MDR Transition and Technical Files

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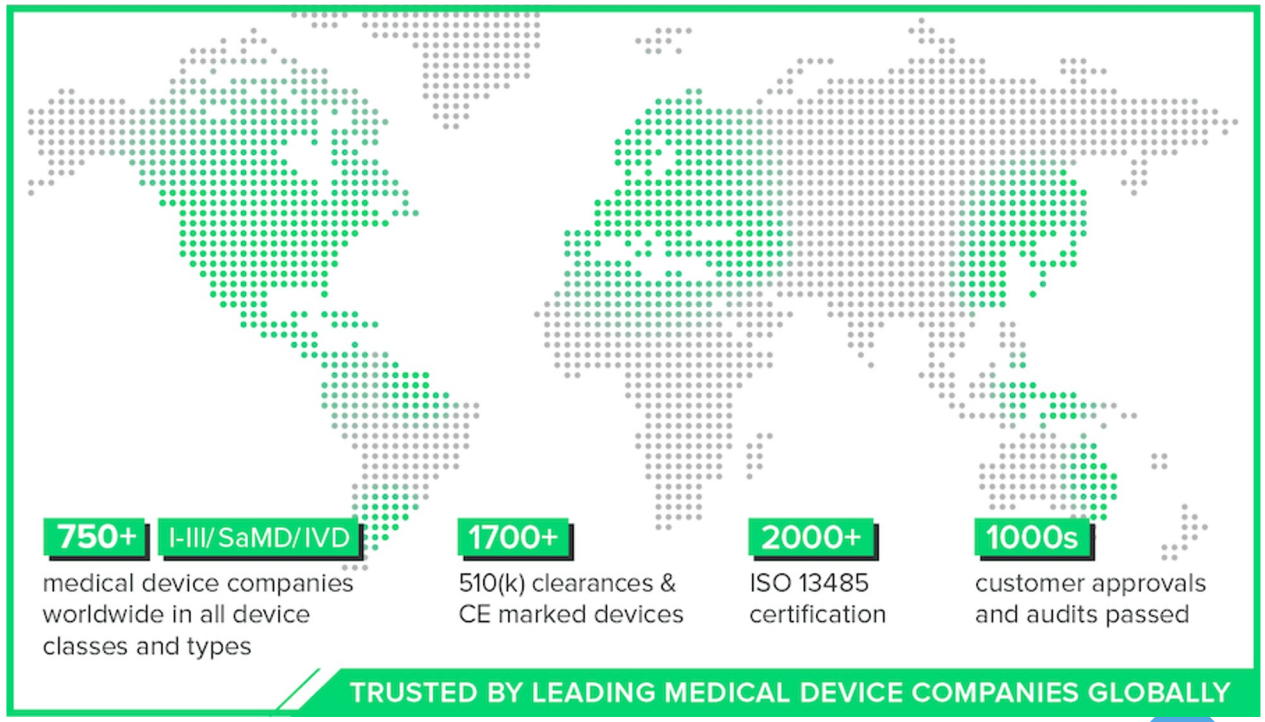

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Rook Quality Systems is a consulting firm dedicated to helping startup to mid-sized medical device companies develop and maintain effective and efficient quality systems.

Experience

Nearly a decade working with class I-III devices, SaMD, and IVDs. Supporting companies in the very early stages of QMS and device creation, from design through commercialization and post-market monitoring.

Expertise

Rook's team of eight Certified Auditors are experts in FDA regulations, MDSAP audits, ISO 13485:2016 compliance, and MDR conformity and provide support during an external or regulatory audit.

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Webinar Outline

- Background on EU MDR
- Clinical Evaluation Requirements
- Risk Management Impacts
- Preparing MDR Technical Files
  - What are the minimum requirements for a Technical File?
  - Who reviews the Technical File?

Background on EU MDR

European Union Medical Device Regulation was adopted on April 5, 2017.

EU MDR is the set of regulations that governs the production and distribution of medical devices in Europe and is legally binding.

It is intended to ensure a high standard of quality and safety for medical devices being produced in or supplied into the European market.

MDR replaces the Medical Device Directive (MDD) that has been the standard for medical device regulation in the EU since 1993

Poly Implant Prothése (PIP) scandal in France triggered change when non-medical grade silicone was used in breast implants, resulting in a massive recall and a prison sentence for the founder of the company.

