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Implants for surgery — Active implantable medical devices —

Part 5: Circulatory support devices

Implants chirurgicaux — Dispositifs médicaux implantables actifs —

Partie 5: Appareils annexes circulatoires

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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.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

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.

ISO 14708-5 was prepared by Technical Committee ISO/TC 150, *Implants for surgery*, Subcommittee SC 6, *Active implants*.

ISO 14708 consists of the following parts, under the general title *Implants for surgery — Active implantable medical devices*:

— *Part 1: General requirements for safety, marking and for information to be provided by the manufacturer*

— *Part 2: Cardiac pacemakers*

— *Part 3: Implantable neurostimulators*

— *Part 4: Implantable infusion pumps*

— *Part 5: Circulatory support devices*

— *Part 6: Particular requirements for active implantable medical devices intended to treat tachyarrhythmia (including implantable defibrillators)*

Introduction

This part of ISO 14708 specifies requirements for safety and performance of active implantable circulatory support devices. It is not intended to be used for extracorporeal perfusion devices, cardiomyoplasty, heart restraint devices, and counter-pulsation devices such as extra- or intra-aortic balloon pumps. It amends and supplements ISO 14708-1:2000, hereinafter referred to as ISO 14708-1. The requirements of this part of ISO 14708 take priority over those of ISO 14708-1.

Heart failure (HF) is a major public health problem. It is estimated that worldwide more than 5 million people die per year due to heart failure. The number of newly diagnosed cases is more than 550 000 per year in the USA alone (AHA[13]). In 2001, nearly 53 000 patients in the United States died of HF as a primary cause. Further, heart failure is implicated as a contributing factor in more than 250 000 deaths each year in the USA alone (Yusuf[29]). Particularly at a higher risk for heart failure are the elderly (> 60 years), who account for 70 % of heart failure patients (Haldeman et al[18]), and for whom congestive heart failure is the leading cause of hospitalization. From 1990 to 1999, the annual number of hospitalizations has increased from approximately 810 000 to over 1 million for HF as a primary diagnosis and from 2,4 million to 3,6 million for HF as a primary or secondary diagnosis (Koelling TM et al,[30]). The economic costs are enormous. It has been estimated that in 2005, the total direct and indirect cost of HF in the United States is equal to $27,9 billion (AHA[13]). Worldwide, it is estimated that over $900 billion per year is spent and almost one third of patients are younger than 60. Heart transplantation in recent years has become an effective treatment for end-stage heart failure. Unfortunately the number of donor hearts is limited to just about 3 000 worldwide, available only to a small fraction of patients who need heart transplants. Future drug discoveries and/or biological therapies such as cell regeneration and gene therapy hold promise for the future in the treatment of chronic heart failure. However, as of today, mechanical circulatory devices remain the only alternative to heart transplantation and will continue to be a viable treatment for end-stage heart failure for the foreseeable future.

Within this part of ISO 14708, the following terms are used to amend and supplement ISO 14708-1:

“Replacement”: the clause of ISO 14708-1 is replaced completely by the text of this particular part of ISO 14708.

“Addition”: the text of this particular part is additional to the requirements of ISO 14708-1.

“Amendment”: the clause of ISO 14708-1 is amended as indicated by the text of this particular part of ISO 14708.

“Not used”: the clause of ISO 14708-1 is not applied in this particular part of ISO 14708.

Subclauses, figures, or tables that are additional to those of ISO 14708-1 are numbered starting from 101; additional annexes are lettered AA, BB, etc.

Implants for surgery — Active implantable medical devices —

Part 5: Circulatory support devices

1 Scope

This part of ISO 14708 specifies requirements for safety and performance of active implantable circulatory support devices. It is not applicable to extracorporeal perfusion devices, cardiomyoplasty, heart restraint devices and counter-pulsation devices, such as extra- or intra-aortic balloon pumps.

This part of ISO 14708 specifies 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.

2 Normative references

The following referenced documents are indispensable for the application 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 5198, *Centrifugal, mixed flow and axial pumps — Code for hydraulic performance tests — Precision grade*

ISO 5840, *Cardiovascular implants — Cardiac valve prostheses*

ISO 7198, *Cardiovascular implants —Tubular vascular prostheses*

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

ISO 14155[1], *Clinical investigation of medical devices for human subjects — Good clinical practice*

ISO 14708-1, *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, *Medical devices — Application of risk management to medical devices*

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

IEC 60601-1-1, *Medical electrical equipment — Part 1-1: General requirements for safety — Collateral standard: Safety requirements for medical electrical systems*

1) To be published. (Revision of ISO 14155-1 and ISO 14155-2)

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

IEC 60601-1-8, *Medical electrical equipment — Part 1-8: General requirements for basic safety and essential performance — Collateral Standard: General requirements, tests and guidance for alarm systems in medical electrical equipment and medical electrical systems*

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

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.

3.101
accessory device
separate part of a circulatory support system that is not essential to the primary function of the circulatory support system

NOTE Examples are programming units, monitoring units and alternative power supply units.

3.102
artificial valve
prosthetic valve
component of the circulatory support system that directs the unidirectional flow of the blood into and out of the pump

3.103
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 replacement

3.104
cavitation
sudden formation and collapse of low pressure bubbles in the blood by means of mechanical forces

3.105
clinical study
evaluation of a device in humans

3.106
conduit
component of the circulatory support system that connects the pump to the patient's circulation

3.107
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

3.108
diastolic pressure
arithmetic average of diastolic blood pressure (when the left ventricle is not contracting), over a sufficient number of cycles to filter out cyclic variation, of the minimum aortic pressures in a pulsatile pressure waveform

3.109
dp/dt
time derivative of pressure giving the rate of change of pressure with respect to time

NOTE dp/dt is expressed in millimetres of mercury per second, mmHg/s (kiloPascal per second [kPa/s] in SI units).

3.110
dQ/dt
time derivative of flow giving the rate of change of flow with respect to time

NOTE dQ/dt is expressed in units of litres per minute per second.

3.111
drive line
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.

3.112
durability
ability of an item to perform a required function under given conditions of use and maintenance, until a limiting state is reached

NOTE 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.

3.113
ejection/fill
E/F
ratio between the ejection time period and the filling time period of the blood pump cycle

NOTE E/F is identical to S/D (systolic/diastolic) when related to the natural heart.

3.114
extracorporeal component
component or subsystem of the circulatory support system that is kept external to the patient (outside of the body)

3.115
failure
termination of the ability of an item to perform a required function

NOTE 1 After failure, the item has a fault.

NOTE 2 “Failure” is an event, as distinguished from “fault”, which is a state.

NOTE 3 This concept as defined does not apply to items consisting of software only.

3.116
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 A fault is often the result of a failure of the item itself, but might exist without prior failure.

