INTERNATIONAL STANDARD

ISO 14708-4

Second edition
2022-02

Implants for surgery — Active implantable medical devices —

Part 4: Implantable infusion pump systems

Implants chirurgicaux — Dispositifs médicaux implantables actifs —
Partie 4: Systèmes de pompe à perfusion implantables

Reference number
ISO 14708-4:2022(E)

ISO copyright office
CP 401 • Ch. de Blandonnet 8
CH-1214 Vernier, Geneva
Phone: +41 22 749 01 11
Email: copyright@iso.org
Website: www.iso.org

Published in Switzerland

Contents

Page

Foreword

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

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

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

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

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

This document was prepared by Technical Committee ISO/TC 150, *Implants for surgery,* SC 6, *Active implants,* in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/JTC 16, *Active implantable medical devices,* in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

This second edition cancels and replaces the first edition (ISO 14708-4:2008), which has been technically revised.

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

— the title of this document has been modified;

— 9.4 additions have been deleted;

— 11.101 has been deleted;

— 14.2 replacement has been deleted;

— 14.101 has been deleted;

— 14.5 has been added;

— Clause 17 has been revised;

— 19.2 replacement has been deleted;

— 19.3 replacement has been deleted;

— 19.101 has been deleted;

— 19.7 has been added;

— 23.2 amendment has been deleted;

— Clause 27 has been revised;

— 28.8 additions have been deleted;

— 28.10 additions have been deleted;

— 28.12 addition has been deleted;

— 28.101 through 28.103 has been deleted;

— 28.31 and 28.32 has been added.

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

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

Introduction

An *implantable infusion pump system* is a device that delivers either a constant infusion rate or a variable infusion rate from which a medicinal substance is delivered via an implanted catheter to site-specific locations within the human body. An external programmer might be used to adjust device parameters.

Requirements for physiologic sensing functions of *implantable infusion pump systems* are not included in this edition of this document but might be considered in future editions.

Implants for surgery — Active implantable medical devices —

Part 4: Implantable infusion pump systems

1 Scope

This document specifies particular requirements for active implantable medical devices intended to deliver a medicinal substance to site-specific locations within the human body, to provide basic assurance of safety for both patients and users. It amends and supplements ISO 14708-1:2014. The requirements of this document take priority over those of ISO 14708-1.

This document is applicable to active implantable medical devices intended to deliver medicinal substances to site-specific locations within the human body.

This document is also applicable to some non-implantable parts and accessories of the devices defined in Clause 3.

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

NOTE This document is not intended to apply to non-implantable infusion systems.

2 Normative references

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

ISO 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/TS 10974, *Assessment of the safety of magnetic resonance imaging for patients with an active implantable medical device*

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

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 61000-4-3, *Electromagnetic compatibility (EMC) — Part 4–3: Testing and measurement techniques — Radiated, radio-frequency, electromagnetic field immunity test*

3 Terms and definitions

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

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

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

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

3.1
bolus
specific amount of fluid (dose or volume) delivered once for a prescribed length of time (duration)

3.2
catheter access port
port allowing access to the delivery catheter

3.3
fluid pathway
internal surfaces of the *implantable infusion pump system* (3.4) which are in direct contact with a medicinal substance

Note 1 to entry: This also includes catheters and refill kits.

3.4
implantable infusion pump system
active implantable medical device intended for delivery of a medicinal substance to a specific location within the human body

Note 1 to entry: For purposes of this document, an *implantable infusion pump system* can be a single article, or a set of components and accessories. Not all of these components or accessories might be required to be partially or totally implanted, e.g. programmers.

3.5
infusion rate accuracy
closeness of the true (actual) infusion rate to the programmed rate

3.6
maximum infusion rate
highest rate selectable by the user

3.7
minimum infusion rate
lowest rate selectable by the user

3.8
magnetic resonance conditional
MR conditional
item with demonstrated safety in the MR environment within defined conditions including conditions for the static magnetic field, the time-varying gradient magnetic fields and the radiofrequency fields

[SOURCE: ASTM F2503-20, 3.1.11]

3.9
pump
implantable part of an *implantable infusion pump system* (3.4) containing the *reservoir* (3.12), energy source and, in some cases, control electronics

3.10
refill access port
port allowing access to the *reservoir* (3.12)

3.11
repeatability
ability to consistently deliver the same results over time, under the same conditions

Note 1 to entry: A method for calculating *repeatability* is given in Annex B of ISO 11631:1998.

3.12
reservoir
space designed to hold fluid

3.13
reservoir volume
fluid volume of the *reservoir* (3.12) that can be discharged

3.14
service life
period after implantation when the *implantable infusion pump system* (3.4) remains within stated specifications and characteristics

4 Symbols and abbreviated terms

The text in Clause 4 of ISO 14708-1:2014 applies with the following addition:

DUT device under test

5 General requirements for active implantable medical devices

5.1 General requirements for non-implantable parts

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

5.2 General requirements for software

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

5.3 Usability of non-implantable parts

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

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

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

5.5 General requirements for risk management

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

5.6 Misconnection of parts of the active implantable medical device

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

6 Requirements for particular active implantable medical devices

6.1 Implantable infusion pump system specifications

The specifications (e.g. *infusion rate accuracy* and *repeatability*) stated by the manufacturer in the accompanying documentation (see 28.8) shall be maintained over the *service life* and over the range of environmental conditions and characteristics (e.g. *reservoir volume*) stated by the manufacturer.

NOTE Minimum environmental conditions for atmospheric pressure are specified in Clause 25.

Infusion rate accuracy shall be stated for all selectable rates (including *bolus* rates).

The manufacturer shall provide a plot of *infusion rate accuracy* versus environmental conditions and characteristics (e.g. *reservoir volume*) that affect *infusion rate accuracy*. For variable rate *implantable infusion pump systems,* the plot shall contain curves for *minimum infusion rate*, *maximum infusion rate*, and at least one rate in between the *minimum infusion rate* and *maximum infusion rate*.

The method of computing and determining the *infusion rate accuracy* shall be clearly stated in the accompanying documentation. Environmental test conditions used to establish *infusion rate accuracy* shall also be stated. Environmental conditions and characteristics that affect *infusion rate accuracy* shall be clearly stated in the accompanying documentation.

For all selectable infusion rates, the *repeatability* of the actual rate shall also be stated. The method of computing and determining the stated *repeatability* shall be clearly described in the accompanying documentation.

Compliance is checked by inspection of accompanying documentation and test procedures and reports, supported by the manufacturer's calculations, as appropriate.

6.2 Septum puncture test

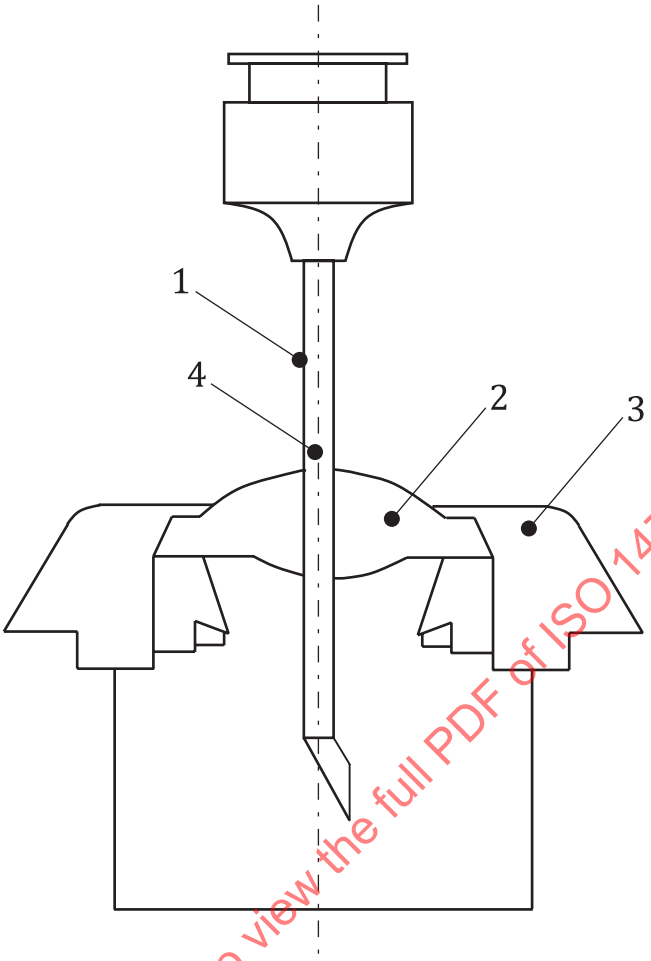
A septum that allows entry to an access port (e.g. *refill access port* or *catheter access port*), shall be able to withstand repeated insertions of a hypodermic needle while maintaining the integrity of the *reservoir* throughout the *service life*.

