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Implants for surgery — Active implantable medical devices —

Part 5: Circulatory support devices

Implants chirurgicaux — Dispositifs médicaux implantables actifs —
Partie 5: Dispositifs d'assistance circulatoire

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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 of 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 www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 150, *Implants for surgery*, Subcommittee SC 6, *Active implants*.

This second edition cancels and replaces the first edition (ISO 14708-5:2010), which has been technically revised. The main change compared to the previous edition is as follows:

— alignment to the revised ISO 14708-1:2014.

A list of all parts in the ISO 14708 series can be found on the ISO website.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

This document specifies requirements for safety and performance of active implantable circulatory support devices. It amends and supplements ISO 14708-1:2014, hereinafter referred to as ISO 14708-1. The requirements of this document take priority over those of ISO 14708-1.

Heart failure is a major public health problem. It is estimated that worldwide more than 5 million people die per year due to heart failure. In addition, it accounts for a large portion of health care expenditure and rehospitalisation (see Reference [35]). Circulatory support devices are needed for promoting myocardial recovery following acute heart failure as well as long-term support until eventual transplantation or permanent therapy. Circulatory support devices may be fully implanted, partially implanted, or delivered by percutaneous approach. The growth of heart failure is expected to increase with the aging population (see Reference [30]).

The requirements of this document supplement or modify those of ISO 14708-1.

In this document, terms printed in italics are used as defined in Clause 3. Where a defined term is used as a qualifier in another term, it is not printed in italics unless the concept thus qualified is also defined.

Information is also provided in Annex A that explains the relationship between ISO/TR 14283, ISO 14708-1 and this document.

Notes on this document are provided in Annex B for information.

Annex C provides guidance on pre-clinical in vitro and in silico evaluation. Annex D provides information device hazards, associated failure modes, and evaluation methods. All annexes are informative.

Implants for surgery — Active implantable medical devices —

Part 5: Circulatory support devices

1 Scope

This document specifies requirements for safety and performance of active implantable circulatory support devices, including type tests, animal studies and clinical evaluation requirements.

NOTE The device that is commonly referred to as an active implantable medical device can in fact be a single device, a combination of devices, or a combination of a device or devices and one or more accessories. Not all of these parts are required to be either partially or totally implantable, but there is a need to specify main requirements of non-implantable parts and accessories if they could affect the safety or performance of the implantable device.

The tests that are specified in this document are type tests and are to be carried out on a sample of a device to assess device behavioural responses and are not intended to be used for the routine testing of manufactured products.

Included in the scope of this document are:

— ventricular assist devices (VAD), left or right heart support;

— total artificial hearts (TAH);

— biventricular assist devices (biVAD);

— percutaneous assist devices;

— paediatric assist devices.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 10993-1:2018, *Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process*

ISO 14708-1:2014, *Implants for surgery — Active implantable medical devices — Part 1: General requirements for safety, marking and for information to be provided by the manufacturer*

ISO 14971:2019, *Medical devices — Application of risk management to medical devices*

IEC 60068-1:2013, *Environmental testing — Part 1: General and guidance*

IEC 60068-2-27:2008, *Environmental testing — Part 2-27: Tests — Test Ea and guidance: shock*

IEC 60068-2-31:2008, *Environmental testing — Part 2-31: Tests — Test Ec: rough handling shocks, primarily for equipment-type specimens*

IEC 60068-2-64:2008, *Environmental testing — Part 2-64: Tests — Test Fh: vibration, broadband random and guidance*

IEC 60601-1:2018, *Medical electrical equipment — Part 1: General requirements for basic safety and essential performance*

IEC 60601-1-2:2014, *Medical electrical equipment — Part 1-2: General requirements for basic safety and essential performance — Collateral standard: Electromagnetic compatibility — Requirements and tests*

IEC 60601-1-6:2010, *Medical electrical equipment — Part 1-6: General requirements for basic safety and essential performance – Collateral standard: Usability*

IEC 60601-1-10:2007, *Medical electrical equipment — Part 1-10: General requirements for basic safety and essential performance — Collateral standard: Requirements for the development of physiologic closed-loop controllers*

IEC 60601-1-11:2015, *Medical electrical equipment — Part 1-11: General requirements for basic safety and essential performance — Collateral standard: Requirements for medical electrical equipment and medical electrical systems used in the home healthcare environment*

IEC 62304:2006, *Medical device software — Software life cycle processes*

IEC 62366-1:2015, *Medical devices — Part 1: Application of usability engineering to medical devices*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 14708-1 and ISO 14971 and the following apply.

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

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

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

3.1
accessory device
separate part of a circulatory support system that is not essential to the primary function of the circulatory support system

Note 1 to entry: Examples are programming units, monitoring units and alternative *power source* (3.18) units.

3.2
artificial valve
prosthetic valve
component of the circulatory support system that directs the unidirectional flow of the blood into and out of the pump

3.3
atrial cuff
connector between the right or left atrial ring after resection of the natural ventricle and the inlet of the right or left blood pump in *total artificial heart* (3.31) replacement

3.4
biVAD
biventricular assist device
configuration in which two VADs are used to support both ventricles respectively

3.5
cavitation
sudden formation and collapse of low-pressure bubbles in the blood by means of mechanical forces

3.6
circulatory support device
electromechanical device that is used to partially or completely replace the left and/or right ventricular function of a failing heart

3.7
conduit
component of the circulatory support system that connects the pump to the patient's circulation

3.8
controller
component of the circulatory support system that contains the logic, circuitry and/or software to control the driving mechanism that enables the system to perform its primary function

3.9
diastolic pressure
arithmetic average of minimum pressures in a pulsatile pressure waveform over a sufficient number of cycles to filter out cyclic variation

3.10
display
component of the circulatory support system that allows data pertaining to the operation of the system to be observed

3.11
driveline
tube and/or cable that connects a driver or energy source to the pump

EXAMPLE The tube that connects a pneumatic console to a pneumatically driven pump.

3.12
durability
ability of an item to perform a required function under given conditions of use and maintenance, until a limiting state is reached

Note 1 to entry: A limiting state of an item should be characterized by the end of the useful life, unsuitability for any economic or technological reasons, or other relevant factors.

3.13
DUT
device under test

3.14
ejection/fill
E/F
ratio between the ejection time period and the filling time period of the blood pump cycle

Note 1 to entry: E/F is identical to S/D (systolic/diastolic) when related to the natural heart.

3.15
failure
termination of the ability of an item to perform a required function

Note 1 to entry: After failure, the item has a *fault* (3.16).

Note 2 to entry: "Failure" is an event, as distinguished from "fault", which is a state.

Note 3 to entry: This concept as defined does not apply to items consisting of software only.

3.16
fault
state of an item characterized by inability to perform a required function, excluding the inability during preventive maintenance or other planned actions, or due to lack of external resources

Note 1 to entry: A fault is often the result of a *failure* (3.15) of the item itself but might exist without prior *failure*.

3.17
labelling
marking
any written, printed, electronic information, or graphical matter affixed to a medical device or any of its containers or wrappers, or accompanying the medical device related to identification, technical description and use, but excluding shipping documents

3.18
power source
source of energy (battery, mains)

3.19
pulsatile flow
characteristic of the output of a pump where the flow is time dependent

3.20
pulse pressure
difference between the systolic and *diastolic pressure* (3.9) readings

Note 1 to entry: It represents the force that the heart generates each time it contracts.

3.21
pump output
performance measure for a circulatory support system indicating the volume of blood pumped into the host circulatory system per minute

Note 1 to entry: The pump output is expressed in litres per minute or its equivalent in other units.

3.22
volume displacement
pump displacement
pump that imparts its pumping action by changing the volume of the pumping chamber

EXAMPLE By displacement of a diaphragm or pusher plate.

3.23
reliability
probability that an item can perform a required function under given conditions for a given time interval (t1, t2) for a specified confidence level

Note 1 to entry: It is generally assumed that the item is in a state to perform this required function at the beginning of the time interval.

Note 2 to entry: The term "reliability" is also used to denote the reliability performance quantified by this probability[11].

3.24
rotary pump
pump that imparts its pumping action directly on the blood by a rotating mechanism

3.25
safe and effective
reasonable assurance that a device will not induce harm to the recipient and that it will provide clinical benefit for the recipient for its conditions of use

3.26
safety
freedom from unacceptable risk

Note 1 to entry: See ISO/IEC Guide 51.

3.27
sales packaging
packaging that protects and identifies the device during storage and handling by the purchaser

Note 1 to entry: The sales packaging should be enclosed in further packaging, for example a “shipping package”, for delivery.

3.28
service life
period after implantation when the circulatory support system remains within stated specifications and characteristics

Note 1 to entry: The service life of the components of the system can vary (implanted components might have longer lifetimes versus the peripheral components which are replaceable).

3.29
stroke volume
amount of blood pumped by the ventricle of the heart in one contraction

3.30
transcutaneous energy transmission system
TETS
system used to send electrical energy wirelessly into a device implanted inside the body

3.31
total artificial heart
TAH
circulatory support system that replaces the pumping function of a patient’s native heart

3.32
ventricular assist device
VAD
circulatory support system that augments the function of either one or both ventricles of the patient's native heart by capturing blood from the atrium(a) or ventricle(s) and providing work to pump blood into the pulmonary and/or systemic circulation

4 Symbols and abbreviations

The text in ISO 14708-1:2014, Clause 4 applies.

5 General requirements for active implantable medical devices

5.1 General requirements for non-implantable parts

The text in ISO 14708-1:2014, 5.1 applies.

5.2 General requirements for software

The text in ISO 14708-1:2014, 5.2 applies.

5.3 Usability of non-implantable parts

The text in ISO 14708-1:2014, 5.3 applies.

5.4 Data security and protection from harm caused by unauthorized information tampering

The text in ISO 14708-1:2014, 5.4 applies.

5.5 General requirements for risk management

The text in ISO 14708-1:2014, 5.5 applies.

5.6 Misconnection of parts of the active implantable medical device

The text in ISO 14708-1:2014, 5.6 applies.

5.7 Wireless coexistence and wireless quality of service

When communication with any part of an active implantable medical device is provided through wireless communication channels, the manufacturer shall evaluate wireless coexistence and wireless quality of service through the risk management process and apply the appropriate risk control measures to protect the patient from harm (see 27.6).

Testing of wireless communication channels, for EMC, is performed in accordance with IEC 60601-1-2:2014.

Compliance is checked by the inspection of the risk management file.

6 Requirements for particular active implantable medical devices

6.1 Intended clinical use/indications

The intended use and indications for the device system shall be described. The intended use describes what the device system does (e.g. provides circulatory support), where it may be used safely (e.g. hospital, home, ground and/or air transport vehicles), and the intended duration of use. The indications are the disease(s) or condition(s) the device will diagnose, treat, prevent, cure, or mitigate and a description of the target population for which the device is intended without causing unreasonable risk of illness or injury associated with use of the device.

Compliance is checked by the inspection of the manufacturer's documentation.

6.2 System description

6.2.1 General

A comprehensive description of the system shall be documented, including discussions on the principles of operation, rationale for key design choices, system configurations, system components, and system performance and operating limits.

Compliance is checked by the inspection of the manufacturer's documentation.

The rationale for key design choices, for example:

— approaches taken to minimize blood component damage;

— methods for thermal management;

— choice of drive mechanisms;

— power management scheme;

— choice of connectors to prevent misuse;

— reliability considerations;

— adequacy of anatomic fit;

— electromagnetic compatibility (EMC)/ interference;

— driveline damage resistance;

— exposure to environmental conditions;

— human factors.

