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Congenius Whitepaper

Guide for start-ups

Regulatory Affairs & Design Assurance essentials for MedTech Start-ups marketing a new medical device in the EU

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1. Introduction & Overview

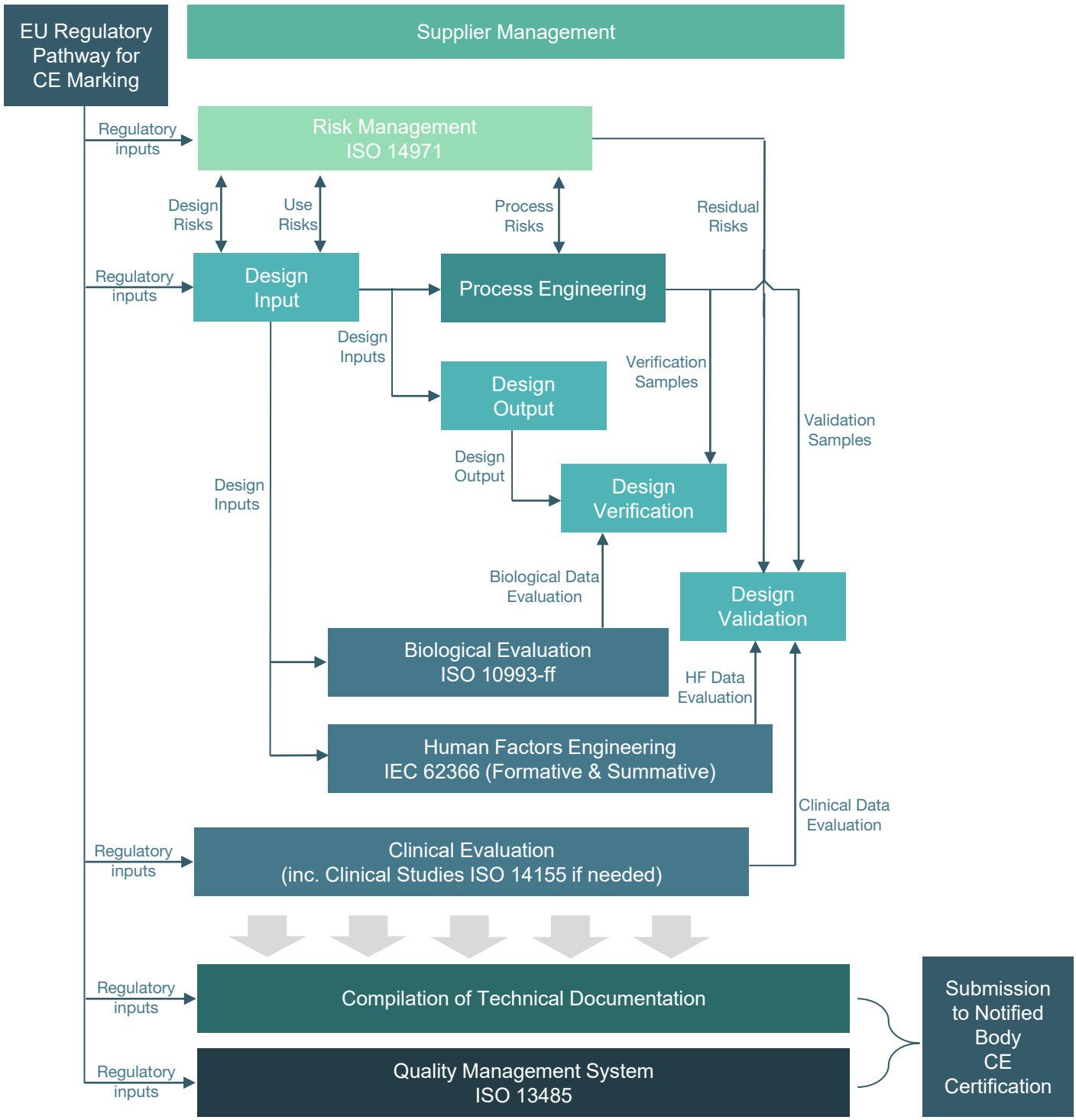
Introduction

Start-ups that want to bring a medical device to market are inevitably confronted with a plethora of questions regarding compliant product development. With often limited time and budget, adhering to the many industry regulations can prove challenging. Prioritisation of the “strictly necessary” tasks is therefore key to maximise efficiency on the journey to medical device certification.

