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BUSINESS ASSURANCE

DNV GL NEMKO PRESAFE

Your partner in this journey

SAFER, SMARTER, GREENER

SUMMARY

INTRODUCTION

As your partner in this journey and facing the current European requirements and the increased technical level and criticity of our assessments as your Notified Body, it was developed this material to guide you to the essential issues related to the MDD Directive , i.e. 93/42/EEC and its amendments.

This is an informative guide based on main requirements and the references are cited under the document.

Access MDD 93/42/ECC Directive

Access Harmonized Standards

If you have some doubt related to this guide or any requirement please CLICK HERE to send us your doubts. The more specific you are in your questions, the better we can support you. We are looking forward for your contact!

HAVE A GOOD READING!

1. Instructions to Your Technical File

Before start going to the technical content of this MDD Guidance, please find on Item 1 below the instructions about how to you organize and present your Technical File (TCF).

Please ensure that your next Technical Files submitted are according this guidance, that will permit to us be more effective when analyzing your data during the audit on site and also when submitting your documentation to the Notified Body.

Observe structure below to prepare the folders for the Technical File. Please observe on table below how shall be Named the Folders and the content for each folder.

Name of the Folder	Content of the Folder
03_Declaration of conformity	Declaration of Conformity signed, dated and scanned. REFERENCE: Read: EN ISO /IEC 17050-1:2010 Conformity assessment. Supplier's declaration of conformity. General requirements Access: Chapter 4.4 "EU declaration of conformity". PAGE: 57 *In English.*
04_QA Documentation	- Procedures of Tests and Inspections (from raw material entrance and while process); - Procedures of Clinical Evaluation - Procedure of Post Marketing (Clinical) Follow Up; - Procedure of Management Risk; - Procedure for validation (if applicable); - Device history record (quality control inspections), of the product that will be choosen by the auditor. - Flow-chart of manufacture process, describing the steps of production flow including the steps of inspection. *In English.*
05_Essential Requirements Checklist	- MDD Check List in .doc and page of signatures shall be scanned. The specific documents fulfilling the clauses of the essential requiremets are expected to be referred uniquely. Access here the "Essential Requirements Check List". *In English.*

06_Test Reports_Preclinical evaluation	- Performance Test Reports in English - Biocompability Reports in English Please consider: - Each test report shall be followed by a Critical Analysis by manufactures about the results. - Manufacturer shall evidence that LAB is accredited. - In case of using a Non- Harmonized Standard, a proper GAP Analysis in English shall be presented to evidence how the harmonized standard is being attended by means of other standards. *In English.*
07_Risk Management and Usability	- File of Risk Management and Usability. Plans, procedures, reports and risk analysis sheet. *In English.*
08_Labels and IFU	Use subfolders to organize: - Instruction for Use; - Label; - Packaging instruction; If you have more than one model of same product, the different model shall be organized in different subfolders. - Procedure of Translation (Reference: MEDDEV 2.5/5 rev.3 (7 kB) Translation procedure). *In English.*
09_Technical documents (other)	- Material Specifications (Raw material, end product, packaging); - Design; - Packing validation; - Shelf-life; - Stability and Transportation; - Product cleaning *In English.*
11_Clinical evaluation	- Clinical Evaluation Report; - Plan of Research, Clinical Evaluation Procedure, literature, CV of Researchers, evidence that equivalente devices have CE mark. - Check List Clinical Evaluation Literature Route completed as "Yes", "No" or Not Applicable. For "No" or "Not Applicable" include justification. For "Yes" inform the related documents. - Declarations of interests for each participant of clinical evaluation Please read A11 – Page 56 of MEDDEV 2.7.1 for Reference; *In English.*

12_Sterilization process	- For sterile medical devices: method for sterilization, validation report, tests results, bioburden monitoring (when applicable). - For non sterile medical devices, but intended to be sterilized by the end user: method for sterilization, Documents for evidence that sterilization method suggested on Instruction for Use was validated. *In English.*
13_EC REP agreement	- Contract with EU Representant properly signed, dated and covering all products that are being certified *In English.*
14_List of Devices	- List of products with description and codes of all models covered in this technical file. *In English.*
15_PMS and PMCF	- Procedure and report of Post-Market Surveillance PMS and Post-Market Clinical Follow-up Plan (if applicable). I*In English.*

- The documents shall be presented in pdf informing page, searcheables and with markers to facilitate the search of specific content;
- The Subject of File shall be in English always containing the code or number of document and the version. Example: Ex: RT001_Clinical evaluation report_rev.01.
- Please not use to name the files "ç" or long subjects - that may corrupt the file;
- The accepted language of Competent Authority of Presafe is English. All documents and critical analysis of test reports shall be presented in English.

