IMDRF International Medical Device Regulators Forum

IMDRF Training

Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices

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International Affairs Office
ANVISA – Brazilian Health Regulatory Agency
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Essential Principles of Safety and Performance

2008

GHTF/SG1/N41R9:2005

GHTF

FINAL DOCUMENT

Title: Essential Principles of Safety and Performance of Medical Devices

Authoring Group: GHTF Study Group 1

Endorsed by: The Global Harmonization Task Force

Date: May 20, 2005

Abraao Carvalho, GHTF Chair

This document was produced by the Global Harmonization Task Force, a voluntary international group of representatives from medical device regulatory authorities and trade associations from Europe, the United States of America (USA), Canada, Japan and Australia.

The document is intended to provide *non-binding* guidance to regulatory authorities for use in the regulation of medical devices, and has been subject to consultation throughout its development.

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2012

GHTF/SG1/N68:2012

GHTF

FINAL DOCUMENT

Global Harmonization Task Force
(revision of GHTF/SG1/N41:2005)

Title: Essential Principles of Safety and Performance of Medical Devices

Authoring Group: Study Group 1 of the Global Harmonization Task Force

Date: November 2nd, 2012

Dr. Kazunari Asanuma, GHTF Chair

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IMDRF International Medical Device Regulators Forum

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Title: Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices

Authoring Group: IMDRF Good Regulatory Review Practices Group

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Yuan Lin, IMDRF Chair

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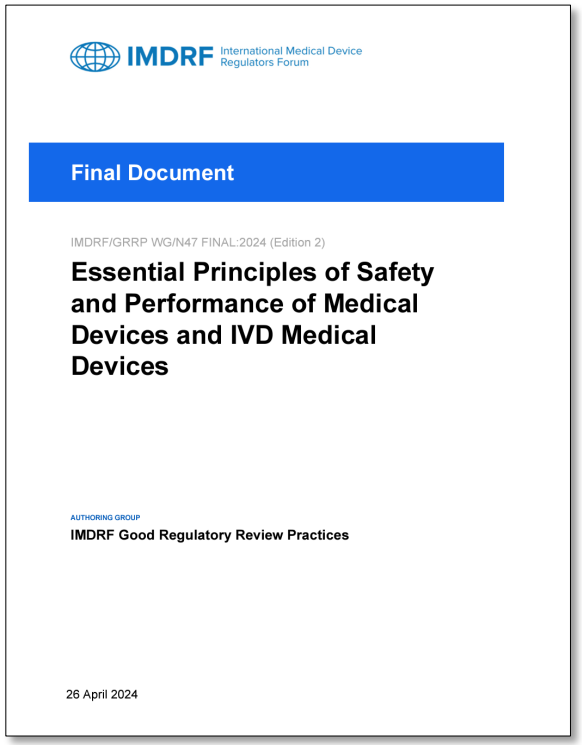
37 pages

2024



IMDRF International Medical Device Regulators Forum

Final Document

IMDRF/GRRP WG/N47 FINAL:2024 (Edition 2)

Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices

AUTHORING GROUP

IMDRF Good Regulatory Review Practices

26 April 2024

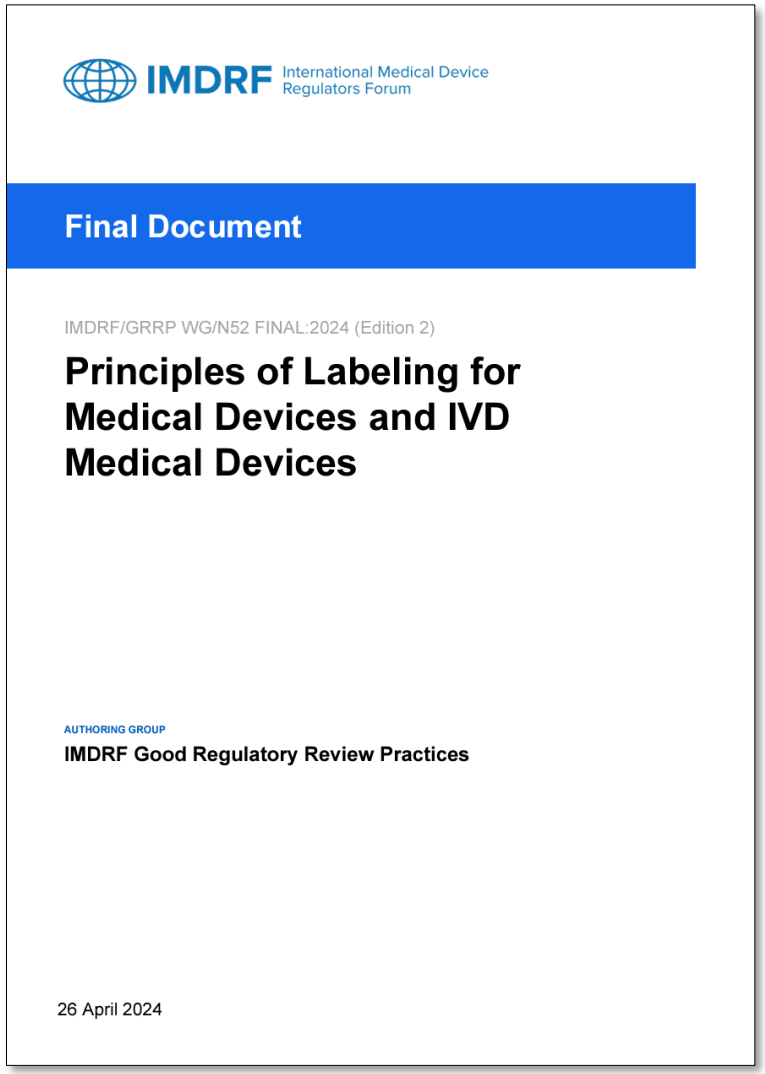
42 pages

Essential Principles of Safety and Performance

Why adopt or update these essential principles?

1) Patient safety
2) Rapid technological advancements
3) Equitable access
4) Market confidence
5) Global harmonization
6) Data privacy and security
7) Adapting to novel risks
8) Clinical efficacy
9) Innovation and industry growth
10) Ethical and social considerations

Essential Principles of Safety and Performance



Other important IMDRF document is directly linked to Safety and Performance Principles

IMDRF/GRRP WG/N52 FINAL:2024 (Edition 2) Principles of Labelling for Medical Devices and IVD Medical Devices

