Medical Devices Regulation

# Technical Documentation Submissions
# Lessons Learnt

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5th May 2021



By Royal Charter

# Your Speakers Today

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*BSI*

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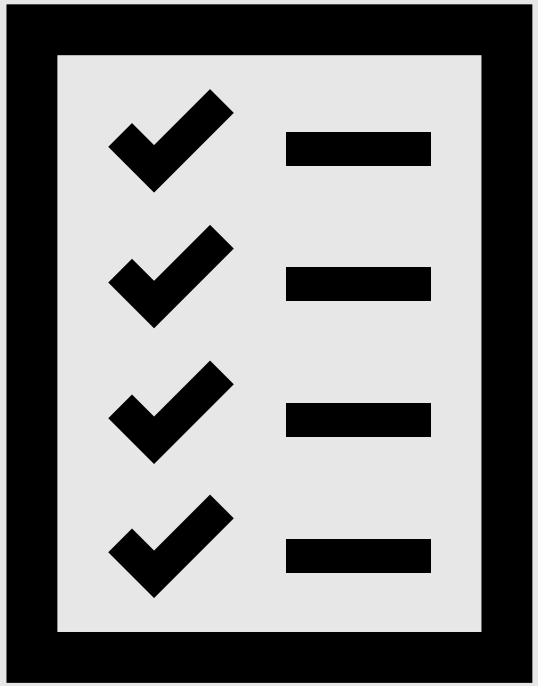
# The most common reasons for delays in technical documentation reviews are:

- **Incomplete Submissions** - all the information needed for the review not provided
- **Poor structuring of Technical Documentation** – information present but difficult to locate.

# Agenda

1. MDR Technical Documentation Review Process
2. Common Gaps/Questions from MDR Technical Reviews
3. Improving Technical Documentation Submissions
4. Questions



**How confident are you that you understand the MDR Requirements in relation to Technical Documentation Submissions?**

a) Very Confident

b) Slightly Confident

c) Enough to Survive

d) Don’t have a clue!

# MDR Technical Documentation Review Process

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# MDR Annex II - Technical Documentation (TD)

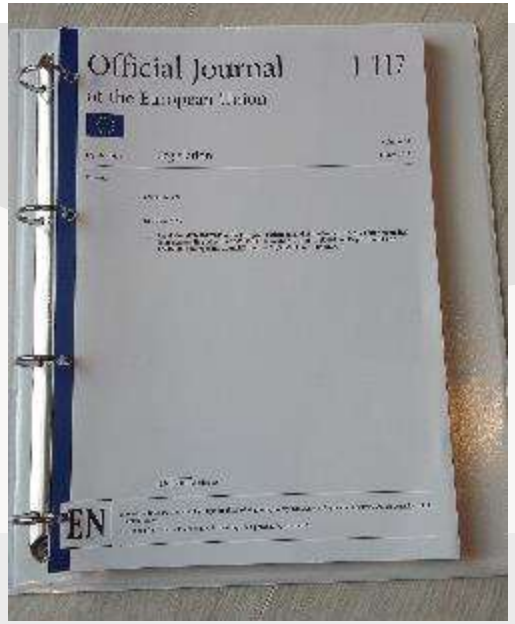


*ANNEX II*

**TECHNICAL DOCUMENTATION**

The technical documentation and, if applicable, the summary thereof to be drawn up by the manufacturer shall be presented in a clear, organised, readily searchable and unambiguous manner and shall include in particular the elements listed in this Annex.

1. DEVICE DESCRIPTION AND SPECIFICATION, INCLUDING VARIANTS AND ACCESSORIES
2. INFORMATION TO BE SUPPLIED BY THE MANUFACTURER
3. DESIGN AND MANUFACTURING INFORMATION
4. GENERAL SAFETY AND PERFORMANCE REQUIREMENTS
5. BENEFIT-RISK ANALYSIS AND RISK MANAGEMENT
6. PRODUCT VERIFICATION AND VALIDATION



# Annex II Technical Documentation

1. Device Description
2. Information to be supplied by the manufacturer
3. Design and Manufacturing Information
4. General Safety and Performance Requirements
5. Benefit-Risk analysis and risk management
6. Product verification and validation

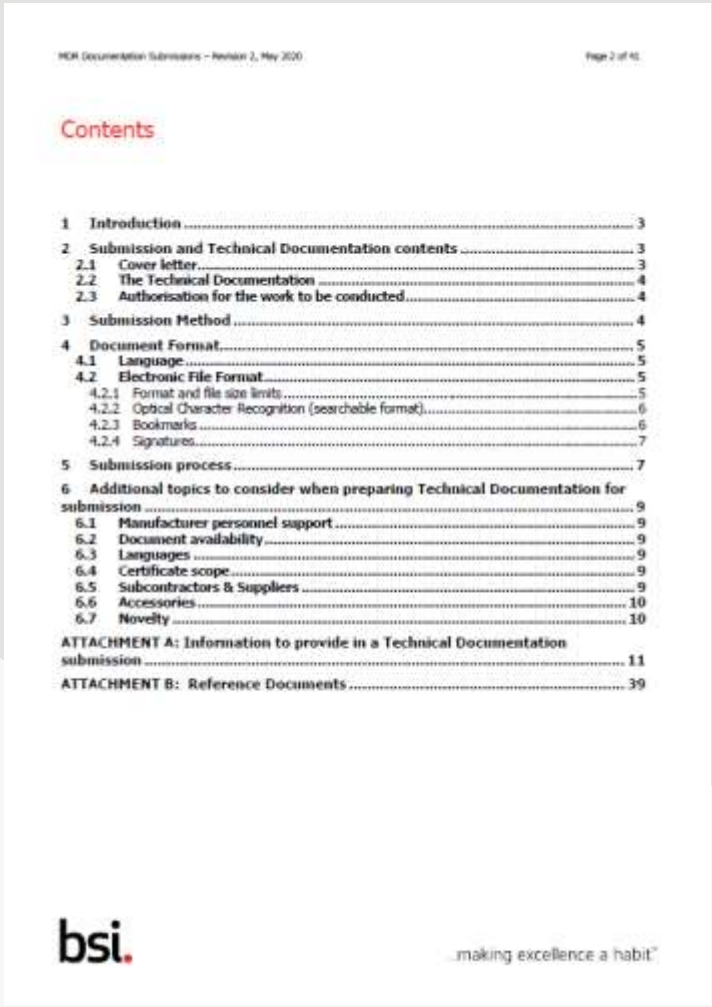
# Annex III Technical Documentation on Post-Market Surveillance