Reference and Guides for Technical Documentation:

- IMDRF/RPS WG/N9FINAL:2014 Non-In Vitro Diagnostic Device Market Authorization Table of Contents (nIVD MA ToC)
- IMDRF/RPS WG (PD1)/N27R1 Assembly and Technical Guide for IMDRF Table of Contents (ToC) Submissions
- (ToC-based submissions)
- Points to Consider in the use of the IMDRF Table of Content for Medical Device Submissions pre-RPS
- Global Harmonization Task Force, GHTF SG 1, "Summary Technical Documentation for Demonstrating Conformity to the Essential Principles of Safety and Performance of Medical Devices (STED)."
- Global Harmonization Task Force, GHTF SG 1, "Summary Technical Documentation (STED) for Demonstrating Conformity to the Essential Principles of Safety and Performance of In Vitro Diagnostic Medical Devices."
- NB-MED/2.5.1, "Technical documentation"
- NBOG's Best Practice Guide, "Guidance on Design-Dossier Examination and Report Content"

2. Let's talk about Management Risk?

The scope of the risk management process shall include the whole lifecycle of the medical device (e.g. development, production, storage distribution, use and discarge) not only look at harms and hazards only related to the use of the device.

This includes as well outsourced processes to critical subcontractors and crucial suppliers.

Our assessors and/or auditors will challenge the probability levels, severity levels and risk acceptance criteria used, the competence in the risk management team, identified hazards or harms, and the risk control measures identified and the evidence that the risk control measures are implemented.

It is important to consider that Risk Management is a living document and inputs are coming currently from market, from use of the product and from clinical.

Access Consensus Paper for the Interpretation and Application of Annexes Z in EN ISO 14971: 2012

2.1 Who is involved in your risk management?

It is important to ensure that your personnel involved in the risk analysis covers:

- Qualifications related to the medical device incl. production.
- Qualifications related to the technologies involved.
- Qualifications related to the medical device and its use.
- Qualifications related to risk management techniques.

Important: The clinical competence will be checked. In general it should be some one that is actually using the device as part of the daily work. This may depend of the type of device, but if no evident clinical experience is part of the team, a deeper explanation and justification are required.

2.2 The Risk Management Plan

Risk Management Plan shall be prepared for each single medical device or family of medical devices Ensure that your plan cover the following elements, as minimum:

- Scope including which medical devise the risk management plan is valid for and the description of life cycle phases
- Intended use of the particular medical device
- Assignment of responsibilities and authorities, including the competence area for each member of the risk management team.
- Severity levels and probability levels of occurrence of harm for the particular medical device and a documented justification behind the levels. Except of new, innovative medical devices, the probability and severity levels shall be quantitative.
- Criteria for risk acceptability, based on the manufacturer's policy for determining acceptable risk, including criteria for accepting risks when the probability of occurrence of harm cannot be estimated. A justification for the chosen risk acceptance criteria shall be documented.
- Verification activities (verifying the implementation and effectiveness of risk control measures)
- Activities related to PMS and review of the post marketing surveillance data.

If the plan changes during the life-cycle of the medical device, a record of the changes shall be maintained in the risk management file.

2.3 The Risk Management File

Ensure that your RM File covers:

- Risk Policy
- Risk Management Plan
- Risk analysis
- Risk evaluation
- Implementation and verification of risk control measures
- Assessment of acceptability of residual risks

Ensure the following elements:

