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Title: Essential Principles of Safety and Performance of Medical Devices

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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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Preface

The document herein was produced by the Global Harmonization Task Force, a voluntary group of representatives from medical device regulatory authorities and the regulated industry. The document is intended to provide non-binding guidance for use in the regulation of medical devices, and has been subject to consultation throughout its development.

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1 Introduction

The primary way in which the GHTF achieves its goals is through the production of a series of guidance documents that together describe a global regulatory model for medical devices. The purpose of such guidance is to harmonize the documentation and procedures that are used to assess whether a medical device conforms to the regulations that apply in each jurisdiction. Eliminating differences between jurisdictions decreases the cost of gaining regulatory compliance and allows patients earlier access to new technologies and treatments.

This document has been developed to encourage and support global convergence of regulatory systems. It is intended for use by Regulatory Authorities, Conformity Assessment Bodies and industry, and will provide benefits in establishing, in a consistent way, an economic and effective approach to the control of medical devices in the interest of public health. It seeks to strike a balance between the responsibilities of Regulatory Authorities to safeguard the health of their citizens and their obligations to avoid placing unnecessary burdens upon the industry. Study Group 1 of the GHTF supports and encourages regulatory harmonization but recognises that some Regulatory Authorities may have to reflect different local needs when they introduce new regulations on conformity assessment. However, Regulatory Authorities that are developing conformity assessment schemes or amending existing ones are encouraged to consider the adoption of the system described in this document, as this will help to reduce the diversity of schemes worldwide and facilitate the process of harmonization.

The GHTF has identified as a priority the need to harmonize essential safety and performance criteria for a medical device that allow the manufacturer to demonstrate its product is suitable for its intended use. This goal was achieved through the publication of guidance on the subject entitled *Essential Principles of Safety and Performance of Medical Devices* (SG1/N020 of June 30, 1999) that applied to the majority of medical devices but not to *in vitro* diagnostic devices. **This current document supersedes that earlier one.** The major difference between them is the expanded scope; this document now includes medical devices for the *in vitro* examination of specimens derived from the human body.

The regulatory requirements of some countries do not, at this time, align fully with this guidance.

Study Group 1 of the Global Harmonization Task Force (GHTF) has prepared this guidance document. Comments or questions about it should be directed to either the Chairman or Secretary of GHTF Study Group 1 whose contact details may be found on the GHTF web page[1].

[1] www.ghtf.org

2 Rationale, Purpose and Scope

2.1 Rationale

Consistent identification, selection and application of safety and performance principles to a medical device offers significant benefits to the manufacturer, user, patient or consumer, and to Regulatory Authorities since it allows its manufacturer to design, manufacture and demonstrate the device is suitable for its intended use. Moreover, eliminating differences between jurisdictions decreases the cost of gaining regulatory compliance and allows patients earlier access to new technologies and treatments.

2.2 Purpose

To describe six **general requirements** of safety and performance that apply to all medical devices.

To provide a comprehensive list of **design and manufacturing requirements** of safety and performance, some of which are relevant to each medical device. These are grouped as:

- Chemical, physical and biological properties.
- Infection and microbial contamination.
- Manufacturing and environmental properties.
- Devices with a diagnostic or measuring function.
- Protection against radiation.
- Requirements for medical devices connected to or equipped with an energy source.
- Protection against mechanical risks.
- Protection against the risks posed to the patient by supplied energy or substances.
- Protection against the risks posed to the patient for devices for self-testing or self-administration.
- Information supplied by the manufacturer.
- Performance evaluation including, where appropriate, clinical evaluation.

Note: the manufacturer selects which of the design and manufacturing requirements are relevant to a particular medical device, documenting the reasons for excluding the others. The Regulatory Authority and/or Conformity Assessment Body may verify this decision during the conformity assessment process.

2.3 Scope

This document applies to all products that fall within the definition of a medical device that appears within the GHTF document *Information Document Concerning the Definition of the Term "Medical Device"*, including those used for the *in vitro* examination of specimens derived from the human body.

