Medical Devices: Evidence and Research

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EXPERT OPINION

The Essential Principles of Safety and Effectiveness for Medical Devices and the Role of Standards

This article was published in the following Dove Press journal:
Medical Devices: Evidence and Research

Saleh S Altayyar

Purpose: A medical device may be of any type such as appliance, in vitro usable reagents, apparatus, instrument, machine, implement, material, software or other related articles. Either as a single entity or in combination, these devices are used by the skilled persons as per the manufacturer's instructions to prevent, diagnose, treat, monitor, alleviate the disease, compensate for an injury, investigate, replace, modify or support the anatomy in human beings.
Methods: Using standards is a voluntary process unless and until it is identified as a mandatory one by the regulatory authority. The manufacturers must demonstrate that the medical devices they manufacture meet the relevant Essential Principles of Safety and Performance and are freely accessible to public.
Results: Various national and international standards (not recognized by the regulatory authority), industrial standards, manufacturer-developed Standard Operating Procedures (not related to international standards), non-recognized standards, and state-of-the-art techniques are in process in terms of performance, material, design, methods, process or practices.
Conclusion: The regulatory authority needs to ensure whether the manufacturer has implemented the risk management processes and met the regulatory requirements set. The responsibility towards medical devices safety and performance lies with both manufacturer and the regulatory authority.
Keywords: essential principles of safety and performance, effectiveness, medical devices performance, medical devices safety

Introduction

The operation of an active medical device relies on an electrical energy source as compared to the energy directly generated from the human gravity or body. Without any substantial modification, medical devices aim to transfer substances, energy, and other components between the patient.[1] Precisely, an active medical device is considered to be as a standalone software. Every medical device is designed with a purpose considering both safety and performance so that its intended action is performed without flaws. When a medical device is properly handled based on the instructions of the manufacturer, it produces the effect expected from the device as per the manufacturer and the medical condition, and declared to be clinically effective.[2] When designing and manufacturing the medical devices, the manufacturer should not compromise on the clinical safety conditions of its users, patients or any other persons involved. Similar measures should be followed when using the device for the intended purpose and using it as per the manufacturer's specified conditions and instructions for use.[3] Generally, the design for medical devices is regulated by essential principles of safety and performance with respect to their design and construction.[4] A device is designed to relieve pain

Correspondence: Saleh S Altayyar
Biomedical Technology Department, College of Applied Medical Sciences, King Saud University, P.O.Box 53831, Riyadh 11593, Saudi Arabia
Tel +966505456035
Email stayyar@ksu.edu.sa

submit your manuscript | www.dovepress.com
DovePress
http://doi.org/10.2147/MDER.S235467

whereas the manufacturer must clinically prove that the device relieves the pain. A close association exists between clinical effectiveness, performance, and safety.

The medical devices regulation is a rapid and vast evolving field that is usually complicated by legal issues. For instance, meanings of legal terms are occasionally non-uniform even throughout one regulatory system. This paper offers a standard framework that implements the regulatory systems with the most developed medical device regulations. Non-technical memory anchors, graphics, tables, and language are utilized for presenting a brief review of medical device safety issues and regulatory philosophy. The paper commences by discussing how safety is a risk management issue, and to what level optimum safety and performance is required to cooperate among all who are entailed in the medical device life span. The critical aspects of medical device regulations are presented using the existing regulatory tools of the Global Harmonization Task Force (GHTF), a common framework for regulatory development, and all the key documents issued in the last 20 years. The first steps toward successful simplification and harmonization are understanding the common framework and different phases in the life span of a medical device.

The objective of this paper is to offer harmonized Essential Principles that can be achieved in the designing and manufacturing of medical devices and in Vitro Diagnostic (IVD) medical devices to assure that they are safe and operate as required. The global implementation of a common set of fundamental designing and manufacturing requirements offers substantial advantages among manufacturers, regulatory authorities (RAs), users, and patients/consumers. Mitigating differences between jurisdictions lowers the cost of achieving regulatory compliance and enables patients' earlier access to new treatments and technologies.

This paper emphasizes on the Essential Principles of Safety and Effectiveness for Medical Devices and the role played by Standards. The outcome of the paper would be the identification of manufacturer obligations and responsibilities to find any risks associated with their medical devices, demonstration of the device benefits that outweigh the risks, and device conformity to the essential principles of safety and performance. It is a must for the regulatory authority to help the manufacturers identify relevant documents and data which are required for the conformity assessment and ensure that the manufacturer has provided an adequate demonstration of compliance to the essential principles of safety and performance.

