Review Article

Methods for Medical Device Design, Regulatory Compliance and Risk Management

ABSTRACT

Despite the evolution of design controls and compliance as vital elements in the medical device development process, as stipulated by both domestic and international regulations and standards, there needs to be a comprehensive model that describes the comprehensive approach to medical device design. This gap exists because design controls and regulatory compliance have become integral to the medical device design process, mandated by regulations and standards at both national and international levels.

The medical device sector prioritizes design controls and compliance with regulatory requirements in isolation. On the other hand, the integration of design controls and compliance, such as those associated with projects involving complex medical device designs, have not been considered nearly enough. This review focuses on the integration of design controls and compliance in the medical device sector.

Keywords: Medical Devices, Medical Device Industry, Design Controls, Regulatory Compliance, Risk Management.

1. INTRODUCTION

Medical device development is an intricate process that necessitates design control implementation. These controls form a systematic framework of procedures and practices designed to manage and ensure the safety and quality of a medical device throughout its development process **[1]**. Regulatory organizations, such as the Food and Drug Administration (FDA) in the United States, require implementing design controls, which are also critical for adherence to international standards like ISO 13485. Design controls cover several phases of the device development process, including design planning, input requirements, design output, validation, verification, and the transition of design to manufacture. The fundamental objectives of the underlying design controls are to ensure that the device meets user needs, functions as intended, maintains safety and efficacy standards, and adheres to regulatory requirements. Design controls enable medical device manufacturers to systematically identify and manage risks, track design alterations, maintain documentation, and ensure that the final product fulfils all stated requirements and standards **[2,3]**.

Design control defines the procedures for medical device but the two most important aspects of medical device design include patient safety and device efficacy. These principles are specified in an international standard, IEC-60601-1, which mentions guidelines for performance and safety standards for medical electrical equipment to safeguard both patients and operators. The FDA plays a crucial role in maintaining these standards, ensuring patient safety by thoroughly evaluating and monitoring medical products for effectiveness and

potential risks. Failure to adhere to IEC-60601-1 guidelines and testing procedures can pose significant public safety hazards, potentially leading to FDA recalls. These recalls aim to protect public health by removing or correcting products that violate laws or pose risks and cover a range of items such as medical devices, pharmaceuticals, and food products. Notable recalls have included Tylenol for tampering, Vioxx for heart risks, and Takata airbags for explosive defects. Overall, device manufacturers must essentially comply with IEC 60601 to ensure regulatory approval, safeguard patient safety, access global markets, maintain industry credibility, and mitigate legal risks associated with medical device development and marketing **[4,5]**.
In this review, we discuss the methods and best practices to ensure basic safety and essential performance as specified in the IEC-60601-1 framework and incorporated into the design controls.

2. DEFINITION OF A MEDICAL DEVICE

The FDA describes a medical device as "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or any other similar or related article, including a component, part or an accessory, which is:"

- recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,

- intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes**[6].**

Medical devices sold in the United States and medical and non-medical radiation-emitting products are solely upon approval from the Center for Devices and Radiological Health (CDRH), a division of the Food and Drug Administration (FDA). Devices involving drugs and biologics, or those that emit radiation, might also be regulated by different FDA centers and subject to additional rules **[7]**.

The following regulatory requirements apply to the distribution of medical devices in the United States: Establishment, Premarket Notification 510(k) (unless exempt) and Premarket Approval (PMA), Medical Device Listing, Investigational Device Exemption (IDE) for studies, Labeling Requirements, Medical Device Reporting (MDR), and Quality Systems Regulation **[8]**.

Regulations guiding device development include various exceptions, special categories, and exemptions. For instance, devices tested solely for consumer preference may be exempt if not intended to establish safety or effectiveness. Additionally, devices used exclusively in research on veterinary and laboratory animals are also exempt. Humanitarian Device Exemptions may be granted for devices intended to treat conditions affecting fewer than 4,000 individuals annually in the USA **[9]**. Expanded access may be granted for emergency, ongoing use, compassionate, and therapeutic applications **[10].**

Manufacturers of devices that do not qualify for exemptions must either obtain Premarket Approval (PMA) or complete a Premarket Notification 510(k). If clinical data is required to support the 510(k) application or PMA, an IDE may also be necessary **[11]**.

2.1 Medical Device Design Phases

Creating an effective healthcare solution that meets patient or doctor needs requires significant effort and coordination for a medical device manufacturer **[12]**. This process involves ensuring all function groups within a medical device manufacturer company are aligned, clearly defining the scope based on the needs of the end user, fostering cross-team collaboration, adhering to specifications and guidelines established by product definitions, mitigating risks, and maintaining the highest quality standards. To design and develop successful medical devices, the manufacturer must ensure the product not only meets customer needs but also complies with regulatory requirements. The model described here is intended to help designers proactively manage the complexities of medical device design **[13]**.