3.117
fully implantable
implanted circulatory support system with no skin penetrations (i.e. percutaneous lead)

3.118
hazard analysis
identification of hazards and their initiating causes

3.119
labelling
marking
any written, printed, 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

3.120
monitor
component of the circulatory support system that allows data pertaining to the operation of the system to be displayed

3.121
peak flow
maximum flow rate during ejection of blood from a pump into the host circulatory system

3.122
peak pressure
maximum pressure generated by the circulatory support system

3.123
percutaneous lead
lead (electrical or otherwise) that crosses the patient's skin to connect implantable parts of a circulatory support system to extracorporeal parts of the system

3.124
power supply
source of energy

3.125
pulsatile flow
characteristic of the output of a pump where the flow is time-dependent (flow varies with time during one beat)

3.126
pump fill
filling phase of a volume displacement pump

NOTE Diastole is used to describe only the filling phase of the host's native ventricle(s).

3.127
pump output
performance measure for a circulatory support system indicating the volume of blood pumped into the host circulatory system per minute

NOTE The pump output is expressed in litres per minute or its equivalent in other units.

3.128
pump/pulse rate
performance measure for a circulatory support system indicating the number of complete pump cycles per minute

NOTE The pump rate is expressed in beats per minute.

3.129
pump stroke volume
performance measure for a circulatory support system indicating the volume pumped into the host circulatory system per beat by a pump with pulsatile flow

NOTE The pump stroke volume is expressed in millilitres.

3.130
pump volume
volumetric capacity of the pump

3.131
pump displacement
volume displacement
pump that imparts its pumping action by changing the volume of the pumping chamber

EXAMPLE By displacement of a diaphragm or pusher plate.

3.132
reliability
probability that an item can perform a required function under given conditions for a given time interval (t1, t2)

NOTE 1 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 The term “reliability” is also used to denote the reliability performance quantified by this probability [see 191-02-06 of IEC 60050-191 definition of reliability (performance)].

3.133
remote access device
component of the circulatory support system that allows modification and/or monitoring of the controller and the operation of the system

3.134
rotary pump
pump that imparts its pumping action directly on the blood by a rotating mechanism

3.135
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

3.136
safety
freedom from unacceptable risk

[ISO/IEC Guide 51:1999, definition 3.1]

3.137
safety hazard
potentially detrimental effect on the patient, other persons, animals, or the surroundings, arising directly from the circulatory support system

3.138
sales packaging
packaging that protects and identifies the device during storage and handling by the purchaser

NOTE The sales packaging should be enclosed in further packaging, for example a “shipping package”, for delivery.

3.139
stroke volume
amount of blood pumped by the ventricle of the heart in one contraction

3.140
systolic pressure
arithmetic average, over a sufficient number of cycles to filter out cyclic variation, of the peak aortic pressures in a pulsatile pressure waveform

3.141
transcutaneous energy transmission system
TETS
system used to send electrical energy wirelessly into a device implanted inside the body

3.142
total artificial heart
TAH
circulatory support system that replaces the pumping function of a patient's native heart

3.143
ventricular assist system
ventricular assist device
VAS/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 abbreviated terms

This clause of ISO 14708-1 applies.

5 General requirements for non-implantable parts

This clause of ISO 14708-1 applies.

6 Requirements for particular active implantable medical devices

Addition

6.101 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) and where it may be used safely (e.g. hospital, home, ground and/or air transport vehicles). 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.

6.102 System description

6.102.1 General

A comprehensive description of the system should be documented, including discussions on the principle(s) of operation, design consideration(s), system configuration(s), system component(s), and system performance and operating limits.

Design specifications for the complete system include the full range of system operating limits for each parameter (e.g. beat rates, E/F ratio, rotation speeds, power), system operational modes (e.g. manual, automatic), system component configurations (e.g. hospital, home, power sources, optional display, optional subsystems, optional console), alarm thresholds, and all associated tolerances on each of these parameters.

6.102.2 Principle of operation

A discussion of the operating principle of the system should include the blood pumping mechanism, connections to the cardiovascular system, power system, and control mechanisms.

6.102.3 Design consideration

The rationale for key design choices should be given. This should include, but is not limited to, approaches taken to minimize blood component damage, methods for thermal management, choice of drive mechanisms, a power management scheme, reliability considerations, adequacy of anatomic fit, and patient interaction.

6.102.4 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.

6.102.5 System performance and operating limits

The entire performance range of the system shall be given, even if some operation conditions are not expected to be used clinically or might cause the system to malfunction.

6.103 Design analysis

A comprehensive analysis should be performed for the integrated system, the various component configurations, as well as for each system component for all safety and effectiveness issues, including human factors. The *in vitro*, *in vivo*, and clinical testing performed to address each issue should be identified.

6.104 Risk analysis

Risk analysis, part of the risk management process, should 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 (see 19.2).

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

6.105 Human factors

Human factors evaluation should consist of both integrated system testing and subsystem testing. The user interface, both hardware and software, should 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 62366.

6.106 *In vitro* design evaluation and system performance testing

6.106.1 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. 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.

6.106.2 Initial design evaluation of the pump system

6.106.2.1 Pump performance test

The pump performance test shall evaluate the ability of its design to meet the specification. The test shall be conducted using blood or a blood analogue solution that mimics critical characteristics of blood, such as viscosity, temperature and density as they might affect pump performance of the particular devices.

6.106.2.2 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 hemolysis, cavitation, and thrombus formation. Such studies include computational fluid dynamics (CFD) or flow visualization study (see Annex DD.4). These study results should be used for justification of design improvement of the device.

6.106.2.3 Vibration measurement

A vibration test shall be conducted over the entire range of operating speed to ensure that critical speed resonance (induced either mechanically or by magnetic bearing control systems) will not cause unacceptable mechanical instability. It might be necessary to positively restrict the operating speed range to avoid critical speeds.

NOTE For further information on vibration testing, see ISO 14708-1.

6.106.2.4 Cavitation observation

Because cavitation can have highly damaging effects on both the device material surfaces and on the formed elements of the blood and small bubbles are capable of embolising to distal organs, it is essential that cavitation be avoided under all designed operating conditions. Potential cavitation phenomena should be investigated in the laboratory and/or via computational fluid dynamics (CFD) simulation. The critical cavitation conditions, NPSHR (net positive suction head required) shall be provided for rotary devices and dynamic cavitation potential in pulsatile devices (particularly in the prosthetic valves) should be investigated.

NOTE For further information on cavitation in rotary devices, see ISO 5198.

Characteristics of the test fluid might have a significant effect on cavitation behaviour. Justification for the test fluid in terms of its cavitation potential compared to blood should be documented.

6.106.3 System characterization

6.106.3.1 General

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

6.106.3.2 Test set-up

All applicable parameters should be documented and reported.

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 (i.e., 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.

Ventricular assist device (VAD) and total artificial heart (TAH) system performance (e.g. alarms, back-up systems, information displayed, measurement accuracy and precision, and failures) should be monitored and reported as specified in ISO 14708-1 and with alarms conforming to IEC 60601-1-8.

6.106.3.3 Test articles

6.106.3.3.1 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.

6.106.3.3.2 Substitution of device components

If a device component (e.g. biological prosthetic valves, vascular graft or atrial cuff) is substituted by its alternative, justification shall be provided.

6.106.3.4 Test equipment

6.106.3.4.1 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.

6.106.3.4.2 Mock circulatory loop

In vitro models used to appropriately simulate the natural heart, as appropriate, and the vascular compliance and resistance, shall be documented, and justified as to the necessary physiological limits prescribed.

