device **(note 5)**, *if applicable*		
Primary packaging		
Secondary packaging		
Labeling/Labeling inspection		
Final inspection		
Sterilization *if applicable*: **specify the process**		
Product release		

The following items should be documented:

- Flow-chart of manufacturing and in-process controls
- Description of the manufacturing methods
- Description of the manufacturing environment, including its classification,
- Identification of the manufacturing sites and QMS certification of subcontractors, if applicable**(note 3)**

Note 1: These are the main manufacturing components, additives and primary packaging of which change can affect conformity with the essential requirements of the Directive.

Note 2: Describe the main manufacturing stages mentioned in the manufacturing flow-chart.

Note 3: In case manufacturing steps are sub-contracted, specify the Quality Management System certification owned by the sub-contractor, as well as the certifying body and provide copies of current certificates.

Note 4: The nature of ongoing manufacturing controls and of the final product is to be sent. Control criteria for critical characteristics of the medical device, included when controls are subcontracted, have to be specified.

Note 5: If applicable, intermediate cleaning stage(s) has(have) to be specified.

Identification of special processes			
Validated process	**Applicable**		**Standard**
Coating	☐ Yes	☐ No	
Cleaning	☐ Yes	☐ No	☐ PR NF S 94-091
Primary Packaging	☐ Yes	☐ No	☐ EN ISO 11607

Identification of special processes				
Validated process	**Applicable**		**Standard**	
Sterilization	☐ Yes	☐ No	☐ EN ISO 11135-1 ☐ EN ISO 11137 ☐ EN ISO 17665-1 ☐ EN ISO 11737-1	☐ other to precise
Comprising validation of method for determining bioburden	☐ Yes	☐ No		
Other process(es) : identification	☐ Yes	☐ No		

21. Validation of processes such as cleaning, disinfection, primary packaging, sterilization, etc

21-A. In case of an initial application:

Note 1: Where compliance has been established by equivalence, the equivalence must be demonstrated and documented.

21-A.1 Cleaning/disinfection process applied to the device, if applicable

Method and validation report and/or re-validation of the cleaning/disinfection process applied to the device **for removal of process agents utilized during manufacturing.** These provisions apply to intermediate cleaning processes and to final cleaning process.

The validation report of the process applied must include the following elements:

- Description of the installation and the process
- Standard(s) claimed
- If applicable, identification of the sub-contractor involved in the product validation and/or application of the process in routine : name and address, certification owned by said sub-contractor, technical agreement
- Review of the characteristics of the devices involved : component materials, geometry, surface condition, porosity, etc
- Where appropriate, identification of the families defined by the manufacturer, including a description of the parameters that define these families (material, surface condition, size/volume/area, shape, manufacturing process, etc) and identification of the MD used for validation (“worst case”, referent of the family, etc)
- Identification of the contaminants (chemical, particulate and microbiological) coming from the manufacturing process of the product and cleaning process.
- Compatibility of the cleaning /disinfection method with the device
- Protocol and report for the process qualification (parameters, acceptance criteria, results including cytotoxicity and systemic toxicity tests, if required) and conclusion on the process qualification
- Monitoring parameters of the routine process

21-A.2 Primary packaging process

a) For non sterile devices

- Detailed description of the primary packaging
- Specifications of the packaging items: nature and grade of materials, physical and chemical characteristics, biocompatibility, demonstration of compatibility with the device and with the labeling system
- Justification of the shelf-life, if applicable, in connection with the device performances (results of stability studies).

b) For sterile devices:

✓ **terminally sterilized devices** (reference standard: EN ISO 11607-1 and -2)
✓ **or devices obtained by aseptic processing** (filtration/aseptic filling/lyophilization) **:**

- Detailed description of the packaging system maintaining sterility
- Specifications of the packaging items : nature and grade of the materials, physical and chemical characteristics, biocompatibility, compliance with standards and European Pharmacopoeia monographs, demonstration of

compatibility with the device, the sterilization process, the forming and/or sealing process and with the labeling system and the printing/writing system, shelf-life limitations

•Microbial barrier properties, description of the sterile barrier system

•Performance tests carried out after sterilization (seal strength, seal width, peel open characteristics, etc) : provide the performance qualification report

- Justification of the shelf-life (stability studies) :
  - ✓ in connection with maintenance of the sterile state : verification of the integrity of the sterile barrier system and the sterility of the device,
  - ✓ in connection with the device performances (if not handled with item 17 above).

