

IVD 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

Prior to placing a device on the market, manufacturers shall undertake an assessment of the conformity of that device, in accordance with the applicable conformity assessment procedures set out in Article 9 of EU Council Directive 98/79/EC on In Vitro Diagnostic Medical Devices (IVD Directive, IVDD)

The application documentation for the Assessment of the Quality Management System as described in this document is aligned with the requirements of IVDD Annex IV (section 3.1) and Annex VII (3.1).

The technical documentation must allow assessment of the conformity of the product with the requirements (e.g. as listed in Annex I) of the IVDD. The technical documentation must include the elements as described in IVDD, Annex III (section 3) and Annex VIII (3) and the elements described in the appendix A of this document.

Medical Devices Notified Body BSI and IVD manufacturers both have an interest in speeding up the review of technical documentation (dossier, technical file, renewal application, etc.) and reducing time to issue certification.

As a Notified Body, BSI receives technical documentation for submission, which we review as part of the certification process. We have created this guide to help you submit documentation that will lead to an efficient review with the minimum rounds of questioning.

The two most frequent reasons for delays to technical documentation reviews are:

- BSI has not been provided with all of the information needed for the review, or
- The information is present within the technical documentation, but is difficult to locate.

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

2 Initial application package for Quality Management System

Per the IVDD, the manufacturer must lodge an application for assessment of its Quality System with a Notified Body.

Under IVDD Annex IV (Section 3.1) and Annex VII (3.1) the application must include the following set of information and documentation:

- the name and address of the manufacturer and any additional manufacturing site covered by the quality system,
- all the relevant information on the product or product category covered by the procedure,
- a written declaration that no application has been lodged with any other notified body for the same product-related quality system,
- the documentation on the quality system,
- an undertaking by the manufacturer to fulfil the obligations imposed by the quality system approved,
- an undertaking by the manufacturer to keep the approved Quality System adequate and efficacious,
- an undertaking by the manufacturer to institute and keep up to date a systematic procedure to review experience gained from devices in the post-production phase.

3 Submission and technical document contents

Three things are required for any technical review:

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

Your submission should therefore contain:

3.1 A cover letter

The cover letter should include an executive summary containing at least the following details:

- The type of review (new product, design change, shelf life extension, etc.)
- A brief product description, including classification and conformity assessment route, analytes and technology involved, etc.
- A BSI reference number (P 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:
 - what is affected (packaging, material change, life, etc.)
 - what is not affected (along with appropriate justification).

* a possible format for this explanation could be a table based on the sections of the dossier, as below:

Dossier section	Affected/Not Affected	Description of evidence submitted; for changes, impact on compliance or rationale for why this section is not affected
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Technical documentation guidance notes

Guidance **ATTACHMENT A** can be found on page 12.

Guidance **ATTACHMENT B** can be found on page 24.

3.2 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.

Please note that, as far as is practical, submissions should be “stand alone”, and not refer to previous submissions for evidence of compliance. The reviewer must be able to assess the documentation in the context of the intended submission, and confirm that it is still relevant within this context. If a submission draws 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.

3.3 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 Authorization form (for existing clients and certificates only).

3.4 Information required to support verification of manufactured product (Annex II List A devices only).

For Annex II List A devices, criteria setting is required; this is carried out in parallel to the technical documentation review. The following will be required:

- Three batches of product must be sent to the Paul Ehrlich Institute (PEI), BSI's chosen reference laboratory, to set criteria.
- These batches must meet the manufacturer's Quality Control (QC) specification and be in the same configuration as the Design Dossier submitted, with components clearly labelled with name, lot number and expiry date, and final draft Instructions For Use IFU.
- On-going batch release will require the following documentation:
 - The final QC release testing for that batch performed by the manufacturer.
 - Labelling (component and box labels as on the batch including lot number, expiry and IFU).

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

4 Submission method

- **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 5 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.

5 Document format

5.1 Language

- The official language of BSI is English, and 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, and subject to BSI terms.
- Technical assessments may be conducted in a local language, as long as BSI is able to allocate assessors with the correct competencies and language capabilities. For any assessment documentation produced in the local language, BSI requires an equivalent and full set of assessment documentation in English to also be available.
- For product specific reviews, BSI requires that the manufacturer's submission is in English. It may be acceptable during a transfer to only have the documentation partially available in English, and for the manufacturer to then translate the full technical documentation within 12 months of the transfer.