According to the FDA, the steps in the development of devices for medical use are: device discovery and concept, preclinical research and prototype development, the route for approval, a review from the FDA, and post-market safety monitoring. The EU MDR does not contain specific articles dedicated to design or manufacturing **[14]**. However, Article 10.1 obligates manufacturers to design and produce devices in compliance with Regulatory guidelines. This is so because of the incorporation of the design and manufacturing requirements into the quality management system requirements in Article 10.9. The contents of EU MDR are similar to ISO13485 **[15]**.

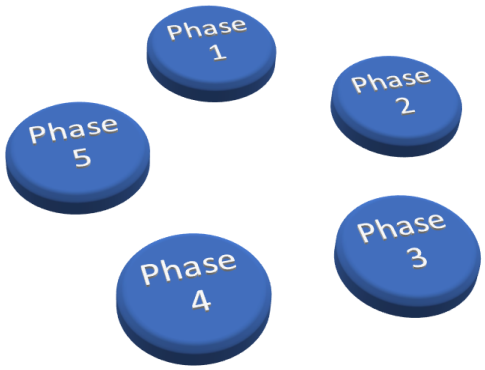

Figure 1 5 Phases of Medical Device Design

2.1.1 Phase I: initiating device development and subsequent analysis of opportunity and risks

In the development of a medical device, the phase of initiation and risk analysis is paramount in determining the feasibility of advancing to subsequent stages. This phase necessitates a meticulous definition of needs, informing a comprehensive risk analysis and establishing the foundation for a robust development plan **[16]**. The development plan typically defines the intended use of the device, identifies analogous market products, understands consumer demands, gathers user requirements, and analyzes typical usage patterns. Key stages include initial design, design reviews, prototyping, user feedback, testing, and clinical trials. Design inputs are bifurcated into user needs and regulatory requirements pertinent to target markets. The cybersecurity requirements for a medical device connected to hospital network are captured at this stage **[81]**. The risk and benefit analysis, initiated early and continually updated throughout the development lifecycle, elucidates the device's potential benefits and risks **[17]**. In accordance with ISO 14971, the plan involving risk management formulated in the initial phase should delineate the stages of production, disposal, industrialization, process validation, design and development, and scope, along with roles, responsibilities, and criteria

for risk acceptability. This comprehensive approach ensures effective risk management, thereby ensuring the efficacy and safety of the medical device **[18]**.

2.1.2 Phase II: critical for evaluating the financial viability, prototype, and formulation of the concept

During the second phase, a formal risk assessment is performed, and regulatory and customer requirements will be gathered, with the first prototype serving as proof of concept. This stage demonstrates the feasibility of the concept in various dimensions and results in the production of a prototype **[19]**. To ascertain customer needs, feedback should be collected through surveys and research involving patients and clinicians, as well as through competitor analysis. Upon identification and documentation of customer needs, initial design and development activities can commence to establish proof of concept through prototyping of the product. The process of identifying client demands must be updated repeatedly through cycles of design, development, and review, much like benefit and risk and benefit assessment. The study on feasibility should encompass steps to elucidate unknown variables, initiate engineering design work, identify critical materials and components, and evaluate the viability of proceeding based on reliability testing data, manufacturer audits, and certification reviews **[20]**. The product concept should be refined by outputs of key materials and components. At each phase, the risk and benefit analysis must be updated as the product's functionalities become more defined and requirements are refined. To design a Failure Modes and Effects Analysis (FMEA) form, this analysis should include data from anticipated misuse, safety-related features, and hazard analysis. As the product concept becomes clearer, the plan for design and development has to be revised to include details of remaining tasks, comprehensive requirements (from users, regulators, distributors, etc.), and sources of verification and validation required to substantiate these requirements. Before progressing to the next stage, it is advisable to share these plans with the Notified Body **[21]**.

2.1.3 Phase III: design validation, verification, and prototype development to meet the regulatory requirements.

Design outputs encompass product drawings, components, materials, parts, product/material specifications, a bill of materials, work instructions, and a user guide. The design and prototyping process culminates in the creation of product prototypes **[22]**. To ensure that design outputs align with the intended inputs derived from user needs and regulatory requirements, it is critical to evaluate the prototypes against all specified criteria. During initial validation, the prototypes must be rigorously evaluated to verify that they meet user needs and intended device functionalities, with continuous planning, design, review, and approval to establish an auditable record of risk mitigation measures. The clinical plan should be initiated if clinical trials are required, and the risk and benefit analysis should be updated accordingly **[23]**. A traceability system must be implemented, with the product registered in the Unique Device Identification database of either the EU or FDA, to enhance user safety through precise adverse event reporting, minimized medical errors, and efficient complaint and recall management. Post-proof of concept, the design and development of the product must be meticulously managed to effectively capture user requirements and translate them into detailed engineering specifications, ensuring that the design adheres to these specifications **[24]**.