Design specifications for the complete system include the full range of system operating limits for each parameter, for example:

— beat rates;

— E/F ratio;

— rotation speeds;

— power consumption;

— flow rate as a function of pressure head (with varying pump rotational speed or beat rate).

Required system components, for example:

— hydrodynamic bearings;

— magnetic bearings.

System operational modes, for example:

— manual;

— automatic.

System component configurations, for example:

— hospital;

— home;

— power sources;

— optional display;

— optional subsystems;

— optional console.

Alarm thresholds, and all associated tolerances on each of these parameters.

Principle(s) of operation, for example:

— blood pumping mechanism;

— connections to the cardiovascular system;

— power system;

— control mechanisms.

6.2.2 System configuration

A detailed physical description of the system shall be given including implantation sites of various implantable components, external wearable units, and external consoles. Size, shape, weight, and volume of the components should be given, as well as the different configurations of system components that can be used to provide support.

Compliance is checked by the inspection of the manufacturer's documentation.

6.2.3 System performance and operating limits

The entire performance range of the system shall be given, even if some operating conditions are not expected to be used clinically or might cause the system to malfunction. The verified *service life* of all components shall also be documented.

Compliance is checked by the inspection of the manufacturer's documentation.

6.3 Design analysis

6.3.1 General

A comprehensive analysis shall be performed for the integrated system, the various component configurations, as well as for each system component for all safety and effectiveness issues, such as tolerance stack-up analysis, and structural analysis. Every software product should possess an adequate level of functional safety and reliability through analysis, design, implementation, system testing, quality assurance, and maintenance of the software product, all of which shall be documented and controlled. Guidance for software design and validation can be found in IEC 62304:2006. The software verification and validation should not only meet requirements for the software integrity itself but should also demonstrate the software is capable of proper operation of the system according to its specifications.

6.3.2 Human factors analysis

6.3.2.1 General

Human factors analysis shall be performed for the device system, the labelling and instructions that are provided, and any training provided to mitigate the risk of harm to the patient by human error. Early stage models or prototypes should be evaluated with representative intended users during formative testing. The intended users of a circulatory support system may be divided into three categories: patients and caregivers, clinicians, and surgeons. Each user group may interact with the system in different use scenarios. Special design considerations and evaluation methods for each user group are outlined in the subclauses below.

6.3.2.2 Patients and caregivers

Patient/caregiver user scenarios are the most important types to consider as they are the ones most affected by any harms caused by human error. Patients and caregivers most commonly interact with the device system peripherals so any human factors formative studies involving all external components provided to a patient should be focused on this user group.

Alarm conditions should be simple and easily discernible so that the patient/caregiver takes the appropriate action upon noticing the alarm. Alarm type redundancy shall be considered for users with disabilities (e.g. visual, audible, and vibratory). All alarms should be distinct and easy for the patient/caregiver to comprehend. Formative studies should be conducted to demonstrate this comprehension and ability to respond with the appropriate action.

The need for patients and caregivers to connect and disconnect peripheral components, such as power sources or data cables, should be minimized as much as possible. Multiple types of connections should

be designed with separate connection configurations so that it is impossible for the patient/caregiver to make an incorrect connection. Also, all connections should be visually and/or tactilely distinct. If there is a need for repeated use in such instances as replacing a battery, use cases should be established that describe the connection interface, the number of expected cycles under normal daily use, and any locking mechanisms involved. All connector/receptacle sets should be designed such that they prevent accidental disconnection. The design may contain keyways that guide connector alignment before the electrical connection is made to prevent inadvertent damage to the pins and are made from durable materials that can withstand repeated use. As with alarms, the formative use studies should be designed to determine if the patient/caregiver subjects can perform these connections appropriately without error or inadvertently damaging connectors. Attention should be paid to training methods for cleaning exit sites during patient training sessions to also minimize infection.

These studies may be conducted with simulated and/or prototype peripherals. Simulated peripherals should have the same connection interfaces and weight as the final product configuration if the design is not complete yet. Any labelling and/or training material that is provided to the patient/caregiver should be written at an 8th grade reading level and use studies conducted to demonstrate comprehension of the instructions provided.

6.3.2.3 Clinicians

The use case considerations for clinicians (e.g. nurses, clinical engineers, first responders) should include performing the same activities as patients or caregivers as well as providing emergency response care (such as CPR) without causing harm to the patient and/or device. If the clinicians are at the hospital, they will typically utilize an external device to connect to the device controller to monitor performance, download log files, and configure device operational parameters. The usability studies for these devices are mostly focused on the controls and presentation of the information provided. If a touch screen is used, the icons, layout, and text size should be designed so that they are easily readable. Early formative studies may be conducted where the screen layouts are presented, and the subjects are studied to observe how well they interface with them.

6.3.2.4 Surgeons/interventional cardiologist

The design of the circulatory support system should take into consideration the commonly used surgical approach, technique, and surgical tools. Implant tools should be optimized for the surgical approach including intrathoracic or percutaneous. Special instructions, warnings, and training should be provided to prevent damage to the device by commonly used surgical tools, such as scalpels, cautery tools, and robotic-assist surgical systems. Formative usability studies for the implant procedure should take place in a simulated operating room or cardiac catherization suite with either a mock patient, cadaver, or animal model and should consist of evaluations for how well the tools are used based on the instructions and training provided.

These human factors studies should be used to provide input to the design team so that the device system can be modified to reduce or eliminate use error. These modifications can take the form of physical design, software updates, labelling, training materials, user instructions, and/or packaging. The risk management file should be updated based on the results of these studies.

6.4 Risk analysis

Risk analysis, part of the risk management process, shall be performed on the system. The risk analysis should include a top-down analysis (such as a hazard analysis or fault tree analysis, FTA), a bottom up analysis (such as failure mode, effects, and criticality analysis – FMECA), as well as an analysis for potential use or user error (human factors analysis). The risk analysis should utilize a method to classify the severity of failure modes, the probability of occurrence, the risk priority number, and the detection method. The analysis should include discussion of methods used to mitigate the criticality of the failure modes and linkage to testing performed to demonstrate device safety. The hazards table in Annex D may be used as a guide for conducting this risk analysis.

NOTE For further information on risk analysis, see ISO 14971:2019.

6.5 Human factors

Human factors evaluation shall consist of both integrated system testing and subsystem testing. This evaluation shall satisfy the requirements of IEC 62366-1:2015 and IEC 60601-1-6:2010. The user interface, both hardware and software, shall be designed to be understandable and compatible with the intended users' anticipated capabilities (e.g. physical, mental, or sensory) to reduce the likelihood of error and/or confusion. Further, appropriate alarms and warnings are necessary and shall be designed to warn users of system or subsystem failures. Guidance for human factors can be found in IEC/TR 62366-2 and ANSI/AAMI HE75. As appropriate, these evaluations shall include but are not limited to the following scenarios:

— home/community;

— transport (air/ground);

— implant procedure (use of surgical tools and implant accessories);

— hospital environment (in-clinic check-up visit and ICU);

— emergency use.

6.6 In vitro design evaluation and system performance testing

6.6.1 Objective

In vitro testing shall include design characterization of the integrated system and its individual system subcomponents against all of its system design specifications. Test set-ups should be reasonably representative of the intended patient population in which pressures, compliances and flow should be at appropriate values (see Annex B). A description of the in vitro testing systems, including all pressures, compliances, and the location of all measurement equipment, as well as the rationale for the test set-up, shall be provided.

In both a volume displacement pump and a rotary pump VAD system, this testing includes the characterization of all-time dependent parameters as they operate with (or as a replacement for) the native heart in a pulsatile environment. In this way, the simulated performance effects of the system on the patient and the patient on the system can be understood.

6.6.2 System characterization

6.6.2.1 General

In vitro system characterization testing is a complete evaluation of the final system design in the simulated use environment.

6.6.2.2 Test set-up

All applicable parameters should be documented and reported. See Annex B for expected physiological parameters.

VAD and TAH system performance, including but not limited to, alarms, back-up systems, information displayed, measurement accuracy/precision, and failures, should be monitored and reported as specified in ISO 14708-1 and with alarms conforming to IEC 60601-1-8.

6.6.2.3 Test articles

6.6.2.3.1 General

At least one clinically representative device system shall be characterized. A complete system is comprised of all system components required for that system to be operational in its intended

environment. If clinical operation of the device can utilize multiple configurations of components and accessories, then testing of each configuration is required. Where the design analysis demonstrates that critical components/sub-assemblies at the extremes of their specifications might impact overall device performance, test articles will be used which characterize that variability.

6.6.2.3.2 Pre-conditioning

The test articles shall be subjected to the following environmental conditions prior to testing, as applicable:

— sterilisation (maximum number of sterilisation cycles for implantable products or products intended for the sterile field);

— environmental (temperature and humidity), may reference ISTA Procedure 2A;

— transportation (vibration, drop, and pressure), may reference ASTM D4169;

— aging (accelerated and real-time), if device is sensitive to aging, may reference ASTM F1980;

— loads and any activity associated with the pre-implant and implant procedures that may impact device performance (e.g. mechanical forces).

6.6.2.3.3 Substitution of device components

If a device component, including but not limited to, biological prosthetic valves, vascular graft, or atrial cuff, is substituted by its alternative, a justification shall be provided.

6.6.2.4 Test equipment

6.6.2.4.1 General

Test equipment required for in vitro system characterization testing of the complete device system shall include a mock circulatory loop and all test measurement equipment.

6.6.2.4.2 Mock circulatory loop

In vitro models used to simulate the natural heart, as appropriate, and the vascular compliance and resistance, shall be documented, and justified as to the necessary physiological limits prescribed. See Annex B for expected physiological parameters.

6.6.2.4.3 Blood analogue fluid

The relevant properties of fluids used to simulate human blood shall be described. Fluids used may be Newtonian (blood analogue). Characteristics of the fluid and its chemical composition shall be given. Justification for necessary blood-matching trade-offs shall be given (e.g. viscosity, temperature, salinity and pH). See Annex B for expected physiological parameters.

6.6.2.4.4 Test measurement equipment

6.6.2.4.4.1 Transducers

All transducers used for the measurement of system parameters shall be specified in the study protocol or test procedure. Transducers shall be appropriate for measuring time dependent waveforms so that any subsequent ensemble averaging to produce representative waveforms can be achieved and any cycle-to-cycle variation can be measured. All transducer characteristics, including amplifier devices (e.g. range, resolution, error, frequency response), shall be given. Calibration schedules and calibration methods used for all transducers are required, as well as evidence that the transducers have been calibrated before use.

6.6.2.4.4.2 Use of the device system as test measurement equipment

Many device systems are capable of measuring, acquiring, manipulating, displaying, and storing desired parameters to be measured. The device system measurement and data handling systems shall be documented and validated against calibrated instruments for accuracy.

6.6.2.4.4.3 Data handling

Systems used for data acquisition, manipulation, display, and storage shall be documented. Data acquisition methods and equipment used shall be specified (e.g. real time, triggering methods, sampling rate, filters, amplification). If any data manipulation (e.g. averaging, smoothing) is performed prior to display and storage of final information, this should be clearly explained, including the algorithms used and documenting evidence of system consistency. Characteristics for the display shall be documented (e.g. accuracy, precision, and error).