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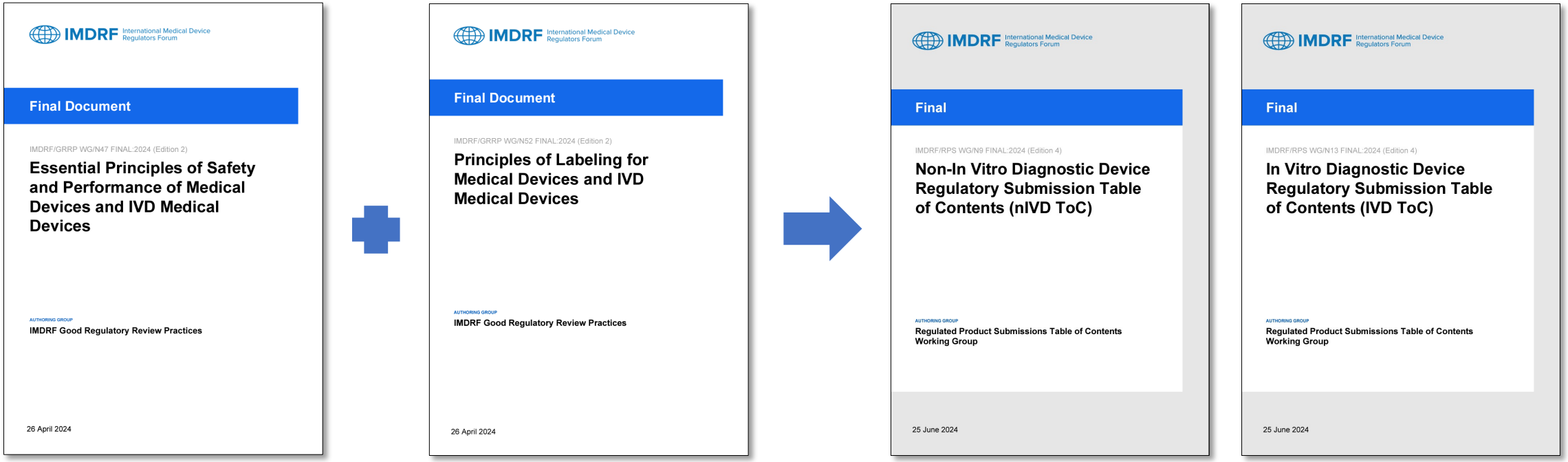
Essential Principles of Safety and Performance

Fundamental design and manufacturing **requirements that provide assurance** that a medical device or IVD is safe and **performs as intended** by the manufacturer



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Essential Principles of Safety and Performance

Safety and Performance

General and specific risk considerations specific to medical devices, IVDs, or both

Includes list of relevant standards/guidance documents

Examples:

- Material characterization
- Clinical evaluation
- Conditions of use
- Diagnostic functions
- Software aspects
- General labeling principles

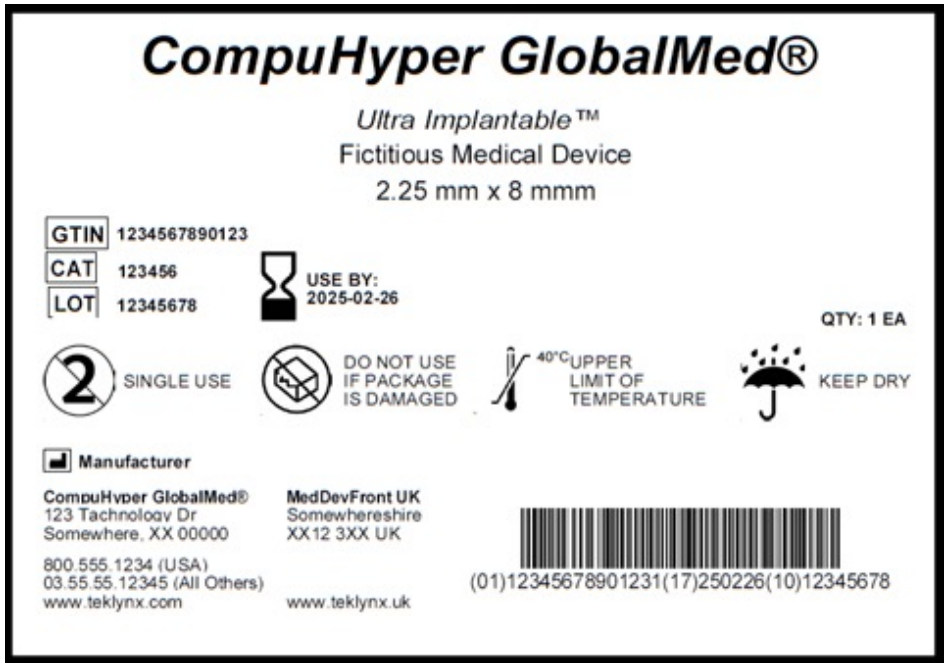
Essential Principles of Safety and Performance

Labeling

Labeling elements and information specific to medical devices, IVDs, or both

Examples:

- Label
- Instructions for use
- Software as a medical device
- Lay users
- Information intended for the patient

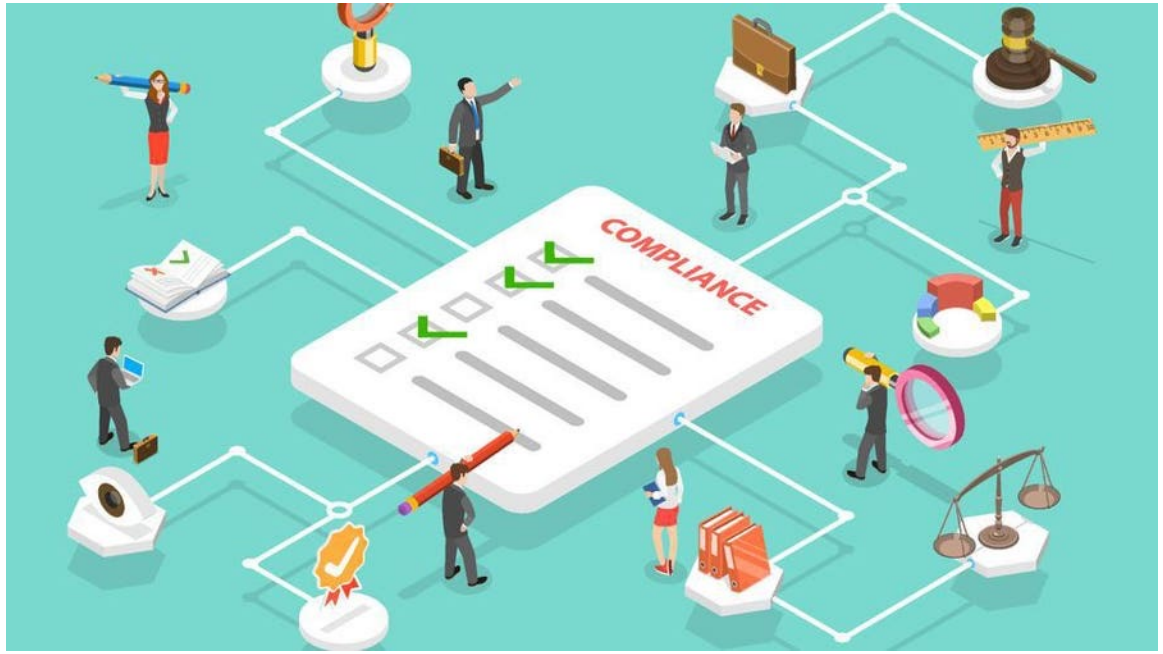


Essential Principles of Safety and Performance

The adoption of these common principles worldwide offers benefits to:

- Manufacturers
- Users
- Patients
- Regulatory authorities

Reducing regulatory compliance costs and enabling faster access to new medical technologies