21-A.3 Sterilization process, if applicable

- Description of the sterilization process and validation report of the method according to the applicable relevant standards:

✓ Steam sterilization: EN ISO 17665:2006

✓ Ethylene oxide: EN ISO 11135:2007

✓ Gamma/beta irradiation: EN ISO 11137-1 : 2016 & EN ISO 11137-2 :2015

✓ Aseptic filtration: EN 13408-1 : 20016

✓ Sterilization by liquid chemical sterilants: EN ISO 14160:2011

- Measures for maintaining process effectiveness (ex: bioburden, OE residues, re-validation, sterilization dose audits, etc)

- Method applied for bioburden determination (counting/identification of the micro-organisms) and validation report of the method.

- Method applied for the detection of pyrogens or bacterial endotoxins and validation of the method

Note 1: Where the microbiological methods are carried out by external laboratories, a copy of the ISO/CEI 17025:2005 accreditation or of the ISO 13485:2003 certification of the laboratory, for the concerned activity, should be provided.

Note 2: For the sterilization process (irradiation or ethylene oxide), refer to "the list of the elements to be provided in the assessment for the sterilization process irradiation or ethylene oxide)".

21-A.4 Other special processes, if applicable:

Description of the process and validation report(s) (OQ and PQ)

Information supplied by the manufacturer

22. Accompanying documents (please refer to the requirements of Annex I section13 of the Directive 93/42/EEC or the Annex I section 14 and 15 of the Directive 90/385/EEC, to product standards, EN 980, etc.)

Please provide the following documents:

- Specific instructions for use of the device or user's manual (or project),
- Labeling (or labeling project) for the different packaging, specifying the intended use of the different labels, if applicable.
- Text and graphic elements for commercial packaging (model)
- *If applicable, documents referenced in the instructions for use, intended for the users (e.g.: surgical technique)*

Note: The manufacturer's address present on the labeling and the IFU shall be the one of the legal entity responsible for placing the medical device on the market. The following information shall be present:

- •street / road
- •number / building / floor / apartment (if relevant)
- •zip code
- •town
- •state / region, if relevant
- •country

The same information is required for the manufacturer's authorized representative address

Risk management

23. Risk management file

The documents shall include:

- Description of the methods for risk analysis, for risk control and identification of the relevant standard (e.g.: NF EN ISO 14971, current version)
- Definition of the life-cycle phases of the device(s): design, ageing, disposal, etc
- Complete risk management file including (according to EN ISO 14971, current version):
  - Risk management plan
  - Summary of the different stages in risk management: risk analysis, risk evaluation, implementation and verification of the measures for risk control, evaluation of any residual risk acceptability, including overall residual risk.
  - Risk management report (results of the review of the risk management process)

Note 1: Risks associated to all phases of the device life-cycle (design, manufacturing, utilization, ageing, disposal) should be evaluated and controlled.

Note 2: It is important to clearly identify and to document the decision criteria and their justification which have led to demonstrate that risks are acceptable regarding the patient benefits

Note 3: All known and foreseeable hazards as well as hazardous situations (combinations or sequences of events) must be identified.

Note 4: The risk acceptability under specific conditions should be considered by reference to the "generally recognized state-of-the-art".

Note 5: The residual risks and their treatment must be identified. A decision should be made regarding the acceptability of the overall residual risk. When the medical benefits are higher than the residual risk, this should be mentioned.

