BSI Transitions

In Vitro Diagnostic Regulation

IVDR Documentation Submissions

Best Practices Guidelines

bsi.

...making excellence a habit.™

Contents

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 Annexes IX to XI of (EU) 2017/746, hereafter referred to as the In Vitro Diagnostic Regulation (IVDR). Subject to classification, most devices will need their Technical Documentation assessed by a Notified Body.
The Technical Documentation submission guidance is aligned to the requirements of the IVDR, described in detail in Annex II and III.
Notified Body BSI (BSI-UK/BSI-NL) and IVD manufacturers both have an interest in speeding up the review of Technical Documentation (Summary of Technical Documentation (STED), initial application, renewal application, etc.) and reducing the time to certificate decision.
The most frequent reasons for delays in the review of the Technical Documentation are:

- Incomplete submissions - BSI has not been provided with all the information needed for the review.
- Poor structuring of the Technical Documentation - The information is present within the Technical Documentation but is difficult to locate.

To reduce the frequency of the above issues, BSI Medical Devices Group proposes the following guidelines, informally known as "IVDR Documentation Submissions: Best Practice Guideline".

2 Submission and Technical Documentation Contents

Three things are required for any technical review:

Context (i.e., an explanation of what is being requested and why),

The Technical Documentation (i.e. objective evidence to demonstrate compliance),

Authorisation for BSI to carry out the work.

The submission should contain:

i. Cover letter,
ii. Technical Documentation,
iii. Authorisation for BSI to carry out the work.

These are discussed in detail in Sections 2.1 to 2.3.

2.1 Cover Letter

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

- Certificate number reference(s) (if known).
- The type of review (new product, design change, shelf life extension, etc.).
- Brief product description, including classification (with Rule according to Annex VIII), conformity assessment route requested, analytes and technology involved.
- BSI Ref. number (Service Management Order (SMO) #) for any other relevant submissions (for example, concurrent applications that may affect the submission).
- An explanation of:
    - What has been submitted and how it demonstrates compliance.

- For changes to existing certification:
    - What is affected (packaging, material change, life, etc.).
    - What is not affected (along with appropriate justification).

Note: A possible format for this explanation could be a table based on the sections of the Technical Documentation, as below:

Technical Documentation section	A/NA?	Description of evidence submitted; for changes, impact on compliance or rationale for why this section is not affected

2.2 The Technical Documentation

The IVDR is a new legislation. For initial approvals, a complete submission with all the relevant Technical Documentation included is required even if the device was previously certified under the IVDD.
To assist manufacturers in determining the correct information to provide to BSI, a comprehensive checklist of various documents required to be submitted as part of the Technical Documentation can be found in the BSI IVDR Technical Documentation Completeness Check form (MDF9003), hereafter referred to as the Completeness Check. Additional guidance is also provided in Appendix A. Supplementary guidance/information can also be found in the associated reference documents listed in Appendix B.
For submissions in the context of scope extensions or substantial change approvals, as far as is practical, submissions should be standalone and not refer to previous submissions as evidence of compliance. The reviewer must be able to assess the documentation in the context of the intended submission and confirm it is still relevant within this context. If a submission draws on information previously submitted to BSI, please include the relevant report or document which demonstrates compliance, rather than directing the reviewer to an earlier review. Overall, this will save time (e.g., in finding the report, confirming that the correct report has been found, confirming whether there have been any changes affecting its relevance to the current application, etc.).

2.1 Authorisation for Work to be Conducted

A signed approved quote will be required before work can commence. If this is not already in place, please contact your BSI Scheme Manager or BSI Sales Team.

3 Verification of Performance

For Class D devices (and others, if requested), kits will be required for testing by an EU Reference Laboratory (EURL) to verify performance. Scientific Opinion of the EURL will be sought for the verification of performance claims made by the Manufacturer (Article 48 (5)). A positive opinion will be needed for certification of the device. This will be discussed in more detail upon application.

3.1 Information Required to Support Verification of Manufactured Product (Class D Only)

Prior to the verification of performance, the EURL must first establish the success criteria. This will be conducted in parallel to the Technical Documentation review. The following will be required:

- Batches of product must be sent to the EU Reference Laboratory to establish criteria.

- These batches must meet the manufacturers QC specification and be in the same configuration as the Technical Documentation submitted, with components clearly labelled with name, lot number, expiry date and final draft IFU.

On-going batch release will require, in addition to sending kits to the EU Reference Laboratory as required, 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 and expiry, as well as the IFU).

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 to request this.
- If the above method is not suitable or does not work, please contact your BSI representative to discuss alternate methods of document submission. Please note, any documents submitted via alternate methods will need to be uploaded to an electronic document management system by our administration team. This may add time and cost to the review.
- **We do not accept hard copies of Technical Documentation**.

5 Document Format

5.1 Language

- The official language of BSI is English, and all submitted Technical Documentation and test results must be in the English language.

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 Sections 5.2.2 to 5.2.4 for further information on text recognition and bookmarks). Other software formats may be acceptable. These files will need to be converted to PDF files with bookmarks and will add time and cost to the review. Significant delays may result if files cannot be easily converted to this format.
- **Manufacturers should submit one PDF for each part below (Table 1). If not possible, for example, for analytical verification, manufacturers are recommended to break it down into sub-sections.**
- **PDF files and attachments should not be file protected or locked as this prevents necessary access and file manipulation for archiving.**
- **File names should be logical and reflect the information covered within that part. The checklist should use the file names.**
- **Documents should be bookmarked to ensure ease of navigation** (see Section 5.2.3 below for more information relating to bookmarking).