3 References

GHTF final documents

SG1/N009 *Labelling for Medical Devices*

SG1/N012 *Role of Standards in the Assessment of Medical Devices.*

SG1/N020 *Essential Principles of Safety and Performance of Medical Devices*

GHTF documents available for public comment

SG1(PD)/N011 *Summary Technical Documentation for Demonstrating Conformity to the Essential Principles of Safety and Performance of Medical Devices.*

SG1(PD)/N029 *Information Document Concerning the Definition of the Term 'Medical Device'.*

SG1(PD)/N043 *Labelling for Medical Devices (revised).*

GHTF document being prepared for public comment

SG1(PD)/N040 *Principles of Conformity Assessment for Medical Devices.*

International standard

ISO 14971:2001 *Medical devices – Application of risk management to medical devices.*

ISO/TR 16142:2004 *Medical Devices – Guidance on the Selection of Standards in Support of the Recognized Essential Principles of Safety and Performance of Medical*

4 Definitions

Clinical evaluation: The review of relevant scientific literature and/or the review and assessment of data collected through clinical investigation.

Clinical investigation: Any designed and planned systematic study in human subjects undertaken to verify the safety and/or performance of a specific device. (Source – ISO/DIS 14155-1)

Device for self-testing/self-administration: Any device intended by the manufacturer to be able to be used by lay persons in a non-clinical environment. (Source – based on European Directive 98/79/EC)

Harm: Physical injury or damage to the health of people or damage to property or the environment. (Source – ISO/IEC Guide 51:1999)

Hazard: Potential source of harm. (Source – ISO/IEC Guide 51:1999)

Intended use / purpose: The objective intent of the manufacturer regarding the use of a product, process or service as reflected in the specifications, instructions and information provided by the manufacturer. (Source – 21 CFR 801.4)

Medical device: Refer to GHTF guidance document: *Information Concerning the Definition of the Term "Medical Device"* (SG1/N029).

Performance evaluation: Review of the performance of a medical device based upon data already available, scientific literature and, where appropriate, laboratory, animal or clinical investigations.

Regulatory Authority (RA): A government agency or other entity that exercises a legal right to control the use or sale of medical devices within its jurisdiction, and may take enforcement action to ensure that medical products marketed within its jurisdiction comply with legal requirements. (Source – EU-Canada MRA)

Risk: Combination of the probability of occurrence of harm and the severity of that harm. (Source – ISO/IEC Guide 51:1999)

Specimen: The discrete portion of a body fluid or tissue or other sample associated with the body taken for examination, study, or analysis of one or more quantity or characteristic to determine the character of the whole.

5 Essential Principles of Safety and Performance of Medical Devices

General Requirements

5.1 Medical devices should be designed and manufactured in such a way that, when used under the conditions and for the purposes intended and, where applicable, by virtue of the technical knowledge, experience, education or training of intended users, they will not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety.

5.2 The solutions adopted by the manufacturer for the design and manufacture of the devices should conform to safety principles, taking account of the generally acknowledged state of the art. When risk reduction is required, the manufacturer should control the risk(s) so that the residual risk(s) associated with each hazard is judged acceptable. The manufacturer should apply the following principles in the priority order listed:

- identify known or foreseeable hazards and estimate the associated risks arising from the intended use and foreseeable misuse,

- eliminate risks as far as reasonably practicable through inherently safe design and manufacture,
- reduce as far as is reasonably practicable the remaining risks by taking adequate protection measures, including alarms,
- inform users of any residual risks.

5.3 Devices should achieve the performance intended by the manufacturer and be designed, manufactured and packaged in such a way that they are suitable for one or more of the functions within the scope of the definition of a medical device applicable in each jurisdiction.

5.4 The characteristics and performances referred to in Clauses 5.1, 5.2 and 5.3 should not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer's instructions.

5.5 The devices should be designed, manufactured and packed in such a way that their characteristics and performances during their intended use will not be adversely affected under transport and storage conditions (for example, fluctuations of temperature and humidity) taking account of the instructions and information provided by the manufacturer.

5.6 The benefits must be determined to outweigh any undesirable side effects for the performances intended.

Design and Manufacturing Requirements

5.7 Chemical, physical and biological properties

5.7.1 The devices should be designed and manufactured in such a way as to ensure the characteristics and performance referred to in Clauses 5.1 to 5.6 of the 'General Requirements'. Particular attention should be paid to:

- the choice of materials used, particularly as regards toxicity and, where appropriate, flammability,
- the compatibility between the materials used and biological tissues, cells, body fluids, and specimens, taking account of the intended purpose of the device.
- the choice of materials used should reflect, where appropriate, matters such as hardness, wear and fatigue strength.