It is intended for use by RAs, Conformity Assessment Bodies (CABs), industry, and other stakeholders, and will provide benefits in establishing, in a consistent way, an economic and effective approach to control the medical devices in the interest of public health. It seeks to strike a balance between the responsibilities of RAs to safeguard the health of their citizens and their obligations to avoid placing unnecessary burdens upon the industry.

Essential Principles of Safety and Performance

A medical device is said to be clinically effective when it exhibits the effect intended by the manufacturer according to the medical condition, for instance, a pain relief medical device should relieve pain as per the manufacturer's intended use. In such a scenario, the manufacturer needs to have clear objectives and scientific proof such as results from clinical tests must be available, inferring that the pain is relieved when using that device. When it comes to performance measurement of medical devices, both technicality and its clinical effectiveness should be considered. For instance, an alarm feature may not be suitable to express clinical effectiveness though it can serve other useful purposes.[5]

When a complication arises while using medical devices, the selection of appropriate medical devices should be decided based on the patient groups. Hence, it is essential for a manufacturer to demonstrate the advantages as well as possible side-effects that may be expected out of the device, though they can outweigh the significant improvements gained in users' quality of life based on clinical evidence. The essential principles of safety and performance govern the medical device's designing and manufacturing, and these principles are segregated broadly into general principles as well as principles with respect to design and construction.[6]

General Principles

Use of Medical Devices Not to Compromise Health and Safety

A medical device is to be devised and developed by assuring that:[6]

- Any risks related to the utilization of the device are compatible with a high level of health and safety and

acceptable risks must be omitted when weighed alongside the aimed advantage to the patient.

- The clinical condition or patient safety, or the health and safety of the user or any other individual will not be compromised under the circumstances and for the objectives for which the device was aimed for.
- A basic concept in the design and development of a medical device is its safety. A well-reasoned and documented investigation of the foreseeable risks is undertaken by a manufacturer to utilize the device and compare these risks with a documented and well-reasoned analysis of the advantages.

Design and Construction of Medical Devices to Conform the Safety Principles

The manufacturer must confirm the solutions adopted with safety principles for the design and construction of a medical device, considering the generally acknowledged framework. The manufacturer must recognize problems and related risks emerging from the use of the device for its aimed purpose, and predictable misuse of the device. Similarly, the manufacturer should reduce or mitigate these risks by implementing a policy of inherently safe design and development. Appropriate protection measures should be assured, if possible, with respect to any risks that cannot be reduced. Lastly, inform users of any residual risks that might emerge due to any shortcomings of the protection measures implemented.[4]

The design and development procedures for a medical device should be considered of any foreseeable hazards or risks that may present or can be constructed by the device when it is utilized as aimed by the manufacturer. Wherever possible, the design and development of the device should reduce the aimed hazards or risk.[5]

Medical Devices to Be Suitable for the Intended Purpose

- A medical device must be designed, packaged, and produced to assure that it is appropriate for one or additional objectives provided in the definition of a medical device in Section 1 of the Medicines and Related substances Act.
- Furthermore, it should be performed in the way aimed by the manufacturer.

Long-Term Safety

A medical device must be designed and developed to assure that it is not subjected to stresses during normal circumstances. The characteristics and performances mentioned in the aforementioned sections are not appropriately influenced and the device is constantly maintained and calibrated with respect to the instructions of manufacturers.[7]

Medical Devices are Not Adversely Affected by Transport or Storage

A medical device must be designed, developed, and packed to assure that the attributes and performance of the device are utilized for its targeted objective and are not negatively affected throughout storage and transport that is conducted considering the instructions and information provided by the manufacturer.

The manufacturer can involve a documented review of complaint history and evidence of testing to explain that the design, packaging, and production of the device assure the performance, and device attributes are not negatively influenced throughout storage and transport.

Benefits of Medical Devices to Outweigh Any Undesirable Effects

The manufacturer must achieve the benefits by using a medical device for the performance aimed to outweigh any undesirable effects emerging from its use. It is essential for identifying and documenting any undesirable effects with the advantages anticipated to be accomplished by using the device to comply with this essential principle. Manufacturers should offer evidence about the consequences or conclusions of the risk analysis based on a documented review of the experience of the manufacturer with a device.