Test: The DUT shall be conditioned at 37 °C ± 1 °C for not less than 12 h to achieve thermal equilibration. Each *pump* septum shall be punctured randomly using the needle specified by the manufacturer for septum puncture and in accordance with the manufacturer's instructions. The needle used for septum puncture shall be replaced if damage to the needle or the needle's tip is noted by the operator. The needle shall completely penetrate the septum and care should be taken not to damage the needle's tip during the test. Puncturing shall be done using a straight-line motion parallel to the septum's axial centre-line as shown in Figure 1.

Septum leakage shall be determined by immersing the test unit in a water bath at 37 °C ± 1 °C and allowing the temperature of the assembly to stabilize for a minimum of 30 min. Leakage shall be determined by air pressure applied slowly to a pressure of twice the *pump's* maximum operating pressure or a minimum of 276 kPa. The septum's exposed surfaces shall be examined for air bubble leakage for 1 min.

The minimum number of punctures for which the septum maintains integrity shall be stated (see 28.8).

Compliance is checked by inspection of accompanying documentation and test reports.



Key

1 needle
2 septum
3 body
4 centre-line

Figure 1 — Septum puncture test

7 General arrangement of the packaging

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

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

8 General markings for active implantable medical devices

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

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

8.3 If special handling measures have to be taken during transport, the shipping packaging shall be marked accordingly.

Compliance is checked by inspection.

8.4 The permissible environmental conditions for transport shall be marked on the outside of the shipping packaging (see ISO 15223-1).

Compliance is checked by inspection.

9 Markings on the sales packaging

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

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

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

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

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

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

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

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

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

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

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

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

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

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

10 Construction of the sales packaging

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

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

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

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

11 Markings on the sterile pack

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

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

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

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

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

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

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

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

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

12 Construction of the non-reusable pack

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

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

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

13 Markings on the active implantable medical device

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

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

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

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

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

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

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

An appropriate test method shall be established to test the *fluid pathway* in addition to external surfaces.

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

Biological safety evaluation of the *implantable infusion pump system* shall include an evaluation for residual monomers, additives, process contaminants, leachables and extractables of the *fluid pathway* materials.

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

14.5 The implantable parts of the *implantable infusion pump system* labelled for use with a medicinal substance shall demonstrate the medicinal substance is not adversely affected while contained in the device (see 28.31 and 28.32).

Compliance is checked by inspection of manufacturer's documentation and drug stability studies.

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

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

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

16 Protection from harm to the patient caused by electricity

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

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

16.3 The text in 16.3 of ISO 14708-1:2014 does not apply.

17 Protection from harm to the patient caused by heat

17.1 Protection from harm to the patient caused by heat

In the absence of an external influence, an implantable part, not intended to supply heat to the patient, shall comply with at least one of the following conditions (a, b, or c) when implanted, and when in normal operation, including recharge:

a) no outer surface greater than 39 °C,

b) no tissue receives a thermal dose greater than the cumulative equivalent minutes (CEM43) dose thresholds in Table 1, or

c) manufacturer's evidence that a higher temperature rise, than indicated in Table 1, is justified for a particular application.

NOTE 1 Examples of external influences include exposure to magnetic resonance imaging (MRI), electrosurgery, external defibrillation, ultrasound, and electromagnetic fields.

NOTE 2 For additional discussion of CEM43, see Annex B.

As the values in Table 1 represent tissue dose thresholds, the manufacturer's risk assessment shall include an analysis of any effects to the patient due to the time/temperature relationship.

Table 1 — CEM43 dose thresholds for various tissues

Tissue	CEM43 dose threshold
muscle	40
fat	40
peripheral nerve	40
skin	21
bone	16
brain	2
BBB (blood brain barrier)	15

The CEM43 value is calculated using Formula (1):

$$\mathrm{CEM43} = \sum_{i=1}^{n} t_i \times R^{(43-T_i)} \quad (1)$$

where

t_i is the i-th time interval in minutes;

T_i is the average temperature of the tissue in °C during the interval t_i;

R is 0,25 for $T < 43$ °C and 0,5 for $T \geq 43$ °C;

n is the number of samples taken during the heating duration.

Formula (1) is valid for temperatures between 39 °C and 57 °C.

Compliance is checked by inspection of a design analysis provided by the manufacturer, supported by the manufacturer's calculations and data from test studies as appropriate.

17.2 Active implantable medical device intended to supply heat

The text in 17.2 of ISO 14708-1:2014 does not apply.

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

18.1 The text in 18.1 of ISO 14708-1:2014 does not apply.

18.2 The text in 18.2 of ISO 14708-1:2014 does not apply.

18.3 The text in 18.3 of ISO 14708-1:2014 does not apply.

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

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

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

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

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

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

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

19.7 The manufacturer shall establish a reliability plan for the *implantable infusion pump system*. The plan shall include a description of the reliability activities and be linked to the appropriate manufacturing controls and post-market activities to ensure the reliability goals are met. Results of the reliability activities shall be documented.

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

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

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

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

NOTE This test checks for damage to a pump even though it might not have leads and electrodes.

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

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

21.2 The text in 21.2 of ISO 14708-1:2014 does not apply.

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

22.1 Diagnostic ultrasound

The text in ISO 14708-1:2014 applies.

22.2 Magnetic resonance imaging

This subclause only applies to devices that are labelled *MR Conditional*.

Implantable parts of an *implantable infusion pump system* and any non-implantable components and accessories which are labelled *MR Conditional* shall be designed and constructed so that no irreversible change to the device or unacceptable risk to the patient results from exposure to MRI. Additional acceptance criteria are listed in Table 2.

Assessment: For an implantable part intended to be used in patients who undergo a magnetic resonance scan in 1,5 T, cylindrical (circular or elliptical cross-section) bore, whole body MR scanners operating at approximately 64 MHz with whole body coil excitation, the requirements of ISO/TS 10974 shall apply. For non-implantable components and accessories, or as an alternative for implantable parts, the manufacturer may demonstrate safety using similar or equivalent means.

NOTE Use in other MR environments requires manufacturer evaluation by similar or other equivalent means.

If device samples are used for testing, they shall meet all manufacturer specifications after testing is completed.

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

Table 2 — Acceptance criteria for test requirements of ISO/TS 10974

Test requirement	ISO/TS 10974 clause number	Acceptance criteria to protect patient from harm
RF field-induced device heating	8	RF-induced heating of adjacent tissue(s) shall not cause an unacceptable risk. This heating value shall be below a limit supported by scientific rationale linked to clinical significance for the adjacent tissue(s). The value used for assessment could be CEM43, applied RF power, temperature, or any other measurable and relevant parameter. If the temperature rise is ≤2 °C, then no further scientific rationale is needed.
Gradient field-induced device heating	9	Gradient induced heating of adjacent tissue(s) shall not cause an unacceptable risk. This heating value shall be below a limit supported by scientific rationale linked to clinical significance for the adjacent tissue(s). The value used for assessment could be CEM43, applied RF power, temperature, or any other measurable and relevant parameter. If the temperature rise is ≤2 °C, then no further scientific rationale is needed.
Gradient field-induced vibration	10	Gradient induced vibration shall not cause an unacceptable risk.
B_0-induced force	11	Magnetically induced force shall be less than the weight of the device or less than a greater specified value that is supported by a scientific-based rationale that the force of this specified value shall not cause an unacceptable risk.
B_0-induced torque	12	Magnetically induced torque shall be less than the worst case gravity-induced torque, which is defined as the product of the weight of the device and the longest linear dimension or less than a greater specified value supported by a scientific-based rationale that a torque of this specified value shall not cause an unacceptable risk.
Gradient field-induced extrinsic electric potential	13	Induced extrinsic electric potential shall not cause an unacceptable risk.
B_0 field-induced device malfunction	14	Device malfunction shall not cause an unacceptable risk.
RF field-induced device malfunction and RF rectification	15	Device malfunction shall not cause an unacceptable risk.
Gradient field-induced device malfunction	16	Device malfunction shall not cause an unacceptable risk.
Combined fields	17	The combined fields test outcome shall not result in an unacceptable risk.

23 Protection of the active implantable medical device from mechanical forces

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

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

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

23.4 The text in 23.4 of ISO 14708-1:2014 does not apply.

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

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

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

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

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

24.2 The text in 24.2 of ISO 14708-1:2014 does not apply.

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

25.1 The text in 25.1 of ISO 14708-1 applies.

25.2 The text in 25.2 of ISO 14708-1 does not apply.

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

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

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

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

27.1 General

Implantable parts of the *implantable infusion pump system* shall not result in an unacceptable risk because of susceptibility to electrical influences due to external electromagnetic fields.

Assessment: The tests in 27.4 to 27.7 shall be used to assess device behavioural responses in meeting acceptance criteria when exposed to electromagnetic (EM) fields representing the general public environment.