- Risk Management Plan is prepared for the particular medical device or family of medical

devices. . If there is more than one device in a risk analysis a justification must be given by the manufacturer in the risk management plan and risk analysis.
- Risk Management Plan has stated the same Intended Use as in the current Instruction for Use
- The Risk Management Plan has documented the Risk Management Team and that the actual team used is in compliance with the team stated in the plan. The Risk management team shall have clinical competence. Make a description to documentation reviewed to verify the clinical competence (e.g. CV)
- Risk Management Plan has documented the severity and probability levels and a justification behind the chosen levels, and levels are qualitative (except of new, innovative medical devices). The levels shall be specific for the type of the particular medical device and with consideration of the production/sales volume. The probability and severity levels used shall be in compliance with the levels stated in the plan.
- Risk Management Plan has documented the Risk Acceptance Criteria based on the top management risk policy and a justification for the risk acceptance criteria is documented. The risk acceptance criteria used shall be in compliance with the risk acceptance criteria stated in the plan.
- The risk analysis method used is identifying hazards and NOT failure. According to ISO 14971, hazards shall be identified because medical devices has hazard associated to normal use.
- The risk analysis is performed specifically for the device in the scope.
- The risk analysis covers ALL product realization processes (in details):
  - Design and development, procurement of critical components and/or services (outsourced processes), incoming inspection, production and packaging process, storage, installation and servicing
  - Delivery process (identification, traceability, shipment and distribution)
  - Post-delivery (including clinical use of the product, storage, etc.
- The initial risk is estimated (before any risk control measures are implemented)
- The risk reduction measures are described detailed enough and proof of effectiveness is documented (e.g. validation of clean room, sterility, welding (e.g. not just human eye), packaging, shipment, calibration, preventive maintenance, documented procedures, training etc.)
- The risk reduction is performed "as far as possible"
- The "Instruction for Use" is not used as risk control measures.
- The risk reduction measures do not produce new risks.
- All individual residual risks are evaluated using the same risk acceptance criteria
- The overall conclusions are explicit and it is clearly documented that medical benefit outweighs all risks combined (especially important if any individual risk is at the acceptance borderline)
- Indicate which specific issues that are followed up through clinical evaluation
- The solutions adopted by are according safety principles, taking account of the generally acknowledged state of the art
- The corresponding information is found in the instructions for use when residual risks are remaining. The relevant risks identified in the clinical evaluation or Post marketing follow up studies etc. are evaluated in the risk analysis (and vice versa).
- The traceability to verification activities can be established (could be as references are to specific documents (i.e. defined versions of especially the IFU and the clinical evaluation report)
- The revision history is traceable (preferably change log should be available) and reviews are performed at least annually, or more frequently if post-market surveillance data necessitates (e.g. customer complaints) or changes in the product realization process.
- The overall conclusion of the risk of the particular medical device is signed by one member of the top management.

Remember that the Risk Management is living documents! During the annual surveillance audits will be checked that design changes, process changes, updates and CAPA are referred back to the RM.

3. Let's talk about Pre-Clinical Data Evaluation?

The manufacturer shall evidence that evaluates the pre-clinical data in a consistent manner and that is meets the requirements of the Medical Devices Directive.

3.1 Biocompatibility

The **EN ISO 10993** series of standards provides the minimum requirements in order to document that the final device is biocompatible and safe for the patient and user.

It is very important to observe that existing literature on the material(s) and the device will be the starting point for any evaluation made by the manufacturer and will be the basis for considering the need for tests.

Tests are required to be performed on animals, but shall be avoided where possible and where the biocompatibility can be demonstrated without.

Any evaluation and/or test shall be performed on the finished product, post-sterilization and manipulations (where relevant). And the biological evaluation by the manufacturer shall be carried out by persons with relevant competence. This competence shall be documented.

3.2 Sterilization method

In case of devices delivered sterile, the chosen method of sterilization must be documented for its suitability related to material(s) and the final device.

When the sterilization method is by ethylene oxide, the residuals in the device must be tested.

Any sterilization method must be validated and it is expected that the validation is very recent for a new device. There must always be a justified plan for frequency of revalidation.

3.3 Stability

Stability of a device is related to the following:

- Material properties being maintained at initial level for the defined lifetime of the device.
- The packaging material is stable throughout the lifetime.
- Sterility being maintained for the defined shelf life of a device.

Stability can be defined initially based on literature, comparison to other devices and through accelerated studies. However, stability must always be ultimately documented through real time studies.

For some devices, it may be needed to define a very short shelf life and through real time studies, followed by extension of the shelf life in accordance with the outcome of the study.

3.4 Animal studies

Any study performed using animals is expected to be in accordance with relevant EU regulation related to the protection of animals used for scientific purposes.

The study design must include objective, methodology, result, analysis, statistics and conclusions as to why the study documents the objective. The number of animals included in the study must be weighed against the need for significant and unambiguous data.