- Post-Market Surveillance (PMS) Plan
- Post-Market Clinical Follow-Up (PMCF) Plan
- Periodic Safety Update Report (PSUR)

Annex XIV – Clinical Evaluation and Post-Market Clinical Follow-Up

# MDR Technical Documentation – Best Practice

- BSI provides this guide.
- A complete and well-organised technical documentation file decreases time and cost of the review.
- Searchable, bookmarked PDF files
- The technical documentation should be available in full in accordance with Annex II.


https://www.bsigroup.com/globalassets/meddev/localfiles/de-de/documents/bsi-md-mdr-best-practice-documentation-submissions-en-gb.pdf

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# MDR Technical Documentation Completeness Check



MDR Technical Documentation Completeness Check







## 3 Supplemental Guidance

Guidance is available from BSI on the best practices in relation to preparation of Technical Documentation from the following link: https://www.bsigroup.com/globalassets/meddev/localfiles/en-gb/documents/bsi-md-mdr-best-practice-documentation-submissions-en-gb.pdf

## 4 Technical Documentation Completeness Checklist

### 4.1 Client Details

| | |
|---|---|
| Manufacturer | |
| Single Registration Number (SRN) | |
| Name of the device(s) the Technical Documentation is associated with | |
| Basic UDI-DIs covered | |
| Impacted BSI certificates (if known) | |
| Date of submission to BSI | |

### 4.2 Technical Documentation Checklist

| Section Title | Item | Location of the requested information; Mark as "N/A" if not applicable and provide a brief justification | BSI Completeness Check (To be completed by BSI) |
|---|---|---|---|
| Overview | Cover letter | | ☐YES ☐NO |
| | MDF4900 – BSI Change Notification Form | | ☐YES ☐NO ☐N/A with justification |
| | Document index | | ☐YES ☐NO |
| | Top level (or summary) Technical Documentation (STED) file | | ☐YES ☐NO ☐N/A with justification |
| BSI Comments - Overview | | | |
| **1. Device Description and Specifications Including Variants and Accessories** | | | |







| Section Title | Item | Location of the requested information; Mark as "N/A" if not applicable and provide a brief justification | BSI Completeness Check (To be completed by BSI) |
|---|---|---|---|
| 1.1 Device Description | 1.1.1 General description including product or trade names, principles of operation, mode of action etc | | ☐YES ☐NO ☐N/A with justification |
| | 1.1.2 Accessories included | | ☐YES ☐NO ☐N/A with justification |
| | 1.1.3 Accessories not included but necessary for use | | ☐YES ☐NO ☐N/A with justification |
| 1.2 Intended Purpose and Intended Users | 1.2.1 Intended purpose including any clinical claims | | ☐YES ☐NO ☐N/A with justification |
| | 1.2.2 Intended users | | ☐YES ☐NO ☐N/A with justification |
| 1.3 Basic UDI-DI & EMDN code | 1.3.1 Basic UDI-DI and any other relevant UDI related information | | ☐YES ☐NO ☐N/A with justification |
| | 1.3.2 EMDN code (previously referred to as CND code) | | ☐YES ☐NO ☐N/A with justification |
| 1.4 Devices covered by technical documentation | 1.4.1 List of type, sizes, configurations, variants etc including catalogue numbers covered by the submitted technical documentation | | ☐YES ☐NO ☐N/A with justification |
| 1.5 Classification | 1.5.1 Classification of the device including all the applicable rules and relevant rationales | | ☐YES ☐NO ☐N/A with justification |
| 1.6 Materials | 1.6.1 Description and identification of key materials incorporated into the device | | ☐YES ☐NO ☐N/A with justification |

# Make a full and thorough MDR submission

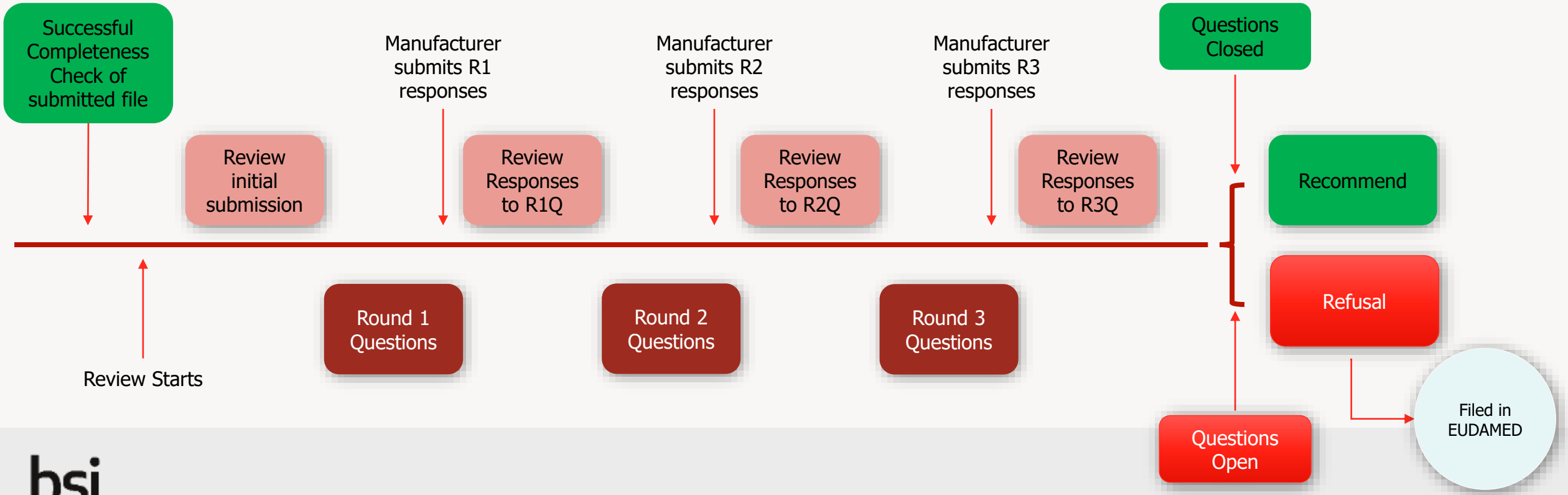
- Completeness Check prior to formal TD review

