

Documentation Submissions

Best Practice Guidelines

**Everything
you need to know
to successfully
submit technical
documentation for
certification.**

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Our mission is to ensure patient safety while supporting timely access to global medical device technology. We strive to set the global standard in thorough, responsive, predictable conformity assessments, evaluations, and certifications.

Our commitment to excellence

Manufacturers tell us they need to work with a highly competent, customer focused Notified Body that understands the specifics of their environment and the importance of complete confidentiality around patent pending new technology.

Our services are designed to align with the steps individual clients need to take to understand what is best practice, how to achieve it and ensure that it remains an ongoing habit.

We provide rigorous quality management reviews and product certifications for medical device manufacturers around the world, and we can do it for you too.

1 Introduction

As a Notified Body, BSI receives significant numbers of submissions; we review all the technical documentation and this can lead to a certification being issued. The technical document received into BSI for submission varies in quality, and therefore we have created this guide to help you submit documentation that will lead to an efficient review with the minimum rounds of questioning, and so increasing your speed to market.

There are two significant reasons for slow review times of a technical document (design dossier, technical file, renewal application, etc):

- BSI is not provided with all of the information needed for the review.
- The information is present within a technical document, but, it is difficult to locate.

BSI Medical Devices proposes the following guidelines informally known as Documentation Submissions: Best Practice Guidelines.

We are a respected, world-class Notified Body dedicated to providing rigorous regulatory and quality management reviews and product certifications for medical device manufacturers — around the world. For more than 100 years, BSI's expertise has provided an assurance of safety and quality to manufacturers in over 150 countries.

Welcome to
your personal
guide to efficient
Technical
Documentation.

2 Submission and Technical Document Contents

2.1 The cover letter

Three things are required for any technical review:

- Context (ie, an explanation of what is being requested and why)
- The technical documentation itself (ie, objective evidence to demonstrate compliance)
- Authorization for BSI to carry out the work.

The submission should therefore contain at least the following details:

- CE Certificate # reference(s);
- The type of review (new product, design change, shelf life extension, etc);
- Brief product description, including model numbers involved, etc;
- BSI Ref. # (EQ or SMO #) for any other relevant submissions (for example, concurrent applications which may affect the submission);
- An explanation of what has been submitted and how it demonstrates compliance;

and, for changes to existing certification:

- An explanation of
 - what is affected (packaging, material change, sterilization, etc) and
 - what is not affected (along with appropriate justification).

2.2 The technical documentation

To assist manufacturers in determining the correct information to provide to BSI, guidance is provided in **Attachment A**. Associated reference documents are listed in **Attachment B** for additional guidance.

2.3 Authorization for the work to be conducted

The following will be required before work can commence:

- A signed approved quote **or**
- A signed BSI Work Authorisation form (for existing clients and certificates only)

Please note that, as far as is practical, submissions should be "stand alone", and not refer to previous submissions for evidence of compliance. The reason is that the reviewer must assess the documentation in the context of the intended submission, and confirm that it is still relevant within this context. If a submission must draw upon information previously submitted to BSI, please include the relevant report or document which demonstrates compliance, rather than directing the reviewer to the earlier review. This will save time (eg, in finding the report, confirming that the correct report has been found, confirming whether or not there have been any changes affecting its relevance to the current application, etc).

Technical documentation guidance notes

Guidance **ATTACHMENT A** can be found on page 11.

Guidance **ATTACHMENT B** can be found on page 26.

A signed BSI Work Authorization form will be required from existing clients before work can commence.

3 Submission Method

3.1 In order to facilitate faster reviews the following is suggested:

- **The preferred route for submissions is via the secure BSI document upload portal.** If you do not have access to the BSI document upload portal, please contact your Scheme Manager or their administrative support for information on how you can set this up for your company.
- **Alternatively, documents may be submitted by email.** This route is normally only feasible for small submissions requiring relatively few documents of small file size.
- **We DO NOT need to receive a hard copy of the information.** If hardcopies are received *in lieu* of electronic files, these will need to be converted to the format described in section 4 below by our administration team. This will add time and cost to the review.

The preferred route for submissions is via the secure BSI document upload portal.

4 Document Format

4.1 Language

- The official language of BSI and BSI's Competent Authority is English, all submissions and test results should be in the English language. Submissions in other languages may result in additional review time and costs for translation which will be passed on to the applicant.
- For Class III design dossiers all documentation must be available in the English language. The primary language for all audit related documents is English.
- Technical files for Class IIa and IIb devices may be accepted in a local language as long as the UK Competent Authority does not require technical files to be in the English language and that BSI is able to allocate technical reviewers with correct competencies and language capabilities.