5.2 Electronic file format

5.2.1 Format and file size limits

- **Documents should ideally be provided as paginated, fully searchable bookmarked PDF files** (see Section 5.2.2 and 5.2.3 for further information on text recognition and bookmarks). Other software formats may be acceptable, but again, these files will need to be converted to PDF files with bookmarks, which will add time and cost to the review. Significant delays may result if files cannot be easily converted to this format.
- PDF files and attachments should not be file protected or locked as this prevents necessary access and file manipulation for archiving.
- Documents should be bookmarked to ensure ease of navigation (see section 5.2.3 for more information on bookmarking).
- Documents should be collated into a single document if possible. If this is not possible due to file size, the submission should be collated into the smallest number of individual files possible. Separate submissions will need to be indexed and consolidated, which may add to the time and cost of the review.

Once BSI has the technical documentation, 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 and attachments should not be file protected or locked.

The preferred document format is a paginated and searchable PDF.

5.2.2 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.

5.2.3 Bookmarks

- Bookmarks are requested to aid in locating major sections of the technical document. At a minimum, the GHTF 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.

5.2.4 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.

5.2.5 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.

GHTF Summary Technical Documentation, STED

GHTF 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.

6 Submission process

6.1 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; you can get in touch here www.bsigroup.com/talk. For existing clients, this will be your Scheme Manager, or a member of the administration team.
- b) If a Work Authorization Form is required, (see section 3.3) 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 IVD Annex II List A devices this will typically be a Design Examination certificate rather than a Quality Assurance certificate).
 - Appropriate box ticked to indicate review service required (CE-Standard/CE-Dedicated FastTrack/CE-Onsite FastTrack).
- c) Once the signed approved quote or Work Authorization Form has been submitted, BSI can assign a reviewer. At that time BSI will assign a unique reference number (SMO) for your review and contact you with that number. We ask that you use those reference numbers in any email correspondence with BSI during the review process.
- d) The review process will begin upon receipt of the submission (Section 3) AND the signed BSI Work Authorization Form/ signed quote.

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

7 Things to consider when preparing a technical document for submission

7.1 Manufacturer personnel support

Please ensure appropriate manufacturer resources (RA, QA, R&D, Manufacturing, etc) are available during CE-Dedicated FastTrack or CE-Onsite FastTrack reviews. The more quickly information can be provided, the more quickly questions can be closed and certificates issued.

7.2 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, 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.

7.3 Certificate scope

Sometimes the addition of new products, or even changes to existing products, can affect the scope of the associated Quality System certificate (e.g. Annex IV certificates). If the scope(s) of the existing certificate(s) do not cover the analyte, product or technology, additional work and time will be required to reissue the affected certificates:

- Sufficient evidence must be provided 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 submission. Your Scheme Manager will coordinate the scope change activities.

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

7.4 Subcontractors

Are there any changes to subcontractors related to the application?

- All significant subcontractors must be added to 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 which 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 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.

7.5 Accessories

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

- A brief description of the accessory/accessories and how they are used with the device(s).
- The classification of the accessories and rationale for classification.

7.6 Novelty

For Annex II List A and List B devices with any new technologies (or analytes) associated with the device:

- This may require additional time. BSI reviewers will still work as per the review process selected, but external consultations may delay the review process, and therefore CE-Dedicated FastTrack and CE-Onsite FastTrack may not be available for your review. Please discuss with your Scheme Manager to select the most appropriate review option.

**ATTACHMENT A:
Information to
provide in your
technical
documentation
submission.**

8 Technical documentation sections and information required

8.1 Administrative information

8.1.1 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, Instructions For Use (IFU) and Declarations of Conformity (DoC).

8.1.2 EU Authorized Representative and Subcontractors

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

8.1.3 File date and issue number

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

8.1.4 Directive(s)

Please indicate which Directive(s) applies.

If the device contains a medical device e.g. Lancet or swab, please confirm if this has been reviewed under the Medical Devices Directive.

8.1.5 Device identification

A complete list of product codes should be provided.