Background on EU MDR

The EU MDR is comprised of 10 Chapters (123 articles within these chapters) and 17 annexes – totaling 218 pages.

In comparison, the EU MDD had 23 articles and 12 annexes – totaling 60 pages.

The EU MDR is almost four times larger than the MDD!

Much higher level of detail.

Additional conditions that must be met for legacy MDD devices. Legacy MDD devices must be recertified in accordance with the MDR.

Some devices have been reclassified to a higher risk.

Background on EU MDR

Nothing from the MDD has been removed. The MDR has expanded upon the MDD requirements with stricter legislation.

The EU MDR includes requirements for:

- **Quality Management Systems (Article 10)**
- **Clinical Evaluations and Investigations (Chapter VI)**
- **UDI/EUDAMED Requirements (Chapter III)**
- **Post-Market Surveillance and Vigilance (Chapter VII)**
- **Device Classification (Annex VIII)**
- **General Safety and Performance Requirements (Annex I)**
- **Technical Documentation (Annex II and Annex III)**
- **Risk Management (Annex I)**
- **CE Marking of Medical Devices (Annex V)**

Background on EU MDR

EU MDR is harmonized with the following ISO standards:

ISO 13485:2016 Medical Devices – Quality Management Systems

ISO14971:2019 Medical Device Risk Management

Various other ISO standards involving device packaging, sterilization, biological evaluation, as well as standards which are particular for certain devices.

List of harmonized standards is available here.

Background on EU MDR

EU MDR requires manufacturers to engage with the following groups:

Competent Authorities

Responsible for transposing the requirements of the EU regulations into national legislation and supervising Notified Bodies.

Notified Bodies

Responsible for reviewing and approving medical devices, as well as performing conformity assessments which are required for issuing declarations of conformity. Designated by the EU member states.

Authorized Representatives

Responsible for coordinating with notified bodies and competent authorities on behalf of manufacturers which are located outside of the European Union.

Background on EU MDR

Key dates for the MDR Transition:

- 26MAY2021: Date of application of the EU MDR (legally binding). Originally set for May 2020 but was delayed due to COVID.
- 26MAY2022: EUDAMED database goes live. Originally set for May 2020 but was delayed.
- 26MAY2024: Certificates issued under MDD become void. Last date for placing devices on the market which were CE marked under the MDD.
- 26MAY2025: Last date for end-users to put MDD devices into service.

UDI Deadlines:

- 26MAY2021: Class III and implantable devices (labeling and packaging)
- 26MAY2023: Class IIa and IIb devices (labeling and packaging)
- 26MAY2025: Class 1 devices (labeling and packaging)
- For reusable devices, direct marking requirements apply two (2) years after the dates listed for labeling and packaging requirements.

MDR Transition's Impact to Manufacturers

Must recertify products that were previously certified under the MDD. Some products may now be within a higher risk classification.

Must perform clinical evaluations.

Must maintain a Technical File in accordance with Annex II.

Must mark products with a UDI.

Must submit product information to the EUDAMED database.

HIGHLY RECOMMENDED to obtain ISO 13485:2016 certification.

HIGHLY RECOMMENDED to establish a ISO 14971:2019 complaint risk management system.

Planning and Conducting Clinical Evaluations

All manufacturers are required to perform clinical evaluations (Article 61).

Manufacturers are required to specify and justify the level of clinical evidence necessary to demonstrate conformity with the relevant GSPR.

Clinical evaluations are based on the following:

- Critical evaluation of relevant scientific literature.
- Critical evaluation of the results of all available clinical investigations.
- Consideration of currently available alternative treatment options, if any.

Planning and Conducting Clinical Evaluations

Clinical evaluations are driven by a clinical evaluation plan (Annex XIV Part A.1) which includes:

- Identification of the GSPR that require support from relevant clinical data
- Specification of the intended purpose of the device
- Clear specification of intended target groups with clear indications and contra-indications.
- Detailed description of intended clinical benefits to patients with relevant and specified clinical outcome parameters.
- Specification of methods to be used for examinations of aspects of clinical safety with clear reference to the determination of residual risks and side-effects
- Indicative list and specification of parameters to be used to determine the acceptability of the benefit-risk ratio for the various indications and for the intended purpose(s) of the device
- Clinical development plan indicating progression from exploratory investigations to confirmatory investigations, and a PMCF with indication of milestones and potential acceptance criteria.