2.1.4 Phase IV: final validation of the product tested pre-launch and approved by a competent authority

In phase 4, operational qualification and performance qualification were concluded, marking critical milestones in the validation process.

Continuing these practices is critical. An effective technique is to execute three small-scale manufacturing pilot runs, each of which produces critical-to-quality data for statistical analysis, therefore confirming the device's process capabilities. These pilot runs should ideally be carried out under the most demanding conditions, including both the lowest and maximum control limits of process inputs. This comprehensive method provides crucial insights into the process window and ensures that the final goods meet approval standards **[25]**.

Using the data acquired, it is crucial to identify quality-sensitive qualities and develop techniques to maintain control over them during mass manufacturing. Equipment maintenance and staff training are critical factors in this regard and should be meticulously planned, even at the component supplier level **[26]**.
Validation and verification (V&V) studies and reports for the product must be extensively reviewed, including elements such as biocompatibility and electrical safety, as appropriate. Additionally, stability testing and shipping trials, which are essential components of technical documentation, should be included at this point **[27]**.
In tandem with the aforementioned evaluation of literature documentation is critical for assuring alignment with established evidence. Vigilance is required to avoid unfounded claims made by marketing gurus.
After completing these rigorous studies assessments, the technical documentation is ready to be submitted. The technical file must thoroughly capture all required evidence, preparing the product for review/audit by a competent authority **[28]**.
This submission procedure process comprises a full review and audit, which is performed by a Notified Body (NB) based on device categorization. The NB assesses both the product(s) and the procedures by analyzing all technical records as well as documentation related to the Device Master Record (DMR), Design History File (DHF), and Device History Record (DHR).

2.1.5 Phase V: launch of the product and post-launch assessment.

Once your product(s) and Quality Management System (QMS) have been approved by a Notified Body, you are prepared to enter the market. A verified and authorized manufacturing strategy is essential to assure the timely delivery of items within budget restrictions while adhering to the medical device safety and quality standards. Continuous verification of the plan's compliance with regulatory standards (such as FDA and/or EU MDR) is crucial. Spot-checking during production, audits, routine inspections, and QMS procedures is crucial for detecting errors caused by batch-to-batch variance, which may go undetected by quality control technicians **[29]**.

Data collecting from many stakeholders, such as users, patients, hospitals, technical operato rs, distributors, and other relevant entities, is critical once a product is launched. Regular examination of this data within the risk management framework, including activities such as Post-Market Clinical Follow-Up (PMCF) and Post-Market Surveillance (PMS) stipulated by the EU MDR, is critical. PMCF's goal is to assure product safety, performance, and longevity while also monitoring contraindications, adverse effects, and new concerns. Furthermore, it confirms the correctness and validity of the benefit-to-risk profile throughout time. It is critical to provide clients with the appropriate documentation and guidance, such as Instructions for Use (IFUs), user guides, training manuals, and promotional materials **[30]**. These documents

should be created in accordance with applicable rules and regulatory requirements, keeping in mind that their necessity may differ depending on the device classification. Implementing an electronic Quality Management System (eQMS) simplifies the management of customer complaints, feedback, product recalls, and overall development processes. Furthermore, if manufacturing is outsourced to a contractor, seamless document sharing guarantees that all relevant information for product manufacturing is readily available **[31]**.

3.1 Role of the International Electrotechnical Commission (IEC)

The IEC introduced the pioneering medical devices standard, IEC 60601-1, in 1970. This standard, titled "Medical electrical equipment – Part 1," is widely recognized globally and addresses general specifications for medical electrical devices and tools, encompassing standards for fundamental safety and necessary activities **[32]**. Integral to the process of designing and developing medical equipment in healthcare settings, the IEC 60601-1 standard holds significant importance. This article will go over the various aspects of designing medical devices in accordance with IEC 60601-1, including its significance, fundamental provisions, procedures for evaluation and certification, common challenges and misconceptions, benefits of adherence, strategies for ensuring compliance, the importance of risk management, and available resources and tools. The IEC 60601-1 standard has constantly played a significant role in shaping the landscape of medical device development. Compliance with the IEC 60601-1 standard is crucial for manufacturers, healthcare practitioners, and patients **[33]**. This standard serves as a key benchmark for determining the efficacy, safety, and effectiveness of medical electrical equipment devices, lowering the risk of harm to both patients and medical personnel. Meeting these stringent requirements proves that manufacturers' medical device designs and innovations comply with the highest quality standards. This approach not only enhances patient safety, but also expedites regulatory approvals and broad commercial acceptance of medical device innovations.