Principles About Design and Construction

Chemical, Physical and Biological Properties

Specific attention must be given to the chemical and physical properties of the materials used in the device when ensuring that the needs of the general principles are achieved with respect to a medical device. Certainly, compatibility between the biological tissues and materials, body fluids, specimens, and cells must be ensured, considering the targeted objective of the device. A medical device must be designed, produced, and packaged to assure that any risks related to residues and contaminants may influence an individual who is engaged in storing,

transporting, or using the device.[8] A medical device must be produced and designed to ensure that the device can be utilized protectively with any substance, gas, and material, which the device might emerge into contact throughout its normal use in routine processes. The device must be designed and produced to ensure that the device allows the medicine to perform as targeted and is compatible with the restrictions and provisions applied to the administered medicine. The quality and safety of the substance should be verified with respect to the instructions for medicines if medical devices include or are aiming to include a substance that might be considered as a medicine.[3]

Infection and Microbial Contamination

The device must be designed to reduce contamination of the device or specimen by the patient, another person, the patient by the specimen or device, and allow it to be easily handled. The animals should be directed to adequate veterinary controls and supervision, if the tissues, cells or substances are originated from animals.[4] Certainly, the production procedure must integrate validated methods of removal, or inactivation with respect to viruses and other transmissible agents. The manufacturer must design medical devices to be supplied in a sterile state when storing and transporting. The adequate standards for air quality of the manufacturing areas should be undertaken in which the device is manufactured.[6] The packaging can withstand the sterilization procedure and is permeable to the sterilizing agent, and able to maintain sterility for a predefined period after the sterilization procedure.

Constructive and Environmental Properties

The manufacturer should entail documented and well-reasoned risk analysis, undertaking all the other devices meant to be used for the targeted objective of the device. The manufacturer should provide all the information for using the device merging with another medical device.[5] The manufacturer should document other medical devices and evidence of adequate testing processes, explaining that all medical devices must operate protectively irrespective of any impairment to the targeted performance. The analysis should list all potential causes and explain the probability and severity of their presence for each risk.

Medical Devices with a Measuring Function

The manufacturer should design and produce a medical device to measure function for assuring the accuracy, preciseness, and stability of a device throughout the limits prescribed based on the targeted objective of the device. Product standards, applicable guidance documents, and pharmacopeia monographs should be considered by manufacturers for assuring the device to be designed and produced in an acceptable way.

Protection Against Radiation

The manufacturer should design and produce a medical device to reduce the exposure of a patient and the user, to the levels of radiation needed to allow the device to act its diagnostic, and therapeutic functions and the targeted objective of the device. The manufacturer should reduce hazardous levels of visible or invisible radiation as it is essential for a medical objective. The reproducibility and tolerance of relevant variable parameters can be assured by using the device.

ISO 14971 Medical device risk management is the standard that describes the requirements to adhere to risk management of medical devices by the manufacturer during the product life cycle. A group of technical experts belonged to the ISO Technical Committee (TC) 210 and IEC TC 62 developed the ISO 14971.[8,9]

Design and Manufacturing Requirements

Classification of Medical Devices

The classification of medical devices is performed as per the risks upon patients, users, and people associated with them. Following is the list of criteria based on which the medical devices are classified.

- The risk to patients, users, and other persons (Probability and severity of harm)
- Degree of invasiveness in the human body
- Duration of use

Manufacturer's Responsibilities

The manufacturer is accountable for the performance of the device as far as the device is utilized according to its intended purposes. There is always a risk associated when using medical devices which can be defined as a combination of probabilities of harm occurrence and the severity of the harm. The manufacturer must use design controls and risk management processes to ensure that the medical device is properly designed, developed

and used as per the indications so that its safety and effectiveness are assured.[10,11]

As per the guidelines, risk control is a process of decision-making based on which certain measures were taken to mitigate the risks up to a certain level or get rid of it.[12] For every medical device, the manufacturer should take a call whether risk reduction measures are required for every hazardous situation and if risks occur, then it should be controlled within the acceptable limits by applying risk control activities.[13]