NOTE 1 Immunity test levels in Clause 27 are based on the reasonably foreseeable maximum disturbance levels anticipated to occur in the general public EM environment.

NOTE 2 27.8 can be used for optional characterization regarding the occupational environment.

NOTE 3 The tests in this clause apply only to the implantable parts. Non-implantable parts are covered by IEC 60601-1–2 (see ISO 14708-1, 5.1).

Compliance is checked by review of appropriate documentation listed in Table 3.

27.2 Test conditions

27.2.1 Acceptance criteria

During testing of all subclauses, the acceptance criteria (pass/fail criteria) shall be based on the manufacturer's intended use of the *implantable infusion pump system* and on the risk assessment (5.5), as follows:

— it is expected that the performance intended by the manufacturer will be maintained, and

— no hazardous situations occur that could lead to an unacceptable risk.

Prior to testing, risks shall be identified, and pass/fail criteria defined, taking into account reasonably foreseeable electromagnetic (EM) disturbances that are likely to occur in the general public environment. The risk assessment process could result in hazardous situations being identified. Since actual risk cannot be observed during testing, it is necessary to observe the performance of the device to see if any hazardous situations occur.

Ideally, pass/fail criteria can be measurable or observable during testing. If not, the manufacturer shall specify an alternative method for determining if the DUT meets the required pass/fail criteria during the test. The use of special hardware or software might be necessary.

If pass/fail acceptance criteria are not met, the manufacturer shall substantiate DUT behavioural responses and explain why the overall risk(s) are acceptable (see Table 3). Irreversible changes in performance, that are outside of manufacturer's specifications, are not allowed.

27.2.2 Test configuration

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

Unless specified otherwise by a particular test, the test setup shall include:

— the *pump*;

— catheters, if necessary, to monitor DUT behavioural responses.

27.2.3 Operating functions, modes, and settings

The *implantable infusion pump system* shall be tested using the functions, modes, and settings, consistent with intended use, that are likely to be the most susceptible to EM disturbances. This can be determined using risk analysis, experience, engineering analysis, or pretesting. If the intended use includes wireless communication technology, the wireless communication function shall be evaluated and tested for EMC in accordance with IEC 60601-1-2.

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

27.3 Documentation

The information listed in Table 3 shall be provided by the manufacturer.

Table 3 — Minimum documentation contents

No.	Item
1	Description of the DUT. For example, the device name, model number, manufacturer, and serial number, or other means of identification.
2	Compliance summary statement. Compliance of the DUT with each test.
3	Unexpected effects on the DUT that were observed during or after the application of the test disturbances. If pass/fail acceptance criteria were not met, the manufacturer shall substantiate DUT behavioural responses and explain why the overall risk(s) are acceptable.
4	Description of the intended use, and any unacceptable risks and associated hazardous situations, resulting from the risk assessment.
5	Pass/fail criteria: how it was determined.
6	Pass/fail criteria: how it was monitored during testing.
7	Name and location of the test facility.
8	Names and functions or equivalent identification of the persons authorizing the test report.
9	Applicability/tests not performed. The decision and justification not to perform a measurement or test shall be documented. Deviations and modifications to tests shall also be described.
10	Description of DUT configuration and test setup for each test, including peripherals and auxiliary equipment used. Description may consist of text or graphics (e.g. photographs, drawings, block diagrams) necessary to convey the information.
11	DUT functions, settings, and operating modes listed by test.
12	DUT software/firmware version.
13	Prototype or production version of the DUT. For prototypes, describe the relationship to production versions.
14	Test data that support the compliance determination for each test performed.
15	Documentation of any special hardware or software needed to perform the tests.
16	Test equipment used, including calibration or maintenance dates.
17	DUT modifications needed in order to pass any of the tests and a statement that they will all be incorporated into production units.

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

This test consists of exposing the DUT to a static (DC) magnetic field.

If the requirements of the B_0 field-induced device malfunction test of 22.2 have been met, then this test is not required. However, this test is not a substitute for any test in 22.2.

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

Test procedure: Place the DUT at the centre of the central plane where the magnetic field is the most uniform. The plane of the largest surface area of the DUT is placed parallel to the central plane (this exposes the *pump's* largest surface to the primary magnetic flux lines which are perpendicular to the central plane). This is the only orientation of the DUT that is required.

After placing the DUT, slowly increase the magnetic field from 0 mT to 50 mT. The duration of exposure shall be adequate to assess any influence on the intended use.

Any ancillary equipment that is needed to operate the DUT or monitor its output during the test shall, as much as possible, be selected and positioned to minimize disruption of the uniform field.

Evaluation of test results: The DUT shall meet the immunity pass/fail criteria determined by the manufacturer. It shall maintain performance, without interruption, up to a test level of 1 mT.

27.5 Protection from magnetic fields over the frequency range 16 Hz to 26 MHz

This test consists of exposing the DUT to a radiated AC magnetic field.

Test equipment:

— a field coil capable of generating a magnetic field as shown in Table 4 at a distance of 5 cm;

NOTE 1 The field coils described in IEC 61000-4-39:2017,Clause 6[5] meet these requirements.

— a signal generator/amplifier capable of providing the drive current necessary to produce the required field strength;

— a magnetic field sensor, voltmeter, measurement receiver, and any other equipment necessary for field levelling;

NOTE 2 A procedure for field levelling is described in IEC 61000-4-39:2017, Clause 8[5].

— a saline tank large enough to hold the DUT and made from materials that are non-conducting and non-magnetic (for example, plexiglass); the saline solution shall have a conductivity of approximately 0,1 S/m.

Table 4 — Magnetic field test levels *H*

Frequency range *f*	**Test amplitude before modulation** *H* A/m rms
16 Hz to 25 Hz	4000/*f*
25 Hz to 500 Hz	160
0,500 kHz to 3 kHz	78/*f*
3 kHz to 150 kHz	26
0,150 MHz to 26 MHz	3.9/*f*

Test procedure: The magnetic field test levels, *H*, as shown in Table 4, are specified at the surface of the saline tank.

Place the DUT into the saline bath with at least 1 cm of saline covering the DUT on all sides. Orient the DUT so that the plane of the largest surface area is aligned with the axis of the field coil. This is the only orientation of the DUT that is required. Centre the field coil over the centre of the DUT at a distance of 5 cm from the surface of the saline tank.

The frequency range of the applied test signals shall be stepped from 16 Hz to 26 MHz, pausing to adjust the signal level and to allow enough time for the DUT behavioural response to be observed. The frequencies shown in Table 5 shall be the minimum incremental steps that are tested.

Table 5 — Minimum frequency steps for the radiated magnetic field test

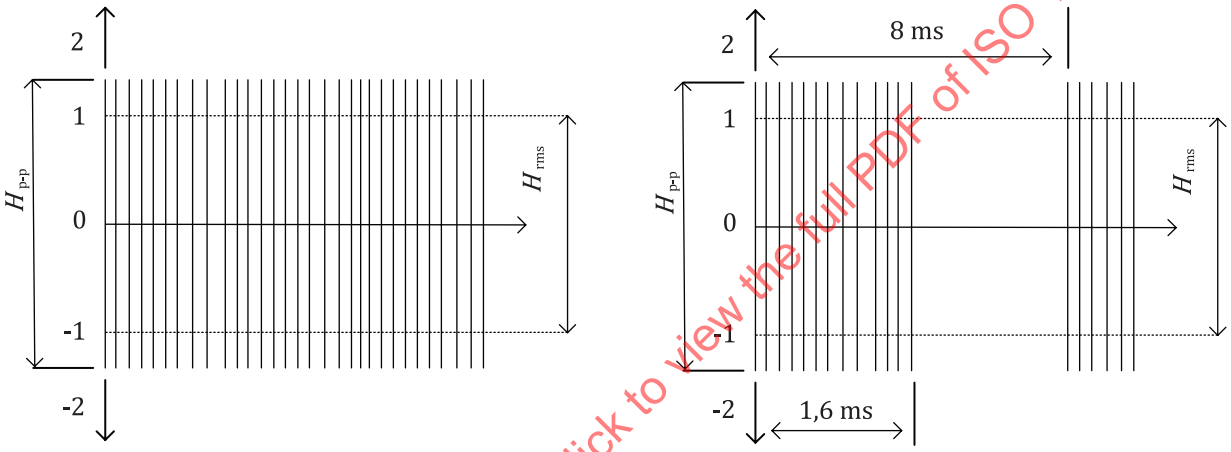
Minimum incremental frequency steps										
Hz	16	25	50	60	100	300	500	800	—	
kHz	1	3	6	10	30	58	85	—	—	
kHz	100	134,2	150	300	500	800	—	—	—	
MHz	1	2	4	6,78	10	13,56	18	21	26	

Over the range of frequencies from 16 Hz to 26 MHz the test signal, *H*, as shown in Table 4, shall be applied as a sinusoidal CW signal at frequencies <50 kHz and as a pulse modulated signal at frequencies from 50 kHz to 26 MHz. See Table 6. An example of 125 Hz, 20 % duty cycle modulation is shown in Figure 2.