- **It is strongly recommended that documents are grouped as shown in Table 1.** 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.

Table 1: Suggested grouping for IVDR Technical Documentation submissions

Parts	IVDR cross-references	BSI Completeness Check - Reference to Technical Documentation Checklist
Part A – Device description and specification including variants and accessories	Annex II Section 1	Section 4.2 - 1
Part B – Information to be supplied by the manufacturer	Annex II Section 2	Section 4.2 - 2
Part C – Design and manufacturing information	Annex II Section 3	Section 4.2 - 3
Part D – General safety and performance requirements	Annex II Section 4	Section 4.2 - 4
Part E – Benefit-Risk Analysis and Risk Management	Annex II Section 5	Section 4.2 - 5
Part F – Product verification and validation Information on analytical performance of the device	Annex II Section 6.1	Section 4.2 – 6.1, 6.2.1 – 6.2.3, 6.2.6 – 6.2.9, 6.3, 6.4,
Part G – Product verification and validation Information on clinical performance and clinical evidence. Performance evaluation report.	Annex II Section 6.2	Section 4.2 – 6.2.4, 6.2.5
Part H – Product verification and validation Stability	Annex II Section 6.3	Section 4.2 – 7.1 – 7.3
Part I - Product verification and validation Software verification and validation	Annex II Section 6.4	Section 4.2 – 4.7
Part K – Product verification and validation Additional information required in specific cases	Annex II Section 6.5	N/A
Part J – Declaration of Conformity	Annex IV	Section 4.2 – 7.4

5.2.2 Optical Character Recognition (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 as 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 documents. As a minimum, sections in IVDR Annex II "Technical Documentation" should be bookmarked (recommendation in Table 1).
- Where possible, individual documents cited as supporting attachments should also 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 organisation 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. Each page should have a unique number irrespective of the total number of pages in the Technical Documentation.
- PDF files are automatically numbered. Where possible, please always provide reference to the pagination in the PDF file as this will aid the Technical Documentation review. Where this is not possible, please make it clear what the page number refers to.
- Pagination is not mandatory, as BSI can add this with our software. Formatting such as this will likely increase the time for review.

5.2.5 Signatures

Signatures are required for any signed document in the file, including BSI work authorisation forms and signed quotes. Signatures can be handled in several ways:

- Documents may be digitally signed.
- Signature pages can be scanned 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.
- All protocols/reports which require approval (as per the legislative requirements & Manufacturer's own procedures and policies), except for the Declaration of Conformity, must have undergone those requisite approvals and be submitted with evidence of those approvals (typically through dated and signed reports, signed protocols, or evidence of approval in an electronic system etc).

6 Submission Process

The following is an overview of the submission process (Figure 1):

a) Notify BSI that you have an application for review. For new clients, this will generally be via a member of the sales team (https://www.bsigroup.com/en-GB/medical-devices/forms/contact-

us/). 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) For IVDR work, a formal quotation will be required.

c) Once the signed approved quote has been submitted, BSI will assign a reviewer. At that time BSI will assign the relevant certificate references and/or a unique identification number ("SMOxxxxxx") for your review and contact you with those references. We ask that you reference those numbers during document submission via the BSI portal or in any email correspondence with BSI during the review process.

d) Manufacturers may be required to complete an IVDR Completeness Checklist prior to the start of the detailed review. This ensures all documents needed to initiate the review have been included as part of the Technical Documentation submission (Appendix A). This ensures much of the first round of questions is not used to ask for key missing information. The requirement for this will be discussed with your Scheme Manager following quote approval.

e) The conformity assessment of the Technical Documentation review can begin upon receipt of a signed quote together with required application documentation (per Annex IX for initial submissions) and BSI acceptance of the IVDR Completeness Checklist, where appropriate.