For healthcare providers, the IEC 60601-1 standard represents a guarantee of safety and dependability ensures safety and dependability in medical device design and development. It ensures that medical devices meet important electrical, mechanical, and functional standards, which reduces the chance of device failure or accident. Compliance with this standard also facilitates the procurement process by allowing healthcare organizations to prioritize devices that satisfy the IEC 60601-1 standard. This promotes consistency in medical product development and ensures uniform equipment quality across numerous medical institutions [34].

IEC 60601-1 has been revised several times over the years to ensure its adaptability and compliance with developing medical technologies. Amendment 1 to IEC 60601-1 was published in 2012, introducing a recent set of improvements. This standard demands the deployment of a structured life cycle method for software development, covers fundamental performance needs, necessitates usability engineering assessments, and considers human aspects [35].

Furthermore, it outlines updated and revised technical requirements for electrical and mechanical hazards, as well as introduces new requirements for product labeling and documentation.

3.1.1 Understanding Basics of IEC 60601-1

The IEC 60601-1 serves as the foundation for the entire range of collateral and specific IEC standards. Depending on the country in which you are seeking approval, designer will adhere to versions 2, 3, or 3.1 **[36]**.

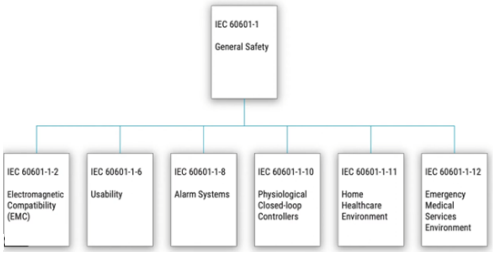

Figure 2 IEC60601-1 Standard

While 60601-1 serves as the fundamental general specification, particular standards branch out to cover particular devices, such as high-frequency surgical equipment, endoscopic tools, and infant incubators. The collateral standards incorporate broad-based requirements, with one or more potentially applicable to your device, including EMC, Usability Engineering Analysis, and considerations for home usage situations **[37]**.

Additionally, there are guidance documents, or the technical reports that are distinct from the general, collateral, and particular standards. An overview of these standards and guidelines can be seen in the diagram above. 60601-1 will always be applicable if the medical device falls within the scope of the general standard, but determining which collateral and particular standards pertain to user specific device, is designers' responsibility.

3.1.1.1 ***IEC60601-1 Compliance***

Below are the steps to follow to obtain 60601-1 approval. It should be noted that the order in which these steps are executed may vary depending on individual circumstances, so it's essential to determine a system that best suits the designer needs **[38]**.

The first step is to Prepare a project plan. It's essential to develop a customized plan that maps out all the relevant steps for achieving compliance with IEC-60601. Being mindful that each project will vary based on the type of device being developed. Your plan may entail additional or fewer tasks compared to others, depending on the specific requirements and characteristics of your device **[39].**

In the second step, standards applicable to your device are determined. This step aims to determine whether your project lies within the scope of the 60601 standards. If not, you may not be using the correct set of guidelines for your device. This stage encompasses essential performance and the basic safety of medical electrical equipment.

When reviewing the clauses of the standards, it is important to pay attention to any asterisks, as these point to the guidance and rationale annex for the clause that offer further insights into the background or intentions behind the standards, which can lead to valuable moments of clarity and understanding **[40]**.

The 60601 requirements encompass the majority of medical electrical equipment, and the FDA may encourage those that are first ruled out of scope to comply with the standard.
Furthermore, it is critical to understand which collateral standards are applicable, as well as any particular or additional requirements that may apply to your device **[41]**.

In the next step, the product is classified. The subsequent step involves classifying your product according to IEC 60601-1, as well as any applicable collateral or particular standards.

For instance, each device must undergo classification regarding protection against electric shock. Devices with a grounded power source are categorized as Class I, while those with an ungrounded source fall under Class II. Additionally, "Other MEE" classification applies to units with an inbuilt battery or power source. Applied parts will also be assessed, with symbols corresponding to their categorization **[42]**.

Additionally, a rating must be determined for protection against water and particulate matter infiltration, which is not mandatory for the general standard. Ratings range from IPX1 (lowest) to IPX8 (highest), each requiring specific humidity tests. For instance, an IPX1 rating or higher necessitates a 7-day humidity test, whereas an IPX0 rating or "ordinary" designation requires a 2-day test **[43]**.

Other categories include the sterilization process, appropriateness for an environment rich in oxygen, mode of operation (continuous or noncontinuous), and whether the device is transportable or stationary. While the latter is not a classification per se, it does impact the testing process, requiring reference to Figure 2 Annex A of IEC 60601-1, edition 3.1.