3.5 Technical performance tests

All electro medical devices must be tested for safety by an accredited laboratory or one approved for Good Laboratory Practice with appropriate scope covered.

In cases where accredited testing is not possible a justification must be provided by the manufacturer.

3.6 The evaluation report by the manufacturer

The result of all pre-clinical data, testing and evaluations must be presented a one report where the manufacturer discusses, evaluates and concludes on each element from the pre-clinical evaluation plan made in the design phase. The reports shall contain, but are not limited to, the following:

A list of all materials in direct or indirect contact with the patient or user, including:

- the concentration of the materials
- indication on particle size
- coatings

Detailed information on biocompatibility testing and biological evaluation and must clearly show the suitability, safety, and, if necessary, biocompatibility of all materials used (biocompatibility testing, please see EN ISO 10993).

For medical devices using particles with at least one dimension below 100 nm:

- agglomeration state / aggregation
- composition (e.g., chemical composition and structure),
- particle size / size distribution
- purity/impurity, shape, solubility (hydrophobicity, lipid solubility, water solubility),
- stability
- surface area, chemistry and charge
- coating characteristics

For medical devices which are made to degrade in-situ

- full composition
- biocompatibility testing in accordance with ISO 10993-13, Biological evaluation of medical devices – Part 13: Identification and quantification of degradation products from polymeric medical devices and ISO 10993-16, Biological evaluation of medical devices – Part 16: Toxicokinetic study design for degradation products and leachables
- degradation profile – how long will it take to degrade in-situ, residuals and clearance.

Detailed information on any studies in animal models, i.e. study objectives, methodology, results analysis, and conclusions including rational and limitations and justification for selection of the model(s).

Detailed information on any simulated use testing including mechanical.

4. Let's talk about Clinical Evaluation?

The reference to compliance the Clinical Evaluation is the MEDDED Guide 2.7/1 Rev04: Clinical Evaluation.

Access the complete Guide: MEDDEV 2.7/1 Rev4 CLINICAL EVALUATION

4.1 The implementation of Rev04 to Presafe

The MEDDEV 2.7/1 REV4 is more robust and bring us deeper details and clarification on steps, process and estructure for clinical evaluation and presentation of the results and some few additional requirements.
All new applications for conformity assessment whether initial, recertification or scope extensions are accompanied by the clinical evaluation reports prepared in accordance with the explanations provided in MEDDEV 2.7.1 rev 4.

For already certified devices you have to prepare the "impact assessment" and "plans for revision" of the content of Clinical Evaluation Reports (and other parts of technical documents if relevant) taking into consideration the level of details explained in MEDDEV 2.7.1 Rev 4. Availability and validity of these plans with the deadline of implementation by December 31, 2018 will be subject to assessment during our periodical or other upcoming audit and/or assessment activities.

4.2 Updating the Clinical Evaluation

Clinical evaluation **is a dynamic process** and the manufacturer has an obligation to revisit the existing evaluation report, for example with the incoming data from "Market Surveillance". **This is a continuous task and the frequency of the updates on the clinical evaluation report (CER) is clearly detailed in the MEDDEV**. See clause "6.2.3 Updating the clinical evaluation" of the guide:

"The clinical evaluation is actively updated:
- when the manufacturer receives new information from PMS that has the potential to change the current evaluation;
- if no such information is received, then

- at least annually if the device carries significant risks or is not yet well established; or
- every 2 to 5 years if the device is not expected to carry significant risks and is well established, a justification should be provided."

4.3 Who should perform the clinical evaluation?

The new MEDDEV also bring us more clear requirements about competence of all recources. Find that on MEDDEV 2.7.1 Rev4 item 6.4 - Page 14.

"The evaluators should have at least the following training and experience in the relevant field:
- a degree from higher education in the respective field and 5 years of documented professional experience; or - 10 years of documented professional experience if a degree is not a prerequisite for a given task."

Declaration of Interest – Observe in A11 page 56 of MEDDEV 2.7.1 rev 4. the clear requirements for the declaration of interest and observe that the declaration of interests should be dated and signed by each evaluator and the manufacturer.

4.4 How is a clinical evaluation performed?

The MEDDEV 2.7/1 Rev4 bring us structured and detailes information about each step for performing a clinical evaluation. See below as reference 6.3 Page 13 of MEDDEV 2.7/1 Rev04.