| Section Title | Item | Location of the requested information; Mark as "N/A" if not applicable and provide a brief justification | BSI Completeness Check (To be completed by BSI) |
|---|---|---|---|
| 3.4 Sites involved in design and manufacturing activities | 3.4.1 Legal Manufacturer (as per EUDAMED registration) | Section 1.2 of ABC-XYZ-035 (Page 5) | ☒YES ☐NO ☐N/A with justification |
| | 3.4.2 European Representatives | Section 1.3 of ABC-XYZ-035 (page 5) | ☒YES ☐NO ☐N/A with justification |
| | 3.4.3 Site with Design responsibility | Section 4.3 of ABC-XYZ-035 (page 16) | ☒YES ☐NO ☐N/A with justification |
| | 3.4.4 Sterilisation subcontractors | Section 4.3 of ABC-XYZ-035 (Page 17) | ☒YES ☐NO ☐N/A with justification |
| | 3.4.5 Other critical subcontractors and crucial suppliers relevant to the device(s) including any copies of certification held by such entities | Section 4.3 of ABC-XYZ-035 (Page 17) | ☐YES ☒NO ☐N/A with justification<br>No critical subcontractors listed |
| BSI Comments – Section 3 | Inclusion of requested information confirmed except no critical subcontractors listed.<br>Please confirm if there any other critical subcontractors and crucial suppliers relevant to the device? If yes, please provide copies of certification held by such entities. | | |

"…….We thought we would send you the top-level documents, and then follow up with more as you need them." - Manufacturer

# MDR TD Review Limitations – some specifics

- 3 rounds of questions
- MDR Annex VII section 4.5.1 specify rationale for time limits for completion of conformity assessment activities
- BSI rationale based on rounds of questions rather than a time limit



# MDR TD Assessment – Timing and Limitations

Completeness Check

Ensuring all documentation is present and generally complete at a glance – not a detailed technical assessment

Three rounds

BSI will be required to reject applications if gaps cannot be addressed in three rounds of questions

In those cases, Manufacturer will be required to resubmit an amended application

# Technical Documentation Assessment – MDCG 2019-13

**5.1. Depth of the assessment**

The depth and extent of the technical documentation assessment of Class IIa / IIb and Class B / Class C devices will be the same as the depth of assessment carried out for Class III and Class IIb implantable and Class D devices.

This means that the technical documentation of a device shall be assessed against all General Safety and Performance Requirements (Annex I) and requirements of Annex II and III. Records of the assessment shall be prepared which allow a third party to understand the functionality of the device and all aspects of the assessment including judgements made by the assessor.

It should be taken into account that every device (i.e. Basic UDI-DI) might include different variants, models or sizes. In that case, the review of the technical documentation will also include the assessment of how the differences among these have been addressed in the technical documentation and whether all of them are in line with the relevant requirements.

Depth and extent of TD assessment to be same irrespective of device classification

TD assessment durations determined by device type (MDA/MDN codes) and complexity rather than device classification;

- Characteristics such as presence of animal tissues, nanomaterials (MDS codes) increase the assessment durations

# It is important to follow the EU Guidance Documents because…

— relating to the sampling of devices, verify that the manufactured device is in conformity with the technical documentation; such requirements shall define the relevant sampling criteria and testing procedure prior to sampling,

— evaluate and verify a manufacturer's compliance with relevant Annexes.

The notified body shall, where relevant, take into consideration available CS, guidance and best practice documents and harmonised standards, even if the manufacturer does not claim to be in compliance.