Table 6 — Pulse modulation rates to be applied

Frequency range *f*	Pulse modulation
<50 kHz	CW
50 kHz to 26 MHz[a]	125 Hz, 20 % duty cycle rectangle wave
134,2 kHz	2,1 kHz, 50 % duty cycle square wave
13,56 MHz	50 kHz, 50 % duty cycle square wave

[a] Includes 134,2 kHz and 13,56 MHz.



a) Unmodulated test signal **b) Pulse modulated test signal**

Key

H_{p-p} peak to peak value of test signal

H_{rms} rms value of test signal

Figure 2 — Example of 125 Hz, 20 % pulse modulation

Any ancillary equipment that is needed to operate the DUT or monitor its output during the test shall, as much as possible, be selected and positioned to minimize disruption of the uniform field.

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

27.6 Protection from EM disturbances over the frequency range 80 MHz to 2,7 GHz

This test consists of exposing the DUT to a radiated electric field.

Test equipment:

— equipment as specified in IEC 61000-4-3 for the radiated electric field; the equipment shall be capable of producing an electric field of 14 V/m rms, before modulation, at the surface of the saline tank;

— a saline tank large enough to hold the DUT and made from materials that are non-conducting and non-magnetic (e.g. plexiglass); the saline solution shall have a conductivity of approximately 0,1 S/m.

Test procedure: Use the setup and procedure as specified in IEC 61000-4-3 unless modified within this subclause. A uniform field area (UFA) of 0,5 m × 0,5 m should be used.

Place the DUT into the saline bath with at least 1 cm of saline covering the DUT on all sides. Orient the DUT so that the plane of the largest surface area faces the antenna. This is the only orientation of the DUT that is required.

The test shall be performed using two antenna polarizations, vertical and horizontal.

The frequency range of the applied test signals shall be swept or stepped from 80 MHz to 2,7 GHz, pausing to adjust the signal level and to allow enough time for the DUT behavioural response to be observed. If stepped, the step size shall not exceed 5 % of the preceding frequency.

Over the range of frequencies from 80 MHz to 2,7 GHz the applied test level shall be 14 V/m rms, before modulation. Test signals shall be 80 % amplitude modulated with a 1 kHz sinewave.

NOTE IEC 61000-4-3 provides a definition of the test signal level and waveshapes.

Any ancillary equipment that is needed to operate the DUT or monitor its output during the test shall, as much as possible, be selected and positioned to minimize disruption of the uniform field.

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

27.7 Protection from proximity fields due to RF wireless communications equipment

Repeat the test of 27.6 for the frequencies and modulations indicated in Table 7.

Table 7 — Proximity field test frequencies and modulations

Test frequency MHz	Pulse modulation[a]
385	18 Hz
450	18 Hz
710	217 Hz
745	217 Hz
780	217 Hz
810	18 Hz
870	18 Hz
930	18 Hz
1 720	217 Hz
1 845	217 Hz
1 950	217 Hz
2 450	217 Hz
6 000	217 Hz

[a] All test frequencies are pulse modulated using a 50 % duty cycle square wave.

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

27.8 Optional characterization testing

27.8.1 General

The test levels in this subclause provide a higher level of evaluation of immunity equivalent to ICNIRP occupational reference levels.

27.8.2 Characterization based on magnetic fields over the frequency range 16 Hz to 26 MHz

Perform the test as described in 27.5 substituting the magnetic field test levels in Table 4 with the test levels in Table 8.

For this test, modulation is not required.

Table 8 — Optional magnetic field test levels *H*

Frequency range *f*	Test amplitude *H* A/m rms
16 Hz to 25 Hz	20 000/*f*
25 Hz to 300 Hz	800
0,300 kHz to 3 kHz	240/*f*
3 kHz to 150 kHz	80
0,150 MHz to 26 MHz	12/*f*

27.8.3 Characterization based on EM disturbances over the frequency range 80 MHz to 2,7 GHz

Perform the test as described in 27.6 using a test level of 32 V/m over the range of frequencies from 80 MHz to 200 MHz. The test may be performed using the same frequency steps as used for 27.6.

For this test, modulation is not required.

NOTE It is not necessary to test above 200 MHz. The test level from 27.6 exceeds the levels of internal electric fields that would occur from ambient ICNIRP occupational levels.

28 Accompanying documentation

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

28.2 The text in 28.2 of ISO 14708-1:2014 does not apply.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

28.22 The accompanying documentation shall warn of precautions to be taken to prevent adverse effects to the patient due to specific adverse environmental conditions (e.g. electromagnetic interference, extreme temperature, variations of pressure).

Compliance is checked by inspection.

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

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

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

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

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

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

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

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

28.31 The manufacturer shall state in the accompanying documentation the duration of time that the medicinal substance is not adversely affected while in the device under labelled conditions.

28.32 The manufacturer shall state in the accompanying documentation the criteria used to establish that the medicinal substance is not adversely affected while in the device. These criteria shall include

at minimum, safety (e.g. impurity) and efficacy (e.g. potency, bio-activity) consistent with the medicinal substance labelling.

Annex A
(informative)

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

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

Essential principles, with clause numbers, of ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of this document and aspects covered
5 Essential principles		
5.1.1 Implants must be designed and manufactured in such a way that, when used under the conditions and for the purposes intended and, where applicable, by virtue of the technical knowledge, experience, education or training, and the medical and physical conditions of intended users, they will perform as intended by the manufacturer and not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which can be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety.	(This principle is fundamental to all aspects of an active implantable medical device addressed by the ISO 14708 series.) 5.3 Requires usability engineering process be applied to non-implantable parts of the active implantable medical device. 5.5 Requires parts of an ISO 14971-compliant risk management process to be applied.	* retained
5.1.2 The solutions adopted by the manufacturer for the design and manufacture of the implants must conform to safety principles, taking account of the generally acknowledged state of the art. When risk reduction is required, the manufacturer must control the risks so that the residual risk associated with each hazard is judged acceptable. The manufacturer must apply the following principles in the priority order listed: — identify known or foreseeable hazards and estimate the associated risks arising from the intended use and foreseeable misuse; — eliminate risks as far as reasonably practicable through inherently safe design and manufacture; — reduce as far as reasonably practicable the remaining risks by taking adequate protection measures, including alarms; — inform users of any residual risks.	(This principle is fundamental to all aspects of an active implantable medical device addressed by the ISO 14708 series. This approach is particularly applicable to the requirements in Clauses 14, 19, and 21.) 5.4 Requires the manufacturer to provide information security when communication with the implantable part is through wireless communication channels. 5.5 Requires parts of an ISO 14971-compliant risk management process to be applied.	* retained
5.1.3 Implants must achieve the performance intended by the manufacturer and be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose.	(This principle is fundamental to all aspects of an active implantable medical device addressed by the ISO 14708 series.)	* retained

Table A.1 *(continued)*

Essential principles, with clause numbers, of ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of this document and aspects covered
5.1.4 The characteristics and performances referred to in 5.1.1, 5.1.2 and 5.1.3 must not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the implant, as indicated by the manufacturer, when the implant is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer's instructions.	19.2 Requires power source depletion indicator.	* retained
	19.3 Defines the methodology to ensure single fault conditions are not a hazard.	* retained
	23.1 Defines drop test for non-implantable parts.	* replacement
	23.2 Defines vibration test for patient carried parts.	* retained
	23.3 Sets test of tensile strength (e.g. leads).	* retained
	23.4 Requires strain relief (e.g. leads).	* does not apply
	23.5 Requires fatigue resistance (e.g. leads).	* retained
	23.6 Requires connections to be reliable.	* retained
	26.1 Requires protection from heat from powered non-implantable parts.	* retained
	28.4 Requires disclosure of maximum proven connector retention strength.	* retained
	28.23 Requires warning against patient entry into hazardous environments.	* retained
5.1.5 Implants must be designed, manufactured and packaged in such a way that their characteristics and performances during their intended use will not be adversely affected by transport and storage conditions (e.g. fluctuations of temperature and humidity) taking account of the instructions and information provided by the manufacturer.	7.2 Requires sterile pack to be protected by sales packaging.	* retained
	10.1 Requires packaging to be durable.	* retained
	10.2 Requires packaging to be protected against the effects of humidity.	* retained
	10.3 Requires markings on the sales package to be indelible.	* retained
	10.4 Requires accompanying documentation to be physically associated with the device.	* retained
	12.3 Requires markings on the sterile pack to be indelible.	* retained
	26.2 Requires device to be protected against the effect of temperature changes.	* retained
5.1.6 All known and foreseeable risks, and any undesirable effects, must be minimised and be acceptable when weighed against the benefits of the intended performance of implants during normal conditions of use.	19.3 Defines the methodology to ensure single fault conditions are not a hazard.	* retained
	19.4 Requires investigation of unintended effects caused by the device.	* retained 19.7 additional requirements