Please indicate which Directive(s) applies.

8.1.6 Device classification

Please indicate the device classification and rationale for classification.

8.1.7 Related previous submissions

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

8.1.8 Accessories

The following information should be provided for any accessories associated with the device:

- A brief description of the accessory/accessories and how they are used with the device(s).
- The classification of the accessories and rationale for classification.

8.2 Technical documentation

8.2.1 Device description

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

- Sufficient information should be provided to distinguish different presentations of the device, and the intended purpose of different design features.
- Ideally for self-test devices and point of care devices or if novel technology is being used, an example of the device may be requested. Talk to your Scheme Manager for confirmation of delivery details. If the device cannot be provided then pictures of the device should be included.

8.2.2 Intended use

The intended use should provide sufficient detail to explain the analyte that is being tested and, ideally how the result relates to a diagnosis. It should include the basic principles of operation (i.e. intended users and environment), the intended patient population of the device.

- Please ensure the intended use has been described consistently throughout the file (e.g. in the IFU, risk management documentation, performance 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 the intended use should be separate from the device description.

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

8.2.3 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 (e.g. SMO/EQ references of reviews) to demonstrate that BSI has been notified of all significant changes (if applicable).

8.2.4 Sales, complaints and vigilance


Please provide sales, complaints and vigilance data for the last five 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 (FSCAs) or Notices (FSNs). This data should include FSCAs or FSNs outside of the EU, if related to a device which is sold in the EU.

8.2.5 Draft Declaration of Conformity

Ideally, the DoC should include:

- Manufacturer's name and address.
- EU Authorized 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 (i.e. Annex and certification).
- Notified Body name and number.
- 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.



Full details of vigilance issues should be provided.

- 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).

8.2.6 Technical standards

The documentation should demonstrate that all relevant standards, both harmonized and product specific e.g. blood glucose, have been considered. 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. This should include 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.

8.2.7 Essential Requirements

It is helpful to provide an Essential Requirements Checklist (ERC) to show how compliance with the Essential Requirements (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 (e.g. test reports),
 - and a rationale for any ERs not considered applicable.
- Where an ER has multiple sub-requirements, either within text or as sub-sections/bullets, ensure all are considered.
- The more specific the references are to documents supporting compliance, the faster the review can be conducted.



**Complete
an Essential
Requirements
Checklist
(ERC).**

Assessment must demonstrate that the benefits outweigh all the residual risks when the device is used as intended.

8.2.8 Risk management

A thorough design 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 Post-Market Surveillance (PMS).

- The risk management documentation should provide a template for preparedness, indicating whether controls (i.e. process validations, performance evaluation, stability, usability 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.

8.2.9 Post-Market Surveillance (PMS)

A Post-Market Surveillance (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.
- A copy of the PMS procedure should also be provided. Please note that the procedure is not the same as the plan – the procedure refers to the manufacturer’s Quality System requirements and is generic to all devices marketed by a manufacturer, whereas the plan 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.

8.2.10 Design responsibility

Identify the name and address of manufacturing site(s) or subcontractor(s) responsible for design.

8.2.11 Product and design specifications

It is helpful to provide a table that links the design inputs/user needs to the design outputs/verification/validation.

8.2.12 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 design and manufacturing subcontractors should be provided e.g. perform final release testing, instrument manufacturers, software development.
- If new critical subcontractors are used, please provide copies of their ISO 13485 certificates. If a critical subcontractor does not have an ISO 13485 certificate from a Notified Body, additional supplier audits may need to be arranged (see Section 7.4 of the main document for further information).
- Validation documents for processes that can affect final product quality should be provided.



See
Attachment B
for links to
guidance for
PMS.

8.2.13 User information

Documents may include labels, Instructions For Use (IFU), 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, please provide photographs or 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.
- Please ensure that any specific requirements of relevant harmonized standards are addressed in the labels and information for use.

8.2.14 Design verification

- Overall, manufacturers should demonstrate that design requirements have been identified in accordance with the intended use, safety and performance requirements, risk assessments, and relevant harmonized and other key standards.
- To this end, the source of design requirements should be indicated. Although compliance to harmonized 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 or summary of the outcomes should be provided. Verification results should be provided for each design requirement. If compliance has been demonstrated without testing, an appropriate rationale should be provided.