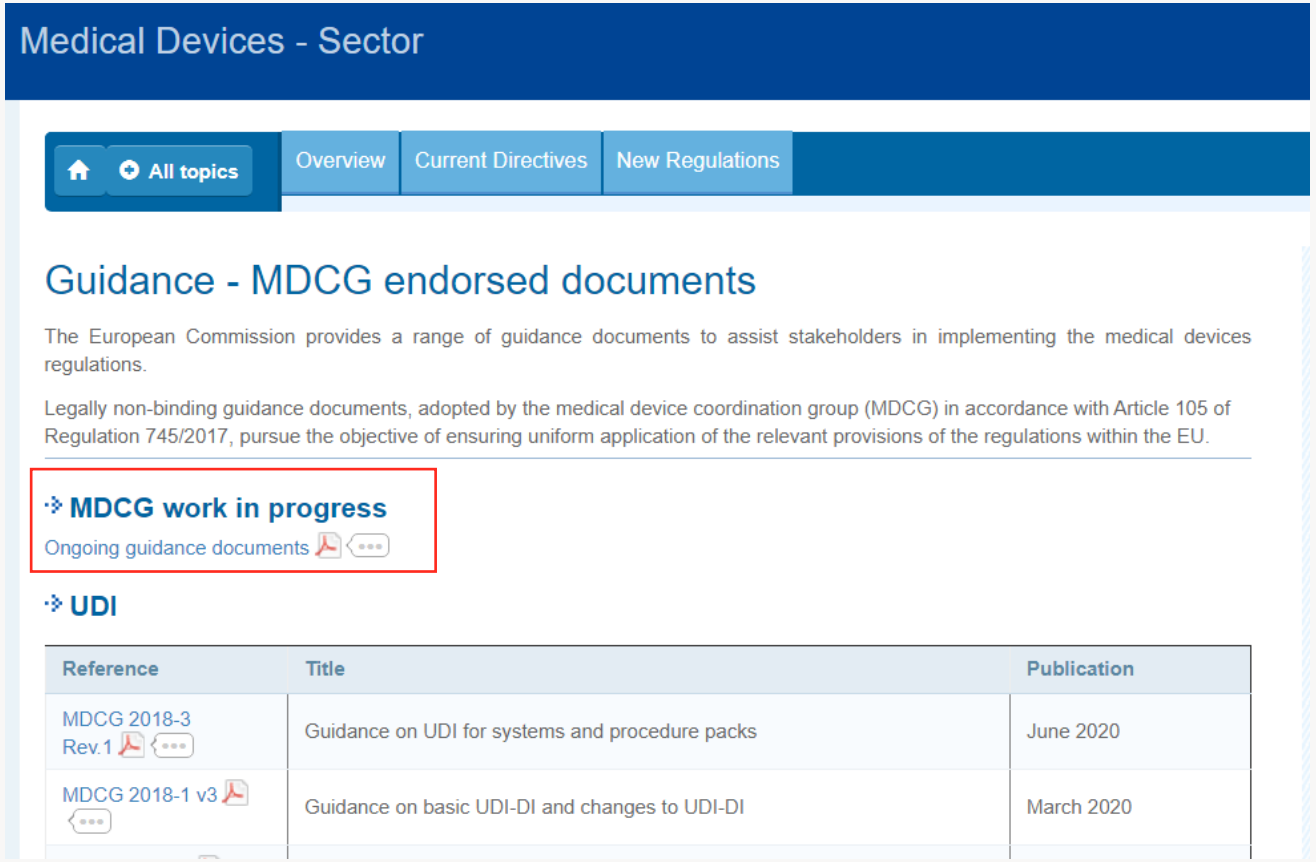
MDR, IVDR - Annex VII Section 4.5.1

# EU MDCG Guidance Documents

https://ec.europa.eu/health/md_sector/new_regulations/guidance_en

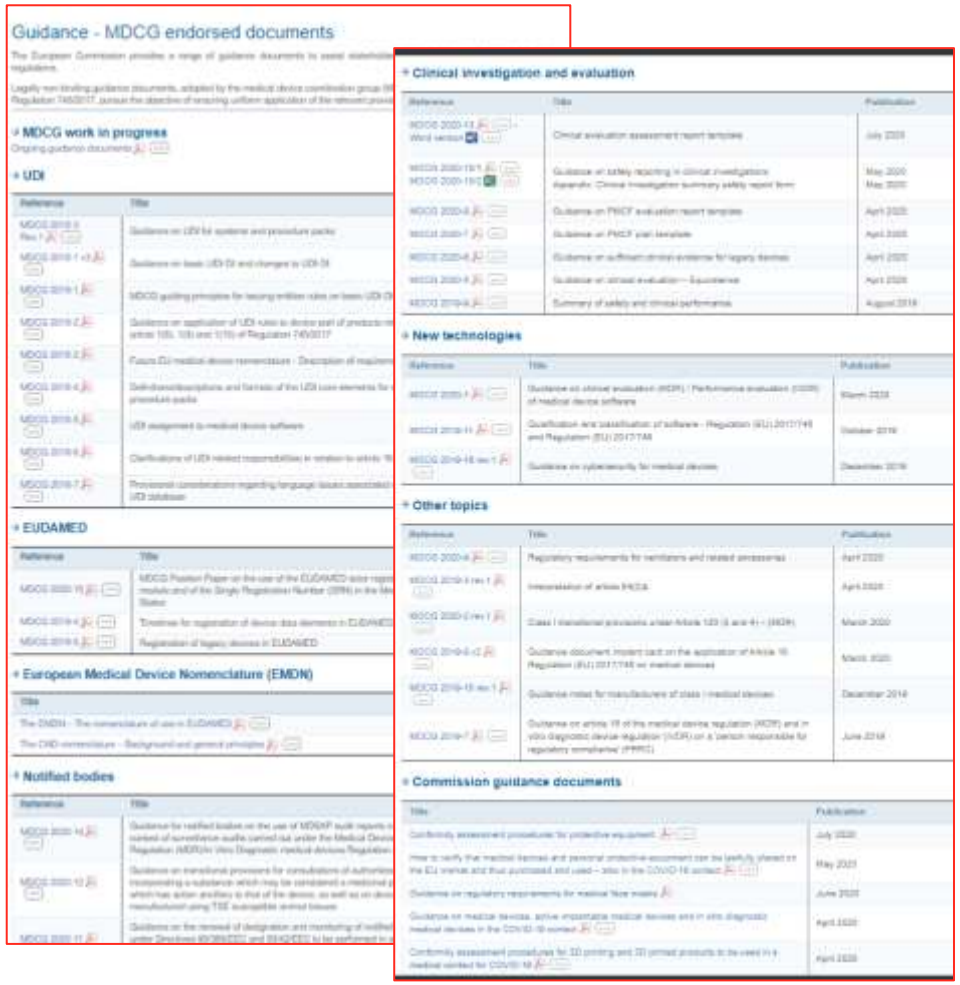
Topic Headings Include:

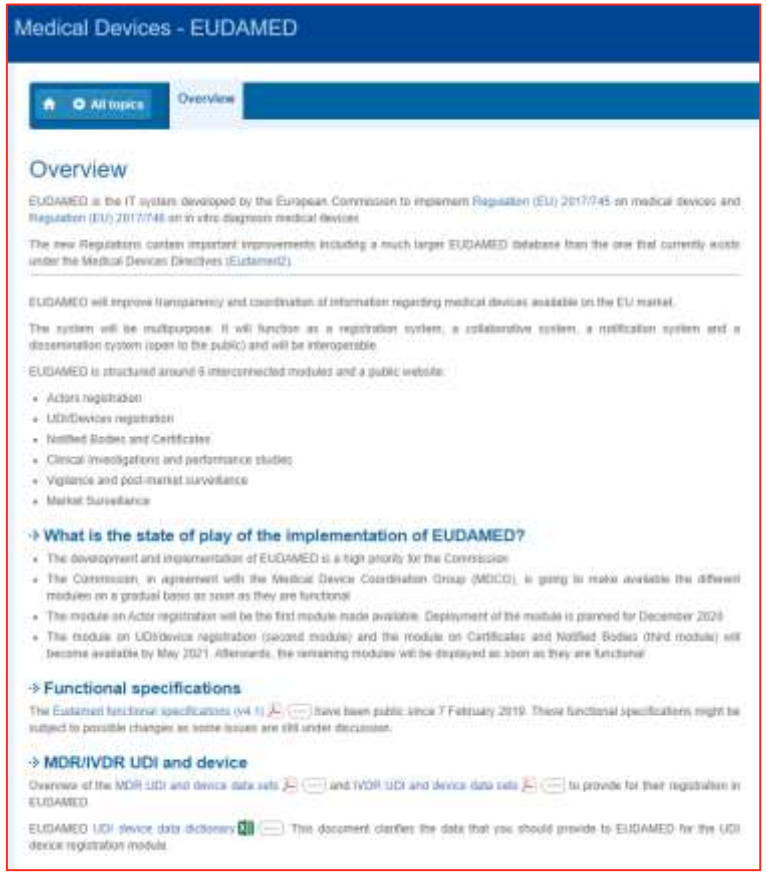
- UDI
- EUDAMED
- European Medical Device Nomenclature (EMDN)
- Notified Bodies
- Clinical Investigation and Evaluation
- New Technologies
- Other Topics
- Commission guidance Documents
- Other Guidance Documents



# MDCG Guidances, EUDAMED

https://ec.europa.eu/health/md_sector/new_regulations/guidance_en
https://ec.europa.eu/health/md_eudamed/overview_en

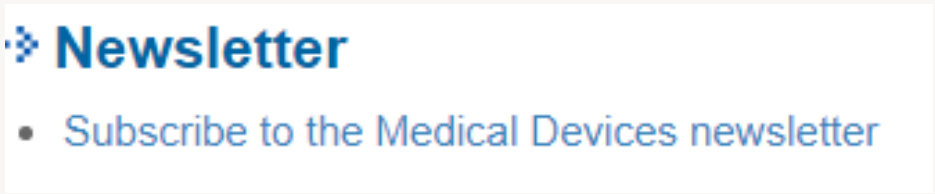



How often are manufacturers checking for changed documents and the impact on processes?