Planning and Conducting Clinical Evaluations

Manufacturers are also required to (per Annex XIV Part A):

- Identify available clinical data relevant to the device and its intended purpose and any gaps in clinical evidence through a systematic scientific literature review
- Appraise all relevant clinical data by evaluating their suitability for establishing the safety and performance of the device
- Generate any new or additional clinical data necessary to address outstanding issues through clinical investigations.
- Analyze all relevant clinical data in order to reach conclusions about the safety and clinical performance of the device including its clinical benefits.

Clinical Evaluation Requirements

The clinical evaluation (per Annex XIV Part A) shall:

- Be thorough and objective
- Consider both favorable and unfavorable data.
- Have a depth an extent proportionate and appropriate to the nature, classification, intended purpose, risks, and manufacturer's claims of the device in question.
- Have results and clinical evidence documented in a clinical evaluation report.

Clinical Evaluation of Equivalent Devices

Clinical evaluation may be based on clinical data relating to a device for which equivalence to the device in question can be demonstrated (Annex XIV Part A.3).

The demonstration of equivalence should consider the following characteristics:

Technical: similar design, used under similar conditions of use, similar specifications and properties, similar deployment methods, similar principles of operation and critical performance requirements.

Biological: same materials or substance sin contact with the same human tissues or body fluids for a similar kind and duration of contact and similar release characteristics of substances, including degradation products and leachables.

Clinical: used for same clinical condition or purpose, in a similar population, has similar relevant critical performance in view of the expected clinical effect for a specific intended purpose.

Post-Market Clinical Follow-Up (PMCF)

Post-Market Clinical Follow-up (PMCF) Requirements are listed in Annex XIV Part B.

PMCF is required unless the manufacturer can justify why PMCF is non-applicable.

- Justifications will be dependent on the nature of the device.
- For example, a low risk-device that has been on the market for an extended amount of time for which there have been no adverse events may not require a PMCF.

Post-Market Clinical Follow-up (PMCF) is documented through the PMCF plan and PMCF evaluation reports.

Post-Market Clinical Follow-Up (PMCF) Plan

PMCF plans are required to include the following information (Annex XIV Part B 6.2):

- the general methods and procedures of the PMCF to be applied, such as gathering of clinical experience gained, feedback from users, screening of scientific literature and of other sources of clinical data;
- the specific methods and procedures of PMCF to be applied, such as evaluation of suitable registers or PMCF studies;
- a rationale for the appropriateness of the methods and procedures referred to in points (a) and (b);
- a reference to the relevant parts of the clinical evaluation report referred to in Section 4 and to the risk management referred to in Section 3 of Annex I;
- the specific objectives to be addressed by the PMCF;
- an evaluation of the clinical data relating to equivalent or similar devices;
- reference to any relevant CS, harmonized standards when used by the manufacturer, and relevant guidance on PMCF; and
- a detailed and adequately justified time schedule for PMCF activities (e.g., analysis of PMCF data and reporting) to be undertaken by the manufacturer.

PMCF Report

Manufacturers are required to analyze the findings of the PMCF and document the results in a PMCF evaluation report that shall be a part of the clinical evaluation report and the technical documentation.

The conclusions of the PMCF evaluation report must be considered for the clinical evaluation and in the risk management processes.

Impact of Clinical Evaluation Changes

Previously under the MDD, manufacturers could choose whether to perform a critical evaluation of either relevant scientific literature or the results of all clinical investigations made.

Now under the MDR, manufacturers must meet the requirements outlined in Annex XIV and must meet both pre-market and post-market requirements.

Impact of Risk Management Changes

Previously under the MDD, manufacturers were required to:

- Eliminate or reduce risks,
- Take adequate protection measures in relation to risks that cannot be eliminated
- Inform users of residual risks

No defined methodology for these activities.

A risk management system was not a requirement of the MDD.

Risk Management Changes

Risk management is now a critical component of the documented General Safety and Performance Requirements outlined in Annex I.

Manufacturers must establish a risk management system (Article 10(2)).

ISO 14971:2019 is the currently recognized standard for risk management.

Risk Management System Requirements

The risk management system must include (per Annex I.3):

- A document risk management plan
- Hazard identification and analysis
- Risk estimation and evaluation
- Risk elimination and control
- The evaluation of the impact of new information and amend controls as necessary.