Next, an isolation diagram is created early in the development lifecycle. Preparation of an isolation diagram in the early stage of the process facilitates the identification of required insulation systems, enabling an effective design plan from the outset. Different requirements apply depending on the isolation barriers involved, and making changes to these barriers after the fact can be costly. Another important consideration is that identifying costly requirements early on provides an opportunity to explore alternative designs, if feasible. The primary concept of the standard revolves around ensuring two levels of protection if the first level fails. The standard prioritizes the protection of both operators and patients and defines "means of protection" (MOP) as follows: 1 MOP: basic insulation and 2 MOPs: reinforced or double insulation. While having two MOPs is not always necessary, if you only have one, make sure that protective earthed parts are present for the specific isolation barrier being considered **[44]**.

In the next step, critical components are identified and manufacturer specification sheets are procured. During this phase, the designer needs to identify critical components from a comprehensive list, including main components, safety isolation components, and flammable components like plastic enclosures and wiring sleeving. Additionally, line filters, whether medical or non-medical, are crucial considerations. Particularly, opting for non-medical line filters may elevate leakage current and potentially lead to test failures; however, it's essential to balance this with electromagnetic compatibility (EMC) test requirements, as non-medical line filters often perform better in this regard. Alongside component identification, gathering essential documents is imperative. These could include UL component certification and Conditions of Acceptance, technical specifications and drawings, certifications for tests and component reports, CB certificate and test reports for power supplies, and label materials **[45]**.

Essential performance identification and preparation of a draft of risk management file (RMF). Identifying and recording essential performance is the key, as it influences your test plan significantly. Essential performance is defined as the competence of a clinical function, but not basic safety, in which any loss or degradation beyond the manufacturer's specified limitations is an unacceptable risk **[46]**.
The process of identifying essential performance requires following the steps outlined in clause 4.3 of IEC 60601-1, edition 3.1, and any specific standards requirements for essential performance, typically found in clause 201.4.3.101. This includes risk analysis duties done by the manufacturer in accordance with the applicable essential performance clauses to define essential performance and specify performance limits between completely functioning and total loss of specified conditions performance in both normal and single fault conditions.

While essential performance commonly applies to critical care equipment, such as anesthesia or ICU monitors, it can also pertain to less critical devices, necessitating analysis for every product. The FDA may request an analysis even if a device lacks essential performance. Any change to the device's intended use can alter its essential performance, and if a predicate device with essential performance was utilized, similar expectations may apply to your device **[47]**.
Regarding the RMF, compliance with ISO 14971 is essential for compliance with 60601-1. It is imperative to conduct risk analysis early in the process. Assembling the RMF involves considerable effort, utilizing the CB scheme technical report (TRF) and lab paperwork. Many compliance statements in the 60601 standards necessitate inspection of the RMF, emphasizing the need for meticulous documentation **[48]**.

The RMF paperwork becomes more manageable if work has been done for ISO 14971:2019. It involves including all RMF and documents of risk management plan (RMP) and completing a "map" of risk management requirements within the TRF.

Ultimately, the documents provided to the test lab must be fully compliant with RMF requirements for general, collateral, and specialized standards. For first-time efforts, filling out RMF requirements of the TRF usually takes nearly 30 days of work.

Drafting your test plan. The 60601 series standards mandate "type testing," involving the testing of a sample device to ensure it meets standards, contrasting with process-based standards like IEC 62366 (Usability Engineering) or IEC 62304 (Software Lifecycle). These samples must resemble final products. While consolidating tests into one plan is generally efficient, EMC (IEC 60601-1-2) requires a separate test plan. Essential performance and risk management documentation must be completed before drafting the test plan. Designers submit a draft test plan to labs for agreement, addressing specific test requirements, including non-applicable tests **[49]**.

For marking and labeling, all device markings, user manuals, and technical descriptions must be reviewed to verify compliance with labeling standards, ensuring readability for the intended user context. Key labeling tests include legibility (tested at 1 meter with 20/20 vision) and durability (labels must remain intact). Construction review ensures the device meets IEC 60601-1 and relevant standards, checking components for compliance, verifying and updating the isolation diagram, and ensuring the test plan covers all relevant tests. This encompasses marking and labeling adherence and ISO standards for biocompatibility **[50]**.

When a test lab is being selected, one needs to consider the quality and reliability of test reports, expertise in required tests, lab location preferences, speed and urgency, reputation, cost vs. service quality, and outsourcing practices. Besides, it is also crucial to provide detailed specifications to the test lab for accurate quotes. This includes outlining the product, its family, version, and relevant testing standards, thoroughly completing the lab's RFQ form, and communicating special requirements early to avoid cost overruns, delays, and retesting.