# Get notified of updates to EU Guidance Documents

https://ec.europa.eu/health/md_sector/overview_en



**Have you already submitted a file for MDR technical documentation review to your Notified Body ?**

a) Yes

b) No, but ready to submit

c) No, we’re not ready yet

# MDR Technical Documentation Lessons Learned

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# Technical Documentation – Overall Feedback

- Generally, new MDR requirements are being clearly addressed
- Some areas continue to evolve with guidance being published and further experience being gained
- "Legacy" device challenges
  - Stand-alone new application file required; not "gap analysis to MDR"
  - Clear organization of files and data
  - Large numbers of reports with no explanation or map will slow review time
    - Consider testing map or summary tables
    - Rationales for applicability of any leveraged tests
    - Justifications needed when historical testing performed does not meet current standards (e.g. ISO 10993 and others)

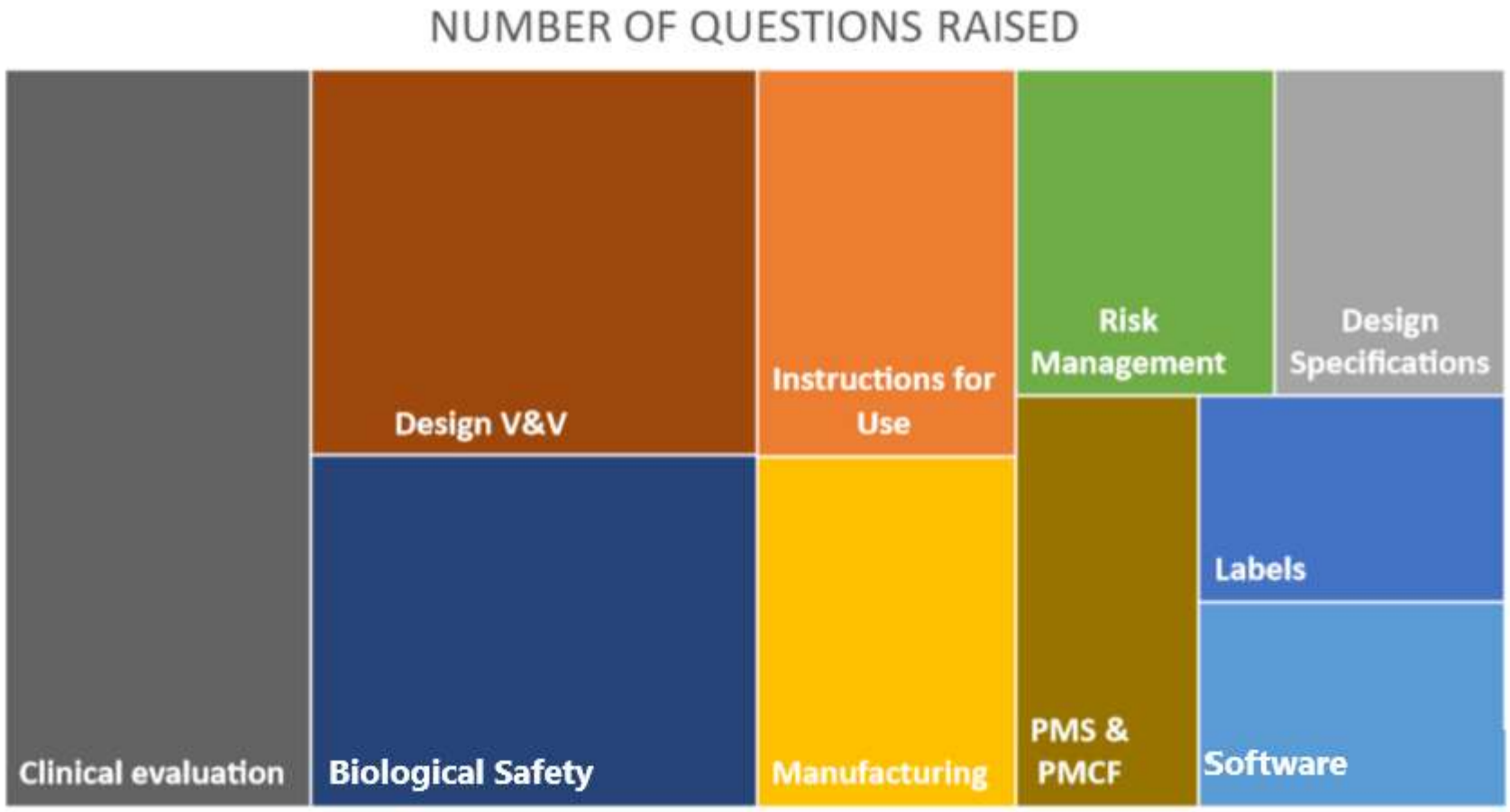
# Technical Documentation – General Feedback

- ✓Know your audience – provide context and evidence
- ✓All relevant reports must be provided - it is not acceptable to reference or leverage tests from the same device or another device that were "previously reviewed by BSI under MDD" without providing these test protocols/reports
- ✓Avoid chain referencing
- ✓Review file fully before submitting

**What have you found most challenging when preparing your technical documentation for submission to your Notified Body?**

a) Biological Evaluation
b) Clinical evaluation
c) Design V&V
d) Design and Manufacturing Information
e) None of the above

# Technical Documentation – Questions Raised



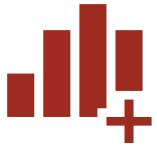

These are early trends and may change with time and more experience

# For "Legacy" MDD Devices – Tell the Story

**Devices with a long history under MDD may have a history of device changes and/or company acquisitions**

While each change was likely reviewed individually under MDD, MDR is a new stand-alone application with no grandfathering and **all testing must be presented and explained clearly**

If it is **not clear what testing was performed on what version, or what other testing was leveraged / justified over time**, please clearly outline this to avoid questions



Please do not present a **"stack" of design verification/validation reports with no context or explanation** – this will increase the review time and cost

Similarly - if it is **not clear which clinical data was obtained on what historic version of the device**, please clearly outline this and justify applicability (equivalence) if the device has changed

Refer to BSI Best Practice Guidelines for additional guidance

# Design V & V – Some common gaps

A clear trace matrix between specifications and relevant reports / sections can reduce review time significantly

Design requirements not fully verified/validated

Missing protocols, reports – provide all referenced in design input/output matrix

Unclear organization of tests for legacy devices

Unclear / hidden rationales for leveraged tests

Evidence of performance over lifetime of device not demonstrated

Test acceptance criteria not met – No justifications for accepting results

Sample sizes, selection criteria and preparation unclear

& many more….