6.6.2.5 Test conditions

A matrix of test conditions should be generated in order to characterize the system over the full range of operational limits using all possible component configurations against all of the design specifications of the device. The VAD system algorithms, if configurable by the clinician, should also be tested in the ON and OFF states to demonstrate they meet their specifications. The testing should simulate the effects of changes in system performance on the patient and the effects of patient changes on system performance. The effects of extremes of operation on both the device and the patient (e.g. test set-up) should be determined. The extremes of operation include the minimum blood flow and maximum blood flow, hypertension, hypotension, responses to changes in flow, pressure and possible inflow/outflow restrictions.

The relevant conditions used to characterize the system should be selected according to the type of the system (e.g. volume displacement or continuous flow, total artificial heart or ventricular assist system). See Annex C for more information.

6.6.2.6 Parameters to be measured

The pump should be characterized over the full operating range with the following parameters as appropriate (see Annex C for more information):

a) blood pump inlet and outlet pressure waveforms;

b) blood pump outlet flow waveform;

c) average outlet pressure from the pump;

d) average inlet pressure to the pump;

e) average pump outlet flow.

6.6.2.7 Data analysis

Data analysis shall be performed to show that the system performance meets the design specifications for the system. This shall include statistical significance calculations comparing actual in vitro system performance to the expected design specification. Further, data analysis of system performance and the expected clinical effects of the system, based upon a review of the literature, should be provided.

6.6.2.8 “Worst case” operating conditions

System characterization data should be evaluated to determine the worst-case modes of operation (e.g. power input, pump flow, pressures, battery life) within the design input specification. A discussion should provide the rationale for the selection of the conditions determined to be worst case and what effect they might have on the device.

6.6.3 Subsystem component testing

6.6.3.1 Design evaluation of the pump subsystem

6.6.3.2 Fluid dynamic analysis

A fluid dynamic characterization of the device should be conducted, and its results should be discussed in terms of how these characteristics relate to the design specification and the results of other in vitro and *in vivo* design evaluations including haemolysis, cavitation, and thrombus formation. Such studies include computational fluid dynamics (CFD) or experimental flow characterization (see Annex C). These study results should be used for justification of design improvement of the device. The contribution of the native heart to the total pump flow should be considered during the analysis or test method development.

6.6.3.3 Cavitation

The device shall not exhibit cavitation under any operating conditions. As applicable, the critical cavitation conditions [e.g. net positive suction head required (NPSHR)] should be provided.

Compliance is checked by the inspection of the design verification record.

6.6.3.4 Control and drive units

6.6.3.4.1 External units

Blood pump controlling and driving units that are carried by patients shall be tested against the design requirement specifications. At a minimum, these units should be qualified by verifying the following requirements.

a) Electrical input (voltage range, ripple, current range, and power requirements).

b) Electrical and/or mechanical output (e.g. voltage, current, power, torque, and pressure).

c) Electrical safety requirements, as specified in IEC 60601-1:2018 shall be met.

d) Software used in the controlling and driving units shall be verified as specified in IEC 62304:2006.

e) The unit alarms should meet the requirements of IEC 60601-1-8 and include multiple types of alarms (e.g. auditory, visual, and vibratory).

f) The external control and drive unit qualification shall also include testing as specified in the following documents:

   1) IEC 60068-1:2013;

   2) IEC 60068-2-64:2008;

   3) IEC 60068-2-27:2008;

   4) IEC 60068-2-31:2008;

   4) IEC 60601-1-10:2007 (for closed-loop controller);

   5) IEC 60601-1-11:2015.

g) Unit enclosure temperature shall be as specified in IEC 60601-1:2018.

h) Biocompatibility of materials that might be in contact with the patient's skin shall also be verified according to the biocompatibility documents within ISO 10993-1:2018.

This list of documents is not all-inclusive, and others may be used as applicable.

6.6.3.4.2 Implantable controllers and drivers

Implantable devices shall comply with the safety, marking and supplied information requirements specified in ISO 14708-1.

6.6.3.4.3 Programming and monitoring units

Peripheral/accessory devices are for the programming of the system, collecting, storing and displaying information in hospitals and/or home environment. As a part of the circulatory support system, programming and monitoring units shall be tested as described in 6.6.3.4.1 External units. Where appropriate, the test levels shall be documented for the intended use environment (e.g. hospital, home, and air/ground transport). See ISO 14708-1. If testing is not to be performed (e.g. the use of qualified off-the-shelf laptops), an equivalency rationale shall be provided.

6.6.3.4.4 Power supplies

Power supplies (including battery chargers) for the circulatory support devices shall meet safety requirements for medical devices as specified in IEC 60601-1:2018, such that at no time is there total loss of power. Electrical input and output (voltage range, ripple, current, and power) as well as overload capabilities and protection shall be verified.

Where appropriate, the test levels shall be documented for the intended use environment (e.g. hospital, home, and air/ground transport).

6.6.3.4.5 Batteries

Battery-powered circulatory support systems should be considered for testing the following:

a) battery voltage from full capacity to the depleted state;

b) effect of current (load) on battery performance (voltage, capacity, and case temperature);

c) effect of time, temperature, load, and cycles on the battery's capacity (aging);

d) battery preventive maintenance and replacement schedule (based on cycles or time);

e) emergency back-up procedure if the battery fails;

f) recharge specifications, for example, charge current, end of charge determination, and recharge time;

g) method to measure battery depletion;

h) method to control hazard from potential gases produced while charging;

i) battery status indicator that gives advance warning of battery depletion. The manufacturer shall define the time interval between the activation of this indicator and the point at which the battery will cease to support the normal operation of the device;

j) auditory, visual, and vibratory warning alarms in the event of battery depletion;

k) appropriateness of parallel redundancy for battery sources;

l) method to measure/identify high discharge temperatures;

m) protection against battery explosion or burst;

n) ease of battery exchange process especially if the battery is implanted.

6.6.3.5 Connectors and driveline

6.6.3.5.1 Electrical and pneumatic connectors

Electrical and pneumatic connectors to and from all power supplies, batteries, controllers, and blood pumps shall be designed to satisfy the pre-conditioning requirements (see 6.6.2.3.2) and following tests, as appropriate:

— connector connect/disconnect cycling;

— connector misalignment;

— fluid and solid contamination ingress.

Conductivity/resistance/pressure shall be measured as appropriate after each of the appropriate tests to ensure design specifications are met.

6.6.3.5.2 Pneumatic driveline

For systems with pneumatic drives, all drivelines to and from the pneumatic supply and the blood pump (the entire gas pathway) shall be pre-conditioned (see 6.6.2.3.2) and then required to maintain pneumatic pressure or alarm while subjected to the following tests:

— tension;

— torsion;

— kink (bend radius);

— pinch;

— jerk;

— vibration;

— flex testing of pneumatic tubing and strain relief(s);

— abrasion;

— aging;

— UV exposure;

— crush resistance;

— cut resistance.

Following subjecting the pneumatic driveline to the insults listed above, the driveline should be:

— visually examined for damage with photographic evidence;

— leak test after insults per manufacturer's acceptance specification.

6.6.3.5.3 Electrical cable

Electrical cables to and from all power supplies, batteries, controllers, and blood pumps shall be pre-conditioned (see 6.6.2.3.2). Following subjecting the electrical cable to the insults listed below, the electrical cable should be visually examined for damage with photographic evidence and evaluated for any change in electrical continuity/resistance according to the manufacturer's acceptance specifications.

Cables are exposed to various types of loads that can cause failure, including (but not limited to) the following:

— tension;

— torsion;

— corrosion;

— jerk;

— vibration;

— UV exposure;

— cut resistance;

— abrasion;

— kink (bend radius);

— pinch;

— multi-dimensional/mode (e.g. simultaneous twist and flex);

— cyclic bend testing.

Manufacturers should consider which among those listed above are relevant, and whether it is appropriate to test for resistance to a single or relatively small number of challenges (e.g. one cut with a knife imposed at a defined force, or five tensile impacts imposed by dropping a known weight secured to one cable end) or endurance to many load cycles. Endurance testing is used to elicit fatigue failure for loads that are expected to be frequently repeated in usage, and the test load and required number of cycles should take real-world usage and target service life into account. Although it is generally sufficient to meet a defined requirement, insight may be gained by continuing a test beyond the requirement to learn if there is an endurance limit and, if so, learn the nature of the failure mode and how far away from the defined requirement failure occurs.

Combining two or more loads in a test may be relevant, especially if there is historical clinical experience or engineering judgment that a combined load presents an important potential failure mode. In such cases, factors of safety applied to exaggerate test loads relative to expected real-world conditions can quickly superimpose to make a test geometrically and unrealistically difficult to pass. Risk management should be applied to balance the degree of safety factor(s) and load combination to devise a test with real-world relevance.

6.6.3.5.4 Vascular grafts, cannulae, blood *conduits*, atrial and apical cuffs

All blood conduits should be evaluated for conformance with ISO 7198.

Inflow conduits and their connectors used with rotary and some pulsatile devices need to withstand significant negative pressures without collapse or entrainment of air. Tests to establish satisfactory performance should be conducted in excess of the maximum negative pressure capable of being generated by the device.

All connections to and from the blood pump and the blood pathway should be evaluated for conformance with specifications with tests such as pull strength, pressure pulsatility, torsion, vibration, kink (bend radius), and seal integrity. Connection interfaces should avoid gaps and steps in the blood flow path that could generate unacceptable levels of microemboli, as assessed by design analysis and in animal trials.

6.6.3.5.5 Artificial/prosthetic valves

If possible, *prosthetic valves* within the device should be tested as part of the *durability* and *reliability* subclauses described in this document and assessed in the final device configuration in that manner.

If the valve design cannot be evaluated in the final device configuration, the valve may be qualified independent of the system in accordance with the ISO 5840 series and a justification shall be provided (see Annex B).

6.6.3.5.6 Transcutaneous energy transmission systems

Transcutaneous energy transmission systems (TETS) send power across the intact skin to an implanted system without the use of wires or tubes that penetrate the skin. Qualification of the energy system should include a theoretical analysis as well as testing. If the TETS is used, specifications for the system should be established and then verified by testing. This testing should be performed at the sub-system level and as a part of the complete circulatory support system testing as specified in 6.6.3.5.

Specifications should include the following testable parameters:

— input power ranges;

— output power ranges;

— maximum power ranges;

— efficiency;

— local temperature rise;

— operational voltage range;

— effect of axial/radial coil misalignment;

— effect of nearby large metal objects;

— specific absorption rate;

— bidirectional transmission of information;

— risk of information transmission *failure*;

— frequency range;

— tissue trauma (e.g. abrasion, pressure, cutaneous injury).

6.7 Electromagnetic compatibility

EMC testing should be conducted for all devices containing electrical and/or electronic components to demonstrate that the system

a) shall not adversely affect the operation/performance of other equipment used in the same environment (emissions), and

b) shall perform in accordance with the design specification in the presence of other equipment (immunity).

Testing in accordance with IEC 60601-1-2:2014 shall be met. Where appropriate, the test levels shall be documented for the intended use environment (e.g. hospital, home and air/ground transport). See Clause 27 for information on protection of the active implantable medical device from electromagnetic (EM) non-ionizing radiation for additional immunity testing requirements.