5.7.2 The devices should be designed, manufactured and packed in such a way as to minimize the risk posed by contaminants and residues to the persons involved in the transport, storage and use of the devices and to patients, taking account of the intended purpose of the product. Particular attention should be paid to tissues exposed and to the duration and frequency of exposure.

5.7.3 The devices should be designed and manufactured in such a way that they can be used safely with the materials, substances and gases with which they enter into contact during their normal use or during routine procedures; if the devices are intended to administer medicinal products they should be designed and manufactured in such a way as to be compatible with the medicinal products concerned according to the provisions and restrictions governing these products and that their performance is maintained in accordance with the intended use.

5.7.4 Where a 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 within that jurisdiction and which is liable to act upon the body with action ancillary to that of the device, the safety, quality and usefulness of the substance should be verified, taking account of the intended purpose of the device.

5.7.5 The devices should be designed and manufactured in such a way as to reduce as far as reasonably practicable and appropriate the risks posed by substances that may leach or leak from the device.

5.7.6 Devices should be designed and manufactured in such a way as to reduce as far as reasonably practicable and appropriate risks posed by the unintentional ingress or egress of substances into or from the device taking into account the device and the nature of the environment in which it is intended to be used.

5.8 Infection and microbial contamination

5.8.1 The devices and manufacturing processes should be designed in such a way as to eliminate or to reduce as far as reasonably practicable and appropriate the risk of infection to patients, users and, where applicable, other persons. The design should:

- allow easy handling,

and, where necessary:

- reduce as far as reasonably practicable and appropriate any microbial leakage from the device and/or microbial exposure during use,
- prevent microbial contamination of the device, or specimen where applicable, by the patient, user or other person.

5.8.2 Where a device incorporates substances of biological origin, the risk of infection must be reduced as far as reasonably practicable and appropriate by selecting appropriate sources, donors and substances and by using, as appropriate, validated inactivation, conservation, test and control procedures.

5.8.3 In some jurisdictions products incorporating tissues, cells and substances of non-human origin may be considered medical devices. In this case, such tissues, cells and substances should originate from animals that have been subjected to veterinary controls and surveillance adapted to the intended use of the tissues. National regulations may require that the manufacturer and/or the Regulatory Authority retain information on the geographical origin of the animals. Processing, preservation, testing and handling of tissues, cells and substances of animal origin should be carried out so as to provide optimal safety. In particular, safety with regard to viruses and

other transmissible agents should be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process.

5.8.4 In some jurisdictions products incorporating human tissues, cells and substances may be considered medical devices. In this case, the selection of sources, donors and/or substances of human origin, the processing, preservation, testing and handling of tissues, cells and substances of such origin should be carried out so as to provide optimal safety. In particular, safety with regard to viruses and other transmissible agents should be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process.

5.8.5 Devices labelled as having a special microbiological state should be designed, manufactured and packed to ensure they remain so when placed on the market and remain so under the transport and storage conditions specified by the manufacturer.

5.8.6 Devices delivered in a sterile state should be designed, manufactured and packed in a non-reusable pack, and/or according to appropriate procedures, to ensure that they are sterile when placed on the market and remain sterile, under the transport and storage conditions indicated by the manufacturer, until the protective packaging is damaged or opened.

5.8.7 Devices labelled either as sterile or as having a special microbiological state should have been processed, manufactured and, if applicable, sterilized by appropriate, validated methods.

5.8.8 Devices intended to be sterilized should be manufactured in appropriately controlled (e.g. environmental) conditions.

5.8.9 Packaging systems for non-sterile devices should keep the product without deterioration at the level of cleanliness stipulated and, if the devices are to be sterilized prior to use, minimize the risk of microbial contamination; the packaging system should be suitable taking account of the method of sterilization indicated by the manufacturer.

5.8.10 The packaging and/or label of the device should distinguish between identical or similar products placed on the market in both sterile and non-sterile condition.

5.9 Manufacturing and environmental properties

5.9.1 If the device is intended for use in combination with other devices or equipment, the whole combination, including the connection system should be safe and should not impair the specified performance of the devices. Any restrictions on use applying to such combinations should be indicated on the label and/or in the instructions for use.