4.2 Electronic File Format

4.2.1 Format and file size limits

- **The preferred document format is PDF.** However, it may be possible to accept the information in any readily available software format including Microsoft Word. Again, time and cost will be added to the review by converting these files to PDF with bookmarks.
- Documents should be **formatted into paginated (if possible) fully searchable PDF files (< 500 Mb) with bookmarks** for ease of locating specific content. The benefit of this is faster review time because of clear organization for the reviewer. Another benefit is quick referencing for future submissions that build upon previous submission history.
- Please submit the information in a single PDF file if possible. If file size prohibits this, please organise the submission into the smallest number of files possible. For typical files, no more than two PDFs should normally be required. To aid this process, please indicate the order in which the documents should be compiled. A logical numbering of files is preferred (e.g. using Part 1 of x, Part 2 of x, Part 3 of x...Part x of x at the beginning of the title of each file).

Once BSI has the information, we will make any adjustments as necessary (eg OCR it, bookmark it, paginate it and add headers and footers as required). The marked-up PDF becomes the final archived version.

PDF files / attachments should not be file protected or locked as this prevents necessary access and file manipulation for archiving.

PDF files and attachments should not be file protected or locked.

The preferred document format is a paginated and searchable PDF.

4.2.2 Optical Character Recognition, OCR, (searchable format)

- Manufacturers scanning directly from a printed page should utilize Optical Character Recognition (OCR) so that as much of the resultant PDF file is searchable as possible.
- Non-searchable submissions will be subjected to OCR conversion adding review time.

4.2.3 Bookmarks

- Bookmarks are requested to aid in locating major sections of the technical document. At a minimum, the GHTEF STED sections should be bookmarked.
- Sometimes random bookmarks based on document headings and subheadings are created when documents are converted to PDF format. These bookmarks should be edited to provide clear document references and to remove excessive, unnecessary or confusing bookmarks.
- Clear organization and easy navigation will make it easier to find documents and will therefore reduce overall time required for the review.

4.2.4 Pagination

- Each page of the submission should have a separate, sequential page number, starting with 1. It doesn't matter how many pages, volumes, or binders are submitted – each page should have a unique number.
- PDF files are automatically numbered. When referencing page numbers, please be clear as to whether the original dossier page or the PDF file page is being used.
- Pagination is not mandatory, as BSI can add this with our software. Documents received without proper pagination however will incur added review time to properly format the submission.

4.2.5 Signatures

Signatures are required for any signed document in the file, including BSI Work Authorization Forms and signed quotes. Signatures can be handled in a number of ways:

- Documents may be digitally signed.
- Signature pages can be scanned in and inserted into the electronic document.
- A 'marker page' can be inserted into the document indicating that the signatures have been provided separately to BSI electronically. BSI will scan and insert these pages into the file, logging the time to do so.

GHTEF Summary Technical Documentation, STED

GHTEF Guidance Document SG1/N063 provides recommendations on the content of summary technical documentation to be assembled and submitted to a Regulatory Authority or Conformity Assessment Body.

5 Submission Process

5.1 The following is a guide to the submission process.

- a) Notify BSI that you have an application for review. For new clients, this will generally be via a member of the sales team (www.bsigroup.com/medical). For existing clients, this will be your Scheme Manager, or a member of the administration team. Email and phone are the preferred means of contact.
- b) If a Work Authorization Form is required, ensure that the form is signed, dated, and completed with the following details:
 - Company Name and Title of Submission.
 - Details of the certificate(s) affected (certificate numbers starting with CE; for Class III devices this will typically be a Design Examination certificate rather than a Quality Assurance certificate).
 - Appropriate box ticked to indicate review speed required (Regular/ Fast Track/ Dedicated/ On-site).
- c) Once the signed approved quote or Work Authorization Form (see Section 2.3 above) has been submitted, BSI can assign a reviewer. At that time BSI will assign a unique identification number (SMO and/ or EQ) for your review and contact you with that number. We ask that you reference those numbers in any email correspondence with BSI during the review process.
- d) The review process will begin upon receipt of the submission (Section 2) AND the signed BSI Work Authorization Form/ signed quote.



**Your contact
at BSI can be
reached by
email or
telephone.**

6 Things to Consider When Preparing a Technical Document for Submission

6.1 Manufacturer Personnel Support

Please ensure appropriate manufacturer resources (RA, QA, R&D, Manufacturing, etc) are available during our On-site or Dedicated reviews. The quicker the information can be provided the quicker questions can be closed out and certificates issued.

6.2 Document Availability

If a pointer system is used for technical documentation, ensure key documents supporting STED sections are made available to the reviewer/ auditor at the time of the initial submission. If these documents are not provided, the submission may be rejected or much of the first round of questions may be devoted to asking for them, which will delay the start of the full review. Please remember that the reviewer must see the manufacturer's conclusions regarding compliance, as well as the objective evidence necessary to support those conclusions.

6.3 Certificate Scope

Sometimes the addition of new products, or even changes to existing products, can affect the scope of the associated Quality System certificate (eg, Annex II excluding section 4). If the scope(s) of the existing certificate(s) do not cover the product or processes affected, additional work and time will be required to reissue the affected certificates:

- Sufficient evidence must be reviewed to support scope change; this may require Quality System or Microbiology audits in addition to the Technical File/ Design Dossier review requested.
- If in doubt, discuss the scope with your BSI Scheme Manager prior to submitting. Your Scheme Manager will coordinate the scope change activities.