It is essential for the manufacturers to identify all the potential hazards associated with the intended use of the medical device, calculate the risks associated with every hazardous situation, and exhibit that they took all the possible measures to reduce the risk associated with the medical device that they manufacture. The manufacturer must address such risks in an adequate manner and outweigh the benefits and significant improvements brought in the users' quality of life rather than the device's side effects. They should also mention the adherence to the essential principles of safety and performance of the manufactured medical device.[12]

Regulatory Authorities (RAs) Responsibilities

The role of the RA is to assure that the manufacturer has followed the risk management processes and met the requirements set by the regulatory authority. Generally, the regulatory authority must create or adopt a checklist that presents all the essential principles of safety and performance to find the relevant documents and data needed for the purpose of conformity assessment. This further helps the manufacturers in understanding the process of demonstrating compliance with the essential principles of safety and performance. Various evaluation activities are included in the conformity assessment that includes an examination of records and procedures conducted by the manufacturer as per the requirements put forth by the regulatory authority.[12]

A checklist was recommended by Global Harmonization Task Force (GHTF) named Summary Technical Documents for Demonstrating (STED) Conformity to essential principles of safety and performance of medical devices, which consists of 21 essential principles that cover six items.[13] The checklist needs to identify whether all the essential principles are applied to the device and even if one principle is not applied, the reason for it, the methods used by the manufacturer to demonstrate the compliance with each essential principle that applies; and the precise identity of the controlled document(s) that offers evidence of compliance with each method used.[14]

Standards Used in Medical Equipment

Regional, national and international level are the three standard levels used in medical devices, some of the standardization bodies are American National Standards Institute (ANSI), Association for the Advancement of Medical Instrumentation (AAMI), European Committee for Standardization (CEN), British Standards Institution (BSI), American Society for Testing and Materials (ASTM), Japanese Industrial Standards Committee (JISC), and German Institute for Standardization (DIN).[15]

In the harmonization of regulatory processes, international standards are very critical components to assure the quality, safety, and performance of medical devices. Using standards is a voluntary act unless it is identified as a mandatory one by the regulatory authority. The term "Recognized standard" denotes that it is not necessarily required to follow, though the manufacturer already complied when it comes to using the recognized standards to showcase the compliance with the relevant Essential Principles for Safety and Performance of medical devices. It is an open choice for the manufacturer to make use of specific premarket requirements and/or other requirements of the Regulatory Authority to adhere to relevant Essential Principles for Safety and Performance of Medical Devices.[12] Furthermore, any mode of demonstration can be used by the manufacturers to showcase that their medical device complies and meets the relevant Essential Principles of Safety and Performance. This may be inclusive of industrial standards, the manufacturer developed Standard Operating Procedures (not related to international standards), compliance with harmonizing or recognized or other standards, national and international standards (not recognized by the regulatory authority).[16]

Conclusion

Medical devices are designed and manufactured with a specific and intended purpose ie, to enhance the patients' quality of life and their safety. To accomplish this, the medical devices must be easy to handle and function as intended by the manufacturer's instructions without compromising the safety of patients, users or patient's clinical conditions. Therefore, medical devices must comply and meet the standards set by the essential principles of safety

and performance. The responsibility towards the medical devices' safety and performance lies with both the manufacturer and the regulatory authority.

Expert Opinion

The objective of this paper is to offer harmonized essential principles that must be achieved in the design and development of medical devices and IVD medical devices for assuring that they are protective and safer as targeted. When achieved, the worldwide adoption of a regular set of basic design and development requirements for medical devices offer assurance about the device and provides substantial advantages to manufacturers, users, patients or consumers, to regulatory authorities, and others. Differences between jurisdictions mitigate the cost of attaining regulatory compliance and offers patients to access new treatments and technologies. This paper has been developed for stimulating and supporting the global convergence of regulatory systems. It is aimed to be used by RAs, industry experts, CABs, and other stakeholders, and will offer advantages to establish an effective and economical approach to the control of medical devices, considering the public health, in a consistent way. It aims to strike a balance between the responsibilities of regulatory authorities to protect the health of their citizens and their responsibilities to ignore any irrelevant stresses upon the industry.

A product must be designed and manufactured based on the expectation of a manufacturer of a medical device that must be safe and effective within its life-cycle. This paper presents basic design and manufacturing requirements, which refer to as essential principles of safety and performance, by the manufacturer. Broad, high-level criteria for design, post-production, and production within the life-cycle of all medical devices and IVD medical devices are provided in essential principles of safety and performance to ensure their safety and performance.