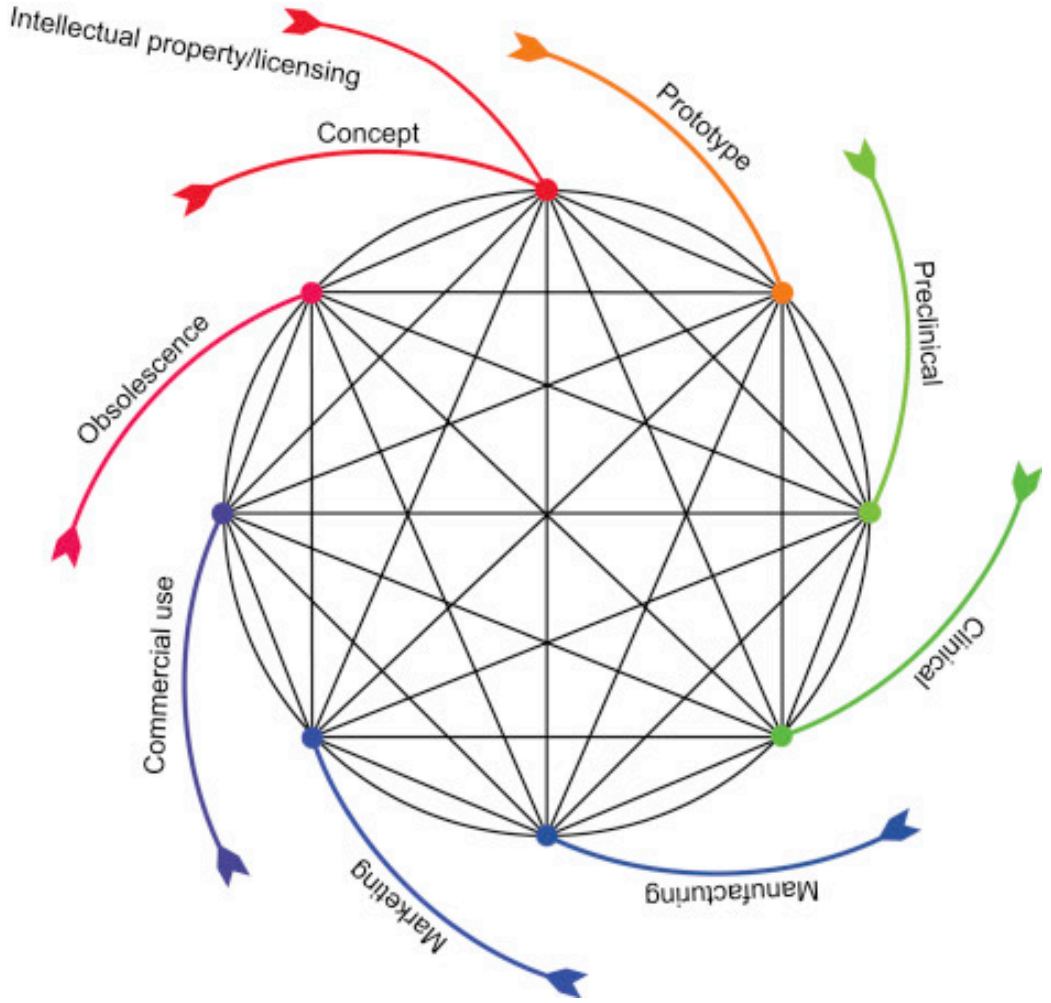


Essential Principles of Safety and Performance

Emphasizes a balance between safeguarding public health and not burdening the industry unnecessarily

Compliance to Essential Principles throughout product life-cycle

- **Design**
- **Production**
- **Postproduction**



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Essential Principles of Safety and Performance

Key terms used in regulatory language

"Should" *indicates that among several possibilities, one is recommended as particularly suitable, without mentioning or excluding others, or that a certain course of action is preferred but not necessarily required, or that (in the negative form) a certain possibility or course of action should be avoided but is not prohibited.*

"May" *is used to indicate that a course of action is permissible within the limits of the standard.*

"Can" *is used as a statement of possibility and capability.*

"Must" *is used only to describe "unavoidable" situations, including those mandated by government regulation.*

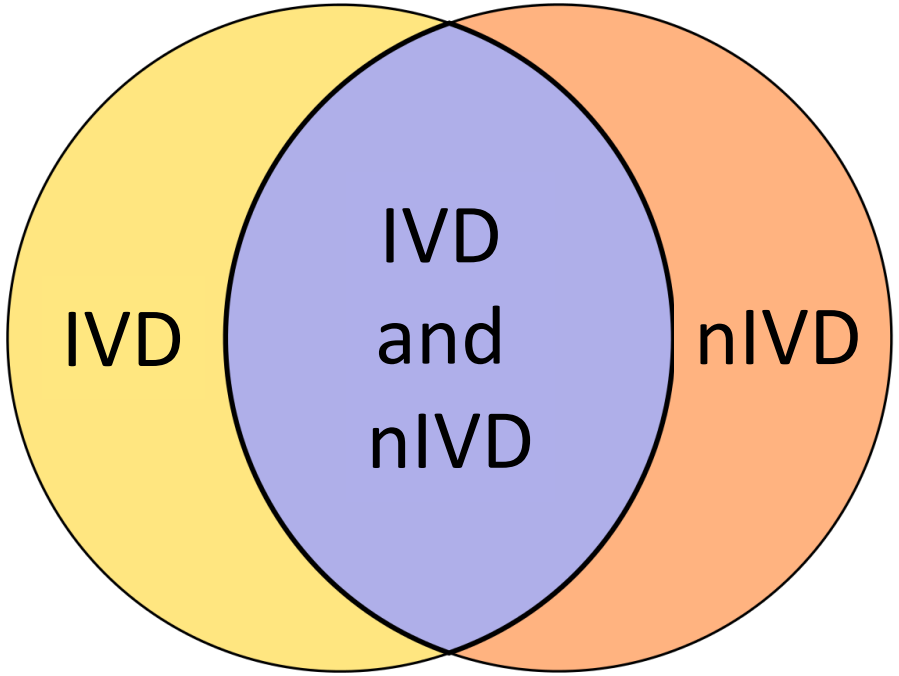
Essential Principles of Safety and Performance

A manufacturer of a medical device or IVD medical device ***is expected to design and manufacture*** *a product that is* ***safe and performs as intended*** *throughout its life cycle.*

Essential Principles Applicable to all Medical Devices and IVD Medical Devices

Essential Principles Applicable to Medical Devices other than IVD Medical Devices

Essential Principles Applicable to IVD Medical Devices



EP's Applicable to all Medical Devices and IVD Medical Devices

General (5.1)

- Performance and Suitability
- Risk Management System
- Risk Management Steps
- Risk Control Measures
- Informing Users
- Risk Reduction for Users
- Performance Maintenance
- Transport and Storage
- Stability
- Balancing Risks and Benefits

- Develop a risk management plan for each device
- Identify and analyze known and foreseeable hazards associated with each device
- Evaluate the risks associated with intended use and foreseeable misuse
- Control or eliminate risks based on specific requirements
- Evaluate the impact of production and post-production information on overall risk
- Adjust control measures if necessary

EP's Applicable to all Medical Devices and IVD Medical Devices

Essential Principle	Guidances	Relevant Standards
5.1	GHTF/SG3/N18:2010 Quality Management System – Medical Devices – Guidance on Corrective Action and Preventive Action and related QMS Processes GHTF/SG3/N17:2008 Quality Management System – Medical Devices – Guidance on the Control of Products and Services Obtained from Suppliers GHTF/SG3/N99-10:2004 Quality Management Systems - Process Validation Guidance GHTF/SG3/N15R8 Implementation of Risk Management Principles and Activities within a Quality Management System ISO 13485:2016 Handbook	ISO 13485: Medical devices — Quality management systems — Requirements for regulatory purposes ISO 14971: Medical devices — Application of risk management to medical devices ISO 23640: In vitro diagnostic medical devices — Evaluation of stability of in vitro diagnostic reagents ISO 24971: In vitro diagnostic medical devices — Guidance on the application of ISO 14971 CLSI EP25: Evaluation of Precision of Quantitative Measurement Procedures