6.8 Materials qualification

The selection of materials for components and devices depends upon knowledge of material properties and behaviour in particular environmental states. Although a criterion for the choice of material in critically designed parts relates to the performance in a field test, it is usual in preliminary design to use appropriate data obtained from standardized tests. All testing should take into account all intended

use environments of the system (e.g. manufacturing process, hospital, home, and air/ground transport). The following considerations are important in material selection and qualification.

a) Elastic properties: stiffness and rigidity.

b) Plastic properties: yield conditions, stress-strain relations, and hysteresis.

c) Time-dependent properties: elastic properties, creep, relaxation, and strain-rate effect.

d) Fracture phenomena: crack propagation, fatigue, and ductile-to-brittle transition.

e) Thermal properties: thermal expansion, thermal conductivity, and specific heat.

f) Chemical interactions with the environment: swelling due to hydration, oxidation, corrosion, diffusion, and leaching and exposure to pharmacologic, wound care, and cleaning chemicals.

g) Surface characteristics: all specialized blood-contacting surface characteristics, any particular surface treatments within the device used to improve material strength, hardness, fatigue life, lubrication, and/or heat dissipation should be described.

6.9 Biocompatibility

The biocompatibility of the materials and components used in the circulatory support system shall be determined in accordance with ISO 10993-1:2018.

6.10 Dynamic haemolysis

The haemolysis levels of the circulatory support system shall be determined and documented.

For assessment of potential damage to red blood cells, dynamic in vitro haemolysis testing of flow devices over the expected operating range using the test procedures described by ASTM F1841 is recommended. Suitable control test pumps for this assessment could be devices with acceptable haemolysis (e.g. comparative commercially used pump model). Paired comparative haemolysis testing should be performed and replicated for the DUT and control test pumps using the same blood pool at the same test conditions in identical flow loops. Test parameters (e.g. blood volume, flow rates, pressures) may need to be adjusted depending upon the operating parameters of the test and control devices. Blood selection and handling (e.g. animal model, blood pooling) should be described using ASTM F1830 as a guide.

6.11 Environmental testing

Environmental testing to the specifications of ISO 14708-1:2014 shall be conducted to demonstrate that the system will perform according to its design specification. If other environmental test documents are used for these evaluations, the test levels used should be justified as to their appropriateness to the intended use environment (e.g. hospital, home, air/ground transport).

6.12 *In vivo* evaluation

6.12.1 Objective

6.12.1.1 General

The objective of an animal study is to perform a pre-clinical validation of the final device by obtaining safety and performance data in a living animal, supporting the suitability of the system prior to first human use. Suitability of the device will be corroborated by safety and performance data. The *in vivo* study plan should be structured according to the intended use of the device in the specified patient population. The plan should describe what system designs require *in vivo* verification beyond planned in vitro design evaluation and performance testing with justification.

6.12.1.2 Safety

Safety shall be assessed in an appropriate animal model based on study endpoints including but not limited to bleeding, thrombogenicity, haemolysis, embolism, neurological events, calcification, pannus formation, end organ dysfunction, infarction, systemic toxicity, infection, corrosion, hermetic integrity, wear, local biological response, clinical pathology, and haemodynamic stability. These study endpoints are based upon clinical observations during the study and/or findings on necropsy. Safety should also be assessed based on the delivery and implantation to the intended anatomic location. Calcification may be assessed for specific devices that have biological/polymeric valves and other polymeric moving parts (such as a polyurethane diaphragm).

6.12.1.3 Performance

Performance shall be assessed based on the ability of the device to provide acceptable circulatory support through a pre-specified timepoint.

6.12.2 Definition of success or failure

Success or failure shall be pre-defined in the study objectives as acceptability criteria that are measurable and shall be based upon the indications for use of the device and intended patient population (see Annex B).

6.12.3 Test articles

The animal study shall utilize the final, finished version of the device. This ensures that study data can be best interpreted for evaluation of safety and usability in clinical use. The test records should refer to build records that describes the system details and processes used to assemble these devices. If the final device design was not used in the animal study, all differences between the tested device and the final device design shall be identified and a justification shall be provided to explain why these differences would not be expected to affect study outcomes. Additionally, justification should be provided on why the final clinical device design presents no new risks to the patient as compared to the design evaluated in the animal study.

6.12.4 Test system

6.12.4.1 Test animals

Animal species, strain, age, gender, weight, identifying features and permanent *markings* shall be recorded. The source(s) of animals shall be recorded with vendor name and address. For record-keeping and health purposes, each animal shall be identified with an ear tag, tattoo, collar, band, subcutaneous transponder, cage card, radiofrequency identification, or any effective and consistent method of animal identification that contains the test facility and/or national identification number.

6.12.4.2 Choice of animal model

An animal model shall be selected according to the following considerations and shall be justified.

a) Non-mammalian species are not appropriate for comparison with human implant conditions for circulatory assist devices.

b) The size and orientation of the heart and major blood vessels shall be considered during the selection for an appropriate animal model of the intended patient population for the device being evaluated.

c) The blood coagulation response of the chosen animal model shall be justified. Anticoagulation used during the evaluation should be carefully documented and assessed for comparison to the specific patient population.

d) The blood coagulation profile including liver function of the chosen animal model shall be screened for bleeding disorders or overactive clotting mechanisms. Anticoagulant and antiplatelet medications used during the evaluation shall be carefully documented and assessed for clinical significance.

e) Red blood cell susceptibility to mechanical stress for the species selected shall be considered and compared to the intended patient population in the evaluation of haemolysis.

6.12.4.3 Sample size and implant duration

Sample size and implant duration shall be appropriate for demonstrating the *safety* and performance of the device within a biological system and shall be justified for the intended use. The sample size calculation shall be performed and/or the number of animals shall be estimated based upon proof-of-concept, exploratory, or pilot studies, in order to detect significant effects and obtain valid results.

6.12.5 Control

Each animal's baseline physical examination and clinical pathology data are used to assess the changes to its health condition. The animal's measured postoperative parameters are compared to preoperative values.

6.12.6 Test equipment

The test institution shall provide detailed equipment information. All measuring equipment shall be calibrated and validated according to manufacturer's standards. The equipment calibration and validation records shall be checked according to the test facility's standard operating procedures.

6.12.7 Preoperative animal care

The test facility shall provide preoperative animal care according to the facility's standard operating procedures, the institution's animal care program, and state and federal policies and regulations (see Annex B).

6.12.8 Implant procedure

The implant protocol and surgical procedure shall include the following, but not be limited to:

a) anaesthesia;

b) device-specific implantation methods;

c) monitoring and animal management;

d) preoperative, intraoperative and postoperative animal care and health management related to device implantation.

6.12.9 Special instructions for early termination

When the implant procedure is considered a failure, and/or the animal reached its humane endpoints rendering euthanasia necessary, another animal should be added to the study. The humane endpoints shall be prespecified prior to the study. Animals that fail to thrive due to conditions unrelated to device function or circumstances beyond the reasonable controls will not be deemed failures and should be excluded from the total number of animals qualified for the study.

Animals that were terminated early or died unexpectedly are subjected to comprehensive necropsy for systemic gross examination including the device *in situ* and collection of tissue samples for histopathological evaluation of major organs, lesions, and local tissues surrounding the implant. The device is explanted for gross assessment, histological examination and engineering analysis. All findings shall be recorded, including observations, root-cause analysis and conclusions regarding the

early termination of the animal in the study. All animals used in the development and testing of devices should be reported including those that are euthanized early and died unexpectedly.

6.12.10 Postoperative care

The postoperative care shall be described in the animal care and use protocol approved for the specific device study by the institution's animal care, welfare and use panel (e.g. Institutional Animal Care and Use Committee or IACUC). Additionally, the test facility shall provide postoperative animal care according to the facility's standard operating procedures, the institution's animal care program, and, state and federal policies and regulations (see Annex B).

6.12.11 Anticoagulation

Use of antithrombotic (anticoagulant and antiplatelet) drugs shall be justified with respect to the intended use of the device and the pharmacological and antithrombotic effects on the animal. If anticoagulant and antiplatelet medications are used, the antithrombotic protocol shall be provided. The administration schedule and the dosage of drugs used, and coagulation panel measurements shall be fully documented.

6.12.12 Adverse events

Possible adverse events associated with the device include death, device/system failures, bleeding, infection, haemolysis, neurological dysfunction, thromboembolic events, cardiovascular dysfunction (e.g. arrythmias, right heart failure, myocardial infarction, valvular incompetence), pulmonary dysfunction, or renal and/or hepatic dysfunction. The definitions of adverse events shall be provided (see Annex B). All adverse events occurring throughout the duration of the study shall be fully documented and adjudicated for device relatedness.

6.12.13 System performance

In order to characterize system performance *in vivo*, the system parameters based on device specifications shall be documented during the course of the study.

6.12.14 Measurement of physiological parameters

The physiological parameters shall be evaluated and documented during the course of the study (see Annex B).

6.12.15 Clinical pathology

6.12.15.1 Timing

Timing of blood collection should be provided during the preoperative, intraoperative, and postoperative periods throughout the study duration.

6.12.15.2 Laboratory analysis

Clinical pathology analysis, such as haematology, serum chemistry, plasma free haemoglobin, coagulation panel, urinalysis and other relevant parameters (see Annex B), shall be documented at each time point.

6.12.16 Necropsy and device retrieval

Protocol for necropsy and device retrieval shall be provided and include, but not be limited to, the following:

a) method of euthanasia;

b) *in situ* photographing;

c) method of fixation of major organs;

d) rinsing and fixation methods for retrieved device.

6.12.17 Macroscopic examination

The test animals shall be subjected to full, detailed gross necropsy and all the observations shall be documented.

The device shall be scrutinized for obvious mechanical changes, corrosion, wear, hermetic integrity, infective vegetations, thrombus, calcification, tissue reaction to the system, examination of the device system components for positioning, and other observations shall be fully documented.

6.12.18 Histological examination

After fixation, the major organs and all gross lesions shall be analysed for microscopic examination and documented.

6.12.19 Explanted device analysis

The protocol for device analyses shall consider but not be limited to the following points.

a) An integrated program of disassembly of the device that facilitates electrical analysis, haemocompatibility analysis (such as gross/microscopic inspection and photography and SEM assessment of blood-contacting surfaces) along with mechanical assessment of parts should be implemented.

b) During disassembly, seals and connections should be assessed. Seals should be examined for integrity and connections in the blood path should be examined for presence of thrombus. Electrical connections should be tested, inspected for corrosion, and shielding should be assessed for integrity.

c) The cables, electrical and mechanical connections, device components and other devices of the system should also be inspected for evidence of damage, wear, degradation, corrosion or other anomalies.

6.12.20 Data analysis

Data analysis shall be conducted for all data collected according to the protocol to demonstrate safety and performance of the device in a living body. Based on these analyses, the feasibility of the device for clinical application shall be assessed against the success criteria defined in the study protocol.