Compliance with the essential principles of safety and performance is an acceptable approach to apply controls comparative to the safety and performance of a device by the regularity authority with jurisdiction, which includes where appropriate a pre-market review. There might be additional requirements that may need to be achieved based on the regulatory authority having jurisdiction and the specific medical device or IVD medical device. Their development can provide advantages from these essential principles of safety and performance, where standards are being considered as part of regulatory compliance.

It is the responsibility of the manufacturer to demonstrate that the devices adhere to the essential principles of safety and performance. The manufacturer should educate the users about device performance and safety which outweigh the risks associated when using the device. In the case of regulatory authority, their responsibility is to ensure whether the manufacturer has implemented the risk management processes and met the regulatory requirements set.

This paper applies to all IVD medical devices and is aimed to recognize and explain essential principles of safety and performance, which can be considered throughout the design and manufacturing process. Some of the important principles of safety and performance do not apply based on the specific medical device or IVD medical device. In such cases, there is a need to provide justifications for their exclusion. These items are required to be met by medical devices when connected with or equipped with an energy source, protection against mechanical risks, information supplied by the manufacturer, protection against the risks posed to the patient for devices for self-testing or self-administration, protection against the risks posed to the patient by supplied energy or substances, and performance evaluation including clinical evaluation where ever appropriate.

Disclosure

The author reports no conflicts of interest in this work.

References

1. IMDRF Good Regulatory Review Practices Group. Essential principles of safety and performance of medical devices and IVD medical devices. 2018. Available from: http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-181031-grrp-essential-principles-n47.pdf. Accessed January 31, 2020.
2. World Health Organization. *Medical Device Regulations: Global Overview and Guiding Principles*. World Health Organization; 2003. Available from: https://apps.who.int/iris/handle/10665/42744. Accessed January 31, 2020.
3. Force GH. Summary technical documentation for demonstrating conformity to the essential principles of safety and performance of medical devices (STED). SG1/N011R17. 2007.
4. Force GH. Essential principles of safety and performance of medical devices. Available from: http://www.imdrf.org/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n41r9-2008-principles-safety-performance-050520.pdf. Accessed January 31, 2020.
5. *The Regulation of Medical Devices in Australia*. Therapeutic Good Administration, Department of Health - Therapeutic Good Administration, Australia; 2002.
6. The Essential Principles for medical devices. Australian medical devices guidance document, 22. 2003. Available from: https://www.omnex.com/training/iso13485/australia/Australia-Device-Essential-Principles.pdf. Accessed January 31, 2020.

7. Guidance on Essential Principles for Safety and Performance of Medical Devices. GN-16. HAS. May 2014. Available from: https://www.hsa.gov.sg/docs/default-source/hprg-mdb/gn-16-r2-guidance-on-essential-principles-for-safety-and-performance-of-medical-devices (18jun-pub).pdf. Accessed January 31, 2020.
8. ISO 14971:2000. *Medical Devices—Application of Risk Management to Medical Devices*. Geneva: International Organization for Standardization; 2000.
9. IEC 60601-1. *Medical Electrical Equipment—Part 1: General Requirements for Basic Safety and Essential Performance*. Geneva: International Electro technical Commission; 2005.
10. Speer J. 8 Reasons why your design controls and risk management processes fail. FDA Regulations and Design Controls and Risk Management and User Needs and Product Development and Design Reviews. June 20, 2016.
11. Medical Control Council. Medical devices and IVD essential principles of safety and performance. July, 2016.
12. ISO 14971. *Medical Devices: Application of Risk Management to Medical Devices*. 2nd ed. International Organization for Standardization: 2007.
13. Speer J. The design controls + risk management connection — verification, validation, & risk controls. *Med Device Online*. 2015;18.
14. Summary technical documentation for demonstrating conformity to the essential principles of safety and performance of medical devices (STED). SG1.GHTF, March 5, 2007.
15. Health Sciences Authority – Health Products Regulation Group. GN-16: guidance on essential principles for safety and performance of medical devices. Available from: https://www.hsa.gov.sg/docs/default-source/hprg/regulatory-updates/gn-16-guidance-on-essential-principles-of-safety-and-performance-of-medical-devices—key-updates.pdf. Accessed January 31, 2020.
16. Role of Standards in the Assessment of Medical Devices. The global harmonization task force (SG1). 2000.