EP’s Applicable to all Medical Devices and IVD Medical Devices

Clinical Evaluation (5.2)

- This evaluation involves analyzing clinical data to confirm a positive balance between benefits and risks for the device
- This data can include reports from clinical investigations or performance evaluations, published scientific literature, and clinical experiences

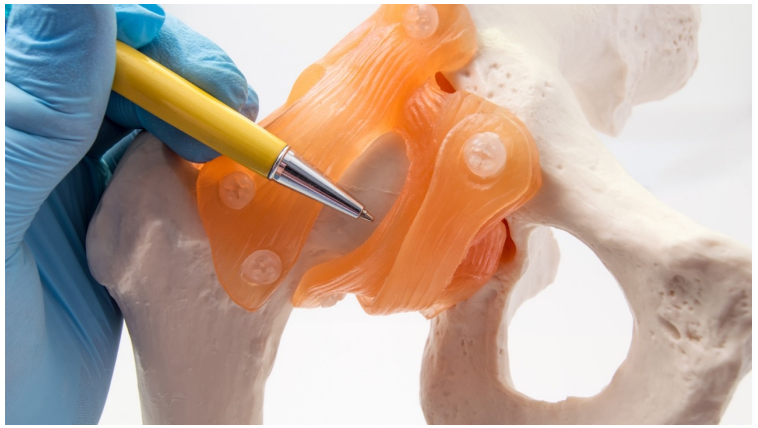
EP's Applicable to all Medical Devices and IVD Medical Devices

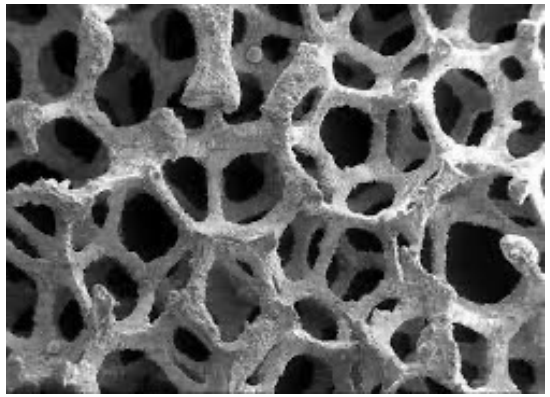
Essential Principle	Guidances	Relevant Standards
5.2	Declaration of Helsinki GHTF/SG5/N1R8:2007 Clinical Evidence – Key Definitions and Concepts GHTF/SG5/N2R8:2007 Clinical Evaluation GHTF/SG5/N3:2010 Clinical Investigations GHTF/SG5/N6:2012 Clinical Evidence for IVD Medical Devices - Key Definitions and Concepts GHTF/SG5/N7:2012 Clinical Evidence for IVD Medical Devices - Scientific Validity Determination and Performance Evaluation GHTF/SG5/N8:2012 Clinical Performance Studies for In Vitro Diagnostic Medical Devices	ISO 14155: Clinical investigation of medical devices for human subjects — Good clinical practice

EP's Applicable to all Medical Devices and IVD Medical Devices

Chemical, Physical, and Biological Properties (5.3)

- Material Selection
- Process Impact
- Research Validation
- Mechanical Properties
- Surface Properties
- Chemical and Physical Specifications
- Contaminants and Residues
- Substance Egress
- Unintentional Substance Ingress
- Infection Risk





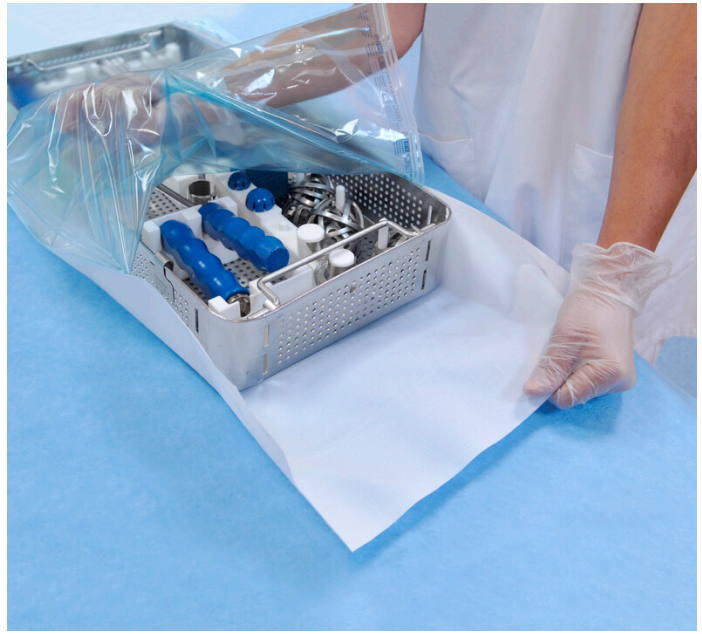
EP's Applicable to all Medical Devices and IVD Medical Devices

Essential Principle	Guidances	Relevant Standards
5.3		ISO 10993: Biological evaluation of medical devices IEC 60601: Medical electrical equipment IEC 61010: Safety requirements for electrical equipment for measurement, control, and laboratory use

EP's Applicable to all Medical Devices and IVD Medical Devices

Sterilization and Microbial Contamination (5.4)

- Facilitate safe cleaning, disinfection, sterilization, and re-sterilization by the user
- Maintain microbial state during transportation and storage
- Validated methods for products labeled as sterile
- Packaging should minimize contamination when devices are provided non-sterile

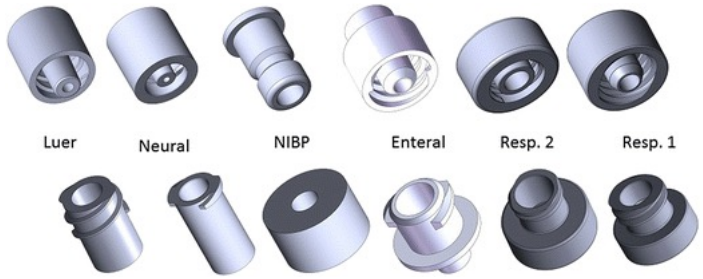


EP’s Applicable to all Medical Devices and IVD Medical Devices

Essential Principle	Guidances	Relevant Standards
5.4		ISO 11135: Sterilization of health care products — Ethylene oxide — Requirements for the development, validation, and routine control of a sterilization process for medical devices ISO 11137: Sterilization of health care products — Radiation — Requirements for the development, validation, and routine control of a sterilization process for medical devices ISO 11138: Sterilization of health care products — Biological indicators ISO 11140: Sterilization of health care products — Chemical indicators ISO 11607: Packaging for terminally sterilized medical devices ISO 10993: Biological evaluation of medical devices ISO 11737: Sterilization of medical devices — Microbiological methods ISO 13408: Aseptic processing of health care products ISO 14644: Cleanrooms and controlled environments ISO 14937: Sterilization of health care products — General requirements for characterization of a sterilizing agent and the development, validation, and routine control of a sterilization process ISO 14698: Cleanrooms and controlled environments — Biocontamination control ISO 17664: Sterilization of medical devices — Information to be provided by the manufacturer for the processing of resterilizable medical devices ISO 17665: Sterilization of health care products — Moist heat