It should be clear how the labelling documents are controlled.

- Test reports should document objectives, acceptance criteria, materials and methods, results, protocol deviations, and conclusions should be provided.
 - If test results are considered representative for a group of devices (i.e. worst case IVD or comparative IVD), then a justification for leveraging protocol(s) and report(s) should be provided.
 - Similarly, if testing has been undertaken on devices that otherwise do not represent the finished goods (i.e. not at final manufacturing scale), a justification for the adequacy of this testing should be provided.
 - If multiple design verification 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.
- An evaluation of the impact of any differences on clinical safety, performance, and testing undertaken should be provided. 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.

8.2.15 Compliance with Common Technical Specifications for Annex II List A devices

This should be in a form of a table tracing the requirements of the Common Technical Specifications (CTS) for the specific analyte to where the requirements have been shown to be met in the Design Dossier or the Quality Control (QC) testing specifications.

8.2.16 Performance evaluation

Performance evaluations/design validation are required for all IVDs.

See Attachment B Section 12.3 for links to these guidance documents.

It is helpful to show how compliance with the Essential Requirements has been achieved. Please include:

- Signed protocols.
- Signed reports with clear conclusions from data.
- Make it as clear as possible where the performance data is used in the IFU. If it is not clear how the performance data from the reports is utilized in the IFU, it will add time and cost to the review for additional questions.

8.2.17 Packaging

- Packaging testing should address requirements for both transit endurance (including inspections for leakage) and shelf life stability, and be undertaken in accordance with relevant standards.
- If all packaging configurations/device combinations have not been tested, a rationale based on worst case (i.e. heaviest and lightest devices, largest and smallest volumes, etc.) should be provided.
- Any change to packaging is considered a significant change.

8.2.18 Stability

- Stability testing covers shelf life, in use (open & on board) and transport studies.
- **Shelf life** is normally considered to be the time the device can be kept in the packaging prior to use/opening. This is not the same as "in use".
- If shelf life testing is based on accelerated age testing, this should be accompanied by a plan for real time testing for three lots/batches. Real time testing should be underway by the time documentation is submitted for review.
- The **in use** stability of the device should consider both opened stability and on board stability relative to other parts of the Dossier (e.g. risk management, clinical evaluation, PMS).
- The **transport** stability of the device should consider the extremes of time and temperature the device could be exposed to during all transport events relative to other parts of the dossier (e.g. supplier control, risk management, clinical evaluation, PMS).

See Attachment B section 12.4 for additional guidance on IVD stability requirements.

Any change to packaging is considered a significant change.

8.2.19 Physical, chemical and biological safety

The submission should clearly indicate whether or not the IVD:

- Utilizes any human or animal-based products.
- Has been assessed to determine the impact of physical, chemical or biological safety.

8.2.20 Software

Appropriate documentation is required if the IVD is either stand-alone software or relies upon software. You can find out more by visiting our website: bsigroup.com/medical-software.

- There should be a rationale for why the software is an IVD and for its classification. If applicable, the software should be broken down into modules based on whether they have an IVD purpose or not. The modules with an IVD purpose must comply with the requirements of the IVD Directive and must carry CE marking. The non-IVD modules are not subject to the requirements for IVDs.
- Ensure all relevant harmonized and non-harmonized software standards have been considered. Ensure the software systems/modules/items have been assigned safety classifications based on standards.
- Include documentation on the IVD 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).
- 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 an IVD purpose must comply with the IVD Directive.

8.2.21 Quality Control (QC) testing

The submission should include QC release testing documentation including any additional pointer documents e.g. QC release specifications.

8.2.22 Self-test

The submission for self-test devices should have the required elements presented clearly to demonstrate conformance to the applicable standard(s). Refer to Attachment B section 11.7 for links to these guidance documents.

8.2.23 Contamination control

It is useful for the submission to include considerations for contamination control e.g. DNA, microorganisms as applicable to the device:

- Summarizing the approach e.g. manufacturing methods, bioburden, preservatives used and/or sterilization. If the device is sterile, include validation and subcontractor details.
- Sterilization validation is reviewed separately by BSI Microbiology experts. Please confirm if this has been reviewed under the Medical Devices Directive, if applicable.
- Please contact your Scheme Manager who will advise you of the documentation requirements relating to sterilization validation.