Ensure key documents supporting STED sections are made available to the reviewer/auditor immediately.

6.4 Subcontractors

Are there any changes to subcontractors related to the application?

- All significant subcontractors must be added to the associated Quality System certificate(s) and the Unannounced Audit Visit schedule, so please ensure that your Scheme Manager and reviewer are aware of any changes. If you are unsure whether a subcontractor is significant, discuss with your Scheme Manager.
- Subcontractors who do not hold a valid ISO 13485 certificate issued by an EU Notified Body or one of its direct subsidiaries (e.g. TUV Americas) may require a subcontractor verification audit, depending on the scope of their activities and the verification activities undertaken by the manufacturer. Please ensure that these details are made clear in the application.
- If design is subcontracted, control of this subcontracted activity must be considered.

6.5 Accessories

Are any new devices or instruments used with the products under review? If a Class III device, for example, requires the use of new Class IIa, Class Im or Class Is equipment which is not within the scope of the existing Quality Management certification, additional technical file reviews may be required for these accessories.

Please provide the following information for any accessories associated with your device:

- Brief description of the accessory/ accessories and how they are used with the device(s).
- Classification of the accessories and rationale for classification.
- Technical Documentation references (file name, issue status, date).
- Evidence of compatibility with the subject devices (eg, in accordance with Essential Requirement 9.1 of 93/42/EEC).

6.6 Novelty

Are any new (new to manufacturer or new to medical device industry) or innovative materials, processes, assemblies or techniques associated with the devices?

- Additional consultations may be required for novel or high risk materials, manufacturing processes, devices or indications. These may include toxicologists, statisticians, or clinicians.
- Some materials (eg medicinal substances or animal tissues and their derivatives) may require additional regulatory consultations.
- BSI reviewers will still work within timescales indicated for the review process selected, but external consultations may fall outside these timescales, and therefore Fast Track and Dedicated review timelines cannot be guaranteed. Please discuss with your Scheme Manager, to select the most appropriate review option.



**ATTACHMENT A:
Information to
provide in your
Technical
Documentation
Submission**

7 Technical Documentation Sections and Information Required

7.1 Administrative information

7.1.1 Manufacturer name and address

The application should identify the name and location of the legal manufacturer who is placing the devices on the market. This should be consistent across the device labels, IFU and Declarations of Conformity.

7.1.2 EU Representative and Subcontractors

The name and location of the EU Representative should be identified. Only one EU Representative should be identified, and this should be consistent across the device labels, IFU and Declarations of Conformity.

7.1.3 File date and issue number

The file status and revision history should be provided. Individual documents should also indicate date, revision history and status.

7.1.4 Directive(s)

Please indicate which Directive and/ or Regulations apply. If a device is governed by multiple Directives or Regulations, all applicable Directives/ Regulations should be identified. For example:

- If the device is intended to be used in accordance with both the MDD and 89/686/EEC (personal protective equipment), ensure that the relevant basic health and safety requirements of Directive 89/686/EEC have been met.
- If the device is also machinery (within Article 2a of 2006/42/EC), ensure fulfilment of the relevant basic health and safety requirements of Directive 2006/42/EC Annex I have been met.
- If the devices have been impacted by subsequent directives/ regulations (e.g. 2005/50/EC, 2003/12/EC, 722/2012) ensure that these are identified and any new requirements met.

Please indicate which Directive and / or Regulations apply.

**Please indicate
the device
classification
and rationale.**

7.1.5 Device identification

A complete list of product codes should be provided.
GMDN Code and Device subcategory/ Generic Device Group should be identified.

7.1.6 Device classification

Please indicate the device classification and rationale. The rationale should address each point of the selected classification rule.

If the device contains multiple components that on their own might be classed differently, please note:

- If several rules apply to the same device, based on the performance specified for the device by the manufacturer, the strictest rules resulting in the higher classification shall apply.
- If multiple classification rules apply, all should be identified.

7.1.7 Related previous submissions

Details of any other submissions relevant to the application, including BSI reference number (SMO and/ or EQ) should be provided.

7.1.8 Accessories

The following information should be provided for any accessories (including Class I) associated with the device:

- Brief description of the accessory/ accessories and how they are used with the device(s)
- Classification of the accessories and rationale for classification
- Technical Documentation references (file name, issue status, date)

Please note (as indicated in Section 6.5), evidence should also be provided within the Technical Documentation to demonstrate compatibility of the devices with any applicable accessories.

7.2 Technical documentation

7.2.1 Device description

The device description should enable understanding of the design, packaging, sterilisation, or other characteristics of the device.

- Sufficient information should be provided to distinguish different variants of the device, and the intended purpose of different design features. For example, if one variant of a device has a coating and another does not, what is the intended purpose of that coating, and why are both variants considered to meet the requirements for safety and performance?
- Pictures and schematics should be provided wherever possible to enable an understanding of the device design features and intended purpose.

7.2.2 Intended use

The intended use should provide sufficient detail to explain the disease conditions the device is intended to treat or monitor, the basic principles of operation (ie intended users and environment), the intended patient population and the indications and contraindications of the device.