This whitepaper provides start-ups with a digestible guide for how to develop their medical devices according to EU MDR 2017 / 745 including the most relevant harmonized standards. With a focus on those tasks that ensure compliance, the following pages outline how the process related to the sequence of these tasks normally works.

Whilst the approach for other markets is very similar to what we outline, this whitepaper is focused primarily on compliance with the EU MDR.

Graphical overview



The diagram above is a graphical overview of the essential regulatory tasks and their sequence. It shows the individual and most important tasks that a start-up must perform to compliantly develop their medical device to achieve CE marking under EU MDR. These individual tasks will be explained in more detail in the following chapters.

2. EU Regulatory Pathway for CE Marking

EU Regulatory Pathway for CE Marking

The regulatory pathway distinguishes how the basic pathway for the device to be developed is defined from a regulatory point of view based on EU MDR 2017/745 compliance. It requires the execution of the following tasks by the manufacturer:

- Define the **intended purpose of your device** (normally defined by Marketing or Product Management)
- Determine whether your product falls under the **definition of a medical device** based on its intended purpose
- **Classify your device** according to MDR 2017 / 745 - Annex VIII
- **Determine the applicable standards** (state of the art) in cooperation with the SMEs involved
- Define the **General Safety and Performance Requirements** (GSPR) according to MDR 2017 / 745 - Annex I that apply to your device
- Determine any **existing equivalent devices** and compare your product with those equivalent devices
- Define the **conformity assessment route** according to MDR 2017 / 745 - Article 52

3. Design Input, Output, Verification & Validation

Design Input

Having clarified the regulatory pathway, the 'Design Input' phase starts. Design inputs relating to device requirements need to be determined and records maintained. These inputs include:

Customer requirements

Customers includes patients, users, health care professionals, payers etc…

Functional, performance, usability & safety requirements

According to the intended purpose of your medical device

Applicable regulatory requirements & standards

Applicable output(s) of risk management

(See Chapter 4 'Risk Management' for more information)

Requirements must be complete, unambiguous, able to be verified or validated, and must not conflict with each other.

Some examples of Design Input documents include; intended use of the device, performance claims, user and patient requirements, physical characteristics, human factors/usability requirements, safety and reliability requirements, toxicity and biocompatibility requirements, and electromagnetic compatibility requirements.

For further details refer to ISO 13485:2016 Chapter 7.3.3.

Design Output

Following the 'Design Input' phase, the 'Design Output' stage follows consecutively. For this topic, design outputs are defined and must:

- Meet the input requirements for design and development
- Provide appropriate information for purchasing, production and service provision
- Contain or reference product acceptance criteria
- Specify the characteristics of the product that are essential for its safe and proper use

The outputs of design must be in a form suitable for verification against the design inputs and must be approved prior to release.

Some examples of Design Output documents include; specifications for raw materials, component parts and sub-assemblies, drawings and parts list, customer training materials, process and materials specifications, finished medical devices, product and process software.

For further details refer to ISO 13485:2016 Chapter 7.3.4.

Design Verification

As the phase ‘Design Output’ concludes, the ‘Design Verification’ stage begins.

In this phase, the design of your medical device must be verified in accordance with planned and documented arrangements to ensure that the design outputs have met the design input requirements.

Your organisation will need to document verification plans that include methods, acceptance criteria and, as appropriate, statistical techniques with rationale for sample size.

The final results of the biological evaluation according to Chapter 5 ‘Biological Evaluation’ should be part of the Design Verification as well.

For further details refer to ISO 13485:2016 Chapter 7.3.6.

Design Validation

Design Validation marks the final phase of the medical device development.

In this final phase, the design validation must be performed in accordance with the planned and documented arrangements to ensure that the resulting device is capable of meeting the requirements for the specified application or intended purpose.

Your organisation will need to **document validation plans** that include methods, acceptance criteria and, as appropriate, statistical techniques with rationale for sample size.

Design validation should be **conducted on a representative product**, with "representative product" meaning initial production units, batches, or their equivalents. You'll also need to record the rationale for the choice of product used for validation.

As part of design validation, **clinical evaluations of the medical device** in accordance with the applicable regulatory requirements **must be performed**. It's important to note that a medical device used for clinical evaluation is not considered to be released for use to the customer.

You can refer to Chapter 6 'Human Factors Engineering' and Chapter 7 'Clinical Evaluation' for more information on these validation topics.