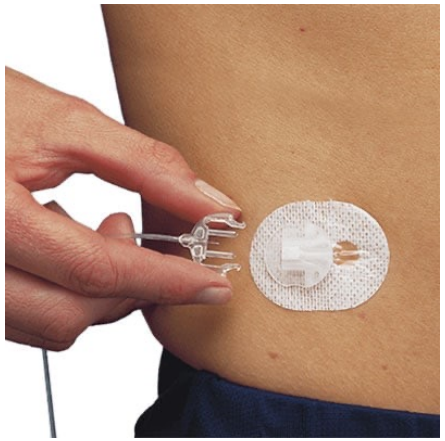
EP's Applicable to all Medical Devices and IVD Medical Devices

Considerations of Environment and Conditions of Use (5.5)



- Devices intended for use alongside other medical devices
  - The entire combination, including connection systems, must ensure safety and not compromise the specified performance

- Consider the intended environment and usage conditions to minimize various risks
  - Risks to users or others caused by physical features, user interface design, and foreseeable external influences like magnetic fields, humidity, temperature, and pressure



- Software interactions, maintenance and calibration mechanisms, unauthorized access risks, ergonomic usability, and safe disposal/recycling

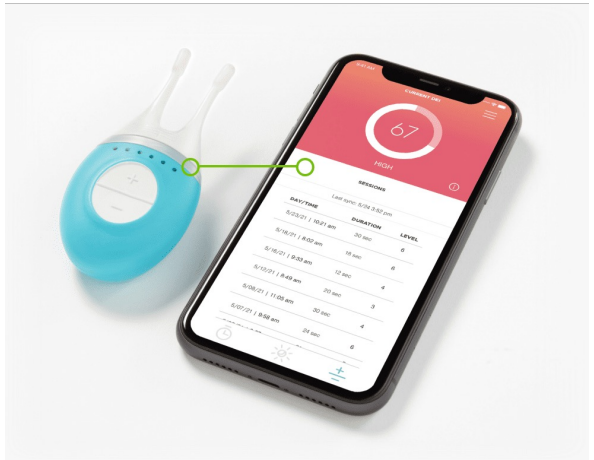
EP’s Applicable to all Medical Devices and IVD Medical Devices

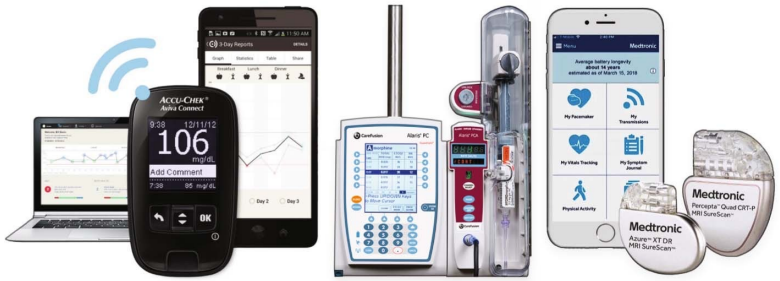
Essential Principle	Guidances	Relevant Standards
5.5		IEC 60601: Medical electrical equipment IEC 61010: Safety requirements for electrical equipment for measurement, control, and laboratory use IEC 62366-1: Medical devices — Application of usability engineering to medical devices IEC/TR 62366-2: Medical devices — Part 2: Guidance on the application of usability engineering to medical devices IEC 80001: Application of risk management for IT-networks incorporating medical devices ISO 80369: Small-bore connectors for liquids and gases in healthcare applications IEC 62304: Medical device software — Software life cycle processes

EP’s Applicable to all Medical Devices and IVD Medical Devices

Devices that Incorporate Software or are Software as a Medical Device (5.8)

- Ensure accuracy, reliability, safety, and performance
- In case of a single fault, measures should be taken to eliminate or reduce resulting risks
- Software should be developed, manufactured, and maintained using up-to-date practices, considering development cycles, risk management, verification, and validation
- When software is intended for use with mobile platforms, the platform's characteristics and usage environment should be considered
- Cybersecurity measures are also essential





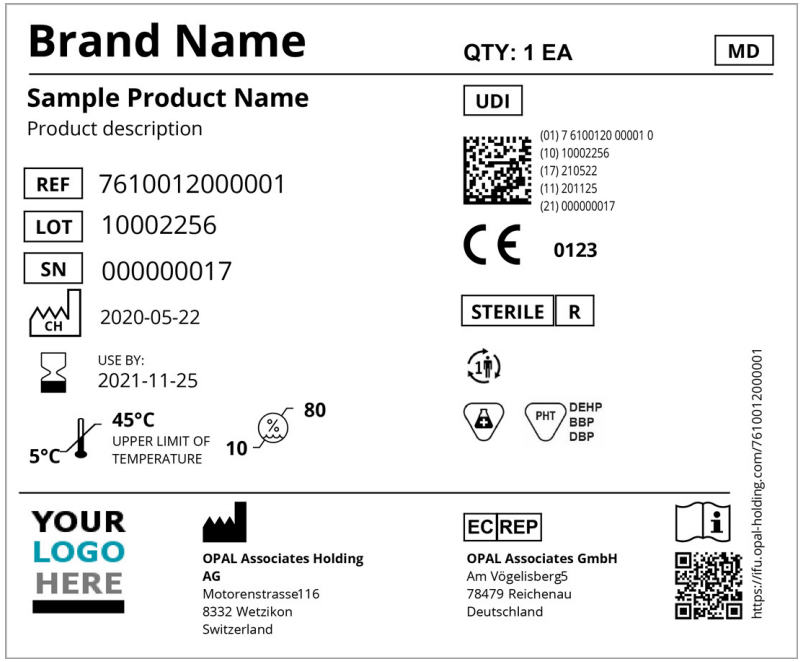
EP's Applicable to all Medical Devices and IVD Medical Devices

Essential Principle	Guidances	Relevant Standards
5.8	IMDRF/SaMD WG/N41FINAL:2017 Software as a Medical Device (SaMD): Clinical Evaluation IMDRF/SaMD WG/N23 FINAL:2015 Software as a Medical Device (SaMD): Application of Quality Management System IMDRF/SaMD WG/N12 FINAL:2014 "Software as a Medical Device": Possible Framework for Risk Categorization and Corresponding Considerations IMDRF/SaMD WG/N10 FINAL:2013 Software as a Medical Device (SaMD): Key Definitions	IEC 62304: Medical device software — Software life cycle processes

EP's Applicable to all Medical Devices and IVD Medical Devices

Labeling (5.10)

- Refer to IMDRF/GRRP WG/N52
- Information needed to distinctively identify the medical device or IVD medical device and its manufacturer
- Accompanied by, or direct the user to any safety and performance information relevant to the user, or any other person, as appropriate
- Information may appear on the device itself, on the packaging or in the instructions for use, or be readily accessible through electronic means, and should be easily understood by the intended user



EP's Applicable to all Medical Devices and IVD Medical Devices

Essential Principle	Guidances	Relevant Standards
5.10	IMDRF/GRRP WG/N52 Principles of Labeling for Medical Devices and IVD Medical Devices	ISO 15223-1: Medical devices — Symbols to be used with medical device labels, labelling, and information to be supplied — Part 1: General requirements ISO 18113: In vitro diagnostic medical devices — Information supplied by the manufacturer ISO 20417: Medical devices — Information to be supplied by the manufacturer