"The clinical evaluation is based on a comprehensive analysis of available pre- and post-market clinical data relevant to the intended purpose of the device in question, including clinical performance data and clinical safety data. There are discrete stages in performing a clinical evaluation:"

Stage 0: Definition of the scope of the clinical evaluation

Highlights on Stage 0: Please check table on Item 7 Page 15 MEDDEV 2.7/1 Rev4 to guide you define scope for products on different stage in their lifecycle of the product. The considerations for setting up a clinical evaluation plan should include different aspects depending of this phase.

Stage 1: Identification of pertinent data

Data generated and held by the manufacturer + Data retrieved from literature

Highlights on Stage 1: Equivalence Demonstration and Search Protocol are vital for the clinical evaluation. The Guide give us in deeper detail about how to comply these requirements: **Appendix A1**- Demonstration of equivalence. **Appendix A4** - Sources of literature. **Appendix A5** - Literature search and literature review protocol, key elements.

Highlight from Appendix A1: "Clinical, technical and biological characteristics shall be taken into consideration for the demonstration of equivalence:

- "Clinical:
- used for the same clinical condition (including when applicable similar severity and stage of disease, same medical indication), and
- used for the same intended purpose, and
- used at the same site in the body, and
- used in a similar population (this may relate to age, gender, anatomy, physiology, possibly other aspects), and
- not foreseen to deliver significantly different performances (in the relevant critical performances such as the expected clinical effect, the specific intended purpose, the duration of use, etc.)."

- "Technical:
- be of similar design, and
- used under the same conditions of use, and
- have similar specifications and properties (e.g. physicochemical properties such as type and intensity of energy, tensile strength, viscosity, surface characteristics, wavelength, surface texture, porosity, particle size, nanotechnology, specific mass, atomic inclusions such as nitrocarburising, oxidability), and
- use similar deployment methods (if relevant), and
- have similar principles of operation and critical performance requirements."

- "Biological: Use the same materials or substances in contact with the same human tissues or body fluids."

"Exceptions can be foreseen for devices in contact with intact skin and minor components of devices; in these cases risk analysis results may allow the use of similar materials taking into account the role and nature of the similar material. Different aspects of equivalence and compliance to different Essential Requirements can be affected by materials.
Evaluators should consider biological safety (e.g. in compliance to ISO 10993) as well as other aspects necessary for a comprehensive demonstration of equivalence. A justification explaining the situation should be provided for any difference."

Stage 2: Appraisal of pertinent data

Appendix A6 – Appraisal of clinical data - examples of studies that lack scientific validity for demonstration of adequate clinical performance and/or clinical safety – bring us detailed information about process.

"In order to determine the value of the data identified in stage 1, the evaluators should appraise each individual document in terms of its contribution to the evaluation of the clinical performance and clinical safety of the device. Uncertainty arises from two sources: the methodological quality of the data, and the relevance of the data to the evaluation of the device in relation to the different aspects12 of its intended purpose. Both sources of uncertainty should be analysed to determine a weighting for each data set."

Follow the guide to the phases: The appraisal plane (9.2 Page 20) > Conduct of Appraisal (9.3 – Page 20) > Evaluation of methodological quality and scientific validity (9.4 – Page 20).

Stage 3: Analysis of the clinical data

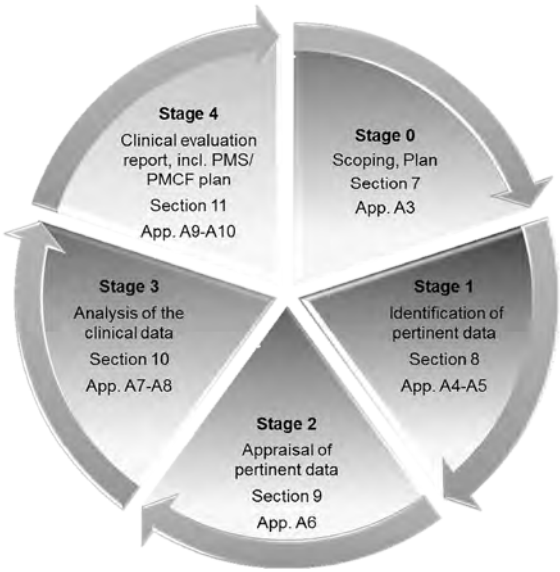
"The goal of the analysis stage is to determine if the appraised data sets available for a medical device collectively demonstrate compliance with each of the Essential Requirements pertaining to the clinical performance and clinical safety of the device, when the device is used according to its intended purpose. In order to demonstrate compliance, the evaluators should use sound methods;

- make a comprehensive analysis;
- determine if additional clinical investigations or other measures are necessary;
- determine PMCF needs.