And for further detail take a look at ISO 13485:2016 Chapter 7.3.7.

4. Risk Management ISO 14971

Risk Management ISO 14971

The aim of the risk management process is to:

Identify the hazards associated with your device

Estimate & evaluate the associated risks based on the design, manufacturing process, or use of the device

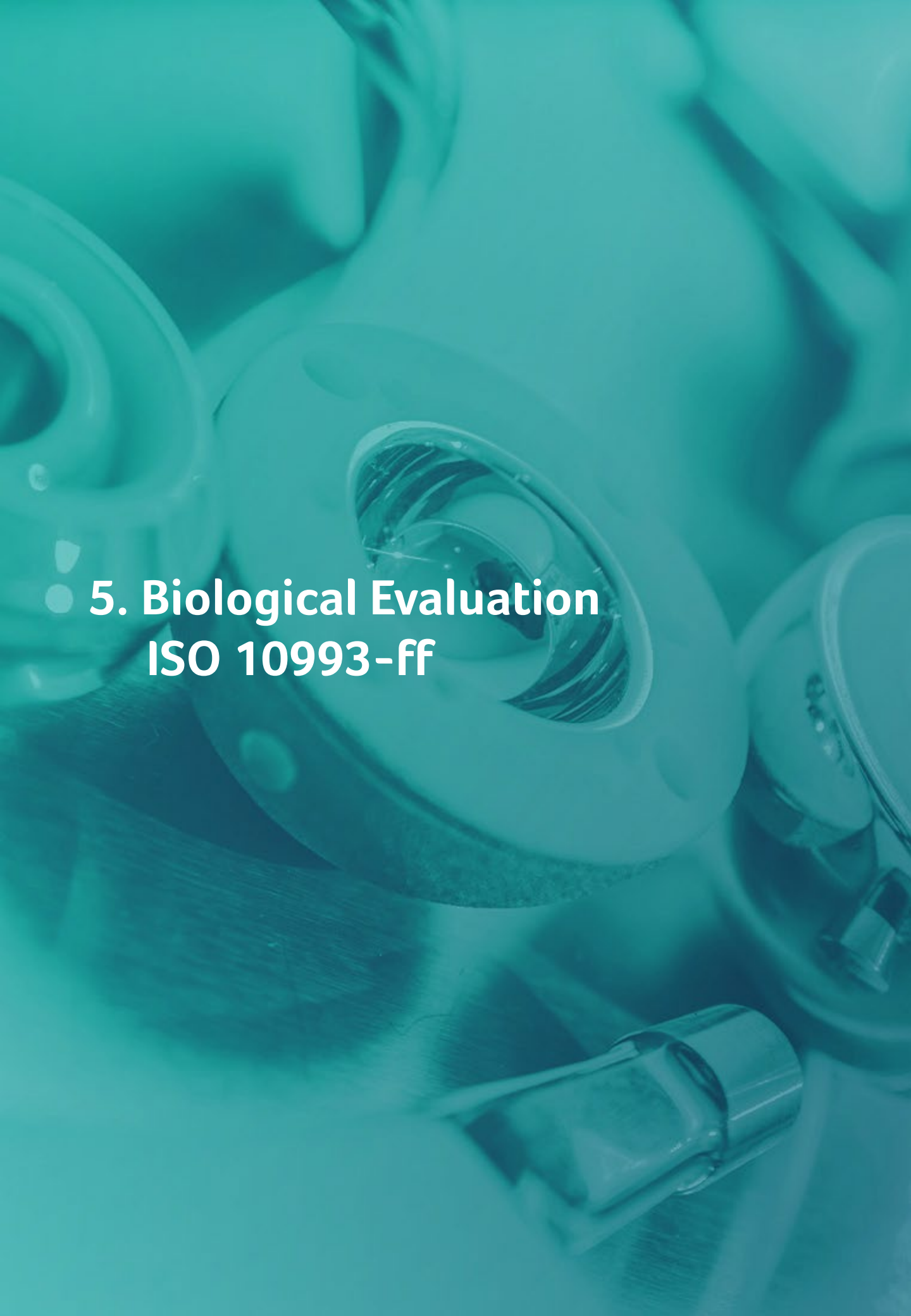
Control these risks

Monitor the effectiveness of the controls

Risk management is a cornerstone activity, starting during pre-market with the 'Design Input' phase and continuing through product development into the post-market phase of the device - for as long as your device is on the market.