Many apply to packaging tests also

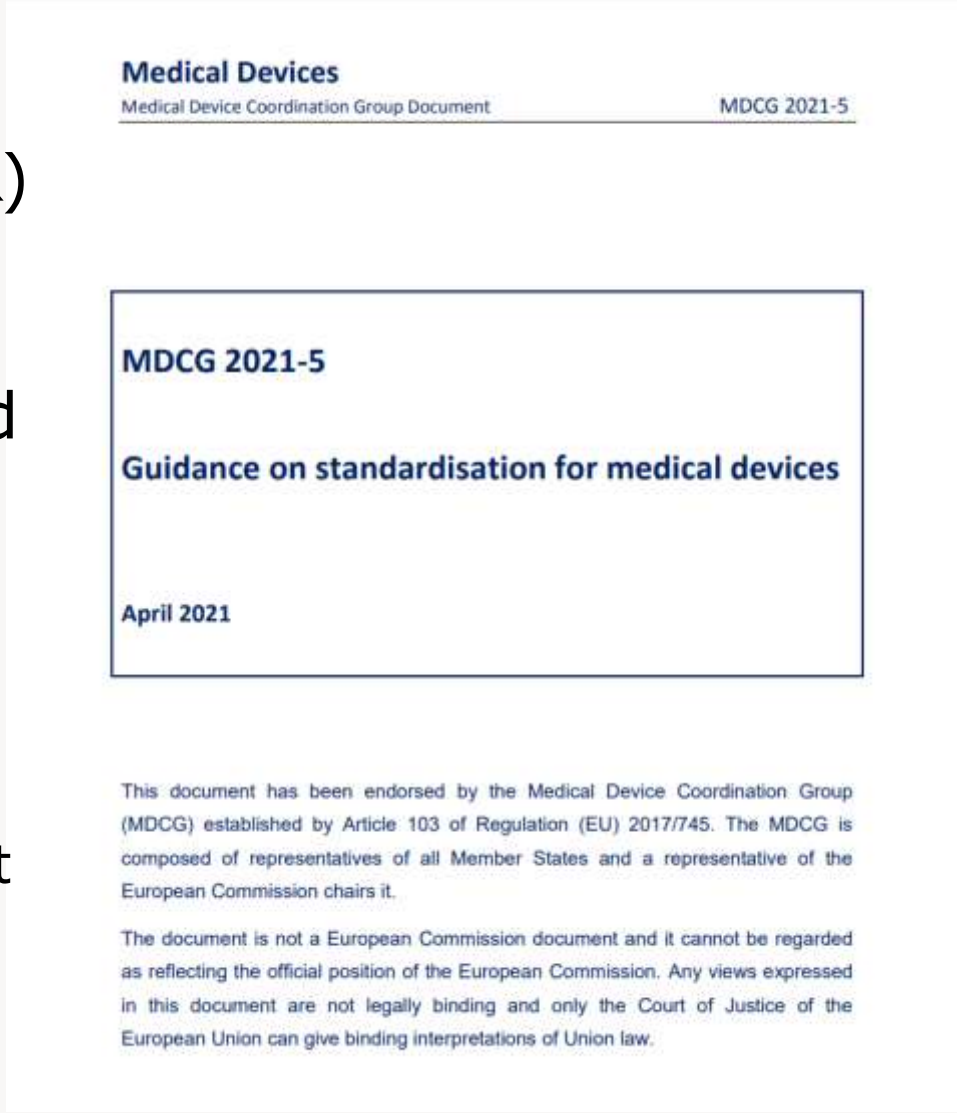
# Design V&V Roadmap – Acme Catheter 2.0

| Specification | Acceptance Criteria | Testing Protocol/Report | Sample Tested | Justification for Sample Tested | Location in TD |
|---|---|---|---|---|---|
| 1.01 – Tensile Strength of Tip | >5N | P/R2013-06 – New Tip Design t=0<br>P/R2013-08 – New Tip Design t=24 | Acme Catheter 2.0 | Same subject device under application | Appendix 83 t=0<br>Appendix 84 t=24 |
| 1.02 – Tensile Strength of Hub | >8N | P/R2011-03 – Acme t=0<br>P/R2011-05 – Acme t=24 | Acme Catheter 1.0 | Hub same as current 2.0 version under application; specification not impacted by tip change to 2.0 | Appendix 86 t=0<br>Appendix 87 t=24 |
| 1.03 – Liquid Leakage | No leaks at <30 psi | P/R2011-03 – Acme t=0<br>P/R2011-05 – Acme t=24 | Acme Catheter 1.0 | Shaft same as current 2.0 version under application; specification not impacted by tip change to 2.0 | Appendix 86 t=0<br>Appendix 87 t=24 |
| 5.11 – Pouch Peel Strength | > 1N/in | P/R2009-02 – CathBot t=0<br>P/R2009-05 – CathBot t=36 | CathBot RX | Pouch and tray design identical to Acme 2.0 and mass of CathBot worst case; same acceptance criteria and testing method; shelf life greater than subject device | Appendix 88 t=0<br>Appendix 89 t=36 |

Other content to consider: Location of protocols; Sample size and justification; standard version used; rationale for any deviation to test methods or difference in acceptance criteria

# Application of Standards

- No standards are yet harmonized to 2017/745 (MDR)
- List of standards to be harmonized is published but this has not yet been completed
- The most current standards are therefore considered state of the art e.g. ISO 14971:2019
- Present a clear gap analysis if older version of standards used
  - For tests, address whether current standards are considered met, conclusion why additional testing was not required
  - Often seeing different versions in a "claimed standards" list compared to test reports, with no gap analysis or explanation – present this proactively
- MDCG 2021-5, Guidance on standardisation for medical devices, April 2021



Medical Devices

Medical Device Coordination Group Document MDCG 2021-5

MDCG 2021-5

Guidance on standardisation for medical devices

April 2021

This document has been endorsed by the Medical Device Coordination Group (MDCG) established by Article 103 of Regulation (EU) 2017/745. The MDCG is composed of representatives of all Member States and a representative of the European Commission chairs it.

The document is not a European Commission document and it cannot be regarded as reflecting the official position of the European Commission. Any views expressed in this document are not legally binding and only the Court of Justice of the European Union can give binding interpretations of Union law.