- Indications and contraindications should be supported by objective evidence (eg, evidence provided in the risk assessment and clinical evaluation reports).
- The intended use must include use of the device as a "medical device" as defined by Article 1 of the respective Directives unless this is otherwise justified.
- Please ensure the intended use been described consistently throughout the file (eg. in the IFU, risk management documentation, clinical evaluation report, and design requirements).
- If the application includes a change to the intended use, all sections of the file should be reviewed for potential impact.
- For clarity it is suggested that this should be separate from the device description.

7.2.3 Market history

All submissions should be accompanied by a market history to enable an understanding of the context of device development.

- If the device is new and has never been marketed by the manufacturer anywhere in the world, please state this explicitly.
- For existing devices:
 - Ensure that a market history is provided indicating the nature and timing of any changes and that any associated documents (i.e. risk analyses, labelling, clinical evaluation reports, verification/ validation data, etc.) account for these changes.
 - Provide evidence (eg SMO/ EQ references of reviews) to demonstrate that BSI has been notified of all significant changes (if applicable).

7.2.4 Sales, complaints and vigilance

Please provide sales, complaints and vigilance data for the last 5 years for your device, if available.

- Sales and complaints data should include sales outside of the EU. A breakdown should be provided to enable evaluation of sales and complaints by region.
- Complaints data should be evaluated rather than just listed. For example, why is the complaints rate considered acceptable? Have any trends been noted, or corrective actions taken? What is the status of these actions?
- Full details of vigilance issues should be provided, including the status of any Field Safety Corrective Actions or Notices. This data should include FSCA or FSN outside the EU, if related to a device which is sold in the EU.

7.2.5 Draft Declaration of Conformity

Ideally, the Declaration of Conformity should include:

- Manufacturer's name and address.
- EU Representative's name and address (if applicable).
- Compliance Statement with relevant Directive, indicating that the manufacturer is exclusively responsible for the Declaration of Conformity (see NB-Med Consensus statement S99/01).
- Conformity route (ie Annex and certification).
- Product name(s), or other unambiguous reference of declaration scope (may be supplemented with an appendix with product codes and descriptions if appropriate). The specific product codes and variants covered by the DoC should be clear.
- Signature line indicating appropriate responsible person and date.

The manufacturer may wish to consider guidance on content of the DoC (see Attachment B for links to this guidance).



Full details of vigilance issues should be provided.

7.2.6 Technical Standards

The documentation should demonstrate that all relevant standards, both harmonized and product-specific, have been considered. This is usually accomplished by means of a list of applicable standards, as well as by reference to appropriate standards in the appropriate documents (eg test reports). See Attachment B for a link to the most up to date list of harmonized standards.

- When identifying applicable standards, indicate if full or partial compliance is being claimed.
- Where key standards have not been applied or not been applied in full, appropriate justification should be provided in the technical documentation. A summary or gap analysis regarding ability to comply with associated Essential Requirements, and a risk analysis & conclusion of acceptability of any compliance gaps should be provided.
- Please indicate if there have been any changes to applicable standards since the technical documentation was last reviewed by BSI. The technical documentation should continue to demonstrate that the files meet the state of the art, including consideration of revised or replaced standards.

7.2.7 Essential Requirements

It is helpful to provide an Essential Requirement Checklist (ERC) to show how compliance with the ERs has been achieved.

- Useful information to provide in an ERC includes: a reference to the ER, an indication as to whether or not it is applicable, details of applicable standards, the location of any supporting information (eg test reports), and a rationale for any ERs not considered applicable.
- The more specific the references are to documents supporting compliance, the faster the review can be conducted.



**Essential
Requirements
Checklist
(ERC)**

Supporting evidence should be provided for any claims made in the labelling.

7.2.8 Manufacturing process and subcontractors

- A detailed overview of the manufacturing processes should be provided. This should clearly identify any special or proprietary processes, and any subcontracted processes.
- The name and location of key manufacturing subcontractors should be provided.
- If new key subcontractors are used, provide copies of their ISO 13485 certificates. If a key subcontractor does not have an ISO 13485 certificate with a valid scope from a Notified Body, additional supplier audits may need to be arranged (see Section 6 for further information).
- Validation documents for processes that can affect final product quality should be provided.

7.2.9 User information

Documents may include labels, instructions for use (IFU), patient implant cards, surgical manuals, brochures, marketing literature, etc

- Legible versions of all levels of labels should be provided (e.g. secondary pack, primary pack) and should be representative of the finished form, showing all included symbols.
- It is sufficient to show information concerning labelling in English only, but items to be translated and the plan for translation should be indicated.
- If possible, provide drawings with the packaging configuration (showing placement of all labels) and label specifications.
- The position of labels on the finished product should be clear. If any of the packaging is printed with information for the user (including pictures/ schematics of the device) this should also be provided.
- It should be clear how the labelling documents are controlled.
- Supporting evidence should be provided for any claims made in the labelling or marketing literature.
- Please ensure that any specific requirements of relevant harmonized standards are addressed in the labels and information for use.