Step 6 involves laboratory testing and a test report preparation. The Risk Management File (RMF) and essential performance are finalized, ensuring all necessary updates are made. Thoroughly reviewing the standard text, rather than relying solely on the Test Report Form (TRF), is crucial. Compliance with ISO 14971, integral to IEC 60601, is assessed through a desk audit of documents, not the RMP. Before submission to a testing facility, it is essential to update the Risk Assessment to align with the RMF. Confirming essential performance for each clinical function is necessary, as complex EP can affect testing time **[51]**.

Pre-testing devices can provide valuable insights, especially for novel technologies. Decision regarding in-house pre-testing or using a test lab depends on your comfort level. Although pre-test of every aspect is not necessary, it helps to assess what is beneficial. If a device fails pre-testing, consider redesigning and reassessing critical components and product classification **[52]**.

For testing, necessary items are prepared in advance, including functional devices, spare parts, labeling, and markings. EMC labs may lack labeling expertise, but reputable ones can assist. Ensure all supporting documentation, such as the RMF and TRF, is ready, and finalize agreements with the test lab. Promptly fulfill deposits, provide component certification, prepare factory inspection paperwork, and align production line test equipment with IEC 60601-1 standard.

Maintain clear communication with test labs, establish timelines for all project phases, and regularly check in with the lab. If testing issues arise, the lab may pause the project for resolution or issue a report on current issues. Incorporate buffer time into your project plan to account for unforeseen challenges, with a recommended additional 2-4 weeks beyond the estimated timeframe **[53]**.

4.1 Regulations For Design Control

Medical device manufacturers must follow Design Control principles to achieve regulatory compliance with entities such as the European Commission, FDA, Health Canada, and others. These guidelines aim to guarantee the safety of potential users of medical devices before they are commercially introduced **[54]**.

While ISO 13485 is widely used in the industry, the FDA has specific quality management and design control requirements. Design controls are outlined in FDA 21 CFR 820.30, which parallels the principles of section 7.3 Design and Development in ISO 13485 guidelines.

The FDA stresses compliance with acceptable quality practices in medical device design by incorporating Current Good Manufacturing Practice (CGMP) requisites into the regulation of the quality system. This regulatory framework offers flexibility for both regulatory compliance and internal design and development processes, ensuring the safety and efficacy of medical devices **[55]**.

Successful implementation of design controls in medical device development requires professionals from several disciplines, including business administration, life sciences, engineering, computer science, and the arts. Design controls provide a complete quality system approach that spans the whole lifecycle of a medical device from design and production, to maintenance, distribution, usage, and obsolescence.

The FDA-defined Design Control clause are as follows:

SECTION A. GENERAL
SECTION B. DESIGN AND DEVELOPMENT PLANNING
SECTION C. DESIGN INPUT
SECTION D. DESIGN OUTPUT
SECTION E. DESIGN REVIEW
SECTION F. DESIGN VERIFICATION
SECTION G. DESIGN VALIDATION
SECTION H. DESIGN TRANSFER
SECTION I. DESIGN CHANGES
SECTION J. DESIGN HISTORY FILE (DHF)

4.1.1 The Control Process for Medical Device Design

The initiation point of Design Control lies in the development and approval of Design Inputs, encompassing the specifications for device design and manufacturing processes to be executed during the production stage **[56]**.

Design control is a comprehensive approach that extends beyond the finalization of design and its transition to the production phase. It continues to influence manufacturing processes, adjusting to changes in the design phase and incorporating feedback received post-production. This iterative process aims to develop a product that meets user needs, incorporating revolutionary changes based on usage patterns and analysis of product failures **[57]**.

The diagram below illustrates how Design Control can be included within the process of waterfall design.

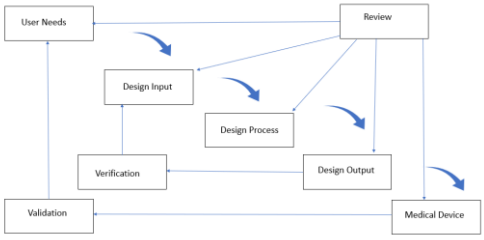

Figure 3 Design Control Implementation using a waterfall model.

The first step is user needs. The requirements are established based on market demand, and the device is developed to meet those requirements. Through a series of iterations, the design of the medical equipment is refined and ultimately transitioned to the production phase for manufacturing. Feedback is essential at every stage of this process to ensure continuous improvement and alignment with user needs **[58]**.

The second step is design inputs. This process is iterative in nature. When an organization identifies a specific need to address, they review and test the suitability of the design input generated from that requirement. This marks the beginning of iteratively translating requirements into device design **[59]**.

The third step is the design process. These design inputs are turned into design output by converting such needs into high-level specifications, which constitute the design output.