Stage 4: The clinical evaluation report

Observe the "**Appendix A.9** – Page 49: Clinical evaluation report- proposed table of contents, examples of contents" that provides an outline for the report. It is highly recommended use this format as it will be of help in reaching the quality needed.
Suggestions for aspects that should be checked for the release of a clinical evaluation report are summarised in **Appendix A10** -Page 55: Proposed checklist for the release of the clinical evaluation report.
That will be a good tool for checking that your method and outcome are in accordance with the expectations.

"The clinical evaluation report should contain sufficient information to be read and understood by an independent party (e.g. regulatory authority or notified body). Therefore, it should provide sufficient detail for understanding the search criteria adopted by the evaluators, data that are available, all assumptions made and all conclusions reached.
The contents of the clinical evaluation report shall be cross-referenced to the relevant documents that support them. It should be clear which statements are substantiated by which data, and which reflect the conclusions or opinions of the evaluators. The report should include references to literature-based data and the titles and investigational codes (if relevant and available) of any clinical investigation reports, with cross-references to the location in the manufacturer's technical documentation.
The amount of information may differ according to the history of the device or technology. Where a new device or technology has been developed, the report would need to include an overview of the developmental process and the points in the development cycle at which all clinical data have been generated."



5. Let's talk about Market Surveillance?

The manufacturer shall ensure systematically review that experience gained from their devices in the post-production phase meets the requirements of the Medical Devices Directive.

The manufacturer have to collect and evaluate data related to their own device for the lifetime of the device to document that performance is as claimed and that it is state of the art.

Data from the post-production phase can be obtained as:

- A formal Post-market clinical follow-up study (PMCF)
- Post-market surveillance program (PMS)
- Incidents/adverse events and vigilance system
- Follow-up from sales and marketing

5.1 Post-market clinical follow-up study (PMCF)

The precondition for placing any device on the market is that it is in conformity with the essential requirements of the MDD. At times the data collected from the pre-market phase cannot fully detect rare complications or problems related to long term use. In such cases a Post-Market Clinical Follow-up (PMCF) is needed to confirm that the residual risks are acceptable.

Access: MEDDEV 2.12-2 Post Market Clinical Follow Up Studies

Access: GHTF Study Group 5, Document SG5/N4: 2010 Post Market Clinical Follow Up Studies

Circumstances whereby PMCF should be instigated:

- innovation, e.g., where the design of the device, the materials, substances, coatings, the principles of operation, the technology or the medical indications are novel
- significant changes to the products or to its intended use for which pre- market clinical evaluation and re-certification has been completed
- high product related risk e.g. based on design, materials, components, invasiveness, clinical procedures;
- high risk anatomical locations;
- high risk target populations e.g. paediatrics, elderly;
- severity of disease/treatment challenges;
- unanswered questions of long-term safety and performance;
- results from any previous clinical investigation, including adverse events or from post-market surveillance activities;
- identification of previously unstudied subpopulations which may show different benefit/risk-ratio e.g. hip implants in different ethnic populations;
- continued validation in cases of discrepancy between reasonable premarket follow-up time scales and the expected life of the product;
- risks identified from the literature or other data sources (e.g. MAUDE) for similar marketed devices;
- interaction with other medical products or treatments;
- verification of safety and performance of device when exposed to a larger and more varied population of clinical users;
- emergence of new information on safety or performance;
- where CE marking was based on equivalence and literature route.

PMCF study may not be needed when the safety and clinical performance are already known from previous use of the device or where other appropriate post-marker data is available and sufficient.

i. PMCF plan

This is a documented and proactive method where the manufacturer investigates specific data related to the CE-marked device.
PMCF studies must be outlined as a well-designed

clinical investigation plan or study plan, and, as appropriate, include:

- clearly stated research question(s), objective(s) and related endpoints;
- scientifically sound design with an appropriate rationale and statistical analysis plan;
- a plan to conduct the study according to the appropriate standard(s);
- a plan of how the analysis of the data and the statistical analysis will be performed and how appropriate conclusion(s) will be drawn.

ii. Objective

The objective is to confirm the safety and the clinical performance throughout the lifetime and as stated in the instruction for use.