6.106.3.4.3 Physiological limits

Mock circulatory loops shall be appropriate to the intended diseased patient population, and not limited to those ranges found within the “normal” population. For those devices used in conjunction with a patient's native heart, the *in vitro* performance testing shall account for native heart rates, and systolic/diastolic pressures and flows.

6.106.3.4.4 Blood analogue fluid

Fluids used to simulate the properties of human blood shall be described. Fluids used may be Newtonian. 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).

6.106.3.4.5 Test measurement equipment

6.106.3.4.5.1 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.

6.106.3.4.5.2 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, calibrated as appropriate, and validated.

6.106.3.4.5.3 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, error).

6.106.3.5 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 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 DD.2 for more information.

6.106.3.6 Parameters to be measured

The following parameters should be measured depending upon the nature of the blood pump design, but not limited to (see Annex DD.3 for more information):

a) blood pump inlet and outlet pressure waveforms;

b) blood pump outlet flow waveform;

c) average outflow pressure from the pump;

d) average inflow pressure to the pump;

e) average pump outflow;

f) maximum achievable operating limits.

6.106.3.7 Data analysis

Data analysis is necessary to show that the system performance meets the design specifications for the system. This should 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.

6.106.3.8 "Worst case" operating conditions

System characterization data should be evaluated to determine the worst-case modes of operation (power input, pump flow, pressures, battery life, etc.) 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.

6.106.4 System component testing

6.106.4.1 Control and drive units

6.106.4.1.1 External units

Blood pump controlling and driving units that are carried by patients should 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, power requirements).

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

c) Electrical safety requirements, as specified in IEC 60601-1 for life support systems, shall be met.

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

e) The unit alarms should meet the requirements of IEC 60417.

f) The external control and drive unit qualification should also include the following testing:

   1) IEC 60068-1;

   2) IEC 60068-2-64;

   3) IEC 60068-2-27;

   4) IEC 60068-2-32.

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

h) Biocompatibility of materials that might be in contact with the patient's skin shall also be verified.

6.106.4.1.2 Implantable controllers and drivers

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

6.106.4.2 Programming and monitoring units

These devices are for the programming of the system, collecting, storing and displaying information in hospitals and/or home environment. As a part of the Life Supporting system these units shall be tested as described in 6.106.4.1.1. Where appropriate, the test levels shall be documented for the intended use environment (e.g. hospital, home and ambulance).

6.106.4.3 Power supplies

Power supplies (including battery chargers) for the mechanical circulatory devices shall meet safety requirements for medical devices as specified in IEC 60601-1. 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, ambulance).

6.106.4.4 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, 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; charge current, end of charge determination, recharge time, etc;

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) audible 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.

6.106.4.5 Connections and connectors

6.106.4.5.1 Electrical connection

Electrical connections to and from all power supplies, batteries, controllers, and blood pumps should be subjected to pull strength, torsion, flex, drop, permeation test and vibration tests. The connection should be tested for electrical/mechanical integrity, resistance to corrosion, proper connector mating, connector connect/disconnect cycling, and conductivity/resistance both before and after each of the appropriate tests to ensure design specifications are met. Conformance to ISO 14708-1 shall be deemed sufficient.

6.106.4.5.2 Lines

For systems with pneumatic drives, all drive lines to and from the pneumatic supply and the blood pump (the entire gas pathway) should be evaluated for pull strength, torsion, drop, vibration, kink (bend radius), and abrasion. Following this testing, the drive lines should be tested for damage, leakage, and any changes in pressure drop in accordance with design specifications.

6.106.4.5.3 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, torsion, vibration, kink (bend radius), and seal integrity. Connection interfaces should avoid gaps and steps in the flow path that could generate unacceptable levels of microemboli, as assessed by design analysis and in animal trials.

6.106.4.6 Artificial/prosthetic valves

If possible, prosthetic valves within the device should be tested as part of the durability and reliability sections 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 ISO 5840 and a justification shall be provided (see Annex CC).

6.106.4.7 Transcutaneous energy transmission systems

Transcutaneous energy transmission systems (TETS) send power across the intact skin to an implanted system without 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 6.106.4.5.

Specifications should include the following testable parameters:

a) input power;

b) output power;

c) maximum power;

d) efficiency;

e) local temperature rise;

f) operational voltage range;

g) effect of primary/secondary coil alignment;

h) effect of nearby large metal objects.

6.107 Electromagnetic compatibility

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 for life support equipment shall be met. Where appropriate, the test levels shall be documented for the intended use environment (e.g. hospital, home and ambulance).

6.108 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. 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 agents.

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.

6.109 Biocompatibility

All surfaces contacting blood and tissue should be biocompatible as defined in ISO 10993-1.

Detailed protocols, raw data, observations, and discussion and interpretation of the results with respect to the intended use of the system and patient safety should be documented.

For assessment of potential damage to blood cells, *in vitro* haemolysis testing of continuous flow devices in accordance with ASTM F1841 is recommended. Suitable control test pumps for this assessment could be devices with acceptable haemolysis (e.g. clinically used pump model).

6.110 Environmental testing

Environmental testing to the specifications of ISO 14708-1 shall be conducted to demonstrate that the system will perform according to its design specification. If other environmental test standards 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, aircraft and ambulance).

6.111 *In vivo* evaluation

6.111.1 Objective

6.111.1.1 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 around 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.

6.111.1.2 Safety

The purpose is to evaluate biocompatibility of the device in an appropriate animal model. Safety shall be assessed based on thrombogenicity, hemolysis, calcification, end organ dysfunction, infection, corrosion, hermetic integrity, wear, and other biocompatibility evaluations compared to clinically acceptable limits. Calcification may be assessed for specific devices that have biological/polymeric valves and other polymeric moving parts (such as a polyurethane diaphragm).

6.111.1.3 Performance

Performance shall be assessed based on the ability of the device to demonstrate biocompatibility and the device's ability to provide circulatory support as specified by the device developer.

6.111.2 Definition of success or failure

Success or failure of a study shall be defined in objective terms or measurable quantities based upon the intended use and the specified patient population (see Annex CC).

6.111.3 Test articles

The device shall be representative of the final clinical designs. The test records should refer to information that describes the system details and processes used to assemble these devices. All items are identical to the clinical model except where described and justification provided.

6.111.4 Test system

6.111.4.1 Test animals

6.111.4.1.1 General

Animal species, quantity, strain and gender, weight, animal supplier name and address shall be recorded. Animal identification, the individual number that corresponds to an ear tag, cage label or equivalent, shall be recorded so that the history of each individual animal is accurate.

6.111.4.1.2 Choice of animal model

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

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

b) The size of the heart and the dimension of the major blood vessels of the selected species shall be similar to those of a human.

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.

6.111.4.1.3 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 justified for the intended use.

6.111.4.2 Control

Each animal's baseline vital signs and blood measurements are used to assess the changes to the animal's condition. The animal's measured post-operative parameters are compared to preoperative values.

6.111.5 Test equipment

The test institution shall provide detailed equipment information. All measuring equipment shall have calibration records checked according to the laboratory's procedures.

6.111.6 Preoperative animal care

The testing laboratory shall provide animal care protocols (Annex CC).

