TECHNICAL REPORT

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Implants for surgery — Essential principles of safety and performance

Implants chirurgicaux — Principes essentiels de la sécurité et les performances

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Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation on the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT) see the following URL: www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 150, *Implants for surgery*.

This third edition cancels and replaces the second edition (ISO/TR 14283:2004), which has been technically revised.

The main changes compared to the previous edition are as follows:

— the previous edition was based on Annex I of the European Council Medical Devices Directive, while this edition is based on guidance documents developed by the Global Harmonisation Task Force (GHTF).

Introduction

The purpose of this document is to harmonize the documentation and procedures that are used to assess whether an implant 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 implants 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.

A further purpose is to provide a basis for the development of technical standards for implants intended to have international applicability.

This document describes fundamental design and manufacturing requirements, referred to as "Essential Principles of Safety and Performance" that, when met, indicate an implant is safe and performs to its specification.

This document is derived and adapted from the previous version of this document (2004) and from guidance documents developed by the Global Harmonization Task Force (GHTF) (GHTF/SG 1 documents N55,[3] N68,[4] N70[5] and N71[6]). In a few cases additional guidance has been provided and in these cases the additional guidance has been clearly identified by means of a Note.

This document is, by its nature, purely informative.

Annex A lists applicable pre-existing national or regional requirements, which can be consulted for comparison with the Essential Principles contained in this report.

The Bibliography provides a list of references that can be used to link these essential principles to standards and guidance documents giving product related requirements and guidance on the analysis of risks associated with the use of implants.

NOTE The GHTF documents listed in the Bibliography are subject to periodic review and can be superseded by later documents. The reader is encouraged to refer to the International Medical Device Regulators Forum (IMDRF) website at http://www.imdrf.org/documents/documents.asp to confirm whether the referenced documents remain current.

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Implants for surgery — Essential principles of safety and performance

1 Scope

This document provides fundamental principles for the design and manufacture of active or non-active implants in order that each implant can achieve its intended purpose.

It is often the case that instruments and other equipment are used in association with implants. These devices might be useful or even essential for the safe implantation and/or use of the implants. This document applies to implants, however, it also applies to associated instruments and equipment to the extent that the design and manufacture of the implants is intended to ensure the safe combination and use of the implants with such devices.

Requirements for the safe operation and use of associated instruments and equipment are contained in other standards.

2 Normative references

There are no normative references in this document.

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

— IEC Electropedia: available at https://www.electropedia.org/

— ISO Online browsing platform: available at https://www.iso.org/obp

3.1
active implant
implant whose operation depends on a source of electrical energy or any source of power other than that directly generated by the human body or gravity and which acts by converting this energy

Note 1 to entry: Implants intended to transmit energy, substances or other elements between an active implant and the patient, without any significant change, are not considered to be active implants.

3.2
clinical data
safety and/or performance information that are generated from the clinical use of a medical device

[SOURCE: GHTF/SG1/N68:2012, 4.0]

3.3
clinical evaluation
assessment and analysis of clinical data pertaining to a medical device to verify the clinical safety and performance of the device when used as intended by the manufacturer

[SOURCE: GHTF/SG1/N68:2012, 4.0]

3.4
clinical investigation
systematic investigation or study in or on one or more human subjects, undertaken to assess the safety and/or performance of a medical device

[SOURCE: GHTF/SG1/N70:2011, 4.0]

3.5
harm
physical injury or damage to the health of people or damage to property or the environment

[SOURCE: GHTF/SG1/N68:2012, 4.0]

3.6
hazard
potential source of harm

[SOURCE: GHTF/SG1/N68:2012, 4.0]

3.7
implant
medical device which is intended

— to be totally introduced into the human body, or

— to replace an epithelial surface or the surface of the eye

by surgical or clinical intervention, and which is intended to remain in place after the procedure

Note 1 to entry: Any medical device intended to be partially introduced into the human body through surgical or clinical intervention and intended to remain in place after the procedure for at least 30 days is also considered an implant.

3.8
information supplied by the manufacturer
see *labelling* (3.12)

3.9
instructions for use
information provided by the manufacturer to inform the device user of the medical device's intended purpose and proper use and of any precautions to be taken

[SOURCE: GHTF/SG1/N70:2011, 4.0]

3.10
intended use
intended purpose
use or purpose for which the implant or medical device is intended as indicated in the product specifications, instructions and information provided by the manufacturer

[SOURCE: GHTF/SG1/N68:2012, 4.0, modified — "the objective intent of the manufacturer regarding the use of a product, process or service as reflected in the" has been replaced by "use or purpose for which the implant or medical device is intended as indicated in the product".]