EP’s Applicable to all Medical Devices and IVD Medical Devices

Protection against the Risks posed by MD and IVD MD intended by the Manufacturer for use by Lay Users (5.12)

- Appropriate Performance:
  - Devices must perform effectively considering lay users' skills and environments
  - Instructions should be clear and easy to understand

- Safety and Accuracy:
  - Ensure safe and accurate use according to instructions
  - Mitigate risks through training if necessary
  - Minimize risk of user error in handling and result interpretation

- User Verification and Warnings:
  - Include methods for users to verify device performance
  - Provide warnings if the device fails or produces invalid results

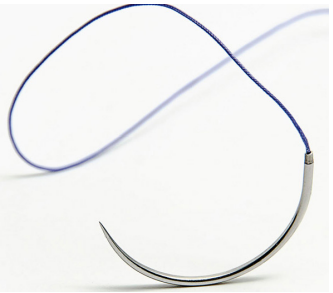
EP’s Applicable to all Medical Devices and IVD Medical Devices

Essential Principle	Guidances	Relevant Standards
5.12		IEC 62366-1: Medical devices — Application of usability engineering to medical devices IEC/TR 62366-2: Medical devices — Part 2: Guidance on the application of usability engineering to medical devices

EP's Applicable to all Medical Devices and IVD Medical Devices

Medical Devices Incorporating Materials of Biological Origin (5.13)

- Source Controls and Origin:
  - Use non-viable or rendered non-viable tissues, cells, or derivatives of animal, plant, or bacterial origin
  - Veterinary controls should be adapted based on animal species and intended use of tissues or derivatives
  - Geographical origin of animals may need to be retained depending on jurisdictional requirements



- Safety Measures in Sourcing & Processing:
  - Sourcing, processing, preservation, testing, and handling must ensure the safety of patients, users and other individuals
  - Special focus on viral safety and preventing other transmissible agents by using validated state-of-the-art elimination or inactivation methods

EP’s Applicable to all Medical Devices and IVD Medical Devices

Essential Principle	Guidances	Relevant Standards
5.13		ISO 22442: Medical devices utilizing animal tissues and their derivatives

EP’s Applicable to all Medical Devices and IVD Medical Devices

Other important EP’s discussed in this section

- Protection against Electrical, Mechanical, and Thermal Risks (5.6)
- Active Medical Devices and Devices Connected to Them (5.7)
- Devices with a Diagnostic or Measuring Function (5.9)
- Protection against Radiation (5.11)

EP's Applicable to all Medical Devices and IVD Medical Devices

Essential Principle	Guidances	Relevant Standards
5.6		IEC 60601: Medical electrical equipment IEC 61010: Safety requirements for electrical equipment for measurement, control, and laboratory use
5.7		IEC 60601: Medical electrical equipment IEC 61010: Safety requirements for electrical equipment for measurement, control, and laboratory use
5.9		IEC 60601: Medical electrical equipment IEC 61010: Safety requirements for electrical equipment for measurement, control, and laboratory use IEC 62366-1: Medical devices — Application of usability engineering to medical devices IEC/TR 62366-2: Medical devices — Part 2: Guidance on the application of usability engineering to medical devices
5.11		IEC 60601: Medical electrical equipment IEC 61010: Safety requirements for electrical equipment for measurement, control, and laboratory use

Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices

Break – 15 minutes

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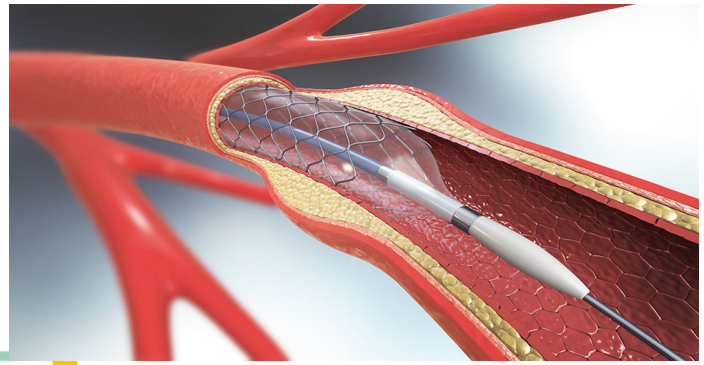
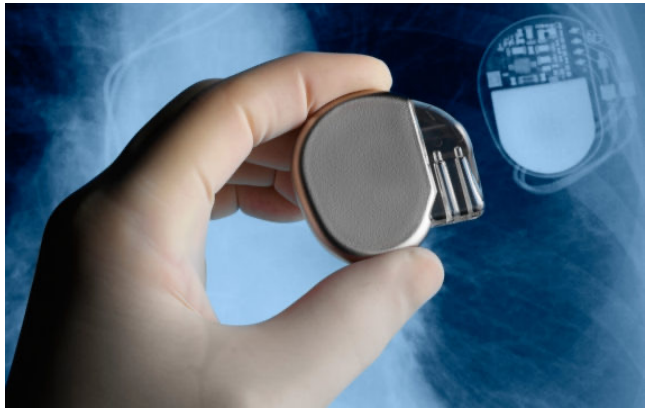
EP's Applicable to Medical Devices other than IVD MD

Additional EP's to the previously listed

- Chemical, Physical and Biological Properties
- Protection against Radiation
- Particular Requirements for Implantable Medical Devices
- Protection against the Risks Posed to the Patient or User by Medical Devices Supplying Energy or Substances
- Medical Devices Incorporating a Substance Considered to be a Medicinal Product/Drug





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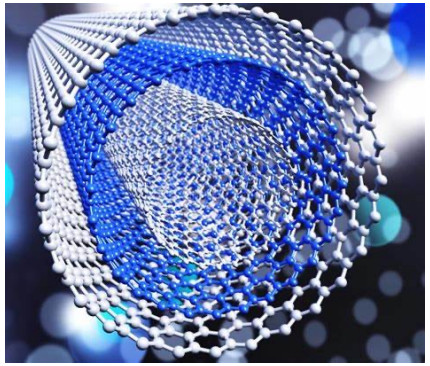
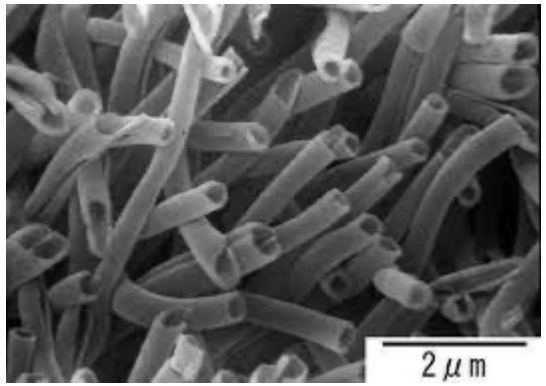
EP's Applicable to Medical Devices other than IVD MD

Chemical, Physical and Biological Properties (6.1)

- Compatibility between the materials used and biological tissues, cells, and fluids
- Design to safely interact with materials, substances, and gases during their use
- Devices must minimize risks related to the release of particles into the body, particularly focusing on nanomaterials, unless they only contact intact skin