6.111.7 Implant procedure

Implant protocol shall include the following, but not be limited to:

a) anaesthesia;

b) device specific implantation methods;

c) monitoring and animal management.

6.111.8 Special instructions for early termination

When the implant procedure is considered a failure and early termination is necessary, another animal should be added to the test. 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.

Such animals are autopsied for histopathological examination of major organs. The device is explanted for gross assessment, histological examination and engineering analysis. All findings shall be recorded, including observations and conclusions regarding the early termination of the animal study. All animals used in the development of devices should be reported including those terminated early.

6.111.9 Post-operative care

The test laboratory shall provide standard protocols for post-operative animal care (see Annex CC).

6.111.10 Anticoagulation

Use of anticoagulants should be justified with respect to the intended use of the device and the pharmacological effect of the anticoagulant on the animal. If anticoagulants are used, the anticoagulation protocol shall be provided. The dosage of drugs used and measurements of relevant coagulation parameters shall be fully documented.

6.111.11 Adverse events

Possible adverse events associated with the device include death, device/system failures, bleeding, infection, hemolysis, neurological dysfunction, thromboembolic events, cardiovascular dysfunction or end organ failure. The definitions of adverse events shall be provided (see Annex CC). All adverse events occurring throughout the duration of the study shall be fully documented and adjudicated for device relatedness.

6.111.12 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.

6.111.13 Measurement of physiological parameters

The physiological parameters of the post-operative animal shall be documented during the course of the study (Annex CC).

6.111.14 Blood measurements

6.111.14.1 Timing

Timing of blood collection should be provided during the pre, intra, and post-operative periods throughout the study duration.

6.111.14.2 Blood parameters

Blood measurements shall include standard clinical parameters such as haematology, blood chemistry, plasma free haemoglobin, blood coagulation, and other relevant parameters (see Annex CC). These measurements shall be documented at each time point.

6.111.15 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.

6.111.16 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, and other observations shall be fully documented.

6.111.17 Histological examination

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

6.111.18 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.

6.111.19 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.

6.112 Reliability

System reliability is defined as the probability of a system to perform its function for a specified period of time under stated conditions (for example, the demonstrated reliability of the VAD system shall be X with at least Y confidence for a Z year mission 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) Each system shall be comprised of components of quality and reliability that are appropriate for their application in the system.

c) VAD/TAH systems used for reliability testing shall be sterilized the maximum number of times permitted for normal use and shall be aged appropriately to reflect the specified device shelf-life, unless justification is provided, prior to *in vitro* reliability testing.

d) 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.

e) Numeric reliability specifications (percent reliability) with confidence intervals (percent confidence) shall be defined for performance testing over the desired life of the system.

f) 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 Nelson[21]).

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

h) 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.

i) 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.

j) Important test parameters (such as flow rate) shall be continuously monitored at a frequency sufficient to enable identification of failure incidents.

k) 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.

l) All failures shall be classified (see 19.2.2).

m) Test documentation should describe the type and frequency of collection of test data necessary for assessing the reliability and maintainability. The rationale for the data to be collected shall be documented.

n) As part of the concept of Total Product Lifecycle, reliability data accumulated during clinical trials might require that a parallel life test be initiated should an unexpected failure mode be discovered and/or redesign be performed. Such a parallel test might require different operating parameters and/or revised test articles.

o) All design changes resulting from failure analyses should be justified and assessed as to their effect on system reliability.

p) 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.

q) Tests on VAD/TAH systems designed to operate from a mains power supply or from batteries should include a schedule of battery/mains operation, based on expected usage. If VAD/TAH operation is not affected when different power supplies are used, a justification may be provided to run the VAD/TAH systems from their mains power supply only for the reliability test and to test the alternate power supplies (e.g. batteries) in separate component tests.

r) The reliability test conditions should be designed to replicate the effects of physiological conditions on the tested device (see Annex CC); 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.

s) Cycling of VAD operating conditions is required to simulate physiological states (such as sleeping, normal activity and exercise; see Pantalos[23]) in order to operate the device through a range of clinically relevant operating conditions. Values of these parameters will depend on design input specifications.

6.113 Clinical evaluation

See ISO 14155 for more information on clinical evaluations.

7 General arrangement of the packaging

This clause of ISO 14708-1 applies.

8 General markings for active implantable medical devices

Addition:

8.101 General

The labelling shall provide the healthcare provider with sufficient information on the safety, use, indications, and performance of the system, as well as traceability information. Table 101 shows information that should be included on the external packaging, sterile packaging, and the device accessories, where applicable.

9 Markings on the sales packaging

This clause of ISO 14708-1 applies in addition to the guidelines specified in Table 101.

Table 101 — General labelling guidelines

		Device / accessories (Clause 8)	External packaging (Clause 9)	Sterile packaging (Clause 11)
1	Name/trademark	X	X	X
2	Address of manufacturer or distributor		X	X
3	Description of device		X	X
4	Intended use of device		X	
5	Relevant characteristics		X	
6	Transport/storage requirements		X	
7	Model designation	X	X	X
8	Lot or serial number	X		
9	Month/year of manufacture		X	X
10	Use before date		X	X
11	Method of sterilization			X
12	Sterile condition declaration		X	
13	STERILE marking			X
14	Non-pyrogenic declaration			X
15	Special purpose (custom-made, exclusive for investigational use)		X	X
16	Identify connection with other devices			X
17	Identify package content		X	X
18	Instructions for opening package			X
19	Internal power source ID without surgical op.	X		
20	Power source identification	X		
21	Self-evident visual indications	X		
All labeling should be legible and durable.				

10 Construction of the sales packaging

This clause of ISO 14708-1 applies.

11 Markings on the sterile packaging

This clause of ISO 14708-1 applies in addition to the guidelines specified in Table 101.

12 Construction of the non-reusable packaging

This clause of ISO 14708-1 applies.

13 Markings on the active implantable medical device

This clause of ISO 14708-1 applies.

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

This clause of ISO 14708-1 applies.

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

This clause of ISO 14708-1 applies.

16 Protection from harm to the patient caused by electricity

This clause of ISO 14708-1 applies.

17 Protection from harm to the patient caused by heat

This clause of ISO 14708-1 applies.

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

This clause of ISO 14708-1 applies.

19 Protection from unintended effects caused by the device

This clause of ISO 14708-1 applies except as follows.

Replacement:

19.1 Line power supplies

A circulatory support system should be provided with a line connected power supply system in addition to, or in place of, a battery power system. When a line connected power supply is included, the following shall be considered:

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

b) power status indicator(s) that confirm line connection and the presence of an output power supply; audible warning alarms in the event of line disconnection and/or power source failure;

c) the redundancy of power sources;

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

Line connected power supply systems shall comply with the electrical safety requirements of IEC 60601-1.

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.

19.2 Risk analysis

See ISO 14971.

19.2.1 A circulatory support system shall be designed so that the failure of any single component part, including software programme(s) shall not cause an unacceptable risk. The manufacturer shall predetermine and document design reliability expectations for the system under stated conditions, identifying all safety critical components and assemblies.