The fourth step is design output. The verification process ensures that the specifications meet the criteria. The output is then utilized as input to update the requirements, and this process is repeated until the Design Output matches the Design Input.
The last phase is manufacturing of the medical device, upon the completion of the final design, it is sent to the production facility for manufacturing at a large-scale **[60]**.

Design control standards require the establishment of a Design History File (DHF), which details the linkages and interactions among all the Design Controls, allowing for the tracking of all changes made when the product is being developed.

Whether choosing a paper- or software-based strategy designed specifically for Design Control, your design history file must be traceable and accessible to each team member.

4.2 Testing: –Validation And Verification

To be successful in the market, every medical equipment must achieve the objectives of functionality, use, and reliability. . In addition to these aspects, end users prioritize device efficacy and safety to address specific problems or conditions, which can, at times be crucial to life. This underscores the importance of medical device iterative testing, verification, and validation **[61]**.

Validation and verification during the design process of medical devices are essential to ensure the alignment of the device with the needs of its intended users and effectively delivers the intended solution. These methods also help ensure that all requirements are met, aiding in regulatory compliance and the creation of high-quality products and manufacturing processes **[62]**.

Verification is an internal process that determines whether a design output fulfils the standards, specifications, or regulations outlined in the design input. On the other contrary, validation is an internal-to-external process that determines whether the product provides the predicted advantages based on the demands of the targeted users **[63]**.

Medical devices come in different shapes, sizes, and levels of intricacy, and the V&V activities must be tailored to the regulatory environment and global standards.

Standardized V&V operations can help speed up the manufacturing and approval processes. Furthermore, automated testing, data collection, and diagnostic tools can further improve the V&V process **[64]**.

When not planned carefully, the iterative nature of V&V can incur significant costs. However, a well-defined test strategy can efficiently manage costs and testing timelines, ensuring timely market readiness of the product.

The complexity of the testing strategy varies depending on the technologies employed and the target markets geographically. A comprehensive test strategy should encompass the following six parameters:

- Targeted geography and standards
- Time to market
- Standards to follow with each version
- Testing Labs – either internal or independent
- Defining test sequences
- Presenting test results

As a result, the tests used in the verification and validation process must be validated themselves. This stage ensures that the tests appropriately measure what is intended, as using an improper test may result in false results about usability and functionality. Designers want an efficient and well-documented V&V procedure that complies with applicable requirements **[65]**.

5. RISK MANAGEMENT OF MEDICAL EQUIPMENT

ISO 13485 and ISO 14971 are widely recognized medical device quality management standards, developed by the International Organization for Standardization (ISO). These guidelines are widely implemented worldwide **[66]**.

In addition to these international standards, there are regional specifications that apply to specific geographical areas. These regional standards are typically adaptations of international standards with minor modifications and limitations to suit local requirements.

- Medical equipment manufactured or sold in the United States are regulated by the FDA.

The American National Standards Institute acts as the representative of ISO standards in the USA. Additionally, two other organizations, namely the American Society for Quality (ASQ) and the Association for the Advancement of Medical Instrumentation (AAMI), play roles in defining standards specific to the US **[67]**.

If a device has been designed in accordance with ISO standards, there is a chance that it may not receive approval from the FDA. This is because the FDA applies its own set of risk management procedures derived from a combination of international and regional standards. These procedures include:

o ISO 14971:2007, Medical devices – The use of risk management to medical equipment (international standard).

o ANSI/AAMI/ISO 14971:2007 (R2010), Medical devices – Using risk management on medical devices (A regional standard containing additions and adjustments to the referred international standard).

In terms of quality management standards, the compliance with the global or regional version of the ISO 13485 standard does not necessarily align with the requirements set forth by the FDA for the US market. The FDA maintains distinct recommendations for quality management designated for medical devices intended for the US market **[68]**. Consequently, while ISO 13485 serves as a globally recognized benchmark for quality management in the medical device industry, its direct applicability to FDA regulations may not suffice. This delineation stems from the nuanced differences between international standards and the regulatory framework maintained by the FDA to ensure safe and efficient medical devices in the United States. Therefore, medical device manufacturers aiming for FDA approval must meticulously adhere to the specific quality management guidelines outlined by the FDA, which may diverge from those delineated in the ISO 13485 standard **[69]**.

o In the context of the European Union, the European Committee for Standardization adopts standards derived from the ISO, while the European Committee for Electrotechnical Standardization develops regional standards influenced by the International Electrotechnical

Commission (IEC)CEN is a bit modified based on the requisites from ISO and written with “EN” prefix **[70]**. For e.g.:

o EN ISO 13485:2012, Medical devices — Quality management systems — The need for regulatory purposes

o EN ISO 14971:2012, Medical devices — Employment of risk management to medical equipment

National members of the European Union employ these standards while including their own prefix. In Switzerland, Swiss Standards publishes standards with the prefix "SN," such as SN EN ISO 14971:2012 and SN EN ISO 13485:2012 **[71]**.

o The Canadian Standards Authority (CSA) is the ISO’s representative organization in Canada.