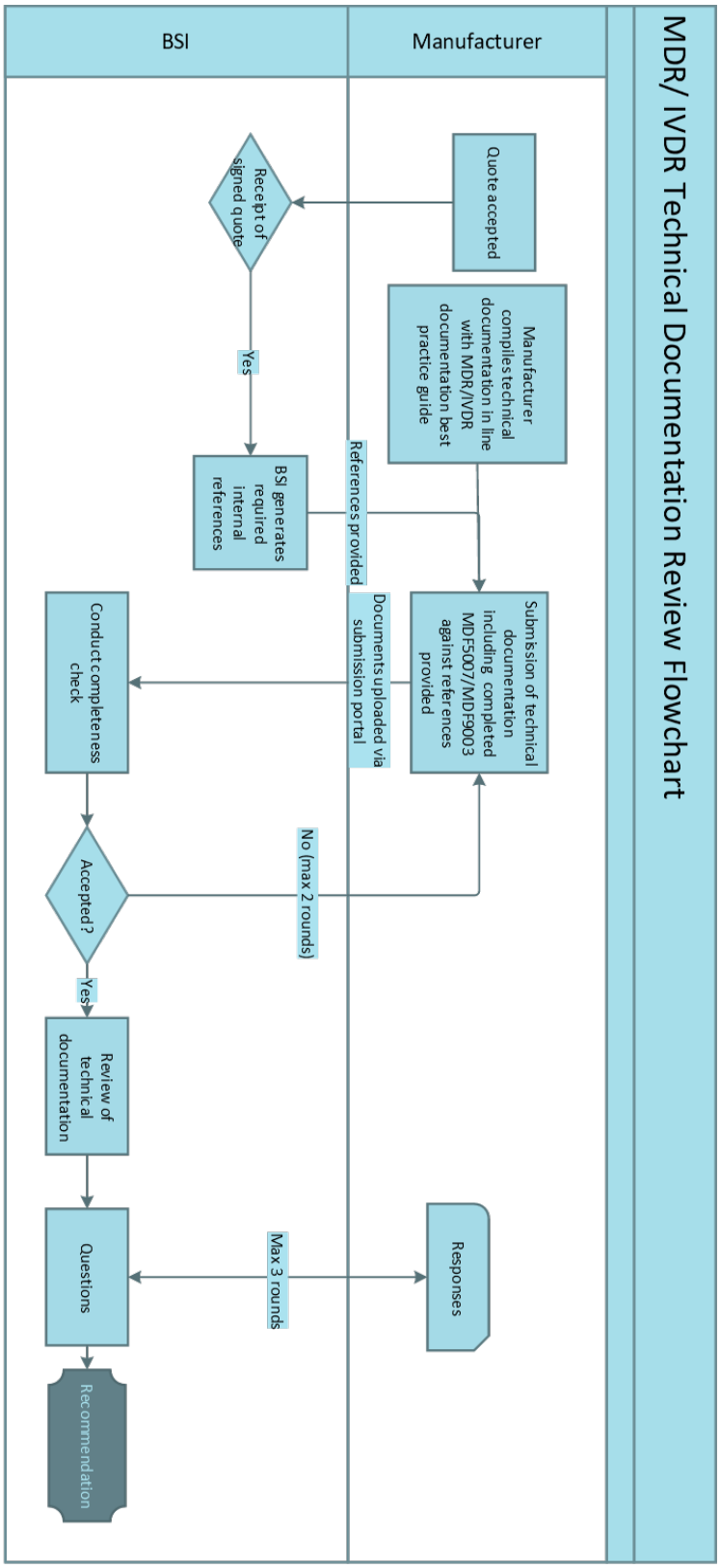

Figure 1: Overview of the BSI submission process and individual responsibilities. Note: Manufacturers must submit the completed Technical Documentation Completeness Checklist and Technical Documentation to BSI at the same time.

7 Additional Topics to Consider When Preparing Technical Documentation for Submission

7.1 Manufacturer Personnel Support

Please ensure appropriate manufacturer resources (RA, QA, R&D, Manufacturing, etc) are available during Technical Documentation review (standard or dedicated). The quicker information can be provided, the more quickly questions can be closed to progress towards certification.

7.2 Document Availability

If a document includes hyperlinks or cross-references to other documents or embedded documents, ensure that these are functional, and all the documents are available. Where appropriate, relevant information must be provided in the IVDR Technical Documentation Completeness Check, to be completed by the manufacturer at the time of submission. If specific essential documents are not provided or incomplete, this may delay the start of Technical Documentation review. Please remember the reviewer must see the manufacturer's conclusions regarding compliance, as well as the objective evidence necessary to support those conclusions. It is possible the technical expert may need additional information and/or documents on initiation of the detailed Technical Documentation review.

7.3 Languages

As part of the quality system, or of the documents defining the manufacturing process, the manufacturer should have procedures for ensuring accurate translation of labelling, instructions for use, product claims in marketing materials, SSPs etc. These are especially important for user instructions where the safety and claimed performance of the device may be compromised through inadequate translation or the SSPs where inaccurate information may be presented to the end-users or patients through inadequate translation.

7.4 Certificate Scope

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

- Sufficient evidence must be reviewed to support the change in scope. This may require QMS audits or microbiology audits, in additional to the Technical Documentation review requested.
- If in doubt, discuss the scope with your BSI Scheme Manager prior to submitting. The Scheme Manager will coordinate the scope change activities.

7.5 Sub-contractors

Are there any changes to sub-contractors related to the application?

- All significant sub-contractors/crucial suppliers must be added to associated QMS certificate(s) and the Unannounced Audit Visit schedule. Please ensure that your Scheme Manager and reviewer are aware of any changes. If you are unsure whether a sub-contractor/supplier is significant, discuss with your Scheme Manager or with the BSI Sales representative at the time of initial quotation.
- Significant sub-contractors/crucial suppliers that 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 sub-contractor

audit, depending on the scope of their activities and the verification activities undertaken by the manufacturer. There may be instances where a verification visit is needed, even if they hold ISO 13485 certification from a Notified Body. Please ensure that these details are made clear in the application.

- If design is sub-contracted, control of this sub-contracted activity must be considered.

7.6 Accessories

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

- Brief description of the accessory(ies) and how they are used with the device(s).
- Classification of the accessories and rationale for classification.

8 Novelty

Are any new technologies (or analytes) associated with the IVD? If so, this may require additional time as consultation with an external expert may be required. BSI reviewers will still work within timescales indicated for the review process selected, but external consultations may not fall within these timescales. As a result, review timelines cannot be guaranteed. Please discuss with your Scheme Manager, to select the most appropriate review option.