3.11
label
written, printed, or graphic information either appearing on the medical device itself, or on the packaging of each unit, or on the packaging of multiple devices

[SOURCE: GHTF/SG1/N70:2011, 4.0]

3.12
labelling
label, instructions for use, and any other information that is related to identification, technical description, intended purpose and proper use of the medical device, but excluding shipping documents

[SOURCE: GHTF/SG1/N70:2011, 4.0]

3.13
manufacturer
natural or legal person with responsibility for design and/or manufacture of a medical device with the intention of making the medical device available for use, under his name; whether or not such a medical device is designed and/or manufactured by that person himself or on his behalf by another person(s)
Note 1 to entry: The term "person" that appears here includes legal entities such as a corporation, a partnership or an association.

[SOURCE: GHTF/SG1/N055:2009, 5.1, modified.]

3.14
medical device
instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific medical purpose(s) of:

— diagnosis, prevention, monitoring, treatment or alleviation of disease,

— diagnosis, monitoring, treatment, alleviation of or compensation for an injury,

— investigation, replacement, modification, or support of the anatomy or of a physiological process,

— supporting or sustaining life,

— control of conception,

— disinfection of medical devices,

— providing information by means of *in vitro* examination of specimens derived from the human body;

and does not achieve its primary intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its intended function by such means

[SOURCE: GHTF/SG1/N71:2012, 5.1, modified — A note on products which might be considered to be medical devices in some jurisdictions but not in others has been deleted.]

3.15
regulatory authority
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 implants marketed within its jurisdiction comply with legal requirements

[SOURCE: GHTF/SG1/N68:2012, 4.0, modified — the abbreviation "RA" has been deleted.]

3.16
risk
combination of the probability of occurrence of harm and the severity of that harm

[SOURCE: GHTF/SG1/N68:2012, 4.0]

4 Application of essential principles

A manufacturer of an implant is expected to design and manufacture a product that is safe and performs as intended. This document describes fundamental principles for design and manufacturing, referred to as "Essential Principles of Safety and Performance", to ensure this outcome.

It is the manufacturer's responsibility to demonstrate conformity of the implant to all the applicable essential principles. If for a particular implant some essential principles are considered to be not applicable, then it is the manufacturer's responsibility to document the reason for excluding these essential principles.

5 Essential principles applicable to implants

5.1 General

5.1.1 Implants must 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, and the medical and physical conditions of intended users, they will perform as intended by the manufacturer and 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 can 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.

5.1.2 The solutions adopted by the manufacturer for the design and manufacture of the implants must conform to safety principles, taking account of the generally acknowledged state of the art. When risk reduction is required, the manufacturer must control the risks so that the residual risk associated with each hazard is judged acceptable. The manufacturer must 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 reasonably practicable the remaining risks by taking adequate protection measures, including alarms; and

— inform users of any residual risks.

5.1.3 Implants must achieve the performance intended by the manufacturer and be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose.

5.1.4 The characteristics and performances referred to in 5.1.1, 5.1.2 and 5.1.3 must 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 implant, as indicated by the manufacturer, when the implant 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.

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

5.1.6 All known and foreseeable risks, and any undesirable effects, must be minimised and be acceptable when weighed against the benefits of the intended performance of implants during normal conditions of use.

5.2 Chemical, physical and biological properties

5.2.1 The implants must be designed and manufactured in such a way as to ensure the characteristics and performance referred to in 5.1. Particular attention must be paid to:

— the choice of materials used, particularly as regards toxicity and where applicable flammability,

— the compatibility between the materials used and biological tissues, cells, and body fluids taking account of the intended purpose of the device,

— the choice of materials used, reflecting, where appropriate, matters such as hardness, wear and fatigue strength.

NOTE Further information is provided in ISO 10993-1.

5.2.2 The implants must be designed, manufactured and packaged 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 implants and to patients, taking account of the intended purpose of the implant. Particular attention must be paid to tissues exposed and to the duration and frequency of exposure.

5.2.3 The implants must 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 implants are intended to administer medicinal products they must 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.

5.2.4 The implants must be designed and manufactured in such a way as to reduce as far as reasonably practicable and appropriate the risks posed by substances that can leach or leak from the implant. Special attention must be given to substances which are carcinogenic, mutagenic or toxic to reproduction.

5.2.5 The **i**mplants must 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 implant taking into account the implant and the nature of the environment in which it is intended to be used.

5.2.6 The **i**mplants must be designed and manufactured in such a way as to reduce as far as reasonably practicable and appropriate risks posed by insufficient cleanliness of the implant. Risks posed by insufficient cleanliness include risks posed by bacterial endotoxins, pyrogens and particulate contaminates.

NOTE The principle in 5.2.6 has been added to the ones in the previous edition, and to the information given in Global Harmonization Task Force guidance documents.