6.13 Reliability

System reliability is defined as the probability of a system to perform its function for a specified period of time under stated conditions (e.g. the demonstrated reliability of the VAD system shall be X with at least Y confidence for a Z year service life).

a) It is desirable to test as much of the integrated system as possible in a test. However, not all system components are suitable for long term life-cycle testing (such as tissue valves) and these components shall be independently life-cycle tested. In this respect, the study document shall make clear what items of the system are being evaluated in a particular life-cycle study.

b) Device systems used for reliability testing shall be pre-conditioned (see 6.6.2.3.2) unless justification is provided, prior to in vitro reliability testing.

c) All implanted components shall be tested in a simulated physiological environment (such as a pH buffered, temperature controlled, saline filled tank) and operated within a pulsatile mock

circulatory loop. If a pulsatile mock loop is not to be used, a scientific justification shall be provided that lack of pulsatility will not invalidate the test (see Reference [31]).

d) The number of systems to be tested under controlled in vitro conditions shall be statistically justified to demonstrate that the stated reliability specifications are met. Statistical methods to be employed in the analysis of the reliability test results shall be described. An example of such a statistical justification is a Weibull calculation (see Reference [33]).

e) Risk analyses based on ISO 14971:2019 suggest some of the most important modes of failure are associated with the implantation and use of the system. These identified failure modes shall be detectable in the reliability test.

f) Definitions of failure events should be based on the termination of the ability of any implanted item to perform a required function or the inability of the implanted components to meet minimum performance specifications.

g) Cases of incipient failure such as breach of hermetic seals, production of significant particulate debris or ongoing corrosion which would ultimately lead to implanted component failure shall be reported.

h) Important test parameters (such as flow rate) shall be continuously monitored at a frequency sufficient to enable identification of failure incidents. The rationale for the data to be collected and frequency of data collection shall be documented.

i) The results of all failure analyses (including component failures that do not result in system failures) shall be documented. All decisions and rationales regarding corrective actions shall be documented.

j) All failures shall be classified according to risk (see 6.4).

k) During the total life cycle of the product, reliability testing may need to be repeated based on additional clinical data accumulated during pre-market and post-market use of the product if such data necessitates a change that could impact device reliability, for example, a design change resulting from a failure analysis that could impact the system reliability.

l) The reliability study might identify wear-out failures and their precursors. The identified wear-out failures and predictive events should be included in a preventative maintenance or device replacement plan (e.g. a reusable controller).

m) The reliability test conditions should be designed to replicate the effects of physiological conditions on the tested device (see Annex B); however, exceptions can be made if a justification can be provided. For example, a more rigorous test of blood immersed contact bearings should be performed using a low viscosity fluid as this would create a condition where less hydraulic dampening would take place than expected.

n) Cycling of device operating conditions is required to simulate physiological states (such as sleeping, normal activity and exercise; see Reference [14]) in order to operate the device through a range of clinically relevant operating conditions. Values of these parameters will depend on design input specifications.

6.14 Clinical evaluation

See ISO 14155 for more information on clinical evaluations.

7 General arrangement of the packaging

7.1 The text in ISO 14708-1:2014, 7.1 applies.

7.2 The text in ISO 14708-1:2014, 7.2 applies.

8 General *markings* for active implantable medical devices

8.1 The text in ISO 14708-1:2014, 8.1 applies.

8.2 The text in ISO 14708-1:2014, 8.2 applies.

9 Markings on the sales packaging

9.1 The text in ISO 14708-1:2014, 9.1 applies.

9.2 The text in ISO 14708-1:2014, 9.2 applies.

9.3 The text in ISO 14708-1:2014, 9.3 applies.

9.4 The text in ISO 14708-1:2014, 9.4 applies.

9.5 The text in ISO 14708-1:2014, 9.5 applies.

9.6 The text in ISO 14708-1:2014, 9.6 applies.

9.7 The text in ISO 14708-1:2014, 9.7 applies.

9.8 The text in ISO 14708-1:2014, 9.8 applies.

9.9 The text in ISO 14708-1:2014, 9.9 applies.

9.10 The text in ISO 14708-1:2014, 9.10 applies.

9.11 The text in ISO 14708-1:2014, 9.11 applies.

9.12 The text in ISO 14708-1:2014, 9.12 applies.

9.13 The text in ISO 14708-1:2014, 9.13 applies.

9.14 The text in ISO 14708-1:2014, 9.14 applies.

10 Construction of the *sales packaging*

10.1 The text in ISO 14708-1:2014, 10.1 applies.

10.2 The text in ISO 14708-1:2014, 10.2 applies.

10.3 The text in ISO 14708-1:2014, 10.3 applies.

10.4 The text in ISO 14708-1:2014, 10.4 applies.

11 Markings on the sterile pack

11.1 The text in ISO 14708-1:2014, 11.1 applies.

11.2 The text in ISO 14708-1:2014, 11.2 applies.

11.3 The text in ISO 14708-1:2014, 11.3 applies.

11.4 The text in ISO 14708-1:2014, 11.4 applies.

11.5 The text in ISO 14708-1:2014, 11.5 applies.

11.6 The text in ISO 14708-1:2014, 11.6 applies.

11.7 The text in ISO 14708-1:2014, 11.7 applies.

11.8 The text in ISO 14708-1:2014, 11.8 applies.

11.9 The text in ISO 14708-1:2014, 11.9 applies.

12 Construction of the non-reusable pack

12.1 The text in ISO 14708-1:2014, 12.1 applies.

12.2 The text in ISO 14708-1:2014, 12.2 applies.

12.3 The text in ISO 14708-1:2014, 12.3 applies.

13 Markings on the active implantable medical device

13.1 The text in ISO 14708-1:2014, 13.1 applies.

13.2 The text in ISO 14708-1:2014, 13.2 applies.

13.3 The text in ISO 14708-1:2014, 13.3 applies.

13.4 The text in ISO 14708-1:2014, 13.4 applies.

13.5 There shall be self-evident visual indications on the device (e.g. connector alignment indicators and arrows).

Compliance is checked by visual inspection and human factors / usability testing in 6.3.2.

14 Protection from unintentional biological effects being caused by the active implantable medical device

14.1 The text in ISO 14708-1:2014, 14.1 applies.

14.2 The text in ISO 14708-1:2014, 14.2 applies.

14.3 The text in ISO 14708-1:2014, 14.3 applies.

14.4 The text in ISO 14708-1:2014, 14.4 applies.

15 Protection from harm to the patient or user caused by external physical features of the active implantable medical device

15.1 The text in ISO 14708-1:2014, 15.1 applies.

15.2 The text in ISO 14708-1:2014, 15.2 applies.

16 Protection from harm to the patient caused by electricity

16.1 The text in ISO 14708-1:2014, 16.1 applies.

16.2 The text in ISO 14708-1:2014, 16.2 applies.

16.3 The text in ISO 14708-1:2014, 16.3 applies.

17 Protection from harm to the patient caused by heat

17.1 Protection from harm to the patient caused by heat

The text in ISO 14708-1:2014, 17.1 applies.

17.2 Active implantable medical device intended to supply heat

The text in ISO 14708-1:2014, 17.2 applies.

18 Protection from ionizing radiation released or emitted from the active implantable medical device

18.1 The text in ISO 14708-1:2014, 18.1 applies.

18.2 The text in ISO 14708-1:2014, 18.2 applies.

18.3 The text in ISO 14708-1:2014, 18.3 applies.

19 Protection from unintended effects caused by the active implantable medical device

19.1 The text in ISO 14708-1:2014, 19.1 applies.

19.2 The text in ISO 14708-1:2014, 19.2 applies.

19.3 The text in ISO 14708-1:2014, 19.3 applies.

19.4 The text in ISO 14708-1:2014, 19.4 applies.

19.5 The text in ISO 14708-1:2014, 19.5 applies.

19.6 The text in ISO 14708-1:2014, 19.6 applies.

19.7 Power supply redundancy: There shall always be a redundant *power source*. Where possible, an emergency battery backup should be designed into the system.

19.8 Power supply management: In case of a single-*fault* condition in the power supply, the device system shall automatically switch to a redundant *power source* without user interaction. The device system shall also provide an alarm notification of the power supply *fault*.

A device system should be provided with a mains connected *power source* system in addition to, or in place of, a battery power system.

When a mains connected *power source* is included, the following shall be considered:

a) emergency back-up procedure if the *power source* fails;

b) power status indicator(s) that confirm mains connection and the presence of an output *power source*; auditory, visual, and vibratory warning alarms in the event of mains disconnection and/or *power source failure*;

c) the redundancy of *power sources*;

d) if the device is intended for out-of-hospital use;

e) line voltage, frequency, current, and physical connection requirements.

Mains connected *power source* systems shall comply with the electrical *safety* requirements of IEC 60601-1:2018.

Compliance shall be confirmed by inspection of the design and its analysis, as documented by the manufacturer. Design analysis shall be supported by the manufacturer's calculations and data from test studies as appropriate.

20 Protection of the active implantable medical device from damage caused by external defibrillators

20.1 The text in ISO 14708-1:2014, 20.1 applies.

20.2 The text in ISO 14708-1:2014, 20.2 applies.

21 Protection of the active implantable medical device from changes caused by electrical fields applied directly to the patient

21.1 The text in ISO 14708-1:2014, 21.1 applies.

21.2 The text in ISO 14708-1:2014, 21.2 applies.

22 Protection of the active implantable medical device from changes caused by miscellaneous medical treatments

22.1 The text in ISO 14708-1:2014, 22.1 applies.

22.2 The text in ISO 14708-1:2014, 22.1 and 22.2 apply.

23 Protection of the active implantable medical device from mechanical forces

23.1 The text in ISO 14708-1:2014, 23.1 applies.

23.2 The text in ISO 14708-1:2014, 23.2 applies.

23.3 The text in ISO 14708-1:2014, 23.3 applies.

23.4 The text in ISO 14708-1:2014, 23.4 applies.

23.5 The text in ISO 14708-1:2014, 23.5 applies.

23.6 The text in ISO 14708-1:2014, 23.6 applies.

23.7 The text in ISO 14708-1:2014, 23.7 applies.

24 Protection of the active implantable medical device from damage caused by electrostatic discharge

24.1 The text in ISO 14708-1:2014, 24.1 applies.

The requirements of IEC 60601-1-2:2014 shall apply to the non-implantable parts.

NOTE While the electrostatic discharge is applied only to the non-implantable parts, operation of the active implantable medical device is evaluated as a system following the test.

Compliance is checked as specified in IEC 60601-1-2:2014.

24.2 This text in ISO 14708-1:2014, 24.2 applies.

25 Protection of the active implantable medical device from damage caused by atmospheric pressure changes

25.1 The text in ISO 14708-1:2014, 25.1 applies.

25.2 The text in ISO 14708-1:2014, 25.2 applies.

26 Protection of the active implantable medical device from damage caused by temperature changes

26.1 The text in ISO 14708-1:2014, 26.1 applies.

26.2 The text in ISO 14708-1:2014, 26.2 applies.

27 Protection of the active implantable medical device from electromagnetic non-ionizing radiation

27.1 General

Implantable parts of the active implantable medical device are expected to maintain their intended use and shall not result in an unacceptable risk because of susceptibility to electrical influences due to external EM fields.

Assessment: The tests of this clause shall be used to assess device behavioural responses when exposed to EM fields representing the general public environment.

For other EM environments (e.g. industrial, air/ground transport, and hospital), the manufacturer might need to adjust immunity test levels according to 27.2.5.

NOTE The tests in this clause apply to the VAD system. Non-implantable (external) parts are exclusively covered by IEC 60601-1-2:2014.

Compliance is checked by review of the risk management file and test reports.

27.2 Test conditions

27.2.1 Acceptance criteria

During testing of the subclauses of Clause 27, the acceptance criteria (pass/fail criteria) shall be based on the manufacturer's intended use of the active implantable medical device and on a risk assessment.

Prior to testing, risks shall be identified, taking into account the reasonably foreseeable EM environment that is likely to occur during its intended use. Immunity test levels in Clause 27 are based on the reasonably foreseeable maximum levels found in the general public EM environment. Each risk shall be evaluated through a design analysis that takes account of any risk control, according to ISO 14708-1:2014, 5.5.4.