8.1 Additional Considerations for Desktop Audits

Surveillance audits will be remote i.e. performed as a "desktop" audit. It is important that all necessary information is included to avoid delays once the reviewer has set aside time to review the file.
Manufacturers should provide the following information:

- Main Technical Documentation body as well as key supporting documents or attachments. In general, if a document is listed as evidence in the General Safety & Performance Requirements checklist or equivalent document, the reviewer(s) may expect to review the corresponding document(s) as evidence of compliance with the relevant General Safety & Performance Requirements.
- A summary of any changes to the device since the last Technical Documentation audit.
- Information on engagement with any global regulatory bodies in respect of legal compliance or other issues.
- Information on any changes to the quality system or management.

Additional review time may be required in the following cases:

- Devices using electronic IFU per Regulation 207/2012.
- Class C software per EN 62304. This requires additional audit time.
- Reviews requiring input from external expert(s).
- Technical Documentation with poor traceability, incomplete or missing information.

APPENDIX A: Information to Provide in a Technical Documentation Submission

Administrative information	
Overview of the submission	The application should clearly state if it is a new certification or scope extension (including changes to design, indications for use etc.) and list any previous related submissions. A summary of details to be included in the cover letter are highlighted in Section 2.1. If a change is being requested, complete relevant information in MDF9900. The document index should include the title of the file and revision history. Individual documents should also indicate date, revision history and status. It is highly recommended for manufacturers to provide a summary of the Technical Documentation (sections in IVDR Annex II or GHTF STED) to aid document review. Manufacturer's must also indicate which regulation applies. If the device contains a medical device e.g. lancet or swab, please confirm this has been reviewed under the medical device regulation.
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. The Single Registration Number (SRN) of the legal manufacturer should be identified. Referred to in IVDR EU 2017/746 Article 10.
Single registration number (SRN)	A Single Registration Number (SRN) is a unique code that is assigned to manufacturers, authorised representatives or importers after they have registered in the European Database on Medical Devices (EUDAMED). Note: Manufacturers are not expected to declare an SRN until this functionality becomes available in EUDAMED.
Device name(s)	State the name(s) of the device as it appears on the labelling and associated documents.
Basic UDI-DIs covered	The submission should include the basic UDI-DI assigned by the manufacturer to the device, as soon as identification of this device becomes based on a UDI system or otherwise a clear identification by means of product code, catalogue number or other unambiguous reference allowing traceability. Refer to IVDR EU 2017/746 Annex VI part C.
Impacted BSI certificates	The certificate identifiers of all BSI certificates currently held by the manufacturer.
Date of submission	This should ideally be presented as DD MMM YYYY to prevent any ambiguity.
Section 1: Device description and specifications including variants and accessories	

Intended purpose	The intended purpose should provide sufficient detail to explain: • What is to be detected and/or measured, and whether it is qualitative, quantitative or semi-quantitative. • Its function (i.e. screening, monitoring, diagnosis or aid to diagnosis, prognosis, prediction or companion diagnostic). • How the result relates to a diagnosis including any specific disorder, condition or risk factor of interest that it is intended to detect, define or differentiate. • It should include the basic principles of operation (i.e. intended users and environment, whether it is automated or not and the type of specimen(s) required). • The intended patient population of the device. • Intended user, as appropriate (e.g. self-testing, near-patient or laboratory professional use etc.). • For companion diagnostics also include the relevant target population and the associated medicinal product(s) ie. International Non-proprietary Name. Please ensure the intended use is 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 this should be separate from the device description. Refer to IVDR EU 2017/746 Annex I 20.4.1. The submission should include the description of the principle of the assay method or the principles of operation of the instrument per Annex II 1.1(d). For instruments of automated assays, the submission should include the description of the appropriate assay characteristics or dedicated assays per Annex II 1.1(i). Additionally, devices with automated assays must include a description of the appropriate instrumentation characteristics or dedicated instrumentation (Annex II 1.1(j)).
Devices covered by the Technical Documentation	The submission should include a description or complete list of the various configurations/ variants of the device that are intended to be made available on the market. Refer to IVDR EU 2017/746 Annex II 1.1.
Classification	The submission should include the classification of the device including the justification for the classification rule(s) applied. Please also include a confirmation and rationale for the device falling under the scope of the IVDR. Refer to IVDR EN 2017/746 Annex VIII and Annex II 1.1.
Device description and specification	The device description should enable understanding of the design, composition and presentation or other characteristics of the device and should include product or trade name. A general description of the device including its intended purpose and intended users should also be provided.

	Please also include a description of all accessories included, not included but required for proper functioning of the device, and other products that are not devices, which are intended to be used in combination with the device. Refer to IVDR EU 2017/746 Annex II 1.1.
Reference to previous and similar generations of the device	The submission should include an overview of the previous generation(s) of the device produced by the manufacturer and an overview of identified similar devices available on the Union or international markets, where such devices exist. 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 initial applications under the IVDR, please confirm whether the device has been previously marketed under the IVDD and whether any changes have been made in comparison to the device on the market under the IVDD. • Market history should include EU and approvals in other geographies. If the device is a system, ensure that the number of units sold is broken down by device component and per year. Refer to IVDR EU 2017/746 Annex II 1.2.
Section 2: Information supplied by the manufacturer	
Labels and instructions for use	Medical devices generally use multiple levels of labelling and it is recognised that not all devices may have the different levels of packaging specified in this section or different terms may be used than those specified here. Legible versions of all applicable levels of labels should be provided (e.g. secondary pack, primary pack) and should be representative of the finished form, showing all included symbols. 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 the device has a sterile package, clearly identify the label for the sterile package. If any of the packaging is printed with information for the user (including pictures / schematics of the device) this should also be provided. Please ensure that any specific requirements of relevant harmonised standards or CS are addressed in the labels and information for use. The submission should include a complete set of: • Labels on the device and on its packaging, such as single unit packaging, sales packaging, transport packaging in the case of specific management conditions. • Instructions for use (IFU) and any material in which claims are made e.g. promotional material. These must be available in all languages for territories in which the product is intended for sale. As a minimum, manufacturers must submit the English IFUs and promotional material at the time of submission. • For self-test and near patient testing devices, manufacturers must provide a clear demonstration of conformity to the specific requirements.