When you perform the risk management for your device, you must follow the requirements set forth in ISO 14971 and also ensure compliance with the general safety and performance requirements of Annex I of the MDR 2017/745 regarding the safety and health of patients, users or, where applicable, third parties.

The residual risks must be assessed in the final risk-to-benefit evaluation performed during the 'Design Validation' phase.



5. Biological Evaluation ISO 10993-ff

Biological Evaluation ISO 10993-ff

The Biological Evaluation starts during 'Design Input' and ends with the 'Design Verification' phase, depending on the Risk Management as per Chapter 4 and the device's intended purpose as per Chapter 2. The aim of the evaluation is to manage the biological risk posed to the patient by using a device.

It is performed according to ISO 10993-ff covering the following disciplines:

- Biological categorisation of medical devices (Chapter 5 / ISO 10993-1)
- Material characterisation (Chapter 6.1 / ISO 10993-1)
- Biological evaluation testing (Chapter 6.2 / ISO 10993-1)
- Overall assessment of biological safety (Chapter 7 / ISO 10993-1)

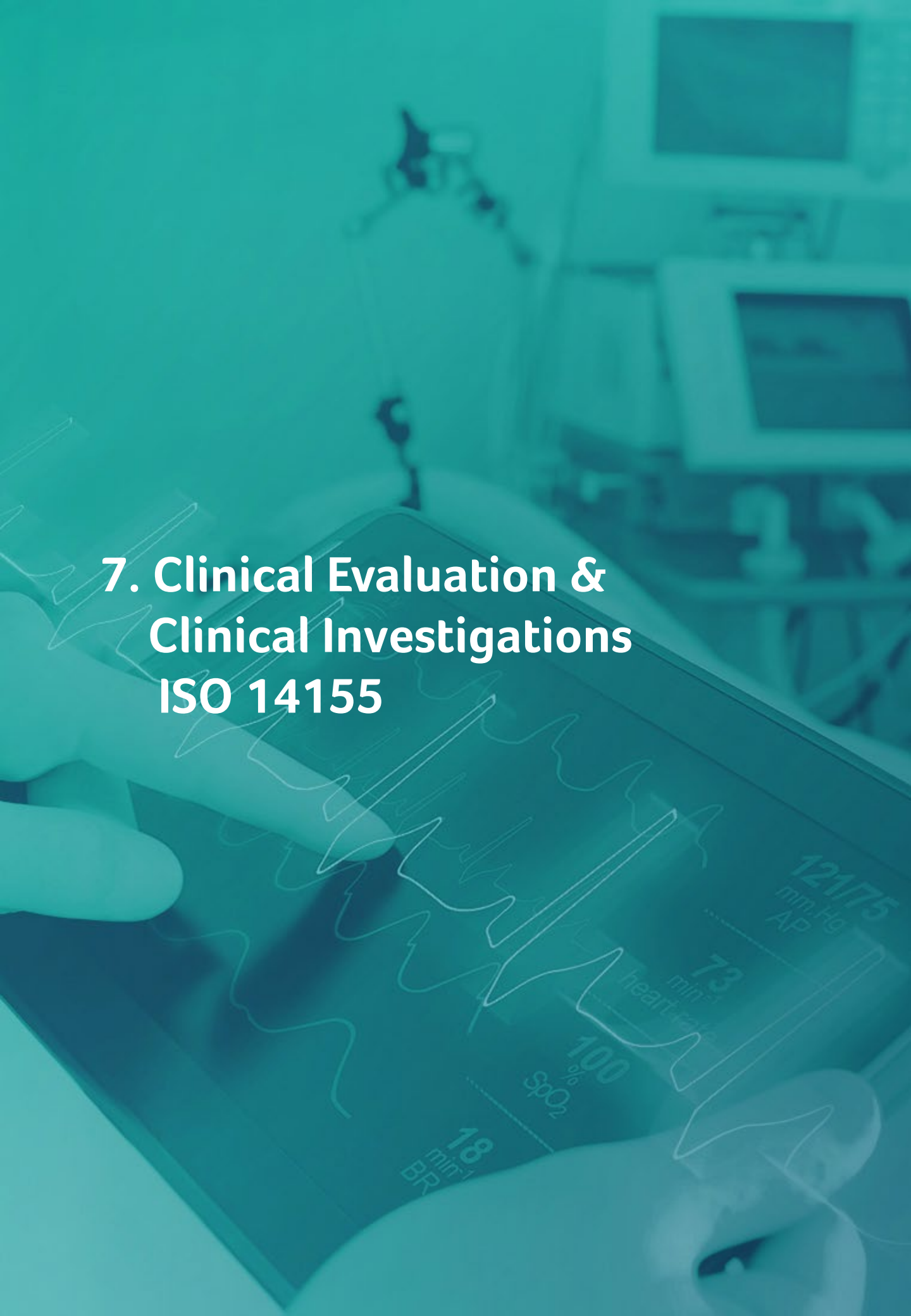
6. Human Factors Engineering IEC 62366

Human Factors Engineering IEC 62366

Human Factors Engineering is performed in accordance with IEC 62366 and is mainly part of the Risk Management process according to Chapter 4 'Risk Management'.

The user tasks to operate the device must be assessed in terms of use risks and their mitigation by a safe and user-friendly design if necessary.

During the 'Design Input & Design Output' phases it must be decided whether **formative human factors studies** need to be performed to influence the design in a positive way related to usability. It must also be decided whether **summative studies** are required to be performed during the final phase of 'Design Validation'. The decisions for both sets of studies is based on the risk assessment for the specific tasks to validate the safe and performant use of the device.



7. Clinical Evaluation & Clinical Investigations ISO 14155

Clinical Evaluation & Clinical Investigations ISO 14155

During Clinical Evaluation it is defined how clinical data on the medical device are collected, assessed, and analysed.

The aim of this activity is to confirm the claims stated in the product's intended purpose under the normal operating conditions of the device, and to show conformity with the relevant General Safety and Performance Requirements set out in Annex I of the MDR.