A risk management system that is compliant with ISO 14971:2019 will be compliant with EU MDR requirements.

What is a Technical File?

A Technical File is a set of organized technical documents that provides evidence that a medical device meets the general safety and performance requirements and conforms to CE-marking legislation.

This documentation must be available for the appropriate authorities to review upon request for all devices.

Previously under the MDD, the contents of technical documentation was left up to the manufacturers and notified bodies.

Now, the contents of this documentation is defined in Annex II of the MDR.

Technical File Requirements

General device description and specifications (Annex II 1.1)

Device labelling, packaging, and instructions for use (Annex II 1.2)

Detailed design and manufacturing documentation (Annex II 1.3)

General Safety and Performance Requirements (GSPR) (Annex II 1.4)

Risk Management and Risk-Benefit information (Annex II 1.5)

Product verification and validation information (Annex II 1.6)

Post-market surveillance information (Annex III)

Declaration of Conformity (Annex IV)

Technical File Requirements

General device description and specifications (Annex II 1.1)

- **Product trade names**
- **Intended use, purpose, population, and target medical conditions**
  - Includes any warnings or contraindications
- **Basic UDI-DI**
- **Device operation, functional elements, accessories, novel features, and configurations or variants**
- **Device materials and other applicable technical specifications**
- **Risk class (class I, IIa, IIb, or III)**
  - Detailed in Annex VIII
- **Predicate and competitor device overview**

Technical File Requirements

Device labeling, packaging, and instructions for use (Annex II 1.2)

- A complete set of labels on the device AND on its packaging
- The IFU should be translated in the languages accepted in the Member States where the device will be sold.

Technical File Requirements

Detailed design and manufacturing documentation (Annex II 1.3)

- Activities performed in the different design stages
- Manufacturing processes involved and their validation and monitoring
- Final product testing/release data
- Identification of manufacturing sites, suppliers, and/or subcontractors

Technical File Requirements

General Safety and Performance Requirements (GSPR) (Annex II 1.4/ Annex I)

- Replaced Essential Requirements Checklist (ERC)
- Outlined in Annex I
- Documented evidence needed to support each element or justification why that element does not apply
- List of harmonized standards applied

Technical File Requirements

Risk Management and Risk-Benefit information (Annex II 1.5)

- **Documented ongoing risk management system**
  - i.e., Risk Management SOP, Plan and Report, documented risk analyses at design and manufacturing phases (FMEAs), Hazard Analyses, risk control measures, etc.
- **Evidence of risk acceptability when weighed against benefits, known as a Benefit-Risk Analysis.**
- **State of the Art (SOTA) should be taken into account.**

Technical File Requirements

Product verification and validation information (Annex II 1.6)

- **Verification/Validation test results**
- **Pre-clinical and clinical data including literature**
- **Testing/study protocol data**
  - i.e., biocompatibility, electrical safety, chemical, electromagnetic compatibility (EMC), software verification/validation, stability, shelf life, etc.
- **Clinical Evaluation Plan (CEP) and Report (CER)**
- **Post-Market Clinical Follow Up (PMCF) Plan and Report**
  - Justification for non-applicability is required for not performing PMCF.

Technical File Requirements

Post-market surveillance information (Annex III)

- **Detailed in Annex III**
- **Post Market Surveillance (PMS) Plan (Article 84) for all devices**
  - Summarizes how required data will be collected and utilized
  - Required for all devices but exceptions for custom-made devices
- **Periodic Safety Update Report (PSUR) for Class IIa, IIb, and III (Article 85)**
  - Includes PMS data collected per PMS Plan, CAPAs, PMCF findings, sales, evaluation of patient population, conclusions
- **Post Market Surveillance Report (PMSR) for Class I (Article 86)**
  - Includes PMS data collected per PMS Plan, CAPAs, conclusions
  - Updated as needed

Technical File Requirements

Post Market Surveillance (PMS) Plan (Article 84) is Required to Cover at least:

- The proactive and systematic process to collect any information referred to in Annex III 1.1.a. The process shall allow a correct characterization of the performance of the devices and shall also allow a comparison to be made between the device and similar products available on the market;
- Effective and appropriate methods and processes to assess the collected data;
- Suitable indicators and threshold values that shall be used in the continuous reassessment of the benefit-risk analysis and of the risk management as referred to in Section 3 of Annex I;
- Effective and appropriate methods and tools to investigate complaints and analyze market-related experience collected in the field;