	Only marketing literature that mentions the device fulfils the requirements of CE marking or includes the CE mark itself is required to be provided. Supporting evidence should be provided in the relevant pre-clinical and clinical sections to substantiate any claims made in the labelling or marketing literature. Refer to IVDR EU 2017/746 Annex I Chapters II and III.
Section 3: Design and manufacturing information	
Materials and components	This shall include a description of the critical ingredients of the device such as antibodies, antigens, enzymes and nucleic acid primers provided or recommended for use with the device. Refer to IVDR EU 2017/746 Annex II 3.1.
System overview	The submission shall include the design stages applied to the device. This should allow the reviewer to understand how the different components/systems fit together. • For devices incorporating instruments and/or software, please provide an overview of the entire system. Please indicate the transition steps and whether manual handling/manipulation are required. • For instruments, please provide a description of the major subsystems, analytical technology and any dedicated computer hardware and software. • Where the device uses software for objective data interpretation or the device is a software in itself, please provide a description of the data interpretation methodology i.e. analysis algorithm. Please state whether this is automated or manual. • For devices intended for self-testing or near-patient testing, manufacturers must include a description of the design aspects that make them suitable for self-testing or near-patient testing. Refer to IVDR EU 2017/746 Annex II 3.1.
Manufacturing information	The manufacturer shall include a detailed overview of the manufacturing processes to enable understanding of the finished device. Please note: The BSI auditors will review more detailed information as part of the QMS audit. Please provide detailed information on: • In-process QC, success criteria and include results from a sample batch. • Final release QC, success criteria and include results from a sample batch. Refer to IVDR EU 2017/746 Annex II 3.2.
Sites involved in design and manufacturing activities	Please identify all sites involved in the manufacture of the finished device including crucial suppliers and significant sub-contractors, indicating which activity is performed at the corresponding site. The following must be clearly identified: • Legal manufacturer. • European representative, if applicable (Article 11). • Site with design responsibility. • Site(s) performing final release testing. • Where sterilisation is performed, if applicable.

	Only one EU Representative should be identified, and this should be consistent across the device labels, IFU and Declaration of Conformity. If significant sub-contractors/crucial suppliers are used, provide copies of their ISO 13485 certificates, if not provided already. If a sub-contractor/supplier does not have an ISO 13485 certificate from a Notified Body, additional supplier audits may need to be arranged and should be discussed during application. If they hold ISO 13485 certification from a Notified Body, there may be instances where BSI would still need to perform a verification visit.
Section 4: General safety and performance requirements (GSPRs)	
Demonstration of conformity with GSPRs	The submission should include information that demonstrates conformity with the general safety and performance requirements set out in Annex I applicable to the device taking into account its intended purpose, and shall include a justification, validation and verification of the solutions adopted to meet those requirements. It is helpful to provide a checklist against the GSPRs, or other documented method to provide evidence of conformity to each requirement. Where a requirement(s) is not applicable, this must be clearly shown, with justification. • Manufacturers must state the method(s) used to demonstrate conformity to the corresponding GSPR. • All applicable harmonised standards, guidelines, regulations and common specifications used must be clearly stated. Where compliance is demonstrated against specific clauses/ sections, Manufacturers must state specific clause(s)/section(s) where partial compliance is demonstrated. • A summary or gap analysis regarding ability to comply with associated general safety and performance 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. This will not be applicable for initial applications. • The **precise** identity of manufacturer document(s) demonstrating evidence of conformity to the corresponding GSPR must be stipulated. The technical reviewer must be able to use this to review compliance in the Technical Documentation, and/or the summary Technical Documentation, if provided. Refer to IVDR EU 2017/746 Annex I and Annex II (4).
Product and design specifications	Manufacturers should provide an overview of the design inputs and key outputs, as well as a design traceability matrix. For self-tests or near-patients tests, the submission should clearly demonstrate how the device meets the requirements and should include: • Data showing the suitability of the device in view of its intended purpose for self-testing or near patient- testing. • Test reports, including results of studies carried out with intended users.

	• Ideally provide an example of the device. Talk to your scheme manager for confirmation/ delivery details and return requirements. If the device cannot be provided, pictures of the device should be included.
	• The information to be provided with the device on its label and its instructions for use including:
	  ○ The type of specimen(s) required to perform the test (e.g. blood, urine or saliva),
	  ○ The need for additional materials for the test to function properly,
	  ○ Contact details for further advice and assistance.
	Refer to IVDR EU 2017/746 Annex I (19) and (20.4.2).