5.3 Infection and microbial contamination

5.3.1 The implants and manufacturing processes must 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 must:

— allow easy handling, and, where necessary:

— reduce as far as reasonably practicable and appropriate any microbial leakage from the implant and/or microbial exposure during use,

— prevent microbial contamination of the implant, by the patient, user or other person.

5.3.2 Implants labelled as having a special microbiological state must be designed, manufactured and packaged to ensure they remain so when placed on the market and remain so under the transport and storage conditions specified by the manufacturer.

5.3.3 Implants delivered in a sterile state must be designed, manufactured and packaged 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.

NOTE Further information is provided in ISO 11607.

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

NOTE Further information is provided in ISO 11135, ISO 11137, ISO 14937 and ISO 17665.

5.3.5 Implants intended to be sterilized must be manufactured in appropriately controlled (e.g. environmental) conditions.

NOTE Further information is provided in ISO 14644.

5.3.6 Packaging systems for non-sterile implants must maintain the integrity and cleanliness of the product and, if the implants are to be sterilized prior to use, minimize the risk of microbial contamination; the packaging system must be suitable taking account of the method of sterilization indicated by the manufacturer.

5.3.7 The labelling of the implant must distinguish between identical or similar products placed on the market in both sterile and non-sterile condition.

5.4 Implants incorporating a substance considered to be a medicinal product/drug

5.4.1 This subclause is not intended to provide guidance on “combination products” as a whole since definitions have yet to be harmonized and practice varies between different jurisdictions.

5.4.2 Where an implant incorporates, as an integral part, a substance which, if used separately, might 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 performance of the implant as a whole must be verified, as well as the safety, quality and efficacy of the substance in the specific application.

5.5 Implants incorporating materials of biological origin

5.5.1 This subclause is not intended to provide guidance on “combination products” as a whole since definitions have yet to be harmonized and practice varies between different jurisdictions.

5.5.2 In some jurisdictions implants incorporating tissues, cells and substances of animal origin might 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 might 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 must be carried out so as to provide optimal safety for patients, users and, where applicable, other persons. In particular, safety with regard to viruses and other transmissible agents (e.g. such as prions) must be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process.

NOTE Further information is provided in ISO 22442 and ISO 14160.

5.5.3 In some jurisdictions implants incorporating human tissues, cells and substances might 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 must be carried out so as to provide optimal safety for patients, users and, where applicable, other persons. In particular, safety with regard to viruses and other transmissible agents must be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process.

5.5.4 In some jurisdictions implants incorporating cells and substances of microbial origin might be considered medical devices. In this case, processing, preservation, testing and handling of cells and substances must be carried out so as to provide optimal safety for patients, users and, where applicable, other persons. In particular, safety with regard to viruses and other transmissible agents must be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process.

5.6 Environmental properties

5.6.1 If the implant is intended for use in combination with other devices or equipment the whole combination, including the connection system must be safe and must not impair the specified performance of the implants. Any restrictions on use applying to such combinations must be indicated on the label and/or in the instructions for use. Connections which the user has to handle, such as fluid, gas transfer or mechanical coupling, must be designed and constructed in such a way as to minimize all possible risks from incorrect connection.

5.6.2 Implants must be designed and manufactured in such a way as to remove or reduce as far as reasonably practicable and appropriate:

5.6.2.1 The risk of injury to the patient, user or other persons in connection with their physical and ergonomic features;

5.6.2.2 The risk of use error due to the ergonomic features, human factors and the environment in which the implant is intended to be used;

5.6.2.3 Risks connected with reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, temperature or variations in pressure and acceleration;

5.6.2.4 The risks associated with the use of the implant when it comes into contact with materials, liquids, and gases to which it is exposed during normal conditions of use;

5.6.2.5 The risk associated with the possible negative interaction between software and the environment within which it operates and interacts;

5.6.2.6 The risks of accidental penetration of substances into the implant;

5.6.2.7 The risks of reciprocal interference with other devices normally used in the investigations or for the treatment given;

5.6.2.8 Risks arising where maintenance or calibration are not possible, including from:

— ageing of materials used,

— loss of accuracy of any measuring or control mechanism,

— excessive increase of leakage currents,

— excess heat generated by the implant.

5.6.3 Implants must 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 must be paid to implants whose intended use includes exposure to or use in association with flammable substances or substances which could cause combustion.

5.6.4 Implants must be designed and manufactured in such a way that adjustment, calibration, and maintenance, where such is necessary to achieve the performances intended, can be done safely.

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

5.7 Implants with a diagnostic or measuring function

5.7.1 Diagnostic implants and implants with a measuring function, must be designed and manufactured in such a way as to provide sufficient accuracy, precision and stability for the intended purpose of the implant, based on appropriate scientific and technical methods. The limits of accuracy must be indicated by the manufacturer.