Table A.1 *(continued)*

Essential principles, with clause numbers, of ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of this document and aspects covered
5.2 Specific principles regarding design and construction		
5.2.1 Chemical, physical and biological properties		
5.2.1 The implants must be designed and manufactured in such a way as to ensure the characteristics and performance referred to in 5.1. Particular attention must be paid to: — the choice of materials used, particularly as regards toxicity and, where applicable, flammability; — the compatibility between the materials used and biological tissues, cells, and body fluids taking account of the intended purpose of the device; — the choice of materials used, reflecting, where appropriate, matters such as hardness, wear and fatigue strength.	14.3 Requires investigation of biocompatibility.	* retained; additional requirement
5.2.2 The implants must be designed, manufactured and packaged in such a way as to minimize the risk posed by contaminants and residues to the persons involved in the transport, storage and use of the implants and to patients, taking account of the intended purpose of the implant. Particular attention must be paid to tissues exposed and to the duration and frequency of exposure.	14.2 Defines test for particulate contamination.	* retained; additional requirement
	14.3 Requires investigation of biocompatibility.	* retained; additional requirement
5.2.3 The implants must be designed and manufactured in such a way that they can be used safely with the materials, substances and gases with which they enter into contact during their normal use or during routine procedures; if the implants are intended to administer medicinal products they must be designed and manufactured in such a way as to be compatible with the medicinal products concerned according to the provisions and restrictions governing these products and that their performance is maintained in accordance with the intended use.	19.5 Demonstrate compatibility with medicinal substances.	* retained
5.2.4 The implants must be designed and manufactured in such a way as to reduce as far as reasonably practicable and appropriate the risks posed by substances that can leach or leak from the implant. Special attention must be given to substances which are carcinogenic, mutagenic or toxic to reproduction.	25.1 Requires implanted parts to withstand pressure changes.	* retained 25.2 does not apply
5.2.5 The implants must be designed and manufactured in such a way as to reduce as far as reasonably practicable and appropriate risks posed by the unintentional ingress or egress of substances into or from the implant taking into account the implant and the nature of the environment in which it is intended to be used.	25.1 Requires implanted parts to withstand pressure changes.	* retained

Table A.1 *(continued)*

Essential principles, with clause numbers, of ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of this document and aspects covered
5.2.6 The implants must be designed and manufactured in such a way as to reduce as far as reasonably practicable and appropriate risks posed by insufficient cleanliness of the implant. Risks posed by insufficient cleanliness include risks posed by bacterial endotoxins, pyrogens and particulate contaminates.	14.1 Requires device to be supplied sterile.	* retained
5.3 Infection and microbial contamination		
5.3.1 The implants and manufacturing processes must be designed in such a way as to eliminate or to reduce as far as reasonably practicable and appropriate the risk of infection to patients, users and, where applicable, other persons. The design must: — allow easy handling, and, where necessary: — reduce as far as reasonably practicable and appropriate either any microbial leakage from the implant or microbial exposure during use, or both; — prevent microbial contamination of the implant, by the patient, user or other person.	14.1 Requires device to be supplied sterile.	* retained
5.3.2 Implants labelled as having a special microbiological state must be designed, manufactured and packaged to ensure they remain so when placed on the market and remain so under the transport and storage conditions specified by the manufacturer.	7.1 Requires device to be supplied in non-reusable pack.	* retained
	7.2 Requires sterile pack to be protected by sales packaging.	* retained
	10.1 Requires packaging to be durable.	* retained
	10.2 Requires packaging to be proof against the effects of humidity.	* retained
	11.7 Requires contents of sterile pack to be declared or visible.	* retained
	11.9 Requires the sterile pack to be marked with the instructions for opening it.	* retained
	12.1 Applies ISO 11607 to the reusable pack.	* retained
	12.2 Shall be apparent if the sterile pack has been opened.	* retained
	14.1 Requires device to be supplied sterile.	* retained
5.3.2 Implants labelled as having a special microbiological state must be designed, manufactured and packaged to ensure they remain so when placed on the market and remain so under the transport and storage conditions specified by the manufacturer.	(Not applicable because 14.1 requires that implantable parts of an active implantable medical device be provided sterile.)	—

Table A.1 *(continued)*

Essential principles, with clause numbers, of ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of this document and aspects covered
5.3.3 Implants delivered in a sterile state must be designed, manufactured and packaged in a non-reusable pack, and/or according to appropriate procedures, to ensure that they are sterile when placed on the market and remain sterile, under the transport and storage conditions indicated by the manufacturer, until the protective packaging is damaged or opened.	7.1 Requires device to be supplied in non-reusable pack	* retained
	7.2 Requires the sterile pack to be protected by sales packaging.	* retained
	10.1 Requires the packaging to be durable.	* retained
	10.2 Requires the packaging to be proof against the effects of humidity.	* retained
	11.7 Requires the contents of sterile pack to be declared or visible.	* retained
	11.9 Requires the sterile pack to be marked with the instructions for opening it.	* retained
	12.1 Applies ISO 11607-1 to the reusable pack.	* retained
	12.2 Shall be apparent if the sterile pack has been opened.	* retained
	14.1 Requires the device to be supplied sterile.	* retained
5.3.4 Implants labelled either as sterile or as having a special microbiological state must have been processed, manufactured and, if applicable, sterilized by appropriate, validated methods.	—	—
5.3.5 Implants intended to be sterilized must be manufactured in appropriately controlled (e.g. environmental) conditions.	14.1 Requires device to be supplied sterile.	* retained
	14.2 Defines test for particulate contamination	* retained; additional requirement
5.3.6 Packaging systems for non-sterile implants must maintain the integrity and cleanliness of the product and, if the implants are to be sterilized prior to use, minimize the risk of microbial contamination; the packaging system must be suitable taking account of the method of sterilization indicated by the manufacturer.	(Not applicable because the subclause requires that the implantable parts of an active implantable medical device be provided sterile.)	—
5.3.7 The labelling of the implant must distinguish between identical or similar products placed on the market in both sterile and non-sterile condition.	(Not applicable because the subclause requires that the implantable parts of an active implantable medical device be provided sterile.)	—
5.4 Implants incorporating a substance considered to be a medicinal product or drug		
5.4.1 This subclause is not intended to provide guidance on “combination products” as a whole since definitions have yet to be harmonized and practice varies between different jurisdictions.		

Table A.1 *(continued)*

Essential principles, with clause numbers, of ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of this document and aspects covered
5.4.2 Where an implant incorporates, as an integral part, a substance which, if used separately, might be considered to be a medicinal product/drug as defined in the relevant legislation that applies within that jurisdiction and which is liable to act upon the body with action ancillary to that of the device, the safety, quality and performance of the implant as a whole must be verified, as well as the safety, quality and efficacy of the substance in the specific application.	14.4 Requirement for quality and safety of incorporated medicinal substances.	* retained
5.5 Implants incorporating materials of biological origin		
5.5.1 This subclause is not intended to provide guidance on "combination products" as a whole since definitions have yet to be harmonized and practice varies between different jurisdictions.		
5.5.2 In some jurisdictions, implants incorporating tissues, cells and substances of animal origin might be considered medical devices. In this case, such tissues, cells and substances should originate from animals that have been subjected to veterinary controls and surveillance adapted to the intended use of the tissues. National regulations can require that either the manufacturer or the Regulatory Authority, or both, retain information on the geographical origin of the animals. Processing, preservation, testing and handling of tissues, cells and substances of animal origin must be carried out so as to provide optimal safety for patients, users and, where applicable, other persons. In particular, safety with regard to viruses and other transmissible agents (e.g. such as prions) must be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process.	(Not applicable to *active implantable medical devices*)	—
5.5.3 In some jurisdictions, implants incorporating human tissues, cells and substances might be considered medical devices. In this case, either the selection of sources, donors or substances of human origin, or both, the processing, preservation, testing and handling of tissues, cells and substances of such origin must be carried out so as to provide optimal safety for patients, users and, where applicable, other persons. In particular, safety with regard to viruses and other transmissible agents must be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process.	(Not applicable to *active implantable medical devices*.)	—