# Clearly present Annex I / GSPR Compliance

Possible Questions

Have applicable and non-applicable requirements been clearly noted with appropriate and relevant rationales?

It may be that certain sub-parts apply while others do not – consider the need for addressing applicability individually

Has the "precise identity of the controlled documents offering evidence of conformity" (Annex II, Section 4.d) been identified for each including document location?

e.g. "Design Verification Testing, Tech Doc Section 8" is not precise and is not fully applicable to each GSPR where it might be listed.

Have applied standards, Common Specifications, and guidances been identified, along with extent of compliance and version / year claimed?

Have all other applicable Directives & Regulations (Animal Tissue, Machinery, PPE, eIFU, etc.) been identified?

If cited standards are in a referenced list and not directly in the GSPR Checklist, is the list of claimed standards traceable?

Are the cited standard versions consistent with those listed in the test reports or has a gap analysis been presented?

# Biological Safety – Common Issues

## No overall biocompatibility assessment of the current version of the device under application

- Test reports for each iterative change over the years, without an overall explanation / assessment of current device
- Make clear the relevance of each test and how the subject device was considered as a new application
- Do not submit every biocompatibility test in a DHF with no explanations
- Overall biological safety assessment by qualified individual/team

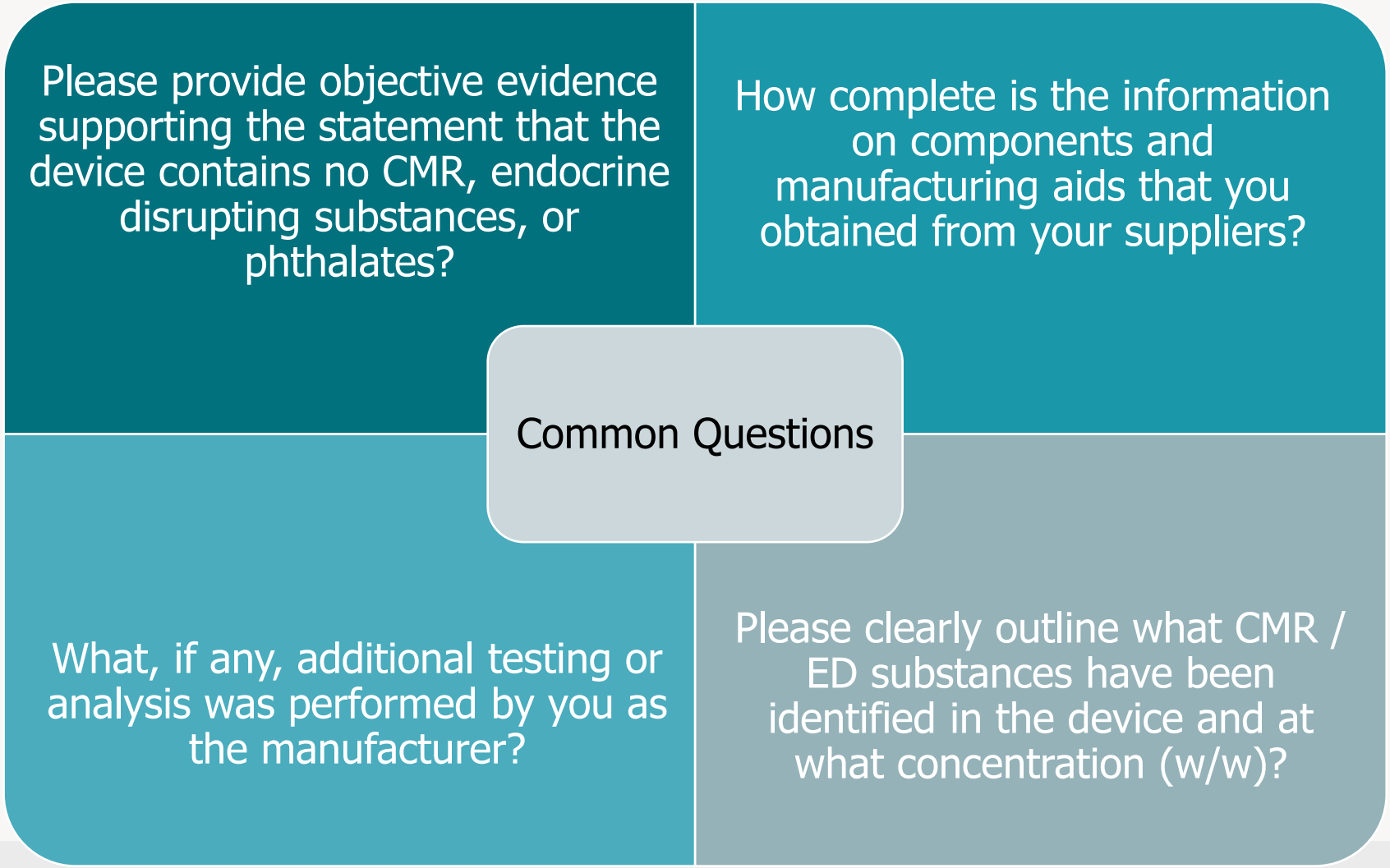
## Context of tests not clear

- Rationales for any tests leveraged comparing device specifics
- Rationale for any device attributes that have changed over time
- Consideration of manufacturing processes & changes
- Details of sample preparation and extractions not sufficiently discussed
- Proactive gap assessment of revised standards

## Other items

- Clear rationales for any tests not conducted/presented
- Chemical characterization testing (especially legacy devices)
  - Justification of test method(s) selected
- Organization: Tests not individually bookmarked and referenced
- No evidence that biological safety evaluation connects to risk management

# GSPR 10.4.2 (CMR / ED Substances)



# Manufacturing & Process Validations

- It is required to include full manufacturing validations in MDR submissions (MDR Annex II, Section 3b)

> (b) complete information and specifications, including the manufacturing processes and their validation, their adjuvants, the continuous monitoring and the final product testing. Data shall be fully included in the technical documentation;

- Protocols and reports of critical process validations are required, not just summary
- Overall summary or Master Validation plan is still helpful to understand overall strategy and process
  - Include pointers to all detailed supporting documents
- Clear link between PFMEAs, manufacturing processes, incoming inspections and inline tests etc. for completeness and control.
- Process validations: what was run, including justifications for tests conducted, sampling rationale, raw data, product range covered.