5.7.2 Any measurement, monitoring or display scale used in association with an implant must be designed in line with ergonomic principles, taking account of the intended purpose of the implant.

5.7.3 Wherever possible values expressed numerically must be in commonly accepted, standardised units, and understood by the users of the implant.

NOTE There is a possibility that considerations of safety, user familiarity, and established clinical practice justify the use of recognized measurement units other than those of the internationally standardized measurement units.

5.8 Protection against radiation

5.8.1 General

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

5.8.2 Intended radiation

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

5.8.3 Unintended radiation

Implants must 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 reasonably practicable and appropriate.

5.8.4 Ionizing radiation

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

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

5.8.4.3 Implants emitting ionizing radiation, intended for therapeutic radiology must 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.

5.9 Implants that incorporate software

5.9.1 Implants incorporating electronic programmable systems, including software must be designed to ensure repeatability, reliability and performance according to the intended use. In the event of a single fault condition, appropriate means must be adopted to eliminate or reduce as far as reasonably practicable and appropriate consequent risks.

5.9.2 For implants which incorporate software, the software must be validated according to the state of the art taking into account the principles of development lifecycle, risk management, verification and validation.

5.10 Active implants and devices connected to them

5.10.1 For active implants, in the event of a single fault condition, appropriate means must be adopted to eliminate or reduce as far as reasonably practicable and appropriate consequent risks.

5.10.2 Implants where the safety of the patients depends on an internal power supply must be equipped with a means of determining the state of the power supply.

5.10.3 Implants where the safety of the patients depends on an external power supply must include an electronic alarm system to signal any power failure by way of an external device used in association with the implant.

5.10.4 Implants intended to monitor one or more clinical parameters of a patient must be equipped with appropriate electronic alarm systems to alert the user of situations which could lead to death or severe deterioration of the patient's state of health by way of an external device used in association with the implant.

5.10.5 Implants must be designed and manufactured in such a way as to reduce as far as reasonably 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.

5.10.6 Implants must 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.

5.10.7 Implants must be designed and manufactured in such a way as to avoid, as far as reasonably practicable, the risk of accidental electric shocks to the patient, user or any other person, both during normal use of the implant and in the event of a single fault condition in the implant, provided the implant is installed and maintained as indicated by the manufacturer.

NOTE Further information is provided in ISO 14708 (all parts).

5.11 Protection against mechanical risks

5.11.1 Implants must 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.

5.11.2 Implants must be designed and manufactured in such a way as to reduce to the lowest practicable level the risks arising from vibration generated by the implants, 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.

5.11.3 Implants must 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.

NOTE The principle in 5.11.3 applies both to audible and electrical noise.

5.11.4 Implants must be designed and manufactured in such a way as to reduce to the lowest practicable level, the risk of error when certain parts within the implant are intended to be connected or reconnected before or during use.

5.11.5 Implant (excluding the parts or areas intended to supply heat or reach given temperatures) and their surroundings must not attain potentially dangerous temperatures under normal conditions of use.

5.11.6 Implant packaging must be designed and manufactured in such a way as to reduce abrasion between packaging and implant to the lowest practicable level.

NOTE The principle in 5.11.6 has been added to the ones in the previous edition, and to the information given in Global Harmonization Task Force guidance documents.

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

5.12.1 Implants for supplying the patient with energy or substances must 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.

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

5.12.3 The function of the controls and indicators must be clearly specified on the implants or associated devices. Where an implant or associated device bears instructions required for its operation or indicates operating or adjustment parameters by means of a visual system, such information must be understandable to the user.

5.13 Label and Instructions for Use

5.13.1 General principles

This subclause describes the general principles that apply equally to all implants.

— The primary purpose of labelling is to identify the implant and its manufacturer, and communicate safety and performance related information to the user, professional or other person, as appropriate. Such information can appear on the implant itself, on packaging or as instructions for use. The following principles are recommended.

— The medium, format, content, legibility, and location of the label and instructions for use must be appropriate to the particular device, its intended purpose and the technical knowledge, experience, education or training of the intended user(s). In particular, instructions for use must be written in terms readily understood by the intended user and, where appropriate, supplemented with drawings and diagrams.

— The information required on the label, might be provided on the implant itself. If this is not practicable or appropriate, some or all of the information can appear on the packaging for each unit, and/or on the packaging of multiple implants.

— Where the manufacturer supplies multiple implants to a single user and/or location, it might be sufficient to provide only a single copy of the instructions for use. In these circumstances, the manufacturer must provide further copies upon request.

— Instructions for use might not be needed or might be abbreviated for implants if they can be used safely and as intended by the manufacturer without any such instructions for use.