Table A.1 *(continued)*

Essential principles, with clause numbers, of ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of this document and aspects covered
5.5.4 In some jurisdictions. implants incorporating cells and substances of microbial origin might be considered medical devices. In this case, processing, preservation, testing and handling of cells and substances must be carried out so as to provide optimal safety for patients, users and, where applicable, other persons. In particular, safety with regard to viruses and other transmissible agents must be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process.	(Not applicable to *active implantable medical devices*.)	—
5.6 Environmental properties		
5.6.1 If the implant is intended for use in combination with other devices or equipment the whole combination, including the connection system must be safe and must not impair the specified performance of the implants. Any restrictions on the use applying to such combinations must be indicated either on the label or in the instructions for use, or both. Connections which the user has to handle, such as fluid, gas transfer or mechanical coupling, must be designed and constructed in such a way as to minimize all possible risks from incorrect connection.	9.9 Requires the implantable connectors to be identified on sales pack.	* retained
	11.8 Requires the implantable connectors to be identified on sterile pack.	* retained
	23.6 Requires the connector retention force to be specified.	* retained
	28.4 Requires disclosure of maximum proven connector retention strength.	* retained
	28.5 Requires the provision of information on accessories that might be required to facilitate the intended use of the device.	* retained
5.6.2 Implants must be designed and manufactured in such a way as to remove or reduce as far as reasonably practicable and appropriate:		
5.6.2.1 The risk of injury to the patient, user or other persons in connection with their physical and ergonomic features;	15.1 Sets the requirement for the surfaces of non-implantable parts.	* retained
	15.2 Requires the implantable parts to have appropriate physical form.	* retained
5.6.2.2 The risk of use error due to the ergonomic features, human factors and the environment in which the implant is intended to be used;	5.3 Requires the usability engineering process be applied to non-implantable parts of the active implantable medical device.	* retained
	5.5 Requires the parts of an ISO 14971-compliant risk management process to be applied.	* retained

Table A.1 *(continued)*

Essential principles, with clause numbers, of ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of this document and aspects covered
5.6.2.3 Risks connected with reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, temperature or variations in pressure and acceleration;	23.1 Defines the drop test for non-implantable parts.	* replacement
	23.2 Defines the vibration test for patient carried parts.	* retained
	24.1 Defines the electrostatic discharge test for non-implantable parts.	* replacement
	25.1 Requires the implanted parts to be proof against pressure changes.	* retained
	26.2 Requires the implantable devices to be undamaged by extremes of temperature in transit.	* retained
	27.1 Defines the requirement for electromagnetic immunity.	* replacement 27.2, 27.3, 27.4, 27.5, 27.6, 27.7, 27.8 additional requirements
5.6.2.4 The risks associated with the use of the implant when it comes into contact with materials, liquids, and gases to which it is exposed during normal conditions of use;	19.3 Requires a design analysis and defines the methodology for the analysis.	* retained
5.6.2.5 The risk associated with the possible negative interaction between software and the environment within which it operates and interacts;	19.3 Requires a design analysis and defines the methodology for the analysis.	* retained
5.6.2.6 The risks of accidental penetration of substances into the implant;	19.3 Requires a design analysis and defines the methodology for the analysis.	* retained
5.6.2.7 The risks of reciprocal interference with other devices normally used in the investigations or for the treatment given;	20.1 Requires the defibrillation protection of external ECG leads.	* retained
	20.2 Defines test to prove defibrillation protection of implanted device.	* does not apply
	21 Requires protection against, for example, diathermy.	* 21.1 retained * 21.2 does not apply
	22 Requires protection against, for example, diagnostic ultrasound.	* retained * 22.2 additional requirements
	28.12 Requirement for warning notices.	* retained
	28.13 Requires warning about monitoring device in case of, for example, diathermy.	* retained
	28.14 Requires a warning not to expose device to therapeutic levels of ultrasound.	* retained
	28.15 Requires a warning about the effect of therapeutic irradiation on implanted devices.	* retained

Table A.1 *(continued)*

Essential principles, with clause numbers, of ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of this document and aspects covered
5.6.2.8 Risks arising where maintenance or calibration are not possible, including from: — ageing of materials used, — loss of accuracy of any measuring or control mechanism, — excessive increase of leakage currents, — excess heat generated by the implant.	17.1 Requires the investigation of local heating caused by faulty implanted device.	* replacement
	17.2 Requires that the supply heat be investigated.	* does not apply
	19.1 Requires a design analysis.	* retained
	19.2 Requires the power source depletion indicator.	* retained
5.6.3 Implants must be designed and manufactured in such a way as to minimize the risks of fire or explosion during normal use and in single fault condition. Particular attention must be paid to implants whose intended use includes exposure to or use in association with flammable substances or substances which could cause combustion.	5 Applies IEC 60601-1 to the NON-IMPLANTABLE PARTS of the active implantable medical device.	* retained
5.6.4 Implants must be designed and manufactured in such a way that adjustment, calibration, and maintenance, where such is necessary to achieve the performances intended, can be done safely.	17.1 Requires the investigation of local heating caused by the implanted device in normal operation or in any single component failure.	* replacement
	19.1 Requires a design analysis.	* retained
	19.2 Requires the power source depletion indicator.	* retained
5.6.5 Implants must be designed and manufactured in such a way as to facilitate the safe disposal of any waste substances.	28.29 Requires the information on proper disposal of the device.	* retained
5.7 Implants with a diagnostic or measuring function		
5.7.1 Diagnostic implants and implants with a measuring function, must be designed and manufactured in such a way as to provide sufficient accuracy, precision and stability for the intended purpose of the implant, based on appropriate scientific and technical methods. The limits of accuracy must be indicated by the manufacturer.	5.1 Applies IEC 60601–1 to the non-implantable parts of the *active implantable medical device* that are connected to or equipped with an electrical power source.	* retained
5.7.2 Any measurement, monitoring or display scale used in association with an implant must be designed in line with ergonomic principles, taking account of the intended purpose of the implant.	5.1 Applies IEC 60601–1 to the non-implantable parts of the *active implantable medical device* that are connected to or equipped with an electrical power source.	* retained
5.7.3 Wherever possible values expressed numerically must be in commonly accepted, standardised units, and understood by the users of the implant.	5.1 Applies IEC 60601–1 to the non-implantable parts of the *active implantable medical device* that are connected to or equipped with an electrical power source.	* retained

Table A.1 *(continued)*

Essential principles, with clause numbers, of ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of this document and aspects covered
5.8 Protection against radiation		
5.8.1 General Implants must be designed and manufactured and packaged in such a way that exposure of patients, users and other persons to any emitted radiation must be reduced as far as reasonably practicable and appropriate, compatible with the intended purpose, while not restricting the application of appropriate specified levels for therapeutic and diagnostic purposes.	(See more particular requirements below.)	
5.8.2 Intended radiation Where implants are designed to emit hazardous, or potentially hazardous, levels of radiation necessary for a specific medical purpose the benefit of which is considered to outweigh the risks inherent in the emission, it must be possible for the user to control the emissions. Such implants must be designed and manufactured to ensure reproducibility of relevant variable parameters within an acceptable tolerance.	(Not applicable to *active implantable medical devices*.)	—
5.8.3 Unintended radiation Implants must be designed and manufactured in such a way that exposure of patients, users and other persons to the emission of unintended, stray or scattered radiation is reduced as far as reasonably practicable and appropriate.	9.1 Requires markings warning of any radioactive substances.	* retained
	18.1 Requires sealed sources.	* does not apply
	18.2 Requires justification of radiation dose on patient.	* does not apply
	18.3 Requires the radiation dose to be as low as is possible.	* does not apply
	28.2 Requires the information to be provided about radioactive substances.	* does not apply
5.8.4 Ionizing radiation	(Not applicable to *active implantable medical devices*.)	—
5.8.4.1 Implants intended to emit ionizing radiation must be designed and manufactured in such a way as to ensure that, where reasonably practicable, the quantity, geometry and energy distribution (or quality) of radiation emitted can be varied and controlled taking into account the intended use.	—	—
5.8.4.2 Implants emitting ionizing radiation intended for diagnostic radiology must be designed and manufactured in such a way as to achieve appropriate image and/or output quality for the intended medical purpose while minimising radiation exposure of the patient and user.	—	—