5.9.2 Devices should be designed and manufactured in such a way as to remove or reduce as far as reasonably practicable and appropriate:

- the risk of injury, in connection with their physical features, including the volume/pressure ratio, dimensional and where appropriate ergonomic features;
- risks connected with reasonably foreseeable external influences or

environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, pressure, humidity, temperature or variations in pressure and acceleration;

- the risks connected to their use in conjunction with materials, substances and gases with which they may come into contact during normal conditions of use;
- the risks of accidental penetration of substances into the device;
- the risk of incorrect identification of specimens;
- the risks of reciprocal interference with other devices normally used in the investigations or for the treatment given;
- risks arising where maintenance or calibration are not possible (as with implants), from ageing of materials used or loss of accuracy of any measuring or control mechanism.

5.9.3 Devices should be designed and manufactured in such a way as to minimize the risks of fire or explosion during normal use and in single fault condition. Particular attention should be paid to devices whose intended use includes exposure to or use in association with flammable substances or substances which could cause combustion.

5.9.4 Devices must be designed and manufactured in such a way as to facilitate the safe disposal of any waste substances.

5.10 Devices with a diagnostic or measuring function

5.10.1 Devices with a measuring function, where inaccuracy could have a significant adverse effect on the patient, should be designed and manufactured in such a way as to provide sufficient accuracy, precision and stability for their intended purpose of the device. The limits of accuracy should be indicated by the manufacturer.

5.10.2 Diagnostic devices should be designed and manufactured in such a way as to provide sufficient accuracy, precision and stability for their intended use, based on appropriate scientific and technical methods. In particular the design should address sensitivity, specificity, trueness, repeatability, reproducibility, control of known relevant interference and limits of detection, as appropriate.

5.10.3 Where the performance of devices depends on the use of calibrators and/or control materials, the traceability of values assigned to such calibrators and/or control materials should be assured through a quality management system.

5.10.4 Any measurement, monitoring or display scale should be designed in line with ergonomic principles, taking account of the intended purpose of the device.

5.10.5 Wherever possible values expressed numerically should be in commonly accepted, standardised units, and understood by the users of the device.

Note: While SG1 generally supports convergence on the global use of internationally standardised measurement units, considerations of safety, user familiarity, and established clinical practice may justify the use of other recognised measurement units.

5.11 Protection against radiation

5.11.1 General

5.11.1.1 Devices should be designed and manufactured and packaged in such a way that exposure of patients, users and other persons to any emitted radiation should be reduced as far as practicable and appropriate, compatible with the intended purpose, whilst not restricting the application of appropriate specified levels for therapeutic and diagnostic purposes.

5.11.2 Intended radiation

5.11.2.1 Where devices are designed to emit hazardous, or potentially hazardous, levels of visible and/or invisible radiation necessary for a specific medical purpose the benefit of which is considered to outweigh the risks inherent in the emission, it should be possible for the user to control the emissions. Such devices should be designed and manufactured to ensure reproducibility of relevant variable parameters within an acceptable tolerance.

5.11.2.2 Where devices are intended to emit potentially hazardous, visible and/or invisible radiation, they should be fitted, where practicable, with visual displays and/or audible warnings of such emissions.

5.11.3 Unintended radiation

5.11.3.1 Devices should be designed and manufactured in such a way that exposure of patients, users and other persons to the emission of unintended, stray or scattered radiation is reduced as far as practicable and appropriate.

5.11.4 Instructions for use

5.11.4.1 The operating instructions for devices emitting radiation should give detailed information as to the nature of the emitted radiation, means of protecting the patient and the user and on ways of avoiding misuse and of eliminating the risks inherent in installation.

5.11.5 Ionizing radiation

5.11.5.1 Devices intended to emit ionizing radiation should be designed and manufactured in such a way as to ensure that, where practicable, the quantity, geometry and energy distribution (or quality) of radiation emitted can be varied and controlled taking into account the intended use.

5.11.5.2 Devices emitting ionizing radiation intended for diagnostic radiology should be designed and manufactured in such a way as to achieve appropriate image and/or output quality for the intended medical purpose whilst minimising radiation exposure of the patient and user.

5.11.5.3 Devices emitting ionizing radiation, intended for therapeutic radiology should be designed and manufactured in such a way as to enable reliable monitoring and

control of the delivered dose, the beam type and energy and where appropriate the energy distribution of the radiation beam.

5.12 Requirements for medical devices connected to or equipped with an energy source

5.12.1 Devices incorporating electronic programmable systems, including software, should be designed to ensure the repeatability, reliability and performance of these systems according to the intended use. In the event of a single fault condition in the system, appropriate means should be adopted to eliminate or reduce as far as practicable and appropriate consequent risks.