The risk assessment process, performed in accordance with ISO 14971:2019, will result in hazardous situations being identified (see ISO 14971:2019, Figure C.1). Since actual risk cannot be observed during testing, it will be necessary to observe the performance of the device to see if any hazardous situations occur.

Pass/fail criteria shall be defined prior to testing. Ideally, these criteria can be measurable or observable during testing. If not, the manufacturer shall specify an alternative method for determining that the *DUT* met the required pass/fail criteria during the test. The use of special hardware or software might be necessary.

If the pass/fail acceptance criteria are not met during testing, resulting in intended use not being maintained or unacceptable risk(s), the manufacturer shall substantiate *DUT* behavioural responses and explain why the overall risk(s) are acceptable. In no cases are irreversible changes in performance, outside of specification, allowed.

During testing of the subclauses of Clause 27, the *DUT* shall not be damaged as a result of the test. After the test, the *DUT* shall conform to all manufacturer specifications (see ISO 14708-1:2014, 28.8).

27.2.2 Test configuration and setup

The active implantable medical device shall be tested in representative configurations, consistent with intended use, that are likely to be the most susceptible to EM disturbances. This shall be determined using risk analysis, experience, engineering analysis, or pretesting.

For all tests, provision shall be made to determine the device's behavioural responses, preferably during testing. If the operation of the *DUT* cannot be observed or verified during the test, the manufacturer

shall specify an alternative method for determining that the DUT met the required pass/fail criteria during the test. The use of special hardware or software might be necessary.

27.2.3 Operating functions, modes, and settings

The active implantable medical device shall be tested using the functions, modes, and settings, consistent with intended use, that are likely to be the most susceptible to EM disturbances. This shall be determined using risk analysis, experience, engineering analysis, or pretesting.

Except for the requirements of 5.7, if the intended use includes a wireless communication channel, the wireless communication function shall be evaluated and tested for EMC in accordance with IEC 60601-1-2:2014.

NOTE A wireless communication function does not have to be tested twice for EMC, as it would be tested according to this document and IEC 60601-1-2:2014.

27.2.4 Patient physiological simulation

If simulation of the patient is required to verify normal operation of the active implantable medical device, it shall be provided during immunity testing. Physiological simulation shall not provide an intentional conductive or capacitive connection to earth other than that required by 27.2.2.

27.2.5 Immunity test levels

Test levels in Clause 27 are based on the reasonably foreseeable maximum levels found in the general public EM environment. When a manufacturer knows from experience, published data, or representative measurements that the environment of intended use has unique characteristics that would increase or decrease the EM disturbance levels that form the basis of immunity tests in Clause 27, the manufacturer shall take this into consideration in the risk management process.

NOTE IEC 60601-1-2:2014, Annex E can be used to determine immunity test levels for environments not specified in Clause 27.

27.3 Risk management file and test report file documentation

The information listed in Table 1 shall be provided by the manufacturer and documented in the risk management file or test report file.

Table 1 — Minimum risk management file and test report file contents

No.	Item
1	Description of the intended use, and any unacceptable risks and associated hazardous situations, resulting from the risk assessment.
2	If the procedure specified by Clause 27 or an equivalent procedure is used: — a justification for any special environments identified; — the adjusted reasonably foreseeable maximum EM disturbance levels; — the resulting final immunity test levels; — details of the methods and data sources used in determining the appropriate immunity test levels.
3	Pass/fail criteria: how it was determined.
4	Pass/fail criteria: how it was monitored during testing.
5	Effects on the DUT that were observed during or after the application of the test disturbances, and the duration for which these effects persisted.
6	If the intended use is not maintained during testing, or if a hazardous situation occurs, the manufacturer shall substantiate DUT behavioural responses and explain why they are acceptable and why they are not considered to be an unacceptable risk.

Table 1 *(continued)*

No.	Item
7	Applicability/tests not performed. The decision and justification not to perform a measurement or test shall be documented.
8	DUT configuration during the test, including a block diagram of DUT configuration and all peripherals and auxiliary equipment used.
9	DUT functions, settings and operating modes listed by test.
10	Name and location of the test facility.
11	Names and functions or equivalent identification of the persons authorizing the test report.
12	Description of the DUT. Included the device name, model number, manufacturer, and serial numbers.
13	DUT software/firmware version.
14	Prototype or production version of the DUT. For prototypes, describe the relationship to production versions.
15	Compliance summary statement. Compliance of the DUT with each test.
16	Test data that support the compliance determination for each test performed.
17	Description of any patient-coupled cable termination used.
18	Simulators, accessories and auxiliary equipment, including patient physiological and simulation.
19	Documentation of any special hardware or software needed to perform the tests.
20	Test equipment used, including calibration or maintenance dates.
21	Dwell time for each immunity test requiring a dwell time.
22	DUT modifications needed in order to pass any of the tests. A statement that they will all be incorporated into production units.
23	Photographs of each test setup including DUT and all peripherals and auxiliary equipment used.
24	Deviations from the test plan with an explanation.

27.4 Protection from static magnetic fields of flux density up to 50 mT

The DUT shall not be damaged when exposed to static (non-time-varying) magnetic fields of flux density up to 50 mT.

Test equipment: A field coil capable of generating a magnetic field with a flux density of at least 50 mT in the region to be occupied by the DUT.

Test procedure: The DUT is to be placed in the centre of the field with the field disabled, and the field can be slowly increased to reach the test level. After at least 15 s of exposure to the magnetic field, the DUT shall be removed from the field. No monitoring of DUT performance is required during the test.

Reorient the DUT so that a second orthogonal axis is aligned with the axis of the field, and again subject the DUT to the required field. Repeat again with the third orthogonal axis aligned with the axis of the field.

Evaluation of test results: The DUT shall meet all manufacturer specifications after the test.

27.5 Protection from AC magnetic fields in the range of 1 kHz to 140 kHz

The DUT shall not be damaged when exposed to AC magnetic field strengths up to 150 A/m.

Test equipment: A test apparatus capable of generating a magnetic field as shown in Table 2 in the region to be occupied by the DUT. The levels shown are minimum values to be maintained across the exposure area. A signal generator/amplifier capable of providing the drive current necessary to produce the required field strength.

Table 2 — Minimum magnetic field test levels (RMS)

Frequency kHz	*H* A/m rms
1 to 100	150
100 to 140	15 000/*f*
NOTE *f* is the frequency in kHz.	

Test procedure: Place the DUT, appropriately terminated, within the centre of the field. The frequency range of the applied test signals, from 1 kHz to 140 kHz, may be either swept or stepped. If swept, the rate of sweep shall be approximately 2 min/decade or slower. If stepped, the step size shall be no larger than 1 kHz starting at 1 kHz and no larger than 10 kHz starting at 10 kHz, and the dwell time at each step shall be approximately 10 s. The test signals shall be applied as sinusoidal continuous wave (CW) signals over the entire frequency range. No monitoring of DUT performance is required during the test.

Reorient the DUT so that a second orthogonal axis is aligned with the axis of the field, and again subject the DUT to the required field. Repeat again with the third orthogonal axis aligned with the axis of the field.

Evaluation of test results: The DUT shall meet all manufacturer specifications after the test.

27.6 Protection from proximity fields due to RF wireless communications equipment

The DUT shall remain functionally safe and is expected to maintain the performance necessary for its intended use during exposure to proximity fields from wireless communications equipment.

All test frequencies, modulations, and test levels shall be as specified in IEC 60601-1-2:2014, 8.10.

Evaluation of test results: The DUT shall meet the immunity pass/fail criteria determined by the manufacturer.

28 Accompanying documentation

28.1 The text in ISO 14708-1:2014, 28.1 applies.

At a minimum, the manufacturer's telephone number shall be provided in the accompanying documentation. The manufacturer's email address and web URL may also be provided as an option.

28.2 The text in ISO 14708-1:2014, 28.2 applies.

28.3 The text in ISO 14708-1:2014, 28.3 applies.

28.4 The text in ISO 14708-1:2014, 28.4 applies.

28.5 The text in ISO 14708-1:2014, 28.5 applies.

28.6 The text in ISO 14708-1:2014, 28.6 applies.

28.7 The text in ISO 14708-1:2014, 28.7 applies.

28.8 The text in ISO 14708-1:2014, 28.8 applies.

28.9 The text in ISO 14708-1:2014, 28.9 applies.

28.10 The text in ISO 14708-1:2014, 28.10 applies.

28.11 The text in ISO 14708-1:2014, 28.11 applies.

28.12 The text in ISO 14708-1:2014, 28.12 applies.

28.13 The text in ISO 14708-1:2014, 28.13 applies.

28.14 The text in ISO 14708-1:2014, 28.14 applies.

28.15 The text in ISO 14708-1:2014, 28.15 applies.

28.16 The text in ISO 14708-1:2014, 28.16 applies.

28.17 The text in ISO 14708-1:2014, 28.17 applies.

28.18 The text in ISO 14708-1:2014, 28.18 applies.

28.19 The text in ISO 14708-1:2014, 28.19 applies.

28.20 The text in ISO 14708-1:2014, 28.20 applies.

28.21 The text in ISO 14708-1:2014, 28.21 applies.

28.22 The text in ISO 14708-1:2014, 28.22 applies.

28.23 The text in ISO 14708-1:2014, 28.23 applies.

28.24 The text in ISO 14708-1:2014, 28.24 applies.

28.25 The text in ISO 14708-1:2014, 28.25 applies.

28.26 The text in ISO 14708-1:2014, 28.26 applies.

28.27 The text in ISO 14708-1:2014, 28.27 applies.

28.28 The text in ISO 14708-1:2014, 28.28 applies.

28.29 The text in ISO 14708-1:2014, 28.29 applies.

28.30 The text in ISO 14708-1:2014, 28.30 applies.

28.31 Instructions for use: When placed on the market, each system should be accompanied by instructions for use providing additional information as needed.

a) A complete description of the system including the intended use, indications for use, any warnings, contraindications, instructions for use, and limitations of use.

b) Information allowing the physician to select a suitable device and the corresponding software and accessories.

c) Information constituting the instructions for use allowing the physician and, where appropriate, the patient to use the device, its accessories and software, correctly, as well as information on the nature, scope and times for operating controls and trials and, where appropriate, maintenance measures.

d) Information allowing, if appropriate, certain risks in connection with implantation of the device to be avoided.

e) Information regarding alarm conditions and subsequent corrective action, instructions for restricted activity, and device performance characteristics. Any special operating instructions, any warnings and/or cautions should be given. The manufacturer should decide the type and level of information required taking into consideration such factors as the assumed technical knowledge and skill of the intended user and any novel or unfamiliar features or mode of operation, which might not be self-evident. Internationally recognized symbols should be used.

f) Information regarding risks of reciprocal interference in connection with the presence of the device during specific investigations or treatment.

g) The necessary instructions in the event of the sterile packaging being damaged and, where appropriate, details of the appropriate methods of sterilization.

h) If the device is reusable, information on the appropriate processes to allow re-use, including cleaning, disinfection, packaging and, where appropriate, the method of sterilization of the device to be re-sterilized, and any restriction on the number of reuses.

i) Where devices are supplied with the intention that they be sterilized before use, the instructions for the cleaning and sterilization of the unit shall be such that, if correctly followed, the device still complies with the performance requirements.

j) Details of any further treatment or handling needed before use (e.g. sterilization and final assembly).

k) Detailed information, if appropriate, on the nature of any emitted radiation from the devices, means of protecting the patient and users, and on ways of avoiding misuse and of eliminating the risks inherent in installation.

l) Precautions providing emergency response care (such as CPR) without causing harm to the patient and/or device.