7.2.10 Design verification and validation

Product design specifications should be adequately documented, outlining the key functional characteristics and technical performance specifications for each device, along with verification/ validation tests to substantiate that they have been achieved.

- Overall, manufacturers should demonstrate that design requirements have been identified in accordance with the intended use, safety and performance requirements, risk assessments, and relevant harmonised and other key standards.
- To this end, the source of design requirements should be indicated. Although compliance to harmonised and other key standards is expected, please be aware that testing beyond that required by the standards may be necessary to demonstrate compliance of your device to the relevant Essential Requirements. Design requirements should be mapped to the intended use, performance and risks identified for the device.
- A design verification/ validation strategy document and/ or summary of the outcomes should be provided. Verification/ validation results should be provided for each design requirement. If compliance has been demonstrated without testing, an appropriate rationale should be provided.
- Test reports should document objectives, acceptance criteria, materials & methods, results, protocol deviations, and conclusions.
 - If test results are considered representative for a group of devices (i.e. worst case devices or comparative devices), then a justification for leveraging protocol(s) and report(s) should be provided.
 - Similarly, if testing has been undertaken on prototypes or devices that otherwise do not represent the finished goods, a justification for the adequacy of this testing should be provided.
 - If multiple design verification / validation studies were conducted please provide a flow chart or table that shows how the studies were conducted and highlight which study ultimately demonstrates that the design meets the product performance specifications.
- For line extensions or devices based on "existing" devices, it may be possible to leverage data from testing undertaken on the existing devices. In this case, a rationale for the use of existing data must be provided, including:
 - Evidence of equivalence to the comparative devices – a table showing the similarities and differences greatly speeds the review process. Key things to consider include (but may not be limited to):
 - materials of construction
 - indications for use
 - methods of manufacturing
 - key design features
 - An evaluation of the impact of any differences on clinical safety, performance, and testing undertaken. The evaluation should support the conclusion that the new devices do not represent a worst case in terms of testing as compared to the devices tested.

7.2.11 Risk management

A thorough design, clinical and process Risk Management assessment should be conducted for the entire life-cycle of the device (from initial design concept up to and including device disposal). This should be updated (as appropriate) with data from PMS.

- The risk management documentation should provide a template for preparedness, indicating whether controls (i.e. process validations, biocompatibility, sterilisation, clinical, shelf-life or other key verification / validation tests) have reduced all risks as low as possible (vs. as low as reasonably practicable) to acceptable levels in light of state-of-the-art for the product(s) under review.
- The assessment must demonstrate that the benefits outweigh all the residual risks when the device is used as intended.
- The analysis must demonstrate that appropriate controls (design out then protective measures) have been applied to all risks.
- Information for use may reduce occurrence of some risks, but it cannot reduce the occurrence of residual risks. Please ensure appropriate use and quantification of risk control measures in the risk assessment.
- A copy of Risk Management Procedure(s) that include the definition of any rating systems used for risk analysis and risk acceptability should be provided.

For line extensions and devices based upon existing devices, the manufacturer may conclude that pre-existing risk management documentation is applicable. However, there are always risks associated with even small changes, and a summary to demonstrate that these risks have been considered (and have been adequately mitigated) should be provided.



A thorough design, clinical and process Risk Management assessment should be conducted.

7.2.12 Clinical evaluation

Clinical evaluations are required for all medical devices. For devices without suitable equivalents and/ or insufficient data in the literature, a pre-market clinical investigation may be required. Guidance is available in MedDev 2.7.1, GHTF SG5 N2R8 and EN ISO 14155. See Attachment B for links to these guidance documents.

- It is useful to provide a copy of the procedure for conducting Clinical Evaluation.
- If a pre-market clinical investigation has been conducted, please ensure:
 - appropriate documentation (CIP, letter of “no objection” from the Competent Authority, evidence of Ethics approval, final report, etc) is provided;
 - the final clinical trial protocol agrees with that submitted to the Competent Authority, and evidence that any deviations have been agreed with the CA has been provided;
 - the final report demonstrates that requirements for all safety and performance endpoints have been met;
 - there are no open clinical investigations relevant to your devices with endpoints related to safety or performance claims.
- Representative clinical data must be provided for all indications and variants. Justifications for why one group of data is representative of another must be clearly substantiated.
- If no clinical investigation data is available for the subject device and the Clinical Evaluation relies on a justification of equivalence of comparative devices, the justification must identify and discuss the potential clinical impact of all differences between the subject and comparable devices relative to intended use, technical, or biological factors.
- A justification should be provided (with appropriate evidence) to substantiate the qualifications of individual(s) conducting/ approving the clinical evaluation.
- Some indications or specific clinical benefit claims may require the Notified Body to consult with an external expert (a surgeon or similar). Contracting a confidential source that is mutually agreed with the Manufacturer may be time consuming.

**Clinical evaluations are required
for all medical devices.**

7.2.13 PMS and PMCF

A Post-marketing Surveillance Plan (PMS Plan) commensurate with the product risk, lifetime, and available clinical data should be provided for each device/ device family.