Chemical, physical and biological properties	The manufacturer must demonstrate consideration of risk related to chemical and physical safety, including risk of accidental ingestion. The manufacture must demonstrate risk of infection and/or contamination is reduced as far as possible.
Devices intended to be connected to other devices to operate as intended	For devices used in combination with other devices and/or electrical equipment, the manufacturer must demonstrate safety of the entire combination, including safe calibration, maintenance and disposal. The submission should include a description of the total combination including proof this conforms to the requirements set out in GSPR 13 to maintain the specified characteristics.
Devices with a measuring function	In the case of devices placed on the market with a measuring function, the submission should include a description of the methods used in order to ensure the accuracy as given in the specifications. Units of measurements must conform to the provisions of Council Directive 80/181/EEC.
Protection against radiation	For devices emitting radiation, manufacturers must demonstrate evidence that exposure levels are appropriate for the intended purpose and have been reduced as far as possible. Where relevant, manufacturers must demonstrate control of hazardous levels by the intended user(s). Necessary detail must also be captured in the IFU especially guidance on user protection and avoidance of misuse.
Software	Manufacturers should clearly state whether the device is a software in itself, or whether this is needed for the proper functioning of the device, as intended. The submission should include a description of any software to be used with the device, either as an integral part, or associated with the device in order for its safe use. Manufactures should include a checklist to demonstrate compliance with EN 62304. Refer to IVDR EU 2017/746 Annex II 1.1. The documentation shall contain evidence of software validation as used in the finished device. It shall also address all of the different hardware configurations and, where applicable, operating systems identified in the labelling.

	Include IVD software lifecycle documentation and related procedures (e.g. software development plan, software requirements specification, risk management and issue resolution). Refer to IVDR EU 2017/746 Annex II (6.4).
Electrical safety and electromagnetic compatibility	If the device incorporates or depends on an energy source, manufacturers must demonstrate due consideration for: • Single fault conditions, • Patient safety, • Electromagnetic interference, and, • All risk associated with accidental electric shock. Refer to IVDR EU 2017/746 Annex I (GSPR 17).
Protection against mechanical and thermal risks	Manufacturers must show evidence of the device is able to withstand stresses in the planned work environment(s). Any risks associated with moving parts, substance leakage, vibrations, noise and temperature of accessible parts must also be considered.
Section 5: Benefit-risk analysis and risk management	
Risk management	Manufacturers must provide their risk management procedure, plan detailing the scoring system used and a risk management report concluding whether the risk is un/acceptable. This must be iterative and continue for the lifetime of the device. Manufacturers must demonstrate systematic updates of the corresponding risk management documentation. The risk management documentation should include: • A risk management plan for each device. • A copy of the risk management procedures that include the definitions of any rating systems used for risk analysis and risk acceptability should also be provided. • Identification and analysis of the known and foreseeable hazards associated with each device. • Estimation and evaluation of the risks associated with, and occurring during, the intended use and during reasonably foreseeable misuse. • Elimination or control of the risks identified (refer to IVDR EU 2017/746 Annex I, Section 4). • Evaluation of the impact of information from the production phase and, in particular, from the post-market surveillance system, on hazards and the frequency of occurrence thereof, on estimates of their associated risks, as well as on the overall risk, the benefit-risk ratio and risk acceptability. • Based on the evaluation of the impact of the information, if necessary, amend control measures in line with the requirements of (refer to IVDR EU 2017/746 Annex I, section 4). 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 all known and foreseeable risks, and any undesirable effects shall be minimised and be acceptable when weighed against the evaluated potential benefits to the patients and/or the user arising from the intended performance of the device during normal conditions of use. For 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. Guidance on the risk management process is available in EN-ISO 14971- Medical devices -- application of risk management to medical devices.
Section 6: Product verification and validation	
Specimen type	Manufacturers must stipulate the specimen(s) to be used for the proper functioning of the device, e.g. formalin fixed paraffin embedded tissue, first catch urine sample or plasma ctDNA. Representative data must be generated using all intended specimen types to demonstrate no loss in the functionality of the device. Any time-critical methods must be clearly defined in the IFU, with supporting data in the Technical Documentation. Where applicable, the submission should include a description of the specimen collection and transport materials provided with the device or descriptions of specifications recommended for use. Refer to IVDR EU 2017/746 Annex II 1.1
Performance evaluation and clinical evidence	The submission should include the following evidence of performance evaluation: • Performance evaluation plan and report (Annex XIII section 1.1 and Annex VIII section 1.3.2, respectively) – this must be maintained for the lifetime of the device. • Scientific validity (Annex XIII Section 1.2.1) – used to demonstrate the usefulness of the marker(s) or analyte(s) in the context of the intended use. • Analytical performance plan(s) and report(s) (Annex XIII Section 1.2.2) – see additional detail below. • Clinical performance plan(s) and report(s) (Annex XIII Sections 1.3.1, 2.3.2 and 2.3.3) including, if applicable: o Clinical performance studies – plan and report, if relevant (Annex XIII 2). o Scientific peer-reviewed articles. o For legacy devices, this could also be published experience gained by routine diagnostic testing and/or market data. The **performance evaluation report** will include the individual reports on: - Scientific validity. - Analytical performance.