When placed on the market, an instruction leaflet should be included to provide details allowing the physician to brief the patient on the known contraindications and the associated precautions to be taken. These details should cover in particular:

1) information allowing the lifetime of the energy source to be established;

2) precautions to be taken should changes occur in the device's performance;

3) precautions to be taken regarding exposure, in reasonably foreseeable environmental conditions, to magnetic fields, external electrical influences, electrostatic discharge, pressure or variations in pressure, accelerations;

4) adequate information regarding the medicinal products which the device in question is designed to administer, where appropriate;

5) instructions for use shall be included in the packaging of every device;

NOTE By way of exception, no such instructions for use are needed for devices in Class I or Class IIa if they can be used safely without any such instructions.

6) precautions to be taken against any special, unusual risks related to the disposal of the device;

7) medicinal substances incorporated into the device as an integral part of it, if appropriate;

8) degree of accuracy claimed for devices with a measuring function;

9) recommended environmental conditions for transport, storage, and use (including charging and discharging, if appropriate).

28.32 Patient ID card: The accompanying documentation shall include a patient ID card bearing space for at least the following information:

— model designation and name of the device;

— serial number or lot number of the device;

— identity of the patient;

— date of implantation;

— name and telephone number of the treating physician;

— manufacturer's contact telephone number (see 28.31);

— text that says the patient has an implanted medical device.

Compliance shall be checked by inspection.

28.33 Wireless documentation: For devices using wireless technologies, the accompanying documentation shall address the following topics if applicable (see 5.7):

— a brief description of the wireless quality of service needed for *safe and effective* operation;

— a brief description of the recommended wireless security measures (e.g. such as the WPA2 wireless encryption for IEEE 802.11 technology);

— information about any wireless coexistence issues and mitigations. This can include precautions for proximity to other wireless products, and specific recommendations for separation distances from such products.

Compliance shall be checked by inspection.

Annex A
(informative)

Relationship between the fundamental principles in ISO/TR 14283 and the clauses of this document

Table A.1 — Relationship between the fundamental principles in ISO/TR 14283 and the clauses of this document

Essential principles from ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of ISO 14708-5 and aspects covered
5 Essential principles		
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.	(This principle is fundamental to all aspects of an active implantable medical device addressed by ISO 14708.) 5.3 Requires usability engineering process be applied to non-implantable parts of the active implantable medical device. 5.5 Requires parts of an ISO 14971:2019-compliant risk management process to be applied.	* retained
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; — inform users of any residual risks.	(This principle is fundamental to all aspects of an active implantable medical device addressed by ISO 14708. This approach is particularly applicable to the requirements in Clauses 14, 19, and 21.) 5.4 Requires the manufacturer to provide information security when communication with the implantable part is through wireless communication channels. 5.5 Requires parts of an ISO 14971:2019-compliant risk management process to be applied.	* retained
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.	(This principle is fundamental to all aspects of an active implantable medical device addressed by ISO 14708.)	* retained

Table A.1 *(continued)*

Essential principles from ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of ISO 14708-5 and aspects covered
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.	19.2 Requires power source depletion indicator.	* retained 19.7, 19.8 additional requirements
	19.3 Defines methodology to ensure single fault conditions are not a hazard.	* retained
	23.1 Defines drop test for non-implantable parts.	* retained
	23.2 Defines vibration test for patient carried parts.	* retained
	23.3 Sets test of tensile strength (e.g. leads).	* retained
	23.4 Requires strain relief (e.g. leads).	* retained
	23.5 Requires fatigue resistance (e.g. leads).	* retained
	23.6 Requires connections to be reliable.	* retained
	26.1 Requires protection from heat from powered non-implantable parts.	* retained
	28.4 Requires disclosure of maximum proven connector retention strength.	* retained
	28.23 Requires warning against patient entry into hazardous environments.	* retained
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 (e.g. fluctuations of temperature and humidity) taking account of the instructions and information provided by the manufacturer.	7.2 Requires sterile pack to be protected by sales packaging.	* retained
	10. Requires packaging to be durable.	* retained
	10.2 Requires packaging to be protected against the effects of humidity.	* retained
	10.3 Requires markings on the sales package to be indelible.	* retained
	10.4 Requires accompanying documentation to be physically associated with the device.	* retained
	12.3 Requires markings on the sterile pack to be indelible.	* retained
	26.2 Requires device to be protected against the effect of temperature changes.	* retained

Table A.1 *(continued)*

Essential principles from ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of ISO 14708-5 and aspects covered
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.	19.3 Defines methodology to ensure single fault conditions are not a hazard.	* retained
	19.4 Requires investigation of unintended effects caused by the device.	* retained
5.2 Specific principles regarding design and construction		
5.2.1 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.	14.3 Requires investigation of biocompatibility.	* retained
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.	14.2 Defines test for particulate contamination.	* retained
	14.3 Requires investigation of biocompatibility.	* retained
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.	19.5 Demonstrate compatibility with medicinal substances.	* retained
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.	25.1 Requires implanted parts to withstand pressure changes.	* retained
5.2.5 The implants 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.	25.1 Requires implanted parts to withstand pressure changes.	* retained

Table A.1 *(continued)*

Essential principles from ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of ISO 14708-5 and aspects covered
5.2.6 The implants 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.	14.1 Requires device to be supplied sterile.	* retained
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.	14.1 Requires device to be supplied sterile.	* retained
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.	7.1 Requires device to be supplied in non-reusable pack.	* retained
	7.2 Requires sterile pack to be protected by sales packaging.	* retained
	10.1 Requires packaging to be durable.	* retained
	10.2 Requires packaging to be proof against the effects of humidity.	* retained
	11.7 Requires contents of sterile pack to be declared or visible.	* retained
	11.9 Requires the sterile pack to be marked with the instructions for opening it.	* retained
	12.1 Applies ISO 11607 to the reusable pack.	* retained
	12.2 Shall be apparent if sterile pack has been opened.	* retained
	14.1 Requires device to be supplied sterile.	* retained
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.	(Not applicable because 14.1 requires that implantable parts of an active implantable medical device be provided sterile.)	—

Table A.1 *(continued)*

Essential principles from ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of ISO 14708-5 and aspects covered
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.	7.1 Requires device to be supplied in non-reusable pack.	* retained
	7.2 Requires sterile pack to be protected by sales packaging.	* retained
	10.1 Requires packaging to be durable.	* retained
	10.2 Requires packaging to be proof against the effects of humidity.	* retained
	11.7 Requires contents of sterile pack to be declared or visible.	* retained
	11.9 Requires the sterile pack to be marked with the instructions for opening it.	* retained
	12.1 Applies ISO 11607-1 to the reusable pack.	* retained
	12.2 Shall be apparent if sterile pack has been opened.	* retained
	14.1 Requires device to be supplied sterile.	* retained
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.	—	—
5.3.5 Implants intended to be sterilized must be manufactured in appropriately controlled (e.g. environmental) conditions.	14.1 Requires device to be supplied sterile.	* retained
	14.2 Defines test for particulate contamination.	* retained
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.	(Not applicable because subclause requires that implantable parts of an active implantable medical device be provided sterile.)	—
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.	(Not applicable because subclause requires that implantable parts of an active implantable medical device be provided sterile.)	—
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.	14.4 Requirement for quality and safety of incorporated medicinal substances.	* retained

Table A.1 *(continued)*

Essential principles from ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of ISO 14708-5 and aspects covered
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 can 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.	(Not applicable to active imp active implantable medical devices.)	—
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.	(Not applicable to active implantable medical devices.)	—
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.	(Not applicable to active implantable medical devices.)	—

Table A.1 *(continued)*

Essential principles from ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of ISO 14708-5 and aspects covered
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.	9.9 Requires implantable connectors to be identified on sales pack.	* retained
	11.8 Requires implantable connectors to be identified on sterile pack.	* retained
	23.6 Requires connector retention force to be specified.	* retained
	28.4 Requires disclosure of maximum proven connector retention strength.	* retained
	28.5 Requires provision of information on accessories that might be required to facilitate the intended use of the device.	* retained
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;	15.1 Sets requirement for surfaces of non-implantable parts.	* retained
	15.2 Requires implantable parts to have appropriate physical form.	* retained
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;	5.3 Requires usability engineering process be applied to non-implantable parts of the active implantable medical device.	* Retained 6.3.2, 6.5 additional requirements
	5.5 Requires parts of an ISO 14971:2019-compliant risk management process to be applied	* retained
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;	23.1 Defines drop test for non-implantable parts.	* retained
	23.2 Defines vibration test for patient carried parts.	* retained
	24.1 Defines electrostatic discharge test for non-implantable parts.	* replacement
	25.1 Requires implanted parts to be proof against pressure changes.	* retained
	26.2 Requires implantable devices to be undamaged by extremes of temperature in transit.	* retained
	27.1 Defines requirement for electromagnetic immunity.	* replacement
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;	19.3 Requires a design analysis and defines the methodology for the analysis.	* retained
5.6.2.5 The risk associated with the possible negative interaction between software and the environment within which it operates and interacts;	19.3 Requires a design analysis and defines the methodology for the analysis.	* retained

Table A.1 *(continued)*

Essential principles from ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of ISO 14708-5 and aspects covered
5.6.2.6 The risks of accidental penetration of substances into the implant;	19.3 Requires a design analysis and defines the methodology for the analysis.	* retained
5.6.2.7 The risks of reciprocal interference with other devices normally used in the investigations or for the treatment given;	20.1 Requires defibrillation protection of external ECG leads.	not applicable to circulatory support systems
	20.2 Defines test to prove defibrillation protection of implanted device.	* retained
	21 Requires protection against diathermy.	* retained
	22 Requires protection against diagnostic ultrasound.	* retained
	28.12 Requirement for warning notices.	* retained
	28.13 Requires warning about monitoring device in case of diathermy.	* retained
	28.14 Requires warning not to expose device to therapeutic levels of ultrasound.	* retained
	28.15 Requires warning about the effect of therapeutic irradiation on implanted devices.	* retained
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.	17.1 Requires investigation of local heating caused by faulty implanted device.	* retained
	17.2 Requires that supply heat be investigated.	not applicable
	19.1 Requires a design analysis.	* retained
	19.2 Requires power source depletion indicator.	* retained 19.7, 19.8 additional requirements
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 Applies IEC 60601-1:2018 to the non-implantable parts of the active implantable medical device.	* retained
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.	17.1 Requires investigation of local heating caused by the implanted device in normal operation or in any single component failure.	* retained
	19.1 Requires a design analysis.	* retained
	19.2 Requires power source depletion indicator.	* retained 19.7, 19.8 additional requirements