19.2.2 A comprehensive risk analysis shall be undertaken for the complete system and for each individual system component, taking into consideration human factors. The risk analysis shall include a top-down analysis (e.g. a hazard analysis, fault tree analysis) a bottom up analysis [e.g. failure mode, effects, and criticality analysis (FMECA)], as well as an analysis for potential use or user error (human factors analysis). The risk analysis shall utilize an appropriate method of classifying the severity of failure modes and the probability of occurrence. All failures shall be classified into one of the five categories:

a) catastrophic failure;

b) critical failure;

c) marginal failure;

d) minor failure;

e) negligible failure.

19.2.3 The risk analysis shall include discussion of methods used to mitigate the criticality of the failure modes. In determining the probability of occurrence of a component or system failure the following shall be defined.

a) Statistical methodology employed in the analysis of the reliability test results.

b) The numeric reliability specification(s) (percent reliability) with confidence intervals (percent confidence), for performance testing over the desired life of the system (e.g. the demonstrated reliability of the heart replacement system shall be X with at least Y confidence for a Z year mission life).

c) Statistical justification for the number of systems tested under controlled conditions (e.g. animal and clinical studies) to demonstrate that the stated reliability specifications are met.

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

19.3 Software verification and validation

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. 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.

20 Protection of the device from damage caused by external defibrillators

This clause of ISO 14708-1 applies.

21 Protection of the device from changes caused by high-power electrical fields applied directly to the patient

This clause of ISO 14708-1 applies.

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

This clause of ISO 14708-1 applies.

23 Protection of the active implantable medical device from mechanical forces

This clause of ISO 14708-1 applies.

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

This clause of ISO 14708-1 applies.

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

This clause of ISO 14708-1 applies.

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

This clause of ISO 14708-1 applies.

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

This clause of ISO 14708-1 applies.

28 Accompanying documentation

This clause of ISO 14708-1 applies except as follows.

Replacement:

28.1 Instructions for use

28.1.1 When placed on the market, each device should be accompanied by instructions for use providing additional information as needed.

a) 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 resterilized, and any restriction on the number of reuses.

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

NOTE This requirement relates only to devices intended by the manufacturer to be reusable. It does not relate to devices which a user might decide to reuse outside the manufacturer's recommendations, e.g. those devices marked as 'single use'.

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

j) 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.

28.1.2 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:

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

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

c) 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, etc.;

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

e) instructions for use shall be included in the packaging for 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.

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

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

h) degree of accuracy claimed for devices with a measuring function.

Annex AA
(informative)

Relationship between the fundamental principles in ISO/TR 14283 and the clauses of this part of ISO 14708

Fundamental principles in ISO/TR 14283	Clauses of ISO 14708-1	Clauses of this part of ISO 14708 and aspects covered
3 General principles		
3.1 The implants should be designed and manufactured in such a way that, when used under the conditions and for the purposes intended, they will not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety.	8.1	Retained.
3.2 The solutions adopted by the manufacturer for the design and construction of the implants should conform to safety principles, taking into account the generally acknowledged state of the art. In selecting the most appropriate solutions, the manufacturer should apply the following principles in the following order: a) eliminate or reduce risks as far as possible (inherently safe design and construction); b) where appropriate, take adequate protection measures, including alarms if necessary, in relation to risks that cannot be eliminated; c) inform users of the residual risks due to any shortcomings of the protection measures adopted.	Note 1	
3.3 The implants should achieve the performance intended by the manufacturer and be designed, manufactured and packaged in such a way that they are suitable for one or more of the functions referred to in 3.1 (of ISO/TR 14283:2004), as specified by the manufacturer.	10.4	Retained.
3.4 When the implant is subjected to stresses which can occur during normal conditions of use, the characteristics and performances referred to in 3.1, 3.2 and 3.3 (of ISO/TR 14283:2004) should not be adversely affected to such a degree that the clinical conditions and safety of the patients and, where applicable, of other persons are compromised during the lifetime of the implant as indicated by the manufacturer.	19.2 19.3 23.1 23.2 23.3 23.4 23.5 23.6 26.1 28.4 28.23	Replacement. Replacement. Retained. Retained. Retained. Retained. Retained. Retained. Retained. Retained. Retained.

Fundamental principles in ISO/TR 14283	Clauses of ISO 14708-1	Clauses of this part of ISO 14708 and aspects covered
3.5 The implants should be designed, manufactured and packed in such a way that their characteristics and performances during their intended use will not be adversely affected during transport and storage, when taking into account the instructions and information provided by the manufacturer.	7.2 10.1 10.2 10.3 12.3 26.2	Retained. Retained. Retained. Retained. Retained. Retained. **8.101** Marking of packaging for special handling during transport.
3.6 Any undesirable side-effect should constitute an acceptable risk when weighed against the performances intended.	19.3 19.4	Replacement. Retained.
4 Specific principles regarding design and construction		
4.1 Chemical, physical and biological properties		
4.1.1 The implants should be designed and manufactured in such a way as to guarantee the characteristics and performances referred to in Clause 3 on general principles. Particular attention should be paid to		
a) the choice of materials used, particularly as regards toxicity and, where appropriate, flammability,	14.3	Retained.
b) the compatibility between the materials used and biological tissues, cells and body fluids, taking into account the intended purpose of the implant.	14.3	Retained.
4.1.2 The implants should be designed, manufactured and packed in such a way as to minimize the risk posed by contaminants and residues to the persons involved in the transport, storage and use of the implants and to the patients, taking into account the intended purpose of the product. Particular attention should be paid to the tissues exposed and to the duration and frequency of exposure.	14.2 14.3	Retained. Retained.
4.1.3 The implants should be designed and manufactured in such a way that they can be used safely with the materials, substances and gases with which they enter into contact during their normal use or during routine procedures. If the implants are intended to administer medicinal products they should be designed and manufactured in such a way as to be compatible with the medicinal products concerned according to the provisions and restrictions governing these products and such that their performance is maintained in accordance with the intended use.	19.5	Retained.
4.1.4 If an implant incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product as defined in 2.7 (of ISO/TR 14283:2004) and which is liable to act upon the body with action ancillary to that of the implant, the safety, quality and usefulness of the substance should be verified, taking into account the intended purpose of the implant.	14.4	Retained.
4.1.5 The implants should be designed and manufactured in such a way as to reduce to a minimum the risks posed by substances leaking from the implant.	25	Retained.