In cases where clinical data must be collected by performing clinical investigations, these activities need to be performed according to ISO 14155.

The clinical evaluation and its documentation requires updating throughout the life cycle of the device, with clinical data obtained from the implementation of the manufacturer's Post Market Surveillance and Clinical Follow Up activities referred to in MDR 2017 / 745 Article 84 and Part B of Annex XIV respectively.

8. Software Lifecycle Management IEC 62304

Software Lifecycle Management IEC 62304

Should your medical device contain software (firmware), or, if your medical device is a stand-alone software (e.g., an app), the development process follows the same phases as described in Chapter 3.

However, for software, specific aspects must be considered, both for the software itself and for steps in the development phases. These aspects are governed by IEC 62304 – Software Lifecycle management.

In this standard, medical device software is classified into three safety classes - A, B, and C, with C being the class with the highest safety risk. This safety classification is based on the severity of risks the software may cause to patients or users. Depending on the safety class, specific requirements of IEC 62304 are mandatory and have to be considered during the development of the software.

Requirements for software risk management, including for cybersecurity, are part of the product risk management as described in Chapter 4.

9. Process Engineering

Process Engineering

Process Engineering deals with the physical manufacturing (production) of the device and is an important discipline to be considered during the development phase.

Tasks are handled as follows:

Define the end-to-end Quality Control of the device to be manufactured and delivered to the end-user

Handle & control the manufacturing risks as indicated in Chapter 4 'Risk Management'

Qualify the **manufacturing infrastructure**

Validate manufacturing processes & tests including purity and sterility validation (if applicable)

Create manufacturing documentation

(e.g., production and test instructions)

10. Supplier management

Supplier management

Proper management of development and manufacturing partners and suppliers is essential, especially in start-ups, where many activities are outsourced. It must be insured that the quality of services and goods delivered by the partners and suppliers are under control during the whole lifecycle of the device. These activities are managed via a Quality Assurance Agreement (QAA).