- Ensure that the PMS plan adequately justifies the monitoring of the safety and intended performance of the device.
- If Post-Market Clinical Follow-up (PMCF) is not part of the PMS Plan, please ensure that adequate justification is provided, based on the risk and clinical data available for the device.
- A copy of the Post Market Surveillance procedure should also be provided. Please note that the procedure is not the same as the Plan – the former refers to the manufacturer’s quality system requirements and is generic to all devices marketed by a manufacturer, whereas the latter is specific to the subject device, and can only be generated in light of data from the clinical evaluation and risk evaluation for that device.

See Attachment B for links to guidance for PMS and PMCF.

7.2.14 Biological safety

- Biological safety assessments should be undertaken in accordance with ISO 10993-1. See Clause 7 of this standard for guidance with respect to appropriate report content.
- Additional guidance has been published by MHRA. See Attachment B for a link to this guidance.
- Biocompatibility assessments should include evidence of compliance for the finished device (including consideration of all materials and all manufacturing steps). It is not sufficient to simply state that devices have been manufactured from materials of well-established biological safety – an assessment which takes into account the impact of manufacturing and sterilization processes, intended use, leachable substances, degradation products etc. must be provided.
- The assessment should categorize the nature and duration of body contact for each component and identify any tests that are required or can be waived to establish evidence of compatibility.
- A justification should be provided regarding the qualifications of those involved in planning, executing, and analyzing the biocompatibility assessment.



**For further
guidance refer to
Attachment B.**

7.2.15 Sterilisation validation

Sterilisation validation is reviewed separately by BSI Microbiology experts.

- Appropriate rationales are required if sterilization validation is by adoption into an existing family or sterilisation validation.
- Devices for End-User-Sterilisation also require review of cleaning and sterilisation validation/ adoption with respect to parameters recommended in the IFU.
- Documents should describe:
 - use of “State of the art” process validation methods;
 - the bioburden controls and monitoring;
 - the product qualification (Dose verification, BI suitability testing, SAL calculations);
 - the process qualification (Performance qualification, Dose Map, BI Inactivations).

Additional guidance relating to specific document types is provided below:

Shelf Life Validation should include:

- Protocol (with acceptance criteria for each test performed) and appropriate test references;
- A clear statement of the intended shelf life;
- A clear statement defining the sterilization status of the test samples (1X, 2X sterilized);
- A summary of the accelerated aging parameters (temperature and humidity) and how the aging times were calculated;
- A statement covering Real Time Aging plans;
- A clear delineation of statistically significant sample quantities;
- Actual physical/microbiological test data reports supporting the expiration date, or post aging, claim (peel testing, burst testing, dye testing, etc);
- A summary of the ship testing/ transit simulation testing conducted and applicable test reports.

Sterilization Validation – Radiation should include:

- Protocol;
- Dosimetry mapping data (typically from the sterilization contractor);
- Validation of bioburden testing method & test report;
- Bioburden determination & test reports;
- Calculation or determination of verification dose and full dose;
- Validation of product sterility testing method & test report;
- Sterility testing of verification dose samples & test report.

Sterilization Validation – Ethylene Oxide should include:

- Protocol;
- Summaries regarding commissioning of the sterilization equipment;
- Validation of bioburden testing method & test report;
- Bioburden determination and test reports;
- Biological indicator data;
- All cycle data and test reports (fractional, half, full);
- Validation of product sterility testing method & test report;
- Product sterility testing & test report;
- Sterilant residual analysis reports.

End User Sterilization Product documentation should include:

- Instructions for use that detail the validated sterilization and cleaning parameters. Please be aware that reference to "standard hospital practice" is insufficient;
- Validation report for the sterilization parameters listed in the IFU;
- Validation report for the cleaning parameters listing in the IFU.

7.2.16 Packaging

- Packaging testing should address requirements for both transit endurance and shelf life stability, and be undertaken in accordance with relevant standards.
- A complete packaging BoM and diagrams should be provided to illustrate how each device is packaged.
- If all packaging configurations/ device combinations have not been tested, a rationale based on worst case (ie heaviest and lightest devices, sharp or pointy edges, etc) should be provided.
- Any change to packaging is considered a significant change. For Class III devices, these must be reported to BSI for review and certificate re-issue.

7.2.17 Shelf life and stability testing

- Shelf life is normally considered to be the time the device can be kept in the packaging prior to use. This is not the same as "Lifetime".
- Shelf-life testing is not restricted to the packaging. The device itself should be subject to shelf life testing, or a rationale provided to demonstrate why its characteristics are not expected to degrade over the claimed shelf life.
- If shelf life testing is based on accelerated age testing, this should be accompanied by a plan for real time testing. Real time testing should be underway by the time documentation is submitted for review.

7.2.18 Product lifetime

- The lifetime of the device should be defined, and considered relative to other parts of the dossier (e.g. risk management, clinical evaluation, PMS).
- Product lifetime is normally considered as the time from manufacture until the device ceases to fulfil its intended use. This is not the same as "Shelf Life".