Table A.1 *(continued)*

Essential principles from ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of ISO 14708-5 and aspects covered
5.6.5 Implants must be designed and manufactured in such a way as to facilitate the safe disposal of any waste substances.	28.29 Requires information on proper disposal of the device.	* retained
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.	5.1 Applies IEC 60601–1 to the non-implantable parts of the active implantable medical device that are connected to or equipped with an electrical power source.	* retained 6.6.3.4, 6.6.3.5 additional requirements
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.	5.1 Applies IEC 60601–1 to the non-implantable parts of the active implantable medical device that are connected to or equipped with an electrical power source.	* retained 6.6.3.4, 6.6.3.5 additional requirements
5.7.3 Wherever possible values expressed numerically must be in commonly accepted, standardised units, and understood by the users of the implant.	5.1 Applies IEC 60601–1 to the non-implantable parts of the active implantable medical device that are connected to or equipped with an electrical power source	* retained 6.6.3.4, 6.6.3.5 additional requirements
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.	(See more particular requirements below.)	
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.	(Not applicable to active implantable medical devices.)	—
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.	9.1 Requires markings warning of any radioactive substances.	* retained
	18.1 Requirement for sealed sources.	* retained
	18.2 Requires justification of radiation dose on patient.	* retained
	18.3 Requires radiation dose as low as is possible.	* retained
	28.2 Requires information to be provided about radioactive substances.	* retained
5.8.4 Ionizing radiation	(Not applicable to active implantable medical devices.)	—

Table A.1 *(continued)*

Essential principles from ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of ISO 14708-5 and aspects covered
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.	5.2 Requires implants to be designed according to software life cycle process activities compliant with IEC 62304:2006 and validated.	* retained 6.6.3.4 additional requirements
	19.3 Requires a design analysis and defines the methodology for the analysis.	* retained 6.3 additional requirements
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 life-cycle development, risk management, verification and validation.	5.2 Requires implants to be designed according to software life cycle process activities compliant with IEC 62304:2006 and validated.	* retained 6.6.3.4 additional requirements
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.	19.3 Defines methodology to ensure single fault conditions are not a hazard.	* retained
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.	19.2 Requires power source depletion indicator.	* retained 19.7, 19.8 additional requirements
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.	5.1 Applies IEC 60601–1 to the non-implantable parts of the active implantable medical device that are connected to or equipped with an electrical power source.	* retained 6.6.3.4, 6.6.3.5 additional requirements
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.	5.1 Applies IEC 60601–1 to the non-implantable parts of the ACTIVE IMPLANTABLE MEDICAL DEVICE that are connected to or equipped with an electrical power source.	* retained additional requirements

Table A.1 *(continued)*

Essential principles from ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of ISO 14708-5 and aspects covered
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.	27.1 Defines requirement for electromagnetic immunity.	* replacement
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.	27.1 Defines requirement for electromagnetic immunity.	* replacement
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.	5.1 Applies IEC 60601–1 to the non-implantable parts of the active implantable medical device that are connected to or equipped with an electrical power source.	* retained
	16.1 Sets safety limits for leakage currents from non-implantable parts.	* retained
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 Applies IEC 60601-1:2018 to the non-implantable parts of the active implantable medical device.	* retained
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 Applies IEC 60601-1:2018 to the non-implantable parts of the active implantable medical device.	* retained
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.	5 Applies IEC 60601-1:2018 to the non-implantable parts of the active implantable medical device.	* retained
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.	5.3 Requires usability engineering process be applied to non-implantable parts of the active implantable medical device.	* retained
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.	17.1 Defines requirement for protection from heat.	* retained
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.	10.1 Specifies packaging construction.	* retained

Table A.1 *(continued)*

Essential principles from ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of ISO 14708-5 and aspects covered
15.12 Protection against the risks posed to the patient by energy supplies 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.	19.3 Requires a design analysis and defines the methodology for the analysis.	* retained 6.3 additional requirements
	5.1 Applies IEC 60601–1 to the non-implantable parts of the active implantable medical device that are connected to or equipped with an electrical power source.	* retained
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.	5.1 Applies IEC 60601–1 to the non-implantable parts of the active implantable medical device that are connected to or equipped with an electrical power source.	* retained
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.	13.4 Specifies on-device markings.	* retained 13.5 additional requirements
5.13 Label and instruction 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.	4 Allows use of symbols, abbreviations, and identification colours	* retained
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.	12.3 Requirement that any markings shall be indelible.	* retained
	13.2 Requires implantable parts to be marked with sufficient information to allow for positive identification at the time of implantation.	* retained
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.	—	—

Table A.1 *(continued)*

Essential principles from ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of ISO 14708-5 and aspects covered
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.	—	—
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.	10.4 Requires accompanying documentation to be physically associated with the device.	* retained
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; 3) obtain a paper version of the instructions for use.		
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.	8.1 Requires warnings to be prominent.	* retained
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.	4 Allows use of symbols, abbreviations, and identification colours.	* retained
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.	11.1 Requires identification of manufacturer on sterile pack.	* retained

Table A.1 *(continued)*

Essential principles from ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of ISO 14708-5 and aspects covered
b) The details strictly necessary for a user to identify the implant and its use.	9.3 Requires description of device and model designation on the sales pack.	* retained
	9.4 Requires marking with characteristics sufficient to identify device.	* retained
	9.8 Requires sales pack to bear information about accessories provided.	* retained
	9.10 Requires supplementary description, if 9.3 and 9.4 are inadequate to declare purpose.	* retained
	11.6 Requires description of device and mode designation on the sterile pack.	* retained
	11.7 Requires identification of contents of sterile pack.	* retained
c) The name and address of the manufacturer in a format that is recognizable and allows the location of the manufacturer to be established.	9.2 Requires name and address of manufacturer on the sales pack.	* retained Clause 28 additional requirements
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.	9.2 Requires name and address of manufacturer on the sales pack.	* retained Clause 28 additional requirements
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.	28.7 Requires information about medicinal products which the device is designed to administer	* retained
	28.28 Requires an indication that the device contains medicinal substance derived from human blood or human plasma	* retained
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.	9.3 Requires batch code or serial number on the sales pack.	* retained
	11.6 Requires batch code or serial number on the sterile pack.	* retained
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.	9.7 Requires marking of a “use-before” date.	* retained
	11.5 Requires marking of a “use-by” date.	* retained
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.	9.7 Requires marking and defines format.	* retained
	11.4 Requires marking and defines format.	* retained
i) An indication of any special storage and/or handling condition that applies.	9.11 Requires marking and defines format.	* retained

Table A.1 *(continued)*

Essential principles from ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of ISO 14708-5 and aspects covered
j) If the implant is supplied sterile, an indication of its sterile state and, where appropriate, the sterilization method.	11.2 Requires method of sterilization to be marked.	* retained
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.	8.1 Requires warnings to be prominent.	* retained
	28.12 Requirement for warning notices.	* retained
l) If the implant is intended for single use, an indication of that fact.	28.18 Requires and defines warning notice about reuse of the device.	* retained Clause 28 additional requirements
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.	9.13 Requires marking of special purpose.	* retained
	11.3 Requires marking of special purpose.	* retained
n) If the implant is intended for premarket clinical investigation only, an indication of that fact.	9.13 Requires marking of special purpose.	* retained
	11.3 Requires marking of special purpose.	* retained
o) If the implant is intended for non-clinical research, teaching or testing purposes only, an indication of that fact.	9.13 Requires marking of special purpose.	* retained
	11.3 Requires marking of special purpose.	* retained
p) If the implant is intended for presentation or demonstration purposes only, an indication of that fact.	9.13 Requires marking of special purpose.	* retained
	11.3 Requires marking of special purpose.	* retained
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.	28.1 Requires name and address of manufacturer.	*retained Clause 28 additional requirements
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.	28.1 Requires name and address of manufacturer.	* replacement
c) The implant's intended use/purpose including the intended user (e.g. professional), as appropriate.	28.8 Requires information describing the intended use.	* replacement
d) The performance of the implant intended by the manufacturer.	28.8 Requires information describing the intended use.	* replacement
e) Where the manufacturer has included clinical investigations as part of premarket conformity assessment to demonstrate conformity to the essential principles, a summary of the investigation, outcome data and clinical safety information, or a reference as to where such information can be accessed.	19.4 Requires investigation of unintended effects caused by the device.	* retained

Table A.1 *(continued)*

Essential principles from ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of ISO 14708-5 and aspects covered
f) Any residual risks, contraindications and any expected and foreseeable side effects, including information to be conveyed to the patient in this regard.	28.12 Requires warning notices on hazards arising from interaction.	* replacement
g) Specifications the user requires to use the implant appropriately, for example, if the implant has a measuring function, the degree of accuracy claimed for it.	5.1 Applies IEC 60601–1 to the non-implantable parts of the active implantable medical device.	* retained
h) If the implant contains, or incorporates, a medicinal substance and/or material of biological origin, identification of that substance or material, as appropriate.	28.7 Requires information about medicinal products which the device is designed to administer.	* retained
	28.28 Requires an indication that the device contains medicinal substance derived from human blood or human plasma.	* retained
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). 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.	(Not applicable to active implantable medical devices.)	
j) Any requirements for special facilities, or special training, or particular qualifications of the implant user and/or third parties.	(Not applicable to active implantable medical devices.)	
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:	(Not applicable to active implantable medical devices.)	
— 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.		

Table A.1 *(continued)*

Essential principles from ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of ISO 14708-5 and aspects covered
l) An indication of any special storage and/or handling condition that applies.	7.2 Requires sterile pack to be protected by sales packaging.	* retained
	10.1 Requires packaging to be durable.	* retained
	10.2 Requires packaging to be protected against the effects of humidity.	* retained
	10.3 Requires markings on sales packaging to be indelible.	* retained
	10.4 Requires accompanying documentation to be physically associated with the device.	* retained
	12.3 Requires markings on sales packaging to be indelible.	* retained
	26.2 Requires device to be protected against the effect of temperature changes.	* retained
m) If the implant is supplied sterile, instructions in the event of the sterile packaging being damaged before use.	28.17 Requires instructions on dealing with the contents if the sterile pack has been opened or damaged.	* retained
n) If the implant is supplied non-sterile, the appropriate instructions for sterilization. NOTE 2 Further information is provided in ISO 17664.	(Not applicable because 14.1 requires that active implantable medical device be provided sterile.)	
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.	(Not applicable to active implantable medical devices.)	
p) For implants intended for use together with other implants, medical devices and/or general-purpose equipment:	28.4 Requires information on connector specifications, assembly instructions, and connector performance.	* retained
— 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.	28.5 Requires provision of information on accessories that might be required to facilitate the intended use of the device.	* retained
NOTE 3 Medical devices and equipment intended for use together with the implant include both those designed and manufactured by the implant manufacturer (e.g. associated instruments) and those designed and manufactured by others (e.g. general-purpose equipment).	28.9 Requires information to allow selection of device, accessories and related devices.	* retained
q) If the implant emits hazardous, or potentially hazardous levels of radiation for medical purposes:	9.1 Requires markings warning of any radioactive substances.	* retained

Table A.1 *(continued)*

Essential principles from ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of ISO 14708-5 and aspects covered
— 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;	28.2 Requires information to be provided about radioactive substances.	* retained
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:	28.22 Requires warnings on precautions to avoid adverse environments.	* retained
	28.12 Requires warning regarding known hazards by reciprocal interference.	* replacement
— 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 with 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 with 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.	14.3 Requires investigation of biocompatibility.	* retained

Table A.1 *(continued)*

Essential principles from ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of ISO 14708-5 and aspects covered
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:	28.29 Requires instructions for proper removal and disposal.	* retained
— 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.	28.25 Requires the date of issue or an indication of last revision.	* retained
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.	19.4 Requires investigation of unintended effects caused by the device.	* retained
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.	19.4 Requires that any clinical investigations are conducted according to ISO 14155.	* retained