	- Clinical performance. These will be used to assess conformity of the device against the applicable GSPRs. The conclusions from these reports will also constitute the clinical evidence for the device. Refer to IVDR EU 2017/746 Annex XIII. Analytical performance must be demonstrated per the requirements of Annex I Section 9.1. The submission should include the results and critical analyses of all verification and validation studies undertaken to demonstrate conformity of the device with the requirements of the Regulation under the conditions of the devices intended use. Device claims may be made in the IFU, labelling or any other material e.g. on websites. This should include studies to demonstrate: • Analytical sensitivity, • analytical specificity, • trueness (bias), • precision (repeatability and reproducibility), • accuracy (analytical and clinical), • limits of detection and quantitation, • linearity, • assay cut-off, • sample handling • interfering substances (endogenous and exogenous), • cross-reactivity. Refer to IVDR EU 2017/746 Annex I, Section 9.1 and Annex II, Section 6. This section must also include evidence the device performs as intended by the intended users i.e. usability engineering. **Summary of safety and performance** For Class C & D devices the summary of safety and performance (SSP; Article 29) must also be provided. This should be written clearly and understandable to the intended user and patient (if relevant) and should contain all elements list in Article 29 (Section 2). A draft document in English is acceptable at the time of submission. Once the SSP has been finalised based on the BSI review, manufacturers should submit the final version of the English SSP, in printable PDF format and is printable, searchable before a certificate recommendation can be made. The SSP shall be updated as indicated in Article 56, over the lifetime of the device as needed, and updates should be defined in the Post-Marker Surveillance Plan. For Class C devices without a product specific certificate, the IVDR allows NBs to choose representative devices from the generic device group for the assessment of Technical Documentation. The SSPs for such devices chosen as the representative sample(s) will be validated by the NB as part of the Technical Documentation assessment for those device(s). NBs are also required to upload the unvalidated SSPs

	of the devices that were not chosen as representative devices (but are part of the same generic device group) to EUDAMED. Hence Manufacturers may submit these unvalidated SSPs at any time during the certification process to BSI, but before a BSI Scheme Manager prepares and makes a recommendation for certification based on the completion of all the required conformity assessments (including Technical Documentation assessment) for the relevant generic device group(s).
Post-market surveillance and post-market performance follow-up	**PMS** The submission should include the post-market surveillance plan as defined in Annex III. This must be a proactive and systematic process with appropriate data collection and analysis methods defined. These must be maintained for the lifetime of the device. Please provide sales, complaints and vigilance data for your device from the last 5 years. This should include but is not limited to: • 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, • Serious incident reports, including information from periodic safety update reports and/or field safety corrective actions in the context of total and EU sales, • Records referring to non-serious incidents and data on any undesirable side-effects, • Information from trend reporting, • Publicly-available information about similar medical devices. Complaints data should be evaluated rather than just listed. For example, why is the complaints rate considered acceptable? Have any trends been analysed and noted, or corrective actions taken? What is the status of these actions? Has a comparison of PMS data been made to the expected occurrence in the risk assessment? Full details of vigilance issues should be provided, including the status of any Field Safety Corrective Actions or Notices, the associated CAPAs and patient outcomes. This data should include FSCA or FSN outside the EU, if related to a device which is sold in the EU. Please also ensure that all PMS data at the time of submission if up-to-date. Where applicable, manufacturers must also include a post-market performance follow-up plan (Annex XIII, Part B), or a justification of why this is not applicable. The outcome of this must be documented in the post-market performance follow-up report. Already available data can be submitted and may be requested for legacy devices i.e. devices sold under the IVD Directive. **PSUR** Manufacturers of Class C and D devices shall also prepare an annual periodic safety update report for each device and, where relevant, for each category or group of devices summarising the results and conclusions of the analysis of the post-market surveillance data gathered as defined in the corresponding plan. This shall follow the requirements of Article 81. For Class C devices the PSUR should be made available upon request. For Class D devices the PSUR should be submitted to the Notified Body (Article 87).

	These documents must be updated at least annually.
Product verification by EURL	The manufacturer should provide reference to the common specifications applied, where relevant. If the device is Class D with no common specifications, this must be clearly stipulated.
Section 7: Stability	
Stability including shelf-life	Shelf life is normally considered to be the time the device can be kept in the packaging prior to its first 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. Extensions to shelf life must be reported to BSI for review and certificate re-issue. Shelf life validation should include: • A protocol (with acceptance criteria for each test performed) and appropriate test references. • A clear statement of the intended shelf life. • If applicable, a clear statement defining the sterilisation status of the test samples (1X, 2X sterilised). • 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 (leach testing, fluorescence decay, age of polymerase, etc.). • A summary of the ship testing/transit simulation testing conducted and applicable test reports. The submission should include the claimed shelf life, in-use, sample and shipping stability studies. **Claimed shelf-life** • Testing shall be performed on at least three different lots manufactured under conditions that are essentially equivalent to routine production conditions. The three lots do not need to be consecutive. • Accelerated studies or extrapolated data from real time data are acceptable for initial shelf life claims but shall be followed up with data generated from real time stability studies. • A protocol stating number of lots, acceptance criteria and testing schedule must be provided.