Note 6: The attached guideline provides information on how to complete the file for risk management (reference standard: NF EN ISO 14971, current version)

Conformity to the essential requirements (Annex I):

24. Synthesis (table) of the essential requirements in Annex I comprising:

- Statement of the essential requirements,
- Solutions adopted by the manufacturer to meet each one of the requirements applicable to the device,
- Identification of the documents containing the elements of compliance,
- Identification of standards and other documents (section 14) applied by the manufacturer which demonstrate the conformity

Note 1: The essential requirements considered not applicable by the manufacturer, due to the characteristics of the medical device and its intended use, should be identified as such.

Note 2: In case of joint application of the Medical Devices and "Machines" (2006/42/EC) Directives, explanation should be given as to how the essential requirements relative to this directive applicable to the concerned medical devices were taken into account.
Cf. Interpretative document of the European Commission (August 21, 2009) and NB-MED/2-X/Rec-X on internet sites specified below.

In case of an EC design examination of the product (Annex II.4), some points could also either be subjected to complementary investigations during the audits, or the results of previous audits of the design section (Annex II.3) could be taken into account. As to ensure the conformity of the device, the notified body may perform or ask for any relevant tests on the device.

In case of an EC type examination (Annex III), the manufacturer should make a "type" available to the notified body, who may request other samples as necessary (namely to perform or have the required tests performed to verify whether the standards applied as solutions satisfy the essential requirements).

The LNE/G-MED certification project manager remains at your disposal for any further information regarding the approach, organization, the nature or content of the data to be specifically submitted for your medical device.

The MEDDEV documents, recommendations from the notified organizations or “consensus statement” can be loaded from the following internet sites:
http://ec.europa.eu/health/medical-devices/index_en.htm and http://www.team-nb.org/.

25. Draft declaration of conformity:

The draft declaration of conformity contains the following items :

1) the name and address of the manufacturer or the authorized representative issuing the declaration;
2) a statement that the declaration is issued under the sole responsibility of the manufacturer;
3) a number identifying the product. This number does not need to be unique to each product. It could refer to a product, batch, type or a serial number. This is left to the discretion of the manufacturer;
4) the identification of the product allowing traceability. This is basically any relevant information supplementary to point 1 describing the product and allowing for its traceability. It may where relevant for the identification of the product contain an image, but unless specified as a requirement in the Union harmonization legislation this is left to the discretion of the manufacturer;
5) all relevant Union harmonization legislation complied with; the referenced standards or other technical specifications (such as national technical standards and specifications) in a precise, complete and clearly defined way; this implies that the version and/or date of the relevant standard is specified;
6) the name and identification number of the notified body LNE/G-MED (CE 0459) involved in the conformity assessment procedure;
7) all supplementary information that may be required (for example grade, category), if applicable;
8) the date of issue of the declaration; signature and title or an equivalent marking of authorized person; this could be any date after the completion of the conformity assessment.

ANNEX: Summary of Risk Management File

Reference standard EN ISO 14971, current version

	section of the standard	**Annex**
Risk management plan	3.4	F
What (scope = Medical Device + life cycles concerned Who When How Criteria for risk acceptability Methods of review Methods of verification Activity of collection and review information about production and post-production phase		B D4, D5, D8
Risk analysis Planned activities Results	4	C – E - G - H (DIV) - I (toxicology)
Intended use – Characteristics/safety Identification of hazards Estimation of the risk(s) for each hazardous situation Probability Severity	4.2 4.3 4.4	C H 2.1 D 2 E 2 H 2.4 D 3 E3 and E4 G (tools) H 2.4
Risk evaluation	5	D.4
Risk control	6	
Risk reduction Risk control options analysis Implementation of risk control measures Residual risk Evaluation Risk/benefit analysis Risks arising from risk control measures Completeness of risk control	6.1 6.2 6.3 6.4 6.5 6.6 6.7	 D 5.1 to 5.5 D3.2.3 J J D6
Evaluation of overall residual risk acceptability	7	D7 J
Risk management report	8	
Review : Management plan appropriately implemented? Overall residual risk acceptable? Methods in place to obtain relevant production and post-production information?		
Production and post-production information about :	9	
The medical device Similar medical devices Field Evolution of the state-of-the-art Impact on the : Processes Risk management File		