— Labels must be provided in a human-readable format but can be supplemented by machine-readable forms, such as radio-frequency identification (RFID) or bar codes.

NOTE 1 Further information on a Unique Device Identification (UDI) System for Medical Devices is provided in GHTF guidance document GHTF/AHWG-UDI/N2R3[1].

— Instructions for use can be provided to the user either in paper or non-paper format (e.g. electronic). They can be supplied by various means either with the implant or separate from it. Examples of other means are information downloaded from the manufacturer's website using the internet, and machine-readable sources. The means chosen must be appropriate for, and accessible to, the anticipated user population.

— Where instructions for use are provided on a medium other than paper, the manufacturer must ensure the user has information on how to:

1) view the instructions for use;

2) access the correct version of the instructions for use; and

3) obtain a paper version of the instructions for use.

NOTE 2 The regulatory authority can set the conditions under which such non-paper format must be provided to guarantee a high level of protection of health. Those conditions can specify the types of devices that can use a non-paper format and the requirements the manufacturer needs to respect, such as, that the manufacturer must upon request provide a paper version of the instructions for use free of charge.

— Residual risks which are required to be communicated to the user and/or other person must be included as limitations, contraindications, precautions or warnings in the labelling.

— The use of internationally recognized symbols must be encouraged provided that implant safety is not compromised by a lack of understanding on the part of the user. Where the meaning of the symbol is not obvious to the implant user, e.g. for a newly introduced symbol, an explanation must be provided within the instructions for use.

NOTE 3 Further information is provided in ISO 15223-1.

— Country-specific requirements for the content of the labelling must be kept to the minimum and, where they currently exist, eliminated as the opportunity arises.

— Where national legislation, such as customs statutes, trade agreements and the like, include requirements for additional documentation to accompany the implant, there might be an inconsistency between the additional documentation and the content of implant labelling described in this document. An example is a customs requirement to indicate the "country of origin" of the implant which does not necessarily align with the address of the manufacturer indicated in the labelling according to 5.13.2 c) or 5.13.3 b) of this document.

— Provided that safe and correct use of the implant is ensured, a regulatory authority might authorize labelling to be in one or more language(s) other than its national language(s).

5.13.2 Content of the label

The label must contain the following particulars which can appear on the implant itself, or on the packaging of each unit, or on the packaging of multiple devices.

a) The name or trade name of the implant.

b) The details strictly necessary for a user to identify the implant and its use.

c) The name and address of the manufacturer in a format that is recognizable and allows the location of the manufacturer to be established.

d) For imported implants, the name and postal address of the authorized representative, or importer or distributor established within the importing country/jurisdiction might be required. This information can be added by the authorized representative, importer, or distributor within the country of import, rather than be provided by the manufacturer, in which case, the additional label must not obscure any of the manufacturer's labels.

e) Where appropriate, an indication that the implant contains or incorporates a medicinal or biological substance, e.g. bone cement containing an antibiotic for use in orthopaedics.

f) The batch code/lot number or the serial number of the implant preceded by the word LOT or SERIAL NUMBER or an equivalent symbol, as appropriate, to allow post-market action to be taken if there is a need to trace or recall the implant.

g) An unambiguous indication of the date until when the implant can be used safely, expressed at least as the year and month (e.g. on implants supplied sterile), where this is relevant.

h) Where there is no indication of the date until when it can be used safely, the year of manufacture. This year of manufacture can be included as part of the batch or serial number, provided the date is clearly identifiable.

i) An indication of any special storage and/or handling condition that applies.

j) If the implant is supplied sterile, an indication of its sterile state and, where appropriate, the sterilization method.

k) Warnings or precautions to be taken that need to be brought to the immediate attention of the user of the implant as relevant, and to any other person where appropriate (e.g. "THIS IMPLANT CONTAINS LATEX"). This information can be kept to a minimum in which case more detailed information must appear in the instructions for use.

l) If the implant is intended for single use, an indication of that fact.

NOTE 1 According to Note 5 of GHTF/SG1/N055:2009,[3] any person who changes the intended use of, or modifies, a medical device without acting on behalf of the original manufacturer and who makes it available for use under his own name, is considered the manufacturer of the modified medical device. As a consequence, a reprocessor of a single use implant device would be subject to the same requirements as those applicable to a manufacturer. In those jurisdictions where reprocessing of single use devices is allowed, the fact that a single use device has been reprocessed must be indicated on the label also.

m) If the implant is for use by a single individual and has been manufactured according to a written prescription or pattern (i.e. it is custom made), an indication of that fact.

n) If the implant is intended for premarket clinical investigation only, an indication of that fact.