Fundamental principles in ISO/TR 14283	Clauses of ISO 14708-1	Clauses of this part of ISO 14708 and aspects covered
4.1.6 Implants should be designed and manufactured in such a way as to reduce, as much as possible, risks posed by the unintentional ingress of substances into the implant, taking into account the implant and the nature of the environment in which it is intended to be used.	25	Retained.
4.1.7 Implants should be designed and manufactured in such a way as to minimize the risks to the patient or user by the programming and control systems, including software.	19.3	Replacement.
4.2 Infection and microbial contamination		
4.2.1 The implants and manufacturing processes should be designed in such a way as to eliminate or reduce as far as possible the risk of infection to the patient, user and third parties. The design should allow easy handling and, where necessary, minimize contamination of the implant by the patient or vice versa during use.	14.1	Retained.
4.2.2 Tissues of animal origin should originate from animals that have been subjected to veterinary controls and surveillance adapted to the intended use of the tissues. Information on the geographical origin of the animals should be retained by the manufacturer. Processing, reservation, testing and handling of tissues, cells and substances of animal origin should be carried out so as to provide optimal security. In particular, safety with regard to viruses and other transferable agents should be addressed by implementation of validated methods of elimination or viral inactivation in the course of the manufacturing process.	Note 2	Retained.
4.2.3 Implants delivered in a sterile state should be designed, manufactured and packed in protective packaging which provides a microbial barrier to ensure that they are sterile when placed on the market and remain sterile, under the storage and transport conditions stipulated by the manufacturer, until the protective packaging is damaged or opened.	7.1 7.2 10.1 10.2 11.7 11.9 12.1 12.2 14.1	Retained. Retained. Retained. Retained. Retained. Retained. Retained. Retained. Retained.
4.2.4 Implants delivered in a sterile state should be manufactured and sterilized by an appropriate, validated method.	14.1	Retained.
4.2.5 Implants intended to be sterilized should be manufactured in appropriately controlled (e.g. environmental) conditions.	14.1 14.2	Retained. Retained.
4.2.6 Packaging systems for non-sterile implants should keep the product without deterioration at the level of cleanliness stipulated and, if the implants are to be sterilized prior to use, minimize the risk of microbial contamination. The packaging system should be suitable, taking into account the method of sterilization indicated by the manufacturer.	Note 3	—
4.2.7 The packaging and/or label of the implant should distinguish between identical or similar products sold in both sterile and non-sterile conditions.	Note 3	—

Fundamental principles in ISO/TR 14283	Clauses of ISO 14708-1	Clauses of this part of ISO 14708 and aspects covered
4.3 Construction and environmental properties		
4.3.1 If the implant is intended for use in combination with other devices or equipment, the whole combination, including the connection system, should be safe and should not impair the specified performances of the devices. Any restrictions on use should be indicated on the label or in the instructions for use.	9.9 11.8 23.6 28.4 28.5	Retained. Retained. Retained. Retained. Retained.
4.3.2 Implants should be designed and manufactured in such a way as to remove or minimize as far as possible, the following		
a) risk of injury, in connection with their physical features, including the volume/ pressure ratio, dimensional and where appropriate ergonomic features,	15.1 15.2	Retained. Retained.
b) risks connected with reasonably foreseeable environmental conditions, such as magnetic fields, external electrical influences, electrostatic discharge, pressure, temperature or variations in pressure and acceleration,	23.1 23.2 24 25 26.2 27	Retained. Retained. Retained. Retained. Retained. Retained.
c) risks of reciprocal interference with other devices (such as defibrillators or high-frequency surgical equipment) normally used in the investigations or for the treatment given,	20.1 20.2 21 22 28.12 28.13 28.14 28.15	Retained. Retained. Retained. Retained. Retained. Retained. Retained. Retained.
d) risks which may arise where maintenance and calibration are impossible, including (if applicable) excessive increase of leakage currents, ageing of materials used, excess heat generated by the implant, decreased accuracy of any measuring or control mechanism.	17 19.1 19.2	Retained. Replacement. Replacement.
4.3.3 Implants should be designed and manufactured in such a way as to minimize the risks of fire or explosion during normal conditions and fault conditions. By “risks during normal conditions and fault conditions” are meant those risks which have been determined by a risk analysis. Particular attention should be paid to implants whose intended use includes exposure to flammable substances or to substances which could cause combustion.	5	Retained.
4.4 Implants with a measuring function		
4.4.1 Implants with a measuring function should be designed and manufactured in such a way as to provide sufficient accuracy and stability within appropriate limits of accuracy and taking into account the intended purpose of the implant. The limits of accuracy should be indicated by the manufacturer.	5	Retained.
4.4.1.1 The measurements, monitoring and display scale should be designed in accordance with ergonomic principles, taking into account the intended purpose of the implant.	5	Retained.

Fundamental principles in ISO/TR 14283	Clauses of ISO 14708-1	Clauses of this part of ISO 14708 and aspects covered
4.4.1.2 If an implant or its accessories bears instructions required for the operation of the implant or indicates operating or adjustment parameters by means of a visual system, such information must be understandable to the user and, as appropriate, the patient.	13.4 5	Retained. Retained.
4.4.2 The measurements made by implants with a measuring function should be expressed in units conforming to the provisions of the ISO 31 series.	5	Retained.
4.5 Protection against radiation		
4.5.1 General Implants should be designed and manufactured in such a way that exposure of patients, users and other persons to radiation is reduced as low as possible, compatible with the intended purpose, while not restricting the application of appropriate specified levels for therapeutic and diagnostic purposes.	See more particular requirements below.	—
4.5.2 Intended radiation	Note 2	—
4.5.3 Unintended radiation Implants should be designed and manufactured in such a way that exposure of patients, users and other persons to the emission of unintended, stray or scattered radiation is reduced as far as possible.	9.1 18.1 18.2 18.3 28.2	Retained. Retained. Retained. Retained. Retained.
4.5.4 Instructions	Note 2	—
4.6 Ionizing radiation	Note 2	—
4.7 Principles for implants connected to or equipped with an energy source		
4.7.1 General		
4.7.1.1 Implants incorporating electronic programmable systems should be designed to ensure the repeatability, reliability and performance of these systems according to their intended use. In the event of risks (of the system) as determined by a risk analysis for the particular device/system, appropriate means should be adopted to eliminate or reduce as far as possible their risk.	19.3	Replacement.
4.7.1.2 Implants for which the safety of the patients depends on an internal power supply should be equipped with a means of determining the state of the power supply.	19.2	Replacement.
4.7.1.3 Implants should bear, if practical and appropriate, a code by which they and their manufacturer can be unequivocally identified (particularly with regard to the type of implant). It should be possible to read this code, if necessary, without the need for a surgical operation.	13.3 28.6	Retained. Retained.
4.7.1.4 For implants for which the safety of the patients depends on an external power supply, the external power supply should include an alarm system to signal any power failure.	5	Retained.
4.7.1.5 External devices intended to monitor one or more clinical parameters from an implant should be equipped with appropriate alarm systems to alert the user to situations which could lead to death or severe deterioration of the patient's state of health.	5	Retained.