7.2.19 Medicinal substances/Human blood derivative & recombinant protein/peptides

- The submission should clearly indicate whether or not the device contains any medicinal substances and /or human blood derivatives and/ or recombinant peptides/proteins. Full justification on the primary mode of action of the device and evidence that the above components are ancillary should be provided.
- Devices which incorporate, as an integral part, an ancillary medicinal substance or an ancillary human blood derivative or ancillary recombinant protein/ peptide are subject to requirements of additional European Directives/ Regulations.
- Additional review resources will be required, and under the amending Directive 2007/47/EC, a consultation with one of the Competent Bodies established under Directive 2001/83/EC or EMA (The European Medicines Agency) is required. Information on the medicinal substance (ASMF, if available) or an ancillary human blood derivative (PMF) or ancillary recombinant protein/ peptide itself and as incorporated in the device should be submitted.

Animal derived substances

The submission should clearly indicate whether or not the device utilizes, or is used in conjunction with, any materials of animal origin.

- Manufacturing subcontractors should be consulted if appropriate to establish if any such substances are used during manufacture, even if they do not feature in the final device (eg lubricants or mould release agents which may use animal derived substances). If in doubt, speak with your Scheme Manager before submitting a dossier.
- Evidence demonstrating compliance with the relevant clauses of EN ISO 22442 (parts 1-3) should be provided.
- Devices which incorporate materials from TSE-susceptible species will be subject to Regulation 722/2012 and the conformity assessment route will require Competent Authority consultation.

7.2.20 Software

Appropriate documentation is required if the medical devices are either stand-alone software or rely upon software.

- If medical device is stand-alone software, guidance for the qualification and classification of the software is found in MEDDEV 2.1/6. See Attachment B for a link to this guidance.
- There should be a rationale for why the software is a medical device and for its classification. If applicable, the software should be broken down into modules, some that have a medical purpose and some that do not. The modules with a medical purpose must comply with the requirements of the Medical Device Directives and must carry the CE marking. The non-medical device modules are not subject to the requirements for medical devices.
- Ensure all relevant harmonised and non-harmonised software standards have been considered. Ensure the software systems/ modules/ items have been assigned safety classifications based on standards.
- Include documentation on the medical device software life-cycle processes implemented (e.g. software design/ development, maintenance/ change management, risk management, configuration management, problem resolution, verification, and validation processes).
- Include software development process documentation (e.g. software development plan, software requirements specification, software architecture, software detailed design, software unit testing procedures/ reports, software integration testing procedures/reports, and software system testing) and maintenance process documentation (e.g. software maintenance plan). Note: Some documentation may or may not be required per the standards based on software system/ module/ item risk classification.
- Include software risk assessment documentation (e.g. software hazard analysis, software failure mode and effects analysis, fault tree analysis, traceability). Note: Some documentation may or may not be required per the standards based on software system/ module/ item risk classification.



**Software
Modules with a
medical purpose
must comply with
the Medical Device
Directives.**



ATTACHMENT B:
Reference
Documents

8 Technical Documentation General Guidance

8.1 Technical Documentation General Guidance

- IMDRF/RPS WG/N9FINAL:2014 Non-In Vitro Diagnostic Device Market Authorization Table of Contents (nIVD MA ToC)
<http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-140630-rps-nivd-toc.pdf>
- IMDRF/RPS WG/N13FINAL:2014 In Vitro Diagnostic Medical Device Market Authorization Table of Contents (IVD MA ToC)
<http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-140630-rps-ivd-toc.pdf>
- IMDRF/RPS WG (PD1)/N27R1 Assembly and Technical Guide for IMDRF Table of Contents (ToC) Submissions (ToC-based submissions)
<http://www.imdrf.org/docs/imdrf/final/consultations/imdrf-cons-rps-atg-imdrf-toc-150409.pdf>
- Points to Consider in the use of the IMDRF Table of Content for Medical Device Submissions pre-RPS
<http://www.imdrf.org/docs/imdrf/final/procedural/imdrf-proc-140821-rps-wg-toc.pdf>
- 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)."
<http://www.imdrf.org/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n011-2008-principles-safety-performance-medical-devices-080221.pdf>
- 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."
<http://www.imdrf.org/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n063-2011-summary-technical-documentation-ivd-safety-conformity-110317.pdf>
- NB-MED/2.5.1, "Technical documentation"
http://www.meddev.info/_documents/R2_5_1-5_rev4.pdf
- NBOG's Best Practice Guide, "Guidance on Design-Dossier Examination and Report Content"
http://www.nbog.eu/resources/NBOG_BPG_2009_1.pdf

9 Change Reporting

- NB-MED Reporting of Design Changes and Changes of the Quality System
http://www.team-nb.org/wp-content/uploads/2015/05/nbmeddocuments/Approved_NB-MED_2_5_2_rec_2_november_2008.pdf

10 Regulatory Guidance Organisations

- EC Commission MEDDEV Guidance – various topics http://ec.europa.eu/health/medical-devices/documents/guidelines/index_en.htm
- International Medical Device Regulators Forum (IMDRF) – various topics, access to all GHTF final documents
<http://www.imdrf.org/>
- NB-MED Guidance – various topics <http://www.team-nb.org/>
- MHRA Devices Regulatory Guidance – various topics <http://www.mhra.gov.uk/Publications/Regulatoryguidance/Devices/index.htm>
- GMDN Agency – medical device nomenclature/generic device groups per ISO 15225
<http://www.gmdnagency.com/>