NOTE 2 In this situation, some of the label content listed above might not apply.

o) If the implant is intended for non-clinical research, teaching or testing purposes only, an indication of that fact.

NOTE 3 In this situation, some of the label content listed above might not apply.

p) If the implant is intended for presentation or demonstration purposes only, an indication of that fact.

NOTE 4 In this situation, some of the label content listed above might not apply.

NOTE 5 For guidance on the information to be incorporated within the label for Unique Device Identification (UDI) purposes, refer to the GHTF guidance document on this subject[1)].

5.13.3 Content of the instructions for use

The instructions for use must contain the following particulars:

a) The name or trade name of the implant.

b) The name and address of the manufacturer in a format that is recognizable and allows the location of the manufacturer to be established, together with a telephone number and/or fax number and/or website address to obtain technical assistance.

c) The implant's intended use/purpose including the intended user (e.g. professional), as appropriate.

d) The performance of the implant intended by the manufacturer.

e) Where the manufacturer has included clinical investigations as part of premarket conformity assessment to demonstrate conformity to Essential Principles, a summary of the investigation, outcome data and clinical safety information, or a reference as to where such information can be accessed.

f) Any residual risks, contraindications and any expected and foreseeable side effects, including information to be conveyed to the patient in this regard.

g) Specifications the user requires to use the implant appropriately, e.g. if the implant has a measuring function, the degree of accuracy claimed for it.

h) If the implant contains, or incorporates, a medicinal substance and/or material of biological origin, identification of that substance or material, as appropriate.

i) Details of any required preparatory treatment or handling of the implant before it is ready for use (e.g. checking, cleaning, disinfection, drying, packaging, sterilization, final assembly, calibration, etc.).

NOTE 1 The principle in i) is in addition to information given in the previous edition of this document, and in addition to information given in Global Harmonization Task Force guidance documents.

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1) See the GHTF guidance document GHTF/AHWG-UDI/N2R3[1].

j) Any requirements for special facilities, or special training, or particular qualifications of the implant user and/or third parties.

k) The information needed to verify whether the implant is properly installed and is ready to perform safely and as intended by the manufacturer, together with, where relevant:

— details of the nature, and frequency, of preventative and regular maintenance, and of any preparatory cleaning or disinfection;

— identification of any consumable components and how to replace them;

— information on any necessary calibration to ensure that the implant operates properly and safely during its intended life span;

— methods of eliminating the risks encountered by persons involved in installing, calibrating or servicing the implants.

l) An indication of any special storage and/or handling condition that applies.

m) If the implant is supplied sterile, instructions in the event of the sterile packaging being damaged before use.

n) If the implant is supplied non-sterile, the appropriate instructions for sterilization.

NOTE 2 Further information is provided in ISO 17664.

o) If the implant is reusable, information on the appropriate processes to allow reuse, including cleaning, disinfection, packaging and, where appropriate, the method of re-sterilization. Information must be provided to identify when the implant must no longer be reused, e.g. signs of material degradation or the maximum number of allowable reuses.

p) For implants intended for use together with other implants, medical devices and/or general purpose equipment:

— information to identify such implants, medical devices or equipment, in order to obtain a safe combination and/or;

— information on any known restrictions to combinations of implants, medical devices and equipment.

NOTE 3 Medical devices and equipment intended for use together with the implant include both those designed and manufactured by the implant manufacturer (for example, associated instruments) and those designed and manufactured by others (for example, general purpose equipment).

q) If the implant emits hazardous, or potentially hazardous levels of radiation for medical purposes:

— detailed information as to the nature, type and where appropriate, the intensity and distribution of the emitted radiation;

— the means of protecting the patient, user, or third party from unintended radiation during use of the implant;

r) Information that allows the user and/or patient to be informed of any warnings, precautions, measures to be taken and limitations of use regarding the implant. This information must cover, where appropriate:

— warnings, precautions and/or measures to be taken in the event of malfunction of the implant, or malfunction of devices used in association with the implant, or changes in implant performance that can affect safety;

— warnings, precautions and/or measures to be taken in regards to the exposure to reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external

electrical and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, or temperature;

— warnings, precautions and/or measures to be taken in regards to the risks of interference posed by the reasonably foreseeable presence of the implant during specific diagnostic investigations, evaluations, therapeutic treatment or use (e.g. electromagnetic interference emitted by the implant affecting other equipment);

— if the implant administers medicinal or biological products, any limitations or incompatibility in the choice of substances to be delivered;

— warnings, precautions and/or limitations related to the medicinal substance or biological material that is incorporated into the implant as an integral part of the implant;

— precautions related to materials incorporated into the implant that are carcinogenic, mutagenic or toxic, or could result in sensitization or allergic reaction of the patient or user.

s) Warnings or precautions to be taken related to the disposal of the implant, its accessories and the consumables used with it, if any. This information must cover, where appropriate:

— infection or microbial hazards (e.g. explants, needles or surgical equipment contaminated with potentially infectious substances of human origin);

— environmental hazards (e.g. batteries or materials that emit potentially hazardous levels of radiation);

— physical hazards (e.g. from sharps).

t) Date of issue or latest revision of the instructions for use and, where appropriate, an identification number.