Given the intricacy of the design of medical equipment, targeted risk management approaches are essential to ensure compliance in terms of usability, safety, and regulation. Risk management involves the systematic identification, control, and prevention of potential failures that could pose hazards to users **[72]**. It also entails identifying associated risks and, if they reach an unacceptable level, notifying developers to mitigate them to an acceptable level or below.

Figure 4 Risk Management of a medical device

The diagram above illustrates the various stages of the process of risk management. It commences with hazard identification, followed by the assessment of related risks are based on the potential repercussions and likelihood of hazards **[73]**.

If the assessed risk level surpasses predefined criteria, mitigation strategies are necessary. The level of risk is influenced by factors, including the device itself, the technologies involved, or the company's risk acceptance policy **[74,75]**.

Hazard analysis, also known as risk analysis, is a structured process that evaluates potential problems that could arise from the use of a medical device. The goal is to identify and assess

these risks, and develop strategies to manage them, ensuring the device's safety and efficiency for patients and meeting regulatory requirements **[76]**.

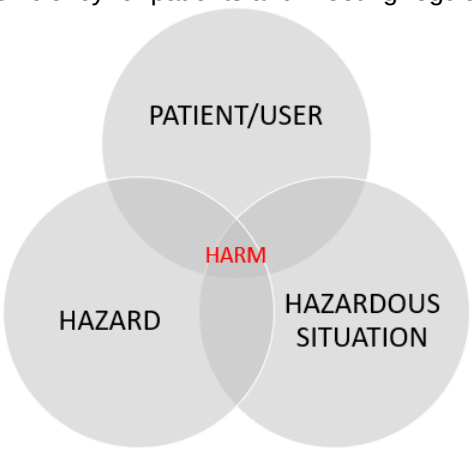

Figure 5 Elements interaction leading to HARM

Conducting a hazard analysis before finalizing a design is considered a best practice. This analysis provides insight into the typical hazards associated with the device. To begin, a primary hazard assessment can be performed by analyzing key components and operational necessities, including raw materials and waste, monitoring and control systems, hardware components, human-device interfaces, and services **[77]**. This process helps identify potential associated hazards. Certain hazards require particular evaluation, like

- Evaluations of raw materials and wastes include toxicity, flammability, and reactivity of the material
- Environmental parameters such as sensitivity to humidity and temperature and more
- Mechanical or electronic risks
- Human factors, like ineffective delivery, medication administration, incomplete or erroneous information, and control over life-sustaining activities, might pose risks to the user interface.
- .

When multiple hazards are recognized, they might be prioritized as per their severity. Sometimes, there may be situations where you lack sufficient information to identify hazards. In such instances, reviewing similar devices and their historical data can aid in hazard identification **[78]**.

In the prototype development phase, conducting a comprehensive hazard and risk analysis becomes essential. For hazard analysis, two approaches are primarily employed: the top-down approach and the bottom-up approach. Bottom-up analysis techniques like Hazard and Operability (HAZOP) and FMEA are employed in analyzing hazards and risks. HAZOP is well-suited for intricate designs with multiple procedural steps, while FMEA is suitable for devices with numerous mechanical components, although it can be time-intensive **[79]**. On the other hand, Fault Tree Analysis employs a top-down methodology to identify undesired top-level outputs by examining combinations and sequences of lower-level events. Using these methods, the risk analysis of a medical device can be completed **[80]**.

6. CONCLUSION

In conclusion, the document emphasizes the critical need for integrating design controls and regulatory compliance in medical device development. The lifecycle of medical device development, from initiation and risk analysis through to post-market surveillance, demands strict adherence to regulatory frameworks like those established by the FDA and international standards such as ISO 13485 and IEC 60601-1.

The process is multifaceted, involving meticulous planning, risk management, and continuous validation to meet user needs and regulatory requirements. The phases—initiation, feasibility assessment, design validation, final validation, and post-launch monitoring—offer a structured approach to ensure technical and regulatory alignment with the device's intended use and safety.

The IEC 60601-1 standard is highlighted as a crucial benchmark, guiding the design, development, and certification of medical electrical equipment. Compliance with these standards ensures patient and user safety, enhances marketability, and facilitates regulatory approval.

Ultimately, the successful design and development of medical devices depend on a harmonized approach that integrates comprehensive design controls with rigorous regulatory compliance. This strategy mitigates risks and ensures the final product meets the highest standards of quality, safety, and efficacy, protecting public health and promoting innovation in the medical device industry.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that they have no known competing financial interests OR non-financial interests OR personal relationships that could have appeared to influence the work reported in this paper.

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