iii. Design

PMCF studies should be designed to address the objective(s) of the study.
PMCF studies can follow several methodologies, for example:

- the extended follow-up of patients enrolled in premarket investigations;
- a new clinical investigation;
- a review of data derived from a device registry; or
- a review of relevant retrospective data from patients previously exposed to the device.

iv. Data analysis and conclusions

The study should:

- be executed with adequate control measures to ensure compliance with the clinical investigation or study plan;
- include data analysis with conclusions drawn according to the analysis plan by someone with appropriate expertise; and
- include a final report with conclusions relating back to original objective(s) and hypothesis/hypotheses.

v. The use of the data

The data and conclusions derived from the PMCF study are used to provide clinical evidence for the clinical evaluation process and risk assessment. This may result in the need to reassess whether the device continues to comply with the Essential Requirements.
Such assessment may result in corrective or preventive actions, for example changes to the labelling/instructions for use, changes to manufacturing processes, and changes to the device design, or public health notifications.
The data collected should be fed into the IFU and risk analysis where relevant.

5.2 Post market surveillance (PMS)

The manufacturer is obliged to implement and maintain surveillance programs in the post-production phase and monitor the safety and the clinical performance of the device. A formal procedure is needed and must take into consideration the type of device in questions. High risk and long term implantable devices may need a more rigorous program than medium to low risk devices. The program shall be justified and shall confirm the positive benefit over risk ratio.

Access: NB-MED 2.12/1 Recommendation Studies

Data collected will typically be:

- Safety reports, for own and similar devices
- Adverse event reports, for own and similar devices
- Results from published literature review relevant to the device in question and equivalent devices
- Further clinical investigations
- Formal PMCF studies
- Feedback from sales and marketing
- Proactive follow-up of long-term use of devices through:
  - customer surveys
  - customer complaints and warranty claims
  - post CE-market clinical trials
  - literature reviews
  - user feed-back other than complaints, either direct to manufacturer or via sales force
  - device tracking/implant registries
  - user reactions during training programmes
  - other bodies (e.g. the CA)
  - the media
  - experience with similar devices made by the same or different manufacturer
  - maintenance/service reports and
  - retrieval studies on explants or trade-ins
  - in-house testing
  - failure analysis

The data shall take the form of a report which

must be updated continuously or whenever needed. The report can be a separate one or included in the overall clinical evaluation report, see procedure on "Assessing and auditing Clinical Data".

The report should include as a minimum but not limited to:

- Specific device identification including the material and/or components
- The regulatory status in markets other than EU
- The total number produced, the number sold and to which countries
- Any recalls when relevant, explained in detail
- All incidents/adverse events, evaluated to be directly related to the device or not, where these originate from
- Information on adverse events for equivalent devices when available
- Positive, in addition to negative follow-up on the performance and safety of the devices for the intended use
- Discussion on the relevance of information collected
- Clear conclusion on the continued relevance and validity of the initial evaluation of clinical data.

The outcome of the surveillance activity may result in need for changes and have an impact on the QMS risk analysis. Presafe should be informed in such case.

PMS is a alive document! During the annual surveillance audit the audit team will review if the manufacturer is actually following this procedure. he data collected shall be reviewed! Please observe that a lack of reported adverse events is not sufficient to prove that the device is safe and performs according to the intended use and does not fulfil the requirement. Collection of information shall be proactive. Not following this requirement may lead to suspension of the certificate.

5.3 Adverse events reporting and vigilance system

The user or the owner of the medical device has an obligation to report any incident to the Competent Authority. The manufacturer and/or the Competent Authority has to take action when an incident is reported.

The MEDDEV 2.12-1 rev 8 of January 2013 gives the full procedure and guidelines for the vigilance system.

5.3.1 Incident reporting

The manufacturer must have a procedure in place in line with the MEDDEV 2.12-1 rev 8. Standardized report forms are available. Please observe the specific section related to devices that are not intended to act directly on the individual (e.g. IVF/ART), when relevant.
Presafe as a Notified Body does not hold a formal role in the vigilance system, but is expected to respond and act if/when contacted by the Competent Authority and/or manufacturer and to make own evaluations in case of incidents, see 5.3.2 for details.