ATTACHMENT B: Reference Documents.

NOTE: Guidance is continuously being updated. These links are intended for reference only. Please ensure that the latest version of the documents is used.

Note: Some of the following links will take you to the home page of the organization responsible for the document listed. You will be able to find the latest version of the document on the website.

9 Technical documentation general guidance

- In Vitro Diagnostic Medical Device Market Authorization Table of Contents (IVD MA ToC) <http://www.imdrf.org/>
- 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 N063: 2011, "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.team-nb.org/nb-med-documents/>
- NBOG 2009-1 Guidance on Design-Dossier Examination and Report Content.
http://www.doks.nbog.eu/Doks/NBOG_BPG_2009_1.pdf

10 Change reporting

- NB-MED 2.5.2 rev 2 Reporting of Design Changes and Changes of the Quality System
<http://www.team-nb.org/nb-med-documents/>
- NBOG-2014-3 Guidance for manufacturers and Notified Bodies on reporting of Design Changes and Changes of the Quality System.
http://www.doks.nbog.eu/Doks/NBOG_BPG_2014_3.pdf
- EC Commission MEDDEV Guidance – various topics

11 Regulatory guidance organizations

https://ec.europa.eu/growth/sectors/medical-devices/guidance_en#meddevs

- International Medical Device Regulators Forum (IMDRF) – various topics. Access to all IMDRF (previously GHTF) final documents:
- GHTF/SG1/N046:2008 Principles of Conformity Assessment for In Vitro Diagnostic (IVD) Medical Devices.
<http://www.imdrf.org/documents/documents.asp>
- NB-MED Guidance – various topics
<http://www.team-nb.org/nb-med-documents/>
- GMDN Agency – medical device nomenclature/generic device groups per ISO 15225.
<http://www.gmdnagency.com/>
- Notified Body Operations Group
<http://www.nbog.eu/>

12 Specific topic guidance

12.1 Quality Management Systems Guidance

- EN-ISO 13485 - Medical devices – Quality management systems – Requirements for regulatory purposes

12.2 Risk Management Guidance

- EN-ISO 14971 – Medical devices – Application of risk management to medical devices

12.3 Performance evaluation guidance

- EN 13612:2002 Performance evaluation of in vitro diagnostic medical devices.
- Clinical evidence IVD medical devices.
- Scientific validity determination and performance evaluation.

Guidance for the documents above can be found at: <http://www.imdrf.org/>

12.4 Stability

- ISO 23640:2015 In vitro diagnostic medical devices – Evaluation of stability of in vitro diagnostic reagents stability

12.5 Post Market Surveillance guidance

- NB-MED Recommendation 2.12/1
<http://www.team-nb.org/nb-med-documents/>

12.6 Declaration of Conformity

- EN ISO /IEC 17050-1:2010 Conformity assessment. Supplier's declaration of conformity. General requirements.
- European Commission Notice 2016/C 272/01 "The 'Blue Guide' on the implementation of EU products rules 2016;" chapter 4.4 "EU declaration of conformity" (page 57-58) where minimum information required in declaration are described.
- NB-Med Consensus statement S99/01:
http://www.meddev.info/_documents/NBRG_ConsensusStatements0403-ver01-2003.pdf

12.7 Standards

- EU Harmonized Standards.
https://ec.europa.eu/growth/single-market/european-standards/harmonised-standards_en
- BSI Online Standards. <https://bsol.bsigroup.com>
- ISO Online Standards <http://www.iso.org/iso/home/standards.htm>
- In vitro diagnostic medical devices – Evaluation of stability of in vitro diagnostic reagents
- In vitro diagnostic test systems – Requirements for blood-glucose monitoring systems for self-testing in managing diabetes mellitus.

12.8 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/DocsRoom/documents/17921/attachments/1/translations>
- BSI Software page: bsigroup.com/medical-software

12.9 Self-tests

- EN 13532:2002 General requirements for In vitro diagnostic medical devices for self-testing.
- ISO 15197:2013 In vitro diagnostic test systems --Requirements for blood glucose monitoring systems for self-testing in managing diabetes mellitus.



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