Fundamental principles in ISO/TR 14283	Clauses of ISO 14708-1	Clauses of this part of ISO 14708 and aspects covered
4.7.2 Protection against electrical risks		
4.7.2.1 Implants should be designed and manufactured in such a way as to avoid, as far as possible, the risk of accidental electric shocks during normal conditions and fault conditions provided the implants are installed correctly. By the "risks during normal conditions and fault conditions" are meant those risks which have been determined by a risk analysis for the particular device(s).	5 16.1	Retained. Retained.
4.7.2.2 Active implants should be designed and manufactured in such a way as to minimize the risks connected with the use of energy sources with particular reference, where electricity is used, to insulation, leakage currents and overheating of the devices.	16.2 16.3 17 26.1	Retained. Retained. Retained. Retained.
4.7.3 Protection against mechanical risks		
4.7.3.1 Implants should be designed and manufactured in such a way as to protect the patient and user against mechanical risks, for example those connected with resistance, stability and moving parts.	5	Retained.
4.7.3.2 Implants should be designed and manufactured in such a way as to minimize the risks arising from vibration generated by the implants, taking into account technical progress and the means available for limiting vibration, particularly at source, unless the vibrations are part of the specified performance.	5	Retained.
4.7.3.3 Implants should be designed and manufactured in such a way as to minimize the risks arising from the noise emitted, taking into account technical progress and the means available to reduce noise, particularly at source, unless the noise emitted is part of the specified performance.	5	Retained.
4.7.3.4 Terminals and connectors to electricity, gas or hydraulic and pneumatic energy supplies which the user has to handle should be designed and constructed in such a way as to minimize all possible risks.	5	Retained.
4.7.4 There should be protection against the risks posed to the patient by energy supplies or substances.		
4.7.4.1 Implants should be designed and constructed in such a way that the proper functioning of the programming and control systems, including software, do not jeopardize the safety of the patient and of the user, taking into account the intended use.	19.3	Replacement.
4.7.4.2 Implants designed to supply energy or administer medicinal substances should be designed and constructed in such a way that the flowrate can be set and maintained accurately enough to minimize the risk to the patient.	5	Retained.
4.7.4.3 Implants designed to administer medicinal products should incorporate suitable means to prevent and/or indicate any inadequacies in the flowrate that could pose a danger.	5	Retained.
4.7.4.4 Implants designed to supply energy or administer medicinal substances should be designed and constructed so that suitable means are incorporated to minimize the risk of accidental release of dangerous levels of energy or the medicinal substance.	5	Retained.

Fundamental principles in ISO/TR 14283	Clauses of ISO 14708-1	Clauses of this part of ISO 14708 and aspects covered
4.8 Information supplied by the manufacturer		
4.8.1 Each implant should be accompanied by the information needed to use it safely and to identify the manufacturer, taking into account the training and knowledge of the potential users. This information comprises the details on the label and the data in the instructions for use. As far as practicable and appropriate, the information needed to use the implant safely should be set out on the implant itself and/or on the packaging for each unit or, if appropriate, on the sales packaging. If individual packaging of each unit is not practicable, the information should be set out in the leaflet supplied with one or more implants. Instructions for use should be included in the packaging for every implant.	10.4 12.3	Retained. Retained.
4.8.2 Where appropriate, this information should take the form of symbols. Any symbol or identification colour used should conform to International Standards. If no standards exist, the symbols and colours should be described in the documentation supplied with the implant.	4	Retained.
4.8.3 The label should bear the following particulars:	5	Retained.
a) the name or trade name and address of the manufacturer;	9.2 11.1	Retained. Retained.
b) the details strictly necessary for the user to identify the implant and the contents of the packaging;	9.3 9.4 9.8 9.10 11.6 11.7	Retained. Retained. Retained. Retained. Retained. Retained. **8.101** Requires additional component information on sterile packaging.
c) where appropriate, an indication that the contents of the packaging are sterile (e.g. “STERILE”);	9.5 11.2 11.3	Retained. Retained. Retained.
d) where appropriate, the batch code or the serial number (SN), preceded by an appropriate identification (e.g. “LOT” or “SN” respectively);	9.3 11.6	Retained. Retained.
e) where appropriate, an indication of the date by which the implant should be used;	9.7 11.5	Retained. Retained.
f) an indication that the implant is for single use;	28.18	Retained.
g) if appropriate, any indication of special purpose (e.g. “custom-made device” or “exclusively for clinical investigations”);	9.12 11.10	Retained. Retained.
h) any special storage and/or handling conditions;	9.11	Retained.
i) any special operating instructions;	Note 4.	—
j) any warnings and/or precautions to take;	Note 5.	—
k) for active implants, month and year of manufacture;	9.6 11.4	Retained. Retained.
l) if applicable, method of sterilization.	11.2	Retained.

Fundamental principles in ISO/TR 14283	Clauses of ISO 14708-1	Clauses of this part of ISO 14708 and aspects covered
4.8.4 If the intended purpose of the implant is not obvious to the user, the manufacturer should clearly state it on the label and in the instructions for use.	9.10	Retained.
4.8.5 Wherever reasonable and practicable, the implants and detachable components should be identified, if appropriate in terms of serial numbers or batches, to allow all appropriate actions to be taken following discovery of any potential risk posed by the implants and detachable components.	8.2 13.1 13.2	Retained. Retained. Retained.
4.8.6 If appropriate, the instructions for use should contain the following particulars:		
a) the details referred to in 4.8.3, with the exception of d), e) and k);	28.1 28.3 28.16 28.18 28.21	Replacement. Retained. Retained. Retained. Retained.
b) the performances referred to in 3.3 (of ISO/TR 14283:2004) and any undesirable side-effects;	28.8	Retained.
c) if the implant should be used with or connected to other medical devices or equipment in order to operate as required for its intended purpose, sufficient details of its characteristics to identify the correct implants or equipment to use in order to obtain a safe combination;	28.4 28.5 28.9	Retained. Retained. Retained.
d) all the information needed to verify whether the implant is properly used and can operate correctly and safely, plus, where appropriate, information allowing the lifetime of the energy source to be established;	28.10	Retained.
e) where appropriate, information to avoid specified risks in connection with implantation of the implant;	28.11	Retained.
f) information regarding the risks of reciprocal interference posed by the presence of the implant during specific investigations or treatment;	28.12	Retained.
g) the necessary instructions in the event of damage to the sterile packaging and, where appropriate, details of appropriate methods of resterilization;	28.17	Retained.
h) if implants are supplied with the intention that they be sterilized before use, the instructions for cleaning and sterilization should be such that, if correctly followed, the implant will still comply with the principles in Clause 3 (of ISO/TR 14283:2004);	28.17	Retained.
i) details of any further treatment or handling needed before the implant can be used (sterilization, final assembly, etc.);	Note 3	—
j) in the case of implants emitting radiation for medical purposes, details of the nature, type, intensity and distribution of this radiation.	Note 2	—
The instructions for use should also include details allowing the medical staff to brief the patient on any contra-indications and any precautions to be taken. These details should cover in particular:		
k) precautions to be taken in the event of changes in the performance of the implant;	28.19 28.20	Retained. Retained.

Fundamental principles in ISO/TR 14283	Clauses of ISO 14708-1	Clauses of this part of ISO 14708 and aspects covered
l) precautions to be taken as regards exposure to, in reasonably foreseeable environmental conditions, e.g., magnetic fields, external electrical influences, electrostatic discharge, pressure or variations in pressure, acceleration, thermal ignition sources, etc.;	28.22	Retained
m) adequate information regarding the medicinal product or products which the implant in question is designed to administer, including any limitations in the choice of substances to be delivered;	28.7	Retained.
n) precautions to be taken against any special, unusual risks related to the disposal of the implant;	28.24	Retained.
o) medicinal products incorporated into the implant as an integral part in accordance with 4.1.4 (of ISO/TR 14283:2004);	28.8	Retained.
p) degree of accuracy claimed for implants with a measuring function.	5	Retained.
4.9 Clinical evaluation If conformity with the fundamental principles for implants should be based on clinical data, such data should be established by either:		
a) a compilation of the relevant scientific literature currently available on the purpose intended by the manufacturer, or	19.4	Retained.
b) the results of all the clinical investigations carried out in a way that protects the human subjects and ensures the scientific conduct of the investigation.	19.4	Retained.