11 Specific Topic Guidance

11.1 Clinical Evaluation Guidance

- Clinical evaluation: Guide for manufacturers and Notified Bodies - MEDDEV 2.7.1
http://ec.europa.eu/health/medical-devices/files/meddev/2_7_1rev_3_en.pdf
- GHTF Study group 5, Document SG5/N8 on Clinical Evidence for IVD Medical Devices
<http://www.imdrf.org/docs/ghtf/final/sg5/technical-docs/ghtf-sg5-n8-2012-clinical-performance-studies-ivd-medical-devices-121102.pdf>
- GHTF Study group 5, Document SG5/N2R8 on Clinical Evaluation
<http://www.imdrf.org/docs/ghtf/final/sg5/technical-docs/ghtf-sg5-n2r8-2007-clinical-evaluation-070501.pdf>

11.1.2 Biological Safety

- EN ISO 10993-1 Biological evaluation of medical devices -- Part 1: Evaluation and testing within a risk management process
- MHRA Guidance on Legislation: Clinical investigations of medical devices – biological safety assessment (November 2013)
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/376937/Biological_safety_assessment.pdf

11.1.3 PMS Guidance

- NB-MED Recommendation 2.12/1
http://www.meddev.info/_documents/R2_12-1_rev11.pdf

11.1.4 PMCF Guidance

- MEDDEV 2.12-2 Post Market Clinical Follow Up Studies
http://ec.europa.eu/growth/sectors/medical-devices/guidance/index_en.htm
- GHTF Study Group 5, Document SG5/N4 on Post Market Clinical Follow Up Studies
<http://www.imdrf.org/docs/ghtf/final/sg5/technical-docs/ghtf-sg5-n4-post-market-clinical-studies-100218.pdf>

11.1.5 Declaration of Conformity

- EN ISO /IEC 17050-1:2010 Conformity assessment. Supplier's declaration of conformity. General requirements
- NB-Med Consensus statement S99/01:
http://www.meddev.info/_documents/NBRG_ConsensusStatements0403-ver01-2003.pdf
- Guide to the implementation of directive based on the New Approach and the Global Approach; chapter 5.4 "EC declaration of conformity" (page 34-35) where minimum information required in declaration are described.
<http://ec.europa.eu/growth/single-market/goods/>

11.1.6 Standards

- EU Harmonised Standards
http://ec.europa.eu/growth/single-market/european-standards/harmonised-standards/medical-devices/index_en.htm
- BSI Online Standards <https://bsol.bsigroup.com>
- ISO Online Standards <http://www.iso.org/iso/home/standards.htm>
- ASTM Standards
<http://www.astm.org/Standards/medical-device-and-implant-standards.html>
<http://www.astm.org/TRACKER/filtrexx40.cgi?index.frm>

11.1.7 Shelf-Life

- ICH Guidelines Q Series
<http://www.ich.org/products/guidelines/quality/article/quality-guidelines.html>

11.1.8 Software Guidance

- MEDDEV 2.1/6 - Guidelines on the Qualification and Classification of Stand Alone Software Used in Healthcare Within the Regulatory Framework of Medical Devices
http://ec.europa.eu/growth/sectors/medical-devices/guidance/index_en.htm

11.1.9 Guidance on devices incorporating ancillary medicinal substances or ancillary human blood derivatives

- MEDDEV 2.1/3 Borderline products, drug-delivery products and medical devices incorporating, as an integral part, an ancillary medicinal substance or an ancillary human blood derivative
<http://ec.europa.eu/DocsRoom/documents/12867>
- EMA/CHMP/578661/2010 - EMA recommendation on the procedural aspects and dossier requirements for the consultation to the EMA by a notified body on an ancillary medicinal substance or an ancillary human blood derivative incorporated in a medical device or active implantable medical device
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000523.jsp&mid=WC0b01ac05800267b9
- MHRA Guidance on legislation: Borderlines between medical devices and medicinal products (June 2013)
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/284493/Borderlines_between_medical_devices_and_medicinal_products.pdf
- MHRA GUIDANCE NOTE No. 8 – A GUIDE TO WHAT IS A MEDICINAL PRODUCT (November 2012)
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/398998/A_guide_to_what_is_a_medicinal_product.pdf

Toronto Office

6205B Airport Road, Suite 414

Mississauga, ON L4V 1E3

T: 416 620 9991

TF: 1 800 862 6752

F: 416 620 9911

Ottawa Office

515 Legget Drive, Suite 110

Ottawa, ON K2K 3G4

T: 613 271 7007

TF: 1 800 862 6752

F: 613 271 9007

Montréal

1, Place Ville Marie, Suite 2901

Montréal, QC H3B 2C4

T: 514 940 1778

TF: 1 800 862 6752

F: 514 866 2115