	○ Where accelerated studies have been performed in anticipation of the real time studies, the method used for accelerated studies shall be described. • The report must state all conclusions and claimed shelf life. **In-use stability** • Data must be generated using at least one lot of reagents reflecting routine use of the device. Data can be generated using real or simulated conditions. This may include open vial stability and/or, for automated instruments, on-board stability. • All performance and stability claims must be supported by data. • Protocol(s) and report(s) stating all conclusions and claimed in-use stability must be submitted. Refer to IVDR EU 2017/746 Annex II 6.3.
Packaging and transit verification	Shipping and transport stability • Data must be generated using at least one lot of the device to evaluate the tolerance to anticipated shipping conditions. • These may be real or simulated studies and shall include extreme variations in temperature. • Manufacturers must submit: ○ The study report (including the protocol, acceptance criteria). ○ The method used for simulated conditions. ○ The conclusion and recommended shipping conditions.
Sterilisation	If the device or aspect(s) of the device include sterilisation, the manufacture must submit the validation protocol(s) and report(s) including a description of the method(s) used. The validation report(s) shall address packaging, sterilisation and maintenance of sterility as well as bioburden testing, pyrogen testing and, if applicable, testing for sterilant residues.
Declaration of conformity	The application should include a copy of the Declaration of conformity (unsigned). The EU Declaration of Conformity should include all of the information listed in IVDR Annex IV.
Additional information required in specific cases	In the case of devices containing tissues, cells and substances of animal, human or microbial origin, the submission should include information on the origin of such material and on the conditions in which it was collected. For example, inactivation of attenuated viruses. Refer to IVDR EU 2017/746 Annex II 6.5.
Companion Diagnostics	Devices classed as companion diagnostics: - Must be essential in developing or generating the supporting information for the corresponding medicinal product. - Must have a corresponding medicinal product. In some instances, a single device may be linked with multiple medicinal products, e.g. panel tests.

	The Technical Documentation requirements for a companion diagnostic are the same as other devices. Additional requirements include: - The International Non-proprietary Name (INN) of the associated medicinal product for which it is a companion test. - The relevant target population and the associated medicinal product(s). - As a minimum, the draft summary of safety and performance and the draft instructions for use will be provided to the relevant Competent Authority (CA) to seek a scientific opinion. - The suitability of the device in relation to the medicinal product will be reviewed by one of the CA designated by the Member States or European Agency for the Evaluation of Medicinal products (EMA). This will be triggered by the NB reviewer and a scientific opinion made available within the timelines set forth in Annex IX (Section 5.2 (d)). - An EU Technical Documentation certificate will not be issued until a scientific opinion has been received from the relevant CA or EMA. - Additional resources may also be required for external independent reviews and/or software review.

APPENDIX B: Reference Documents

NOTE: Guidance related to IVDR issued by MDCG and other entities is evolving at a rapid pace. These links are intended for reference only. Please ensure that the latest version of the documents is used. Gaps with the IVDR have not been assessed for each guidance, but guidance documents are included here for general additional information on specific topics. The following is not an exhaustive list and other relevant guidance documents not listed below may be available under each subject/topic.

B1. Change Reporting

NBOG's Best Practice Guide 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

B2. Regulatory Guidance Organisations

EC Commission MEDDEV Guidance – various topic

https://ec.europa.eu/growth/sectors/medical-devices/regulatory-framework_en

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

https://ec.europa.eu/growth/sectors/medical-devices/getting-ready-new-regulations/manufacturers-ivd_en

Guidance from NBOG (Notified Bodies Operational Group)

https://www.nbog.eu/nbog-documents/

Guidance from CAMD

https://www.camd-europe.eu/resources/

International Medical Device Regulators Forum (IMDRF) – various topics, access to all GHTF final documents

http://www.imdrf.org/documents/documents.asp

B3. Specific Topic Guidance

B3.1 Quality management Systems Guidance

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

B3.2 Risk Management Guidance

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

B3.3 Standards

The EU Commission Implementing Decision on IVD harmonised standards was published on 24 Mar 2020 and can be found here:

http://data.europa.eu/eli/dec_impl/2020/439/oj

BSI Online Standards

https://bsol.bsigroup.com

ISO Online Standards

http://www.iso.org/iso/home/standards.htm

B3.4 Shelf-Life

ICH Guidelines Q Series

http://www.ich.org/products/guidelines/quality/article/quality-guidelines.html

B3.5 Transit testing

ISTA guidelines

https://ista.org/docs/2018_ISTA_Guidelines.pdf

B3.6 Software Guidance

MEDDEV 2.1/6 - Guidelines on the Qualification and Classification of Software in MDR and IVDR Regulations

https://ec.europa.eu/docsroom/documents/37581/attachments/1/translations/en/renditions/pdf

UDI requirements for standalone software that are IVDs in their own right

https://ec.europa.eu/docsroom/documents/31926/attachments/1/translations/en/renditions/pdf

B3.7 Self-tests

EN 13532 General requirements for in vitro diagnostic medical devices for self-testing

ISO 15197 In vitro diagnostic test systems -- Requirements for blood-glucose monitoring systems for self-testing in managing diabetes mellitus.

Find out more about how BSI can support your transition by visiting our website **bsigroup.com/IVDRRevision** or call: +44 345 080 9000

BSI Group America Inc.
12950 Worldgate Drive,
Suite 800,
Herndon,
VA 20170
USA
T: +1 800 862 4977/703 437 9000
F: +1 703 437 9001
E: us.medicaldevices@bsigroup.com

BSI Group - EMEA
Kitemark Court,
Davy Avenue,
Knowlhill,
Milton Keynes MK5 8PP
United Kingdom
T: +44 345 080 9000
F: .+44 1908 814920
E: uk.medicaldevices@bsigroup.com

BSI Group Asia Pac
BSI Group - Hong Kong
23rd Floor, Cambridge House
TaiKoo Place,
979 King's Road,
Island East, Hong Kong
T: +852 3149 3320
F: +852 2743 8727
E: hk@bsigroup.com

BSI Group The Netherlands B.V.,
Say Building,
John M. Keynesplein 9,
1066 EP Amsterdam,
The Netherlands
T: +31 20 3460780
F: +3120 346 07 81
E:. info.nl@bsigroup.com

Visit us online at: *bsigroup.com/medical*