NOTE 1 This principle is fundamental to all aspects of an active implantable medical device addressed by ISO 14708.

NOTE 2 Not applicable to active implantable medical devices.

NOTE 3 Not applicable because 14.1 requires that implantable parts of an active implantable medical device be provided sterile.

NOTE 4 For implantable parts of an active implantable medical device, all operating instructions are provided in the accompanying documentation.

NOTE 5 In the general case, warnings and precautions, except for those dealing with special handling conditions [see 4.8.3 h)] should be described in the accompanying documentation instead of on the label.

Annex BB
(informative)

Relationship between the clauses of this part of ISO 14708 and the fundamental principles listed in Annex AA

Clauses of this part of ISO 14708	Fundamental principles of ISO/TR 14283	Clauses of this part of ISO 14708	Fundamental principles of ISO/TR 14283
4	4.8.2	11.3	4.8.3 c)
5	4.4.1, 4.4.1.1, 4.4.1.2, 4.4.2, 4.7.1.4, 4.7.1.5, 4.7.3.1, 4.7.3.2, 4.7.3.3, 4.7.3.4, 4.7.4.2, 4.7.4.3, 4.7.4.4, 4.8.3, 4.8.6 p)	11.4	4.8.3 k)
		11.5	4.8.3 e)
		11.6	4.8.3 b), 4.8.3 d)
6.101	3.3, 4.7.4.2	11.7	4.8.3 b), 4.2.3
6.102	3.3	11.8	4.3.1
7.1	4.2.3	11.9	4.2.3
7.2	3.5, 4.2.3	11.10	4.8.3 g)
8.1	3.1	12.1	4.2.3
8.2	4.8.5	12.2	4.2.3
8.101	3.5	12.3	3.5
9.1	4.5.3	13.1	4.8.5
9.2	4.8.3 a)	13.2	4.8.5
9.3	4.8.3 b), 4.8.3 d)	13.3	4.7.1.3
9.4	4.8.3 b)	13.4	4.4.1.2
9.5	4.8.3 c)	14.1	4.2.1, 4.2.3, 4.2.4, 4.2.5
9.6	4.8.3 k)	14.2	4.1.2, 4.2.5
9.7	4.8.3 e)	14.3	4.1.1 a), 4.1.1 b), 4.1.2
9.8	4.8.3 b)	14.4	4.1.4
9.9	4.3.1	15.1	4.3.2 a)
9.10	4.8.3 b), 4.8.4	15.2	4.3.2 a)
9.11	4.8.3 h)	16.1	4.7.2.1
9.12	4.8.3 g)	16.2	4.7.2.2
10.1	3.5, 4.2.3	16.3	4.7.2.2
10.2	3.5, 4.2.3	17	4.7.2.2, 4.3.2 d)
10.3	3.5	18.1	4.5.3
10.4	3.3, 4.8.1	18.2	4.5.3
11.1	4.8.3 a)	18.3	4.5.3
11.2	4.8.3 c), 4.8.3 l)	19.1	4.3.2 d)

Clauses of this part of ISO 14708	Fundamental principles of ISO/TR 14283	Clauses of this part of ISO 14708	Fundamental principles of ISO/TR 14283
19.2	3.4, 4.3.2 d), 4.7.1.2	28.3	4.8.6 a) [4.8.3 b)]
19.3	3.4, 3.6, 4.1.7, 4.7.1.1, 4.7.4.1	28.4	3.4, 4.3.1, 4.8.6 c)
19.4	3.6, 4.9 a), 4.9 b)	28.5	4.3.1, 4.8.6 c)
19.5	4.1.3	28.6	4.7.1.3
20.1	4.3.2 c)	28.7	4.8.6 m)
20.2	4.3.2 c)	28.8	4.8.6 b), 4.8.6 o)
21	4.3.2 c)	28.9	4.8.6 c)
22	4.3.2 c)	28.10	4.8.6 d)
23.1	3.4, 4.3.2 b)	28.11	4.8.6 e)
23.2	3.4, 4.3.2 b)	28.12	4.3.2 c), 4.8.6 f)
23.3	3.4	28.13	4.3.2 c)
23.4	3.4	28.14	4.3.2 c)
23.5	3.4	28.15	4.3.2 c)
23.6	3.4, 4.3.1	28.16	4.8.6 a) [3.8.3 c)]
24	4.3.2 b)	28.17	4.8.6 g), 4.8.6 h)
25	4.3.2 b)	28.18	4.8.6 a) [4.8.3 f)]
26.1	3.4, 4.7.2.2	28.19	4.8.6 k)
26.2	3.5, 4.3.2 b)	28.20	4.8.6 k)
27	4.3.2 b)	28.21	4.8.6 a) [4.8.3 h)]
28.1	4.8.6 a) [4.8.3 a)]	28.22	4.8.6 l)
28.2	4.5.3	28.23	3.4
		28.24	4.8.6 n)

Annex CC
(informative)

Rationale

CC.1 General

Since cardiac assist systems provide an ongoing life support function in patients with end stage heart failure, cardiac assist systems should be designed to be highly reliable without introduction of risk from poor design and manufacturing, or inappropriately specified parts and components. Systems should therefore be comprised of components of quality and reliability that are appropriate for their application. Some components should require separate testing and/or analysis to demonstrate appropriate reliability for use in the total system. This would include the failure analysis of prototype laboratory devices and those which malfunction in part or in whole during the animal testing phase of design qualification and proving.

The number of systems to be tested under controlled laboratory conditions or during animal studies should be statistically justified to demonstrate that the stated reliability specifications are met.

It is important that the statistical methods employed in the analysis of the reliability test results be adequately described within design documentation.

The definition of failure of the system under test should be clinically relevant.

EXAMPLE Flow rate for a specified duration that results in irreversible organ damage.

Test documentation should describe the type and frequency of collection of test data necessary for assessing reliability and maintainability. The rationale for the data to be collected should also be documented.

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

All design changes resulting from failure analyses should be justified and assessed as to their effect on system reliability.

Laboratory tests and animal studies should identify wear-out failure mechanisms which should provide a base of information for preventative maintenance plans as appropriate to the design.

The random vibration spectrum specified in ISO 14708-1 is excessively strict for devices implanted where viscoelastic damping is significant, such as in the abdomen or thoracic cavity. Dupuis et al[17] have shown that even when undertaking extreme physical activities such as running, horse riding and athletic long jump, the peak accelerations experienced at the subject's head is never greater than 5,7g (running 3,6g, riding 3,6g, long jump 5,7g).

CC.2 Notes on specific clauses and subclauses

6.106.4.6 Artificial/prosthetic valves

Certain circulatory support devices incorporate valves to reduce backflow. In most cases, these are prosthetic heart valves that have already been approved for human implant. The issue is that valves in these support devices are exposed to peak loading and rates of loading greater than in the clinical environment. This non-clinical loading does cause wear not seen in the clinical environment. As a result, ISO 5840, on heart valves, is specifically intended to exclude valves to be used in circulatory support.