Table A.1 *(continued)*

Essential principles, with clause numbers, of ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of this document and aspects covered
5.8.4.3 Implants emitting ionizing radiation, intended for therapeutic radiology must be designed and manufactured in such a way as to enable reliable monitoring and control of the delivered dose, the beam type and energy and where appropriate the energy distribution of the radiation beam.	—	—
5.9 Implants that incorporate software		
5.9.1 Implants incorporating electronic programmable systems, including software must be designed to ensure repeatability, reliability and performance according to the intended use. In the event of a single fault condition, appropriate means must be adopted to eliminate or reduce as far as reasonably practicable and appropriate consequent risks.	5.2 Requires implants to be designed according to software life cycle process activities compliant with IEC 62304:2006 and validated.	* retained
	19.3 Requires a design analysis and defines the methodology for the analysis.	* retained
5.9.2 For implants which incorporate software, the software must be validated according to the state of the art taking into account the principles of development lifecycle, risk management, verification and validation.	5.2 Requires implants to be designed according to software life cycle process activities compliant with IEC 62304:2006 and validated.	* retained
5.10 Active implants and devices connected to them		
5.10.1 For active implants, in the event of a single fault condition, appropriate means must be adopted to eliminate or reduce as far as reasonably practicable and appropriate consequent risks.	19.3 Defines the methodology to ensure single fault conditions are not a hazard.	* retained
5.10.2 Implants where the safety of the patients depends on an internal power supply must be equipped with a means of determining the state of the power supply.	19.2 Requires the power source depletion indicator.	* retained
5.10.3 Implants where the safety of the patients depends on an external power supply must include an electronic alarm system to signal any power failure by way of an external device used in association with the implant.	5.1 Applies IEC 60601–1 to the non-implantable parts of the ACTIVE IMPLANTABLE MEDICAL DEVICE that are connected to or equipped with an electrical power source.	* retained
5.10.4 Implants intended to monitor one or more clinical parameters of a patient must be equipped with appropriate electronic alarm systems to alert the user of situations which could lead to death or severe deterioration of the patient's state of health by way of an external device used in association with the implant.	5.1 Applies IEC 60601–1 to the non-implantable parts of the ACTIVE IMPLANTABLE MEDICAL DEVICE that are connected to or equipped with an electrical power source.	* retained
5.10.5 Implants must be designed and manufactured in such a way as to reduce as far as reasonably practicable and appropriate the risks of creating electromagnetic interference which could impair the operation of this or other devices or equipment in the usual environment.	27.1 Defines the requirement for electromagnetic immunity.	* replacement

Table A.1 *(continued)*

Essential principles, with clause numbers, of ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of this document and aspects covered
5.10.6 Implants must be designed and manufactured in such a way as to provide an adequate level of intrinsic immunity to electromagnetic disturbance to enable them to operate as intended.	27.1 Defines the requirement for electromagnetic immunity.	* replacement
5.10.7 Implants must be designed and manufactured in such a way as to avoid, as far as reasonably practicable, the risk of accidental electric shocks to the patient, user or any other person, both during normal use of the implant and in the event of a single fault condition in the implant, provided the implant is installed and maintained as indicated by the manufacturer.	5.1 Applies IEC 60601–1 to the non-implantable parts of the *active implantable medical device* that are connected to or equipped with an electrical power source.	* retained
	16.1 Sets the safety limits for leakage currents from non-implantable parts.	* retained
5.11 Protection against mechanical risks		
5.11.1 Implants must be designed and manufactured in such a way as to protect the patient and user against mechanical risks connected with, for example, resistance to movement, instability and moving parts.	5 Applies IEC 60601–1 to the non-implantable parts of the *active implantable medical device*.	* retained
5.11.2 Implants must be designed and manufactured in such a way as to reduce to the lowest practicable level the risks arising from vibration generated by the implants, taking account of technical progress and of the means available for limiting vibrations, particularly at source, unless the vibrations are part of the specified performance.	5 Applies IEC 60601–1 to the non-implantable parts of the *active implantable medical device*.	* retained
5.11.3 Implants must be designed and manufactured in such a way as to reduce to the lowest practicable level the risks arising from the noise emitted, taking account of technical progress and the means available to reduce noise, particularly at source, unless the noise emitted is part of the specified performance.	5 Applies IEC 60601–1 to the non-implantable parts of the *active implantable medical device*.	* retained
5.11.4 Implants must be designed and manufactured in such a way as to reduce to the lowest practicable level the risk of error when certain parts within the implant are intended to be connected or reconnected before or during use.	5.3 Requires the usability engineering process to be applied to non-implantable parts of the *active implantable medical device*.	* retained
5.11.5 Implant (excluding the parts or areas intended to supply heat or reach given temperatures) and their surroundings must not attain potentially dangerous temperatures under normal conditions of use.	17.1 Defines the requirement for protection from heat.	* replacement
5.11.6 Implant packaging must be designed and manufactured in such a way as to reduce abrasion between packaging and implant to the lowest practicable level.	10.1 Specifies packaging construction.	* retained

Table A.1 *(continued)*

Essential principles, with clause numbers, of ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of this document and aspects covered
5.12 Protection against the risks posed to the patient by energy supplies or substances		
5.12.1 Implants for supplying the patient with energy or substances must be designed and constructed in such a way that the delivered amount can be set and maintained accurately enough to guarantee the safety of the patient and of the user.	19.3 Requires a design analysis and defines the methodology for the analysis.	* retained
	5.1 Applies IEC 60601–1 to the non-implantable parts of the *active implantable medical device* that are connected to or equipped with an electrical power source.	* retained
5.12.2 Implants must be fitted with either the means of preventing or indicating any inadequacies, or both, in the delivered amount which could pose a danger. Implants must incorporate suitable means to prevent, as far as possible, the accidental release of dangerous levels of energy or substances from either an energy or a substance source, or both.	5.1 Applies IEC 60601–1 to the non-implantable parts of the *active implantable medical device* that are connected to or equipped with an electrical power source.	* retained
5.12.3 The function of the controls and indicators must be clearly specified on the implants or associated devices. Where an implant or associated device bears instructions required for its operation or indicates operating or adjustment parameters by means of a visual system, such information must be understandable to the user.	13.4 Specifies on-device markings.	* retained
5.13 Label and Instruction for Use		
5.13.1 General principles		
This subclause describes the general principles that apply equally to all implants. The primary purpose of labelling is to identify the implant and its manufacturer and communicate safety and performance related information to the user, professional or other person, as appropriate. Such information can appear on the implant itself, on packaging or as instructions for use. The following principles are recommended.		
The medium, format, content, legibility, and location of the label and instructions for use must be appropriate to the particular device, its intended purpose and the technical knowledge, experience, education or training of the intended user(s). In particular, instructions for use must be written in terms readily understood by the intended user and, where appropriate, supplemented with drawings and diagrams.	4 Allows use of symbols, abbreviations, and identification colours.	* retained * additional abbreviation
The information required on the label, might be provided on the implant itself. If this is not practicable or appropriate, some or all of the information can appear either on the packaging for each unit, or on the packaging of multiple implants, or both.	12.3 Requires that any markings shall be indelible.	* retained
	13.2 Requires implantable parts to be marked with sufficient information to allow for positive identification at the time of implantation.	* retained

Table A.1 *(continued)*

Essential principles, with clause numbers, of ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of this document and aspects covered
Where the manufacturer supplies multiple implants to either a single user or location, or both, it might be sufficient to provide only a single copy of the instructions for use. In these circumstances, the manufacturer must provide further copies upon request.	—	—
Instructions for use might not be needed or might be abbreviated for implants if they can be used safely and as intended by the manufacturer without any such instructions for use.	—	—
Labels must be provided in a human-readable format but can be supplemented by machine-readable forms, such as radio-frequency identification (RFID) or bar codes.	—	—
Instructions for use can be provided to the user either in paper or non-paper format (e.g. electronic). They can be supplied by various means either with the implant or separate from it. Examples of other means are information downloaded from the manufacturer's website using the internet, and machine-readable sources. The means chosen must be appropriate for, and accessible to, the anticipated user population.	10.4 Requires accompanying documentation to be physically associated with the device.	* retained
Where instructions for use are provided on a medium other than paper, the manufacturer must ensure the user has information on how to: a) view the instructions for use; b) access the correct version of the instructions for use; c) obtain a paper version of the instructions for use.	—	—
Residual risks which are required to be communicated either to the user or to another person, or both, must be included as limitations, contraindications, precautions or warnings in the labelling.	8.1 Requires warnings to be prominent.	* retained
The use of internationally recognized symbols must be encouraged provided that implant safety is not compromised by a lack of understanding on the part of the user. Where the meaning of the symbol is not obvious to the implant user, e.g. for a newly introduced symbol, an explanation must be provided within the instructions for use.	4 Allows use of symbols, abbreviations and identification colours.	* retained * additional abbreviation
Country-specific requirements for the content of the labelling must be kept to the minimum and, where they currently exist, eliminated as the opportunity arises.	—	—