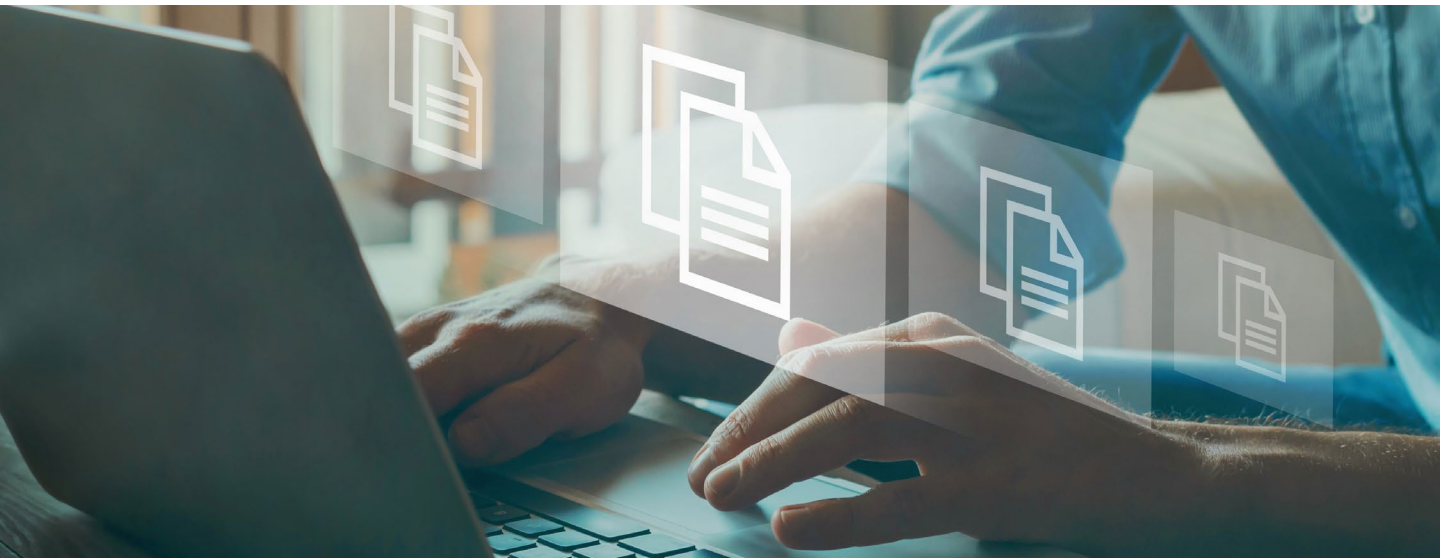
For further details refer to ISO 13485:2016 Chapters 4.1.5 & 7.4.

11. Technical Documentation Annex II & III MDR 2017 / 745

Technical Documentation
Annex II & III MDR 2017 / 745

The Technical Documentation is a comprehensive description of your device intended to demonstrate compliance with MDR 2017 / 745.

The Technical Documentation resulting from the aforementioned development activities must be structured according to the requirements of MDR 2017 / 745 Annex II and III (Post Market). The Technical Documentation is the base documentation for starting the submission process to the Notified Body for CE certification of your device.



12. Quality Management System ISO 13485

Quality Management System ISO 13485

ISO 13485 specifies requirements for a Quality Management System (QMS), where an organisation needs to demonstrate its ability to provide medical devices and related services that consistently meet customer needs and applicable regulatory requirements.