EP’s Applicable to Medical Devices other than IVD MD

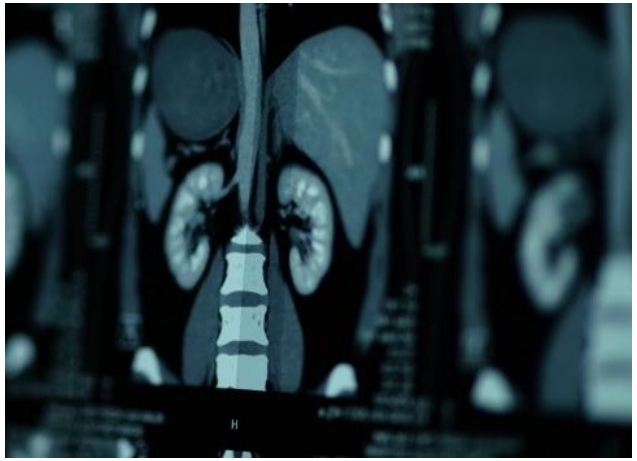
Essential Principle	Guidances	Relevant Standards
6.1		ISO 10993: Biological evaluation of medical devicesIEC 60601 IEC 60601: Medical electrical equipment – Part 1: General requirements for basic safety and essential performance

EP's Applicable to Medical Devices other than IVD MD

Protection against Radiation (6.2)

- Medical devices emitting ionizing radiation intended for medical imaging should be designed and manufactured in such a way as to achieve an image and/or output quality that are appropriate to the intended medical purpose whilst minimizing radiation exposure of the patient, user, and other persons

- Medical devices emitting ionizing radiation should be designed to allow the accurate estimation (or monitoring), display, reporting, and recording of the dose from a treatment



EP’s Applicable to Medical Devices other than IVD MD

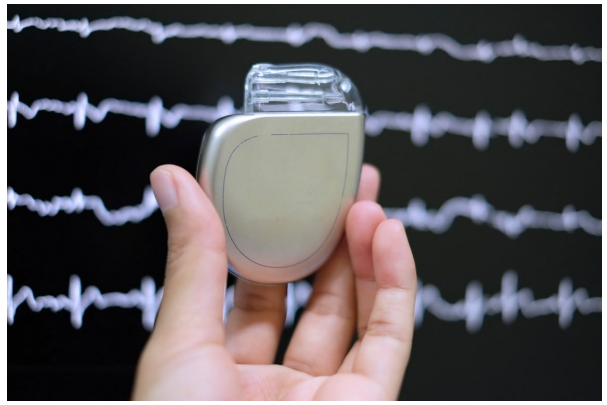
Essential Principle	Guidances	Relevant Standards
6.2		IEC 60601: Medical electrical equipment – Part 1: General requirements for basic safety and essential performance

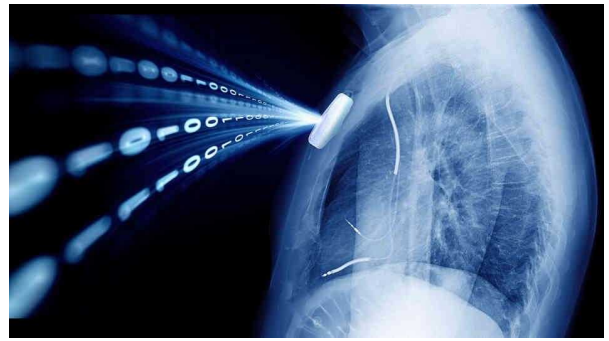
EP's Applicable to Medical Devices other than IVD MD

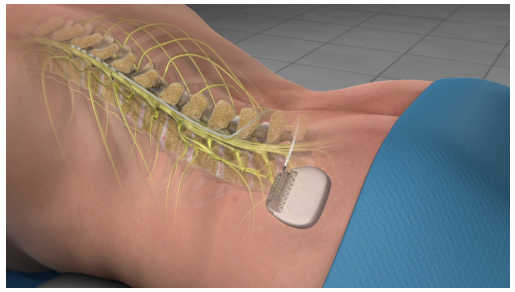
Particular Requirements for Implantable Medical Devices (6.3)

- Implantable medical devices should be designed and manufactured in such a way as to remove or appropriately reduce the risks associated with medical treatment, e.g. the use of defibrillators, high-frequency surgical equipment

- Active programmable implantable medical devices should be designed and manufactured in a manner that allows the unequivocal identification of the device without the need for a surgical operation







EP’s Applicable to Medical Devices other than IVD MD

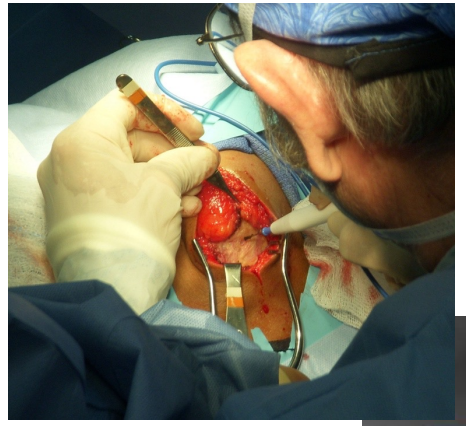
Essential Principle	Guidances	Relevant Standards
6.3		Requirements depend on the type of implantable device

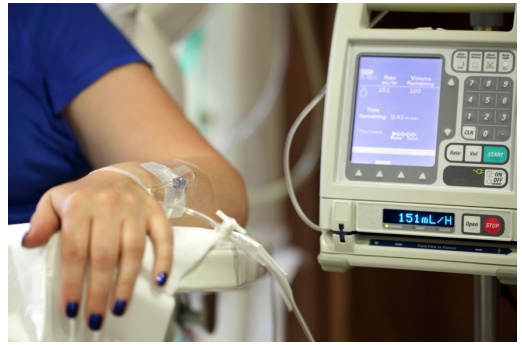
EP's Applicable to Medical Devices other than IVD MD

Protection against the Risks Posed to the Patient or User by Medical Devices Supplying Energy or Substances (6.4)

- Medical devices for supplying the patient with energy or substances should be designed and manufactured in such a way that the amount to be delivered can be set and maintained accurately enough to ensure the safety of the patient, user, and others

- Medical devices should be fitted with the means of preventing and/or indicating any inadequacies in the amount of energy delivered or substances delivered which could pose a danger. Devices should incorporate suitable means to appropriately reduce the risk of accidental release of dangerous levels of energy or substances from an energy and/or substance source





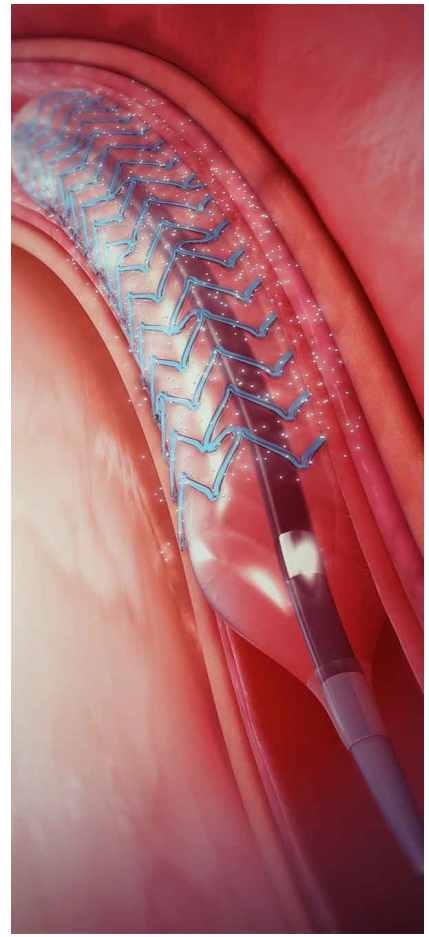
EP’s Applicable to Medical Devices other than IVD MD