5.3.2 Field safety corrective action (FSCA)

This is an action related to devices already on the market. A FSCA may include:

- recall, i.e. the return of the device to the supplier;
- device modification;
- exchange/replacing of devices;
- destruction of devices at point of purchase or after recall;
- retrofit/upgrade by purchaser of based on manufacturer's modification or design change;
- advice by the manufacturer on the use of the device or follow up of patients

The action must be reported and notified via a Field Safety Notice (FSN).

5.3.3 Field safety notice (FSN)

A FSN is a written notice sent by the manufacturer to the user or distributors in relation to a FSCA.
A form template and possible format is available under 2.12 Market Surveillance.

6. Let's talk about Changes to Design and Quality System?

6.1 Reporting of Design Changes and Changes of the Quality System

The manufacturer is obliged to inform Presafe about any planned changes to the device or quality system. This planned change shall be explained and declared in the "Notification on Change Form" and sent to Presafe. Information here will be basis for decision on further activity.

The NBOG's Best Practice Guide NBOG BPG 2014-3 is giving extensive instructions for both manufacturer and Notified Body on how to handle changes on already approved design, devices and quality system. Presafe is therefore adopting the text in this guidance as part of the procedure valid for any change. *(The text on item 6.2 below in Italic come from the NBOG Reference).*

Please go to NBOG BPG 2014-3 – Item 5 – Page 4 - to find details and criteria about "Substantial Use": Item 5 Criteria for "substantial" changes of the Guide for detailed information about criteria for "Substantial Use".

Access the complete GUIDE: NBOG BPG 2014-3

Inform your changes using the: Notification on Change Form. Access here!

6.2 Steps of the manufacturer for the change assessment procedure

The manufacturer shall have documented the responsibilities and authorities throughout implementation of changes and have documented procedures and evidence for

- *Need/wish to change the device, quality system or product range covered by the quality system*
- *Verification and validation to take the decision to effectively modify the product or the product range or the quality system related to its risk management process*
- *The need to update the technical documentation*
- *Definition of a change implementation plan to monitor the change stages and meet the regulatory requirements*
- *Determination whether the change is substantial or not*
- *Decision to implement the change taken and the timing of implementation (dependent on Notified Body review)*
- *Information given to the Notified Body about any substantial change*
- *Final implementation of the change.*

It is recommended that manufacturers contact and discuss with their Notified Body about any questions related to the substantial or not substantial characteristic of the change in order to get a common understanding.

The manufacturer shall establish, maintain and apply a procedure for categorising and implementing any changes to the device design/ type (including software) and/or quality system and/or product range as either substantial or not substantial.

The reporting system of the manufacturer for substantial changes must fulfil the subsequent criteria:

The manufacturer shall inform the Notified Body of the planned substantial changes as soon aspossible without delay.

A notification of any substantial change in the design/devices as well as in the quality system shall include

- *A brief description of the modifications compared to the approved design/devices or the approved quality system.*

» *The reason and origin for the changes/ modifications*
» *In the case of design/device changes, a statement on the relevance to the compliance with the essential requirements*
» *The technical data and documentation supporting above points.*

Manufacturers shall maintain a current listing of devices covered by the certificate and update the Notified Body accordingly.

7. Your Medical Device is Reusable and Re-sterilisable?

The Compliance and Enforcement Group (COEN) issued an important guide to improve the implementation of requirements regard information provided by manufacturer for the processing of resterilisabe medical devices in additional of the harmonized standard **EN ISO 17664 "Sterilization of medical devices - Information to be provided by the manufacturer for the processing of resterilisable medical devices.**

Please access complete the document here:

COEN Working Group – 2014 v 1.0 Instructions For Use for reusable and re-sterilisable Medical Devices

You will find Check Lists in Annex 1 and Annex that will prompt guide you on the implememtation of requireents.

8. Do you want to apply your product to CE Mark?

If you want to apply your product to CE Mark Certification we are available to help you on that and provide you a Certification Proposal.

Please complete the QRF - Quotation Request Form, attach the Instructions for Use or Manual, and send us on mail: **productassurancebrazil@dnvgl.com**

Quotation Request: QRF Form

It is very important to complete technical information about your product as Intention for Use, Classification and MD CODE. Please access NBOG to check the **MD CODE** of your products:

NBOG BPG 2009-3 MD CODES

Need help to check Classification of your product? Please Access:

Classification Guide: MEDDEV 2.4/1

9. References

Internal Procedures Presafe.

Regulation, Guides, Standards cited along this document.

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