Technical File Requirements

Post Market Surveillance (PMS) Plan Requirements (continued):

- Methods and protocols to manage the events subject to the trend report as provided for in Article 88 (Trend Reporting), including the methods and protocols to be used to establish any statistically significant increase in the frequency or severity of incidents as well as the observation period;
- Methods and protocols to communicate effectively with competent authorities, notified bodies, economic operators and users;
- Reference to procedures to fulfil the manufacturers obligations laid down in Articles 83 (Post-market Surveillance System of the Manufacturer), 84 (Post-Market Surveillance Plan) and 86 (Periodic safety update report);
- Systematic procedures to identify and initiate appropriate measures including corrective actions;
- Effective tools to trace and identify devices for which corrective actions might be necessary; and
- A PMCF plan as referred to in Part B of Annex XIV, or a justification as to why a PMCF is not applicable.

Technical File Requirements

The Periodic Safety Update Report (PSUR) (Article 86) shall include:

- The conclusions of the benefit-risk determination
- The main findings of the PMCF (post-market clinical follow-up)
- The volume of sales of the device and estimate evaluation of the size and other characteristics of the population using the device and, where practicable, the usage frequency of the device.

Required for Class IIa, IIb, and III devices.

Updated at least annually for IIb and III and at least every two years for IIa

Made available to the competent authority upon request.

Technical File Requirements

Post Market Surveillance Report (Article 85) shall:

- Summarize the results and conclusions of the analyses of the post-market surveillance data gathered as a result of the post-market surveillance plan (Annex III).

Required for Class I devices.

Updated when necessary.

Made available to the competent authority upon request.

Technical File Requirements

Declaration of Conformity (DoC) (Annex IV)

Detailed in Annex IV

Must not be signed until after the Notified Body (NB) approves conformity

- The Notified Body is not required for Class 1 single-use, non-sterile devices without a measuring function.

Includes product name, catalogue numbers, Single Registration Number (SRN), sole responsibility statement, Basic UDI-DI, risk class, harmonized standards used, identification of NB, and place of issue and person who will sign.

Technical File FAQs

1. Is a Tech File mandatory?
2. Is it required for all device classes?
3. How should the Tech File be structured?
4. Who reviews the Tech File?

Technical File FAQs – Is a Technical File Mandatory?

Yes! Any company intending to sell products in the European Union is required to have a technical file per Article 10 (4).

The technical file is reviewed in order to issue a declaration of conformity for your product.

This declaration of conformity allows you to CE mark your product.

Technical File FAQs

1. Is a Tech File mandatory?
2. Is it required for all device classes?
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4. Who reviews the Tech File?

Technical File FAQs – Are Technical Files Required for All Device Classes?

Yes! While some required documentation may be different or less stringent for Class I devices compared to Class III, a technical file is still required.

Technical documentation requirements can be found in Annex I, Annex II, Annex III, and Annex IV.

Higher risk devices will have more stringent documentation requirements and more evidence needed to demonstrate conformance with GSPR.

Technical File FAQs

1. Is a Tech File mandatory?
2. Is it required for all device classes?
3. How should the Tech File be structured?
4. Who reviews the Tech File?

Technical File FAQs – How should the Technical File be Structured?

There is no specific structure and format within the regulation; however, information is required to be:

- Clear
- Organized
- Readily searchable
- Unambiguous
- Contain all requirements outlined in Annex II

The Notified Body may specify a recommended format for the Technical File.

It is HIGHLY RECOMMENDED to keep an index of all technical file requirements which traces to the corresponding documents. This index can be based off a checklist to ensure all Annex II requirements are met.

Technical File FAQs

1. Is a Tech File mandatory?
2. Is it required for all device classes?
3. How should the Tech File be structured?
4. Who reviews the Tech File?

Technical File FAQs – Who reviews the Technical File?

Class I (non-sterile, single-use, and non-measuring) devices, while still requiring a technical file, do not require a review by the Notified Body. This review should be completed internally.

Class I (sterile, reusable, or measuring), Class IIa, and Class IIb devices require a technical file review by the Notified Body for each product family.

Class III and all implantable devices require a technical file review by the Notified Body for each individual product.

Questions?

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Contact **info@rookqs.com** for more questions, comments, or to set up a meeting. One of our consultants will be sure to reach out to assist!