Essential Principle	Guidances	Relevant Standards
6.4		IEC 60601: Medical electrical equipment – Part 1: General requirements for basic safety and essential performance

EP's Applicable to Medical Devices other than IVD MD

Medical Devices Incorporating a Substance Considered to be a Medicinal Product/Drug (6.5)

- Where a medical device incorporates, as an integral part, a substance which, if used separately may be considered to be a medicinal product/drug as defined in the relevant legislation that applies in that Regulatory Authority and which is liable to act upon the body with action ancillary to that of the medical device, the safety and performance of the medical device as a whole should be verified, as well as the identity, safety, quality and efficacy of the substance in the specific combination product
    - **Note:** This essential principle is not intended to provide definitions for combination products since these definitions are yet to be harmonized and how combination products are handled varies among different regulatory authorities



EP’s Applicable to IVD Medical Devices

Additional EP’s to the previously listed

- Chemical, Physical and Biological Properties
- Performance Characteristics
  - Analytical performance
  - Clinical performance
  - Validated control procedures
- Traceability of Calibrators and Controls
- Standardized Units
- Performance Evaluation

EP's Applicable to IVD Medical Devices

Chemical, Physical and Biological Properties (7.1)

- With regards to chemical, physical, and biological properties for IVD medical devices, attention should be paid to the possibility of impairment of analytical performance due to physical and/or chemical incompatibility between the materials used and the specimens, analyte or marker to be detected and measured (such as biological tissues, cells, body fluids and micro-organisms), taking account of the intended purpose of the device

EP's Applicable to IVD Medical Devices

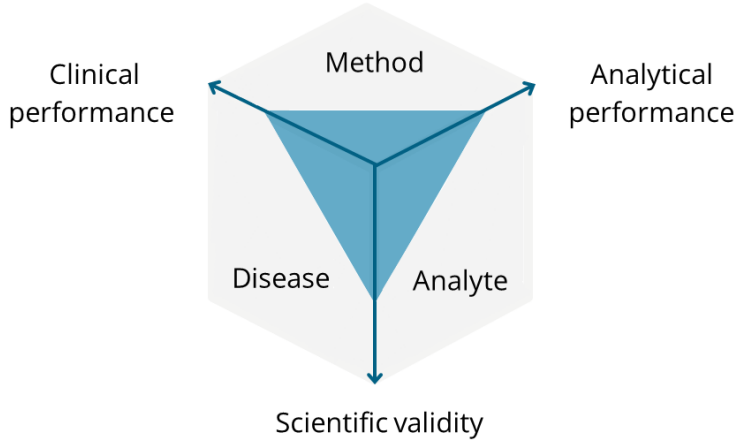
Essential Principle	Guidances	Relevant Standards
7.1		CLSI EP05 - Evaluation of Precision of Quantitative Measurement Procedures CLSI EP06 - Evaluation of Linearity of Quantitative Measurement Procedures CLSI EP07 - Interference Testing in Clinical Chemistry CLSI EP12 - User Protocol for Evaluation of Qualitative Test Performance CLSI EP17 - Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures CLSI EP21 - Evaluation of Total Analytical Error for Quantitative Medical Laboratory Measurement Procedures CLSI EP25 - Evaluation of Stability of In Vitro Diagnostic Reagents CLSI EP28 - Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory ISO 17511 - In vitro diagnostic medical devices — Requirements for establishing metrological traceability of values assigned to calibrators and control materials ISO 23640 - In vitro diagnostic medical devices — Evaluation of stability of in vitro diagnostic reagents

EP’s Applicable to IVD Medical Devices

Performance Characteristics (7.2)

- IVD Medical devices must meet both analytical and clinical performance standards as defined by the manufacturer, based on the device's intended use, patient population, user, and setting

- These performance characteristics must be validated using state-of-the-art methods
  - Analytical performance includes aspects such as traceability of calibrators, accuracy, sensitivity, specificity, and stability
  - Clinical performance covers measures like diagnostic sensitivity, specificity, predictive values, and likelihood ratios



EP’s Applicable to IVD Medical Devices

Performance Characteristics (7.2) [cont’d]

- Proper control procedures should be in place to ensure device accuracy
- If the device uses calibrators or control materials, their accuracy must be confirmed using reference methods. Measurements should be in standard units
- The device's performance should be tested for the intended user, setting, and population
- Test groups should be diverse and representative of the market, especially for infectious diseases

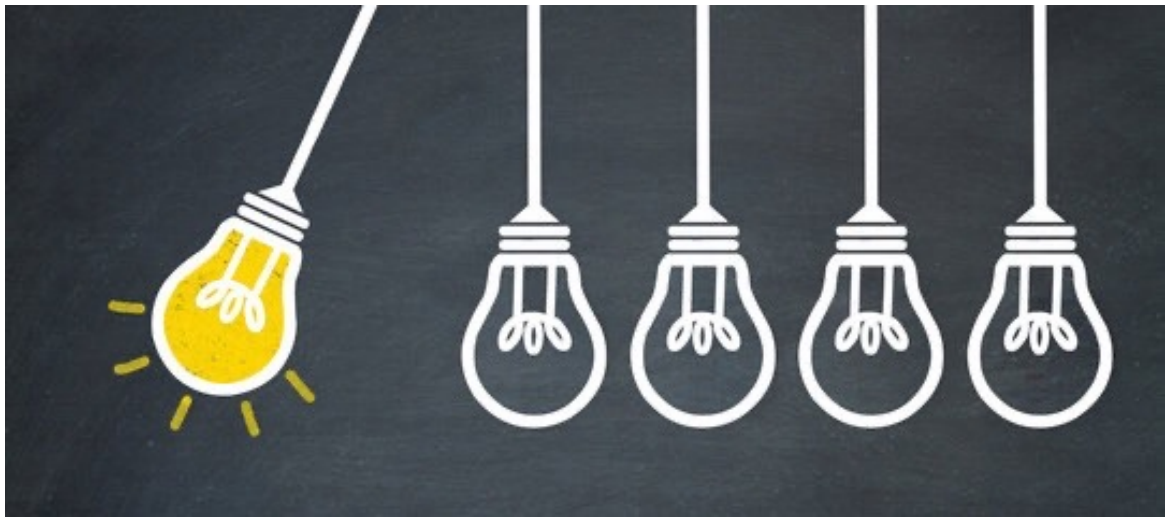
EP’s Applicable to IVD Medical Devices

Essential Principle	Guidances	Relevant Standards
7.2		ISO 10993: "Biological evaluation of medical devices IEC 61010: "Safety requirements for electrical equipment for measurement, control, and laboratory use"

Conclusion

Essential Principles of Safety and Performance for MD and IVD MD

- Trust and reliability in the technologies
- Innovation with responsibility
- Maximize patient well-being while minimizing risks
- High standards
- Contribute to the advancement of medical science



IMDRF International Medical Device Regulators Forum