Ensure English versions are provided

# Inspection Information – why is BSI asking for this?

- Incoming, in-process and final inspection checks and the results (Annex VII 4.5.3)
- Common question – *"Why is this being requested outside the QMS audit?"*
- MDR requires that the NB review this as part of the Annex IX technical documentation assessment (not only QMS audits)

4.5.3. Product verification

Assessment of the technical documentation

For assessment of the technical documentation conducted in accordance with Chapter II of Annex IX, notified bodies shall have sufficient expertise, facilities and documented procedures for:

— the allocation of appropriately qualified and authorised personnel for the examination of individual aspects such as use of the device, biocompatibility, clinical evaluation, risk management, and sterilisation, and

— the assessment of conformity of the design with this Regulation, and for taking account of Sections 4.5.4. to 4.5.6. That assessment shall include examination of the implementation by manufacturers of incoming, in-process and final checks and the results thereof. If further tests or other evidence is required for the assessment of conformity with the requirements of this Regulation, the notified body in question shall carry out adequate physical or laboratory tests in relation to the device or request the manufacturer to carry out such tests.

# Lifetime in Use

- Lifetime of the device should be defined by the manufacturer (GSPR 6)
- How is evidence of performance over lifetime demonstrated in testing and clinical use?
- Post-Market Surveillance & PMCF plans should be suited to gathering data through the device lifetime (Art. 83, Annex XIV)

- Special device types:
- Implants
  - Article 18 (Implant card and information to be supplied to patient): Expected lifetime of the device and any necessary follow-up
  - SSCP: Information about the expected lifetime of the device including data on implant survival rates
- Software
  - Lifetime of the device may be determined by hardware, or other required software

# Clinical Evaluation – Some Common Gaps

| | | | |
|---|---|---|---|
| Equivalence not demonstrated | Incomplete Safety & Performance data with respect to all indications/claims | Clinical benefits and risks not clearly addressed | Clinical benefits not measurable |
| Safety and performance endpoints not clearly defined | Patient population not clearly defined | State of the art not clearly established | Missing or incomplete clinical development plans |
| | Competence of the CER authors/reviewers | & many more…. | |

# Article 18 (Implant Card and Info to be Supplied)

## *What Article 18 documentation should manufacturers submit?*

1. Explanation/justification for the solutions adopted by the manufacturer to meet art. 18 requirements and MDCG guidance.
2. Implant card drawing (back and front) and sticker drawings (if applicable)
3. Implant card specification
    - Physical/mechanical and material/chemical specifications for card (and stickers if applicable)
4. Informative instructions leaflet (or justification for not providing)
5. Art. 18.1 (b-d) information
    - Patient information leaflet
    - screen shots from patient information website, hyperlink to working website etc.
6. Usability validation protocols/reports

# Improving Technical Documentation Submissions

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# TD Submissions - Remember to Include:

- ✓ Information to allow the design stages applied to the device to be understood (Annex II Section 3a)
- ✓ Design Specifications or Design Inputs, etc. (Needed for Annex II Section 3)
- ✓ All Process Validations and associated Validation Plan (Annex II Section 3b)
- ✓ Risk Management Plan (Annex I, GSPR 3a)
- ✓ Clinical Evaluation Plan as well as Clinical Evaluation Report (Annex II Section 6.1c)
- ✓ Device-specific PMS Plan (Annex III), and PMCF Plan (if applicable) including proactive elements (Annex XIV)
- ✓ Incoming, in-process and final inspection checks and the results (Annex VII 4.5.3)

New requirements compared to MDD/AIMDD or often missed

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# TD Submissions - Additional Topics To Consider:

- ✓ Manufacturer personnel support
- ✓ Document availability
- ✓ Languages
- ✓ Certificate scope
- ✓ Subcontractors and Suppliers
- ✓ Accessories
- ✓ Novelty

# Improving TD submissions – Final Thoughts:

- ✓ Regulations and regulators are clear that MDR is a new stand-alone application
- ✓ Make the documentation a numbered, fully searchable, bookmarked PDF and easy for the reviewer to navigate. Know your audience – provide context and evidence – tell the story.
- ✓ Read the salient portions of the MDR and the associated MDCG guidance documents and address these to the best of your ability/understanding
- ✓ **A complete and well-organised technical documentation file decreases the time and cost of the review.**

# BSI Medical Devices – Use Our Resources

https://www.bsigroup.com/en-GB/medical-devices/resources

## Brochures, Guides and Documents


## Webinars


## White Papers and Articles


## Training Resources

| Medical devices regulation (MDR) | |
|---|---|
| Transition from MDD to MDR | 1 day |
| Technical Documentation for CE - Marking | 1 day |
| Requirements of MDR for CE - Marking | 1 day |
| Implementing of MDR for CE- Marking | 3 days |

| Further courses for medical devices manifacturers | |
|---|---|
| Medical Device Single Audit Program (MDSAP) | 2 days |
| ISO 14971 Risk Management | 1 day |
| Creating and Maintaining Technical Files | 1 day |
| Post-market Surveillance and Vigilance | 1 day |
| Clinical Evaluation for Medical Devices | 1 day |
| Process Validation for the Medical Device Industry | 1 day |
| Introduction to Medical Device Software | 1 day |


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# Recap

1. MDR Technical Documentation Review Process
2. Common Gaps or Questions from MDR Technical Reviews
3. Improving Technical Documentation Submissions
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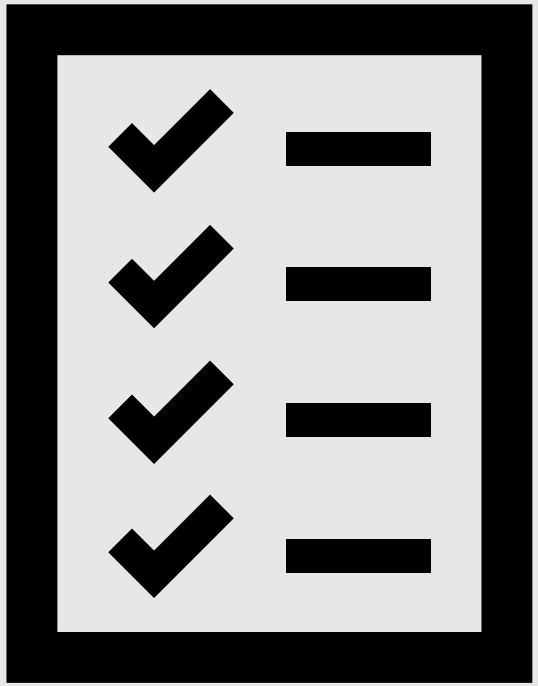

# Questions?

# Available medical devices training courses include:

## CE marking training courses

- MDD to MDR Transition
- Requirements of the MDR  for CE Marking
- Implementation of the MDR for CE Marking
- Introduction to Medical Device Software

## Specialist training courses

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