5.14 Clinical evaluation

5.14.1 For all implants, the demonstration of conformity with essential principles must include a clinical evaluation. The clinical evaluation must review clinical data in the form of any:

— clinical investigation reports,

— literature reports/reviews, and

— clinical experience.

to establish that a favourable benefit-risk ratio exists for the implant.

NOTE Further information is provided in GHTF/SG5/N2R8:2007[9].

5.14.2 Clinical investigations on human subjects must 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 might have specific regulatory requirements for pre-study protocol review or informed consent.

NOTE Further information is provided in ISO 14155.

Annex A
(informative)

Corresponding regulatory requirements

Region/Country	Australia
Name of regulatory body	Therapeutic Goods Administration
Website of regulatory body	www.tga.gov.au
Title of top level text	Therapeutic Goods Act
Section of text where essential principles can be found, if applicable	Therapeutic Goods (Medical Devices) Regulations, 2002: Regulation 2.1, which in turn references Schedule 1 — Essential Principles
Comment, if applicable	The Australian regulations are closely based on the European/GHTF model and TGA routinely accepts CE certificates in lieu of TGA conformity assessment certificates in support of registration of all devices except Class III devices with an integral medicine or component of animal origin.

Region/Country	Brazil
Name of regulatory authority	ANVISA — Agência Nacional de Vigilância Sanitária (*Brazilian Health Surveillance Agency*)
Website of regulatory authority	http://portal.anvisa.gov.br/wps/portal/anvisa-ingles
Title of top level text	ANVISA RDC nº 56/2001, Requisitos essenciais de segurança e eficácia de produtos para saúde (*Essential requirements for health products Safety and Efficacy*) ANVISA RDC nº 185/2001, Regulamento Técnico registro de produtos médicos (*Technical regulation for registration of medical products*)
Section of text where essential principles can be found, if applicable	a) RDC nº 56/2001, Annex, b) RDC nº 185/2001, Annex III.B
Comments, if applicable	a) Official documents only available in Portuguese — English titles supplied for informational purposes b) Available non-official English versions for informational purposes at www.emergogroup.com/resources/regulations-brazil: 1) RDC nº 56/2001, http://www.emergogroup.com/sites/default/files/file/rdc_56_2001_safety_and_efficacy_requirements.pdf 2) RDC nº 185/2001, http://www.emergogroup.com/sites/default/files/file/rdc_185_2001_classification_and_registration_requirements_of_medical_products_0.pdf c) RDC nº 56/2001, Annex — Information of principles, general requirements and requirements related to design and manufacture d) RDC nº 185/2001, Annex III.B — Information of labels and instructions for use of medical products

Region/Country	Canada
Name of regulatory authority	Health Canada, Health Products and Food Branch
Website of regulatory authority	http://www.hc-sc.gc.ca/index-eng.php (French website is available via website tab)

Region/Country	**Canada**
Title of top level text	Food and Drugs Act R.S.C., 1985, c. F-27; Medical Devices Regulations SOR/98–282
Section of text where essential principles can be found, if applicable	Sections 10–20, Medical Devices Regulations SOR/98–282
Comments, if applicable	Note section 9, Medical Devices Regulations SOR/98–282, which places responsibility on the device manufacturer to meet the "essential principles" regardless of device classification

Region/Country	**China**
Name of regulatory authority	China Food and Drug Administration
Website of regulatory authority	http://www.cfda.gov.cn/
Title of top level text(s)	Regulations on Supervision and Administration of Medical Devices
Section of text where essential principles can be found, if applicable	NA
Comments, if applicable	

Region/Country	**European Union (existing legislation)**
Name of regulatory body	European Commission
Website of regulatory body	http://ec.europa.eu/growth/sectors/medical-devices/index_en.htm
Title of top level text(s)	Council Directive 93/42/EEC of 14 June 1993 concerning medical devices Council Directive 90/385/EEC of 20 June 1990 on the approximation of the laws of the Member States relating to active implantable medical devices
Section of text where essential principles can be found, if applicable	Annex I of both directives
Comments, if applicable	Both of the original directives have been amended. In both cases the current consolidated text was published in the Official Journal on 11 Oct 2007. The directives are undergoing revision and will be replaced by a single regulation. Details of the new regulation are given below.