5.12.2 Devices where the safety of the patients depends on an internal power supply should be equipped with a means of determining the state of the power supply.

5.12.3 Devices where the safety of the patients depends on an external power supply should include an alarm system to signal any power failure.

5.12.4 Devices intended to monitor one or more clinical parameters of a patient should be equipped with appropriate alarm systems to alert the user of situations which could lead to death or severe deterioration of the patient's state of health

5.12.5 Devices should be designed and manufactured in such a way as to reduce as far as practicable and appropriate the risks of creating electromagnetic interference which could impair the operation of this or other devices or equipment in the usual environment.

5.12.6 Devices should be designed and manufactured in such a way as to provide an adequate level of intrinsic immunity to electromagnetic disturbance to enable them to operate as intended.

5.12.7 Protection against electrical risks

Devices should be designed and manufactured in such a way as to avoid, as far as possible, the risk of accidental electric shocks during normal use and in single fault condition, provided the devices are installed and maintained as indicated by the manufacturer.

5.13 Protection against mechanical risks

5.13.1 Devices should be designed and manufactured in such a way as to protect the patient and user against mechanical risks connected with, for example, resistance to movement, instability and moving parts.

5.13.2 Devices should be designed and manufactured in such a way as to reduce to the lowest practicable level the risks arising from vibration generated by the devices, taking account of technical progress and of the means available for limiting vibrations, particularly at source, unless the vibrations are part of the specified performance.

5.13.3 Devices should be designed and manufactured in such a way as to reduce to the lowest practicable level the risks arising from the noise emitted, taking account of technical progress and of the means available to reduce noise, particularly at source, unless the noise emitted is part of the specified performance.

5.13.4 Terminals and connectors to the electricity, gas or hydraulic and pneumatic energy supplies which the user has to handle should be designed and constructed in such a way as to minimize all possible risks.

5.13.5 Accessible parts of the devices (excluding the parts or areas intended to supply heat or reach given temperatures) and their surroundings should not attain potentially dangerous temperatures under normal use.

5.14 Protection against the risks posed to the patient by supplied energy or substances

5.14.1 Devices for supplying the patient with energy or substances should be designed and constructed in such a way that the delivered amount can be set and maintained accurately enough to guarantee the safety of the patient and of the user.

5.14.2 Devices should be fitted with the means of preventing and/or indicating any inadequacies in the delivered amount which could pose a danger. Devices should incorporate suitable means to prevent, as far as possible, the accidental release of dangerous levels of energy from an energy and/or substance source.

5.14.3 The function of the controls and indicators should be clearly specified on the devices. Where a device bears instructions required for its operation or indicates operating or adjustment parameters by means of a visual system, such information should be understandable to the user and, as appropriate, the patient.

5.15 Protection against the risks posed to the patient for devices for self-testing or self-administration

5.15.1 Such devices should be designed and manufactured in such a way that they perform appropriately for their intended purpose taking into account the skills and the means available to users and the influence resulting from variation that can reasonably be anticipated in user's technique and environment. The information and instructions provided by the manufacturer should be easy for the user to understand and apply.

5.15.2 Such devices should be designed and manufactured in such a way as to reduce as far as practicable the risk of use error in the handling of the device and, if applicable, the specimen, and also in the interpretation of results.

5.15.3 Such devices should, where reasonably possible, include a procedure by which the user can verify that, at the time of use, that the product will perform as intended by the manufacturer.

5.16 Information supplied by the manufacturer

5.16.1 Users should be provided with the information needed to identify the manufacturer, to use the device safely and to ensure the intended performance, taking account of their training and knowledge. This information should be easily understood.

Note: Further information is provided in *SG1/N009 Labelling for Medical Devices* and in SG1/N043 *Labelling for Medical Devices (revised).*

5.17 Performance evaluation including, where appropriate, clinical evaluation

5.17.1 All data generated in support of performance evaluation should be obtained in accordance with the relevant requirements applicable in each jurisdiction.

5.17.2 Clinical investigations on human subjects should be carried out in accordance with the spirit of the Helsinki Declaration. This includes every step in the clinical investigation from first consideration of the need and justification of the study to publication of the results. In addition, some countries may have specific regulatory requirements for pre-study protocol review or informed consent.

Note: Refer to SG1(PD)/N040 *Principles of Conformity Assessment for Medical Devices* and the work of GHTF Study Group 5 for further information on the use of clinical evaluation to demonstrate compliance with these Essential Principles.