Table A.1 *(continued)*

Essential principles, with clause numbers, of ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of this document and aspects covered
Where national legislation, such as customs statutes, trade agreements and the like, include requirements for additional documentation to accompany the implant, there might be an inconsistency between the additional documentation and the content of implant labelling described in this document. An example is a customs requirement to indicate the "country of origin" of the implant which does not necessarily align with the address of the manufacturer indicated in the labelling according to 5.13.2 c) or 5.13.3 b) of this document.	—	—
Provided that safe and correct use of the implant is ensured, a regulatory authority can authorize labelling to be in one or more language(s) other than its national language(s).	—	—
5.13.2 Content of the label		
The label must contain the following particulars which can appear on the implant itself, or on the packaging of each unit, or on the packaging of multiple devices.		
a) The name or trade name of the implant.	11.1 Requires the identification of manufacturer on sterile pack.	* retained
b) The details strictly necessary for a user to identify the implant and its use.	9.3 Requires the description of device and model designation on the sales pack.	* retained
	9.4 Requires the marking with characteristics sufficient to identify device.	* retained
	9.8 Requires the sales pack to bear information about accessories provided.	* retained
	9.10 Requires supplementary description, if 9.3 and 9.4 are inadequate to declare purpose.	* retained
	11.6 Requires the description of device and mode designation on the sterile pack.	* retained
	11.7 Requires the identification of contents of a sterile pack.	* retained
c) The name and address of the manufacturer in a format that is recognizable and allows the location of the manufacturer to be established.	9.2 Requires the name and address of the manufacturer on the sales pack.	* retained
d) For imported implants, the name and postal address of the authorized representative, or importer or distributor established within the importing country or jurisdiction might be required. This information can be added by the authorized representative, importer, or distributor within the country of import, rather than be provided by the manufacturer, in which case, the additional label must not obscure any of the manufacturer's labels.	9.2 Requires the name and address of the manufacturer on the sales pack.	* retained

Table A.1 *(continued)*

Essential principles, with clause numbers, of ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of this document and aspects covered
e) Where appropriate, an indication that the implant contains or incorporates a medicinal or biological substance, for example, bone cement containing an antibiotic for use in orthopaedics.	28.7 Requires the information about medicinal products which the device is designed to administer.	* retained
	28.28 Requires an indication that the device contains medicinal substance derived from human blood or human plasma.	* retained
f) The batch code, lot number or the serial number of the implant preceded by the word LOT or SERIAL NUMBER or an equivalent symbol, as appropriate, to allow post-market action to be taken if there is a need to trace or recall the implant.	9.3 Requires the batch code or serial number on the sales pack.	* retained
	11.6 Requires the batch code or serial number on the sterile pack.	* retained
g) An unambiguous indication of the date until when the implant can be used safely, expressed at least as the year and month (e.g. on implants supplied sterile), where this is relevant.	9.7 Requires the marking of a “use-before” date.	* retained
	11.5 Requires the marking of a “use-by” date.	* retained
h) Where there is no indication of the date until when it can be used safely, the year of manufacture. This year of manufacture can be included as part of the batch or serial number, provided the date is clearly identifiable.	9.7 Requires the marking and defines format.	* retained
	11.4 Requires marking and defines format.	* retained
i) An indication of either any special storage or handling condition that applies, or both.	9.11 Requires marking and defines format.	* retained
j) If the implant is supplied sterile, an indication of its sterile state and, where appropriate, the sterilization method.	11.2 Requires the method of sterilization to be marked.	* retained
k) Warnings or precautions to be taken that need to be brought to the immediate attention of the user of the implant as relevant, and to any other person where appropriate (e.g. “THIS IMPLANT CONTAINS LATEX”). This information can be kept to a minimum in which case more detailed information must appear in the instructions for use.	8.1 Requires warnings to be prominent.	* retained
	28.12 Requires warning notices.	* retained
l) If the implant is intended for single use, an indication of that fact.	28.18 Requires and defines warning notice about reuse of the device.	* retained
	11.3 Requires marking of special purpose.	* retained
n) If the implant is intended for premarket clinical investigation only, an indication of that fact.	9.13 Requires marking of special purpose.	* retained
	11.3 Requires marking of special purpose.	* retained
o) If the implant is intended for non-clinical research, teaching or testing purposes only, an indication of that fact.	9.13 Requires marking of special purpose.	* retained
	11.3 Requires marking of special purpose.	* retained

Table A.1 *(continued)*

Essential principles, with clause numbers, of ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of this document and aspects covered
p) If the implant is intended for presentation or demonstration purposes only, an indication of that fact.	9.13 Requires marking of special purpose.	* retained
	11.3 Requires marking of special purpose.	* retained
5.13.3 Content of the instructions for use		
The instructions for use must contain the following particulars.		
a) The name or trade name of the implant.	28.1 Requires the name and address of the manufacturer.	* retained
b) The name and address of the manufacturer in a format that is recognizable and allows the location of the manufacturer to be established, together with either a telephone number, fax number, or website address, or all, to obtain technical assistance.	28.1 Requires the name and address of the manufacturer.	* retained
c) The implant's intended use/purpose including the intended user (e.g. professional), as appropriate.	28.8 Requires the information describing the intended use.	* retained
d) The performance of the implant intended by the manufacturer.	28.8 Requires the information describing the intended use.	* retained
e) Where the manufacturer has included clinical investigations as part of premarket conformity assessment to demonstrate conformity to essential principles, a summary of the investigation, outcome data and clinical safety information, or a reference as to where such information can be accessed.	19.4 Requires the investigation of unintended effects caused by the device.	* retained
f) Any residual risks, contraindications and any expected and foreseeable side effects, including information to be conveyed to the patient in this regard.	28.12 Requires warning notices on hazards arising from interaction.	* retained
g) Specifications the user requires to use the implant appropriately, for example, if the implant has a measuring function, the degree of accuracy claimed for it.	5.1 Applies IEC 60601–1 to the non-implantable parts of the active implantable medical device.	* retained
h) If the implant contains, or incorporates, either a medicinal substance or a material of biological origin, or both, and identification of that substance or material, as appropriate.	28.7 Requires information about the medicinal products which the device is designed to administer.	* retained
	28.28 Requires an indication that the device contains medicinal substance derived from human blood or human plasma	* retained
i) Details of any required preparatory treatment or handling of the implant before it is ready for use (e.g. checking, cleaning, disinfection, drying, packaging, sterilization, final assembly, calibration). NOTE 1 The principle in i) is in addition to information given in the previous edition of this document, and in addition to the information given in Global Harmonization Task Force guidance documents.	(Not applicable to *active implantable medical devices*.)	

Table A.1 *(continued)*

Essential principles, with clause numbers, of ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of this document and aspects covered
j) Any requirements for special facilities, or special training, or particular qualifications of either the implant user or third parties, or both.	(Not applicable to *active implantable medical devices*.)	
k) The information needed to verify whether the implant is properly installed and is ready to perform safely and as intended by the manufacturer, together with, where relevant: — details of the nature, and frequency, of preventative and regular maintenance, and of any preparatory cleaning or disinfection; — identification of any consumable components and how to replace them; — information on any necessary calibration to ensure that the implant operates properly and safely during its intended life span; — methods of eliminating the risks encountered by persons involved in installing, calibrating or servicing the implants.	(Not applicable to *active implantable medical devices*.)	
l) An indication of either any special storage or handling condition, or both, that applies.	7.2 Requires the sterile pack to be protected by the sales packaging.	* retained
	10.1 Requires the packaging to be durable.	* retained
	10.2 Requires the packaging to be protected against the effects of humidity.	* retained
	10.3 Requires the markings on sales packaging to be indelible.	* retained
	10.4 Requires accompanying documentation to be physically associated with the device.	* retained
	12.3 Requires the markings on sales packaging to be indelible.	* retained
	26.2 Requires the device to be protected against the effect of temperature changes.	* retained
m) If the implant is supplied sterile, instructions in the event of the sterile packaging being damaged before use.	28.17 Requires the instructions on dealing with the contents if the sterile pack has been opened or damaged.	* retained
n) If the implant is supplied non-sterile, the appropriate instructions for sterilization. NOTE 2 Further information is provided in ISO 17664.	(Not applicable because 14.1 requires that *active implantable medical device* be provided sterile.)	

Table A.1 *(continued)*

Essential principles, with clause numbers, of ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of this document and aspects covered
o) If the implant is reusable, the information on the appropriate processes to allow reuse, including cleaning, disinfection, packaging and, where appropriate, the method of re-sterilization. Information must be provided to identify when the implant must no longer be reused, e.g. signs of material degradation or the maximum number of allowable reuses.	(Not applicable to *active implantable medical devices*.)	
p) For implants intended for use together with either other implants, medical devices or general purpose equipment, or all: — information to identify such implants, medical devices or equipment, in order to obtain a safe combination and/or; — information on any known restrictions to combinations of implants, medical devices and equipment. NOTE 3 Medical devices and equipment intended for use together with the implant include both those designed and manufactured by the implant manufacturer (e.g. associated instruments) and those designed and manufactured by others (e.g. general purpose equipment).	28.4 Requires information on connector specifications, assembly instructions, and connector performance.	* retained
	28.5 Requires the information on accessories that might be required to facilitate the intended use of the device.	* retained
	28.9 Requires information to allow the selection of the device, accessories and related devices.	* retained
q) If the implant emits hazardous, or potentially hazardous levels of radiation for medical purposes: — detailed information as to the nature, type and where appropriate, the intensity and distribution of the emitted radiation; — the means of protecting the patient, user, or third