Region/Country	**European Union (new legislation)**
Name of regulatory body	European Commission
Website of regulatory body	http://ec.europa.eu/growth/sectors/medical-devices/index_en.htm
Title of top level text(s)	REGULATION (EU) 2017/745 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC
Section of text where essential principles can be found, if applicable	Annex I
Comments, if applicable	The date of entry into force was 26 May 2017. The date of application is 26 May 2020.

Region/Country	**Japan**
Name of regulatory authority	Ministry of Health, Labour and Welfare (MHLW) and Pharmaceuticals and Medical Devices Agency (PMDA)

Region/Country	Japan
Website of regulatory authority	http://www.mhlw.go.jp/english/policy/health-medical/pharmaceuticals/ http://www.pmda.go.jp/english/
Title of top level text(s)	Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics, 2014
Section of text where essential principles can be found, if applicable	MHLW Ministerial Notification No. 122
Comments, if applicable	

Region/Country	New Zealand
Name of regulatory body	Medsafe
Website of regulatory body	www.medsafe.govt.nz
Title of top level text	Medicines Act 1981
Section of text where essential principles can be found, if applicable	Not applicable — no equivalent in NZ regulation
Comment, if applicable	New Zealand has no premarket review processes. The agency requires that all devices supplied in New Zealand be included on the WAND database. This is achieved by electronic submission of a notification.

Region/Country	United States of America
Name of regulatory authority	Department of Health and Human Services/Food and Drug Administration
Website of regulatory authority	http://www.fda.gov/MedicalDevices
Title of top level text	Federal Food, Drug, and Cosmetic (FDC) Act of 1938 Medical Device Amendments of 1976 Food and Drug Administration Act of 1988 Safe Medical Devices Act of 1990 Food and Drug Administration Modernization Act of 1997 Medical Device User Fee and Modernization Act of 2002
Section of text where essential principles can be found, if applicable	http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/
Comments, if applicable	

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[2] GHTF/SG1/N044. 2008, *Role of Standards in the Assessment of Medical Devices*

[3] GHTF/SG1/N055. 2009, Definitions of the Terms Manufacturer, Authorised Representative, Distributor and Importer

[4] GHTF/SG1/N68. 2012, *Essential Principles of Safety and Performance of Medical Devices*

[5] GHTF/SG1/N70. 2011, *Label and Instructions for Use for Medical Devices*

[6] GHTF/SG1/N71. 2012, Definition of the Terms 'Medical Device' and 'In Vitro Diagnostic (IVD) Medical Device'

[7] GHTF/SG1/N78. 2012, *Principles of Conformity Assessment for Medical Devices*

[8] GHTF/SG5/N1R8. 2007, *Clinical Evidence — Key Definitions and Concepts*

[9] GHTF/SG5/N2R8. 2007, *Clinical Evaluation*

[10] GHTF/SG5/N3. 2010, Clinical Investigations

[11] ISO 10993-1, *Biological evaluation of medical devices*

[12] ISO 11135, *Sterilization of health-care products — Ethylene oxide — Requirements for the development, validation and routine control of a sterilization process for medical devices*

[13] ISO 11137 (all parts), *Sterilization of health care products — Radiation*

[14] ISO 11607 (all parts), *Packaging for terminally sterilized medical devices*

[15] ISO 13485, *Medical devices — Quality management systems — Requirements for regulatory purposes*

[16] ISO 14155, *Clinical investigation of medical devices for human subjects — Good clinical practice*

[17] ISO 14160, *Sterilization of health care products — Liquid chemical sterilizing agents for single-use medical devices utilizing animal tissues and their derivatives — Requirements for characterization, development, validation and routine control of a sterilization process for medical devices*

[18] ISO 14630, *Non-active surgical implants — General requirements*

[19] ISO 14644, *Cleanrooms and associated controlled environments*

[20] ISO 14708-1 (all parts), *Implants for surgery — Active implantable medical devices*

[21] 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 for medical devices*

[22] ISO 14971, *Medical devices — Application of risk management to medical devices*

[23] ISO 15223-1, *Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied — Part 1: General requirements*

[24] ISO 16061, *Instrumentation for use in association with non-active surgical implants — General requirements*

[25] ISO 16142-1, *Medical devices — Recognized essential principles of safety and performance of medical devices — Part 1: General essential principles and additional specific essential principles for all non-IVD medical devices and guidance on the selection of standards*

[26] ISO 17664, *Processing of health care products — Information to be provided by the medical device manufacturer for the processing of medical devices*

[27] ISO 17665, *Sterilization of health care products — Moist heat*

[28] ISO 22442, *Medical devices utilizing animal tissues and their derivatives*

[29] IEC 60601-1, *Medical electrical equipment*

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