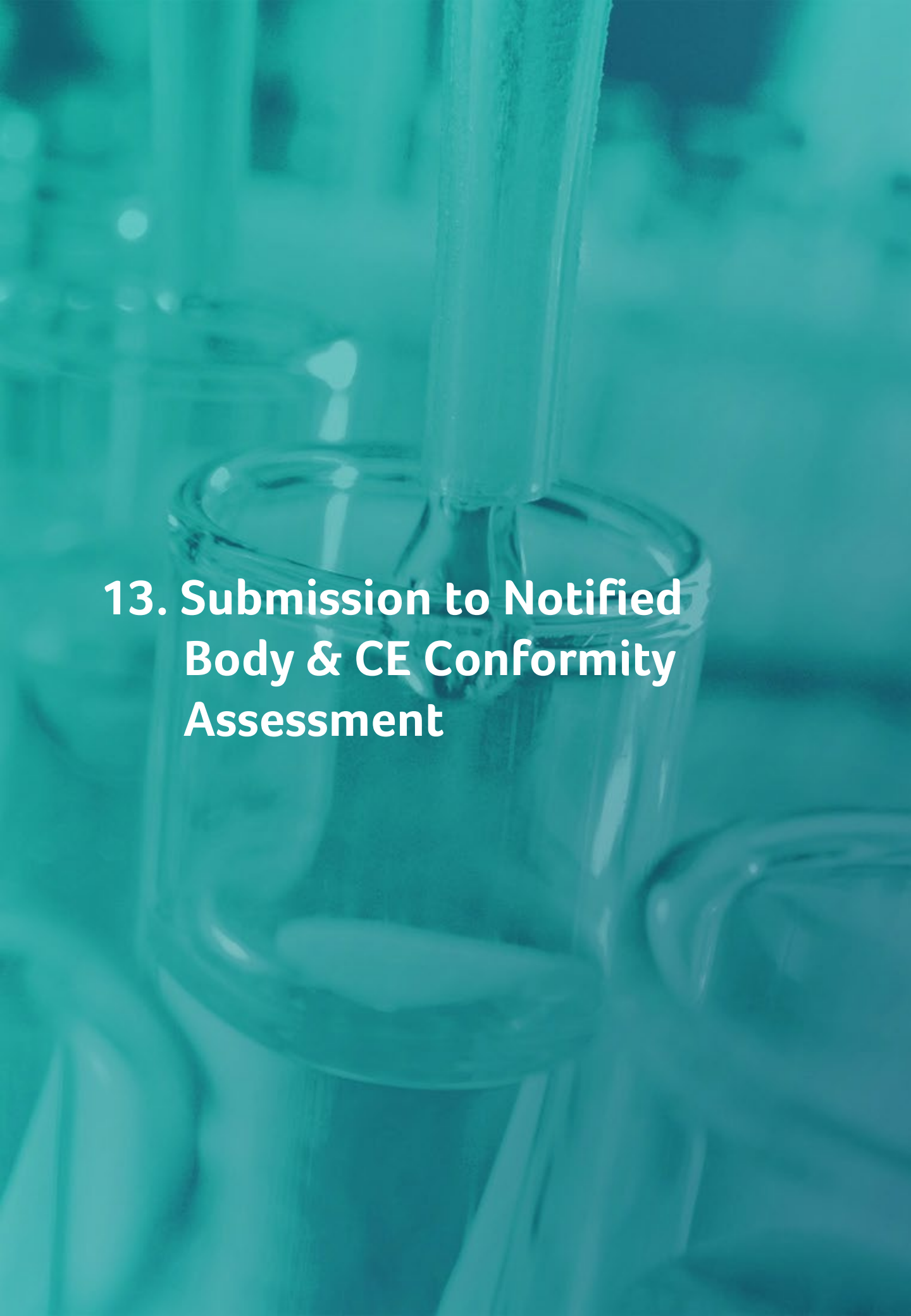
Such organisations can be involved in one or more stages of the lifecycle, including:

- Design and development
- Production
- Storage & distribution,
- Installation
- Servicing of a medical device
- Design & development or provision of associated activities (e.g., technical support)

Introducing a QMS during your start-up's pre-development phase can facilitate a successful path to market access. Here at Congenius, we offer a QMS product – **QMgeniuS** - which fulfils the mentioned requirements and is specifically designed for start-up companies.

'QMgeniuS' can be implemented paper-based or electronically (fully complying with 21CFR11 related to Electronic Records and Electronic Signatures). In close collaboration with your company, one of our experienced consultants builds your system, tailoring it as necessary depending on your company's needs.

The necessary processes and related documents / templates are scoped and then implemented according to your specific requirements. Our smart solution facilitates your certification in a lean way that saves you time and money. Find out more about QMgeniuS here.



13. Submission to Notified Body & CE Conformity Assessment

Submission to Notified Body & CE Conformity Assessment

As soon as you complete and release your Technical Documentation, and your Quality Management System is implemented and shows efficacy, you're ready to begin your application for CE certification.

The application for CE certification starts with the submission of the relevant documentation of the Technical Documentation (refer to Chapter 11) and Quality Management System (refer to Chapter 12) to your relevant Notified Body.

After successful assessment of the Technical Documentation and the Quality Management System by the Notified Body, the CE certificate is issued, and your device may be sold on the European Market.

CE

14. Conclusion

Conclusion

The compliant development of a medical device is extensive, requiring the implementation of various disciplines as described in this whitepaper.

Having worked with a wide range of start-ups, at Congenius we are well prepared to help you tackle the regulatory challenges that can often be as unique as your business itself. Our broad knowledge base across our service offerings aims to support the enhancement of your core business, and by using validated approaches, we ensure cost and time efficiencies to maximise your budget.

Our aim is to provide reassurance and direction as you look to make your mark on the industry, and our team of MedTech experts is ready and happy to help.

Congenius

For more information on Regulatory Essentials for start-ups, feel free to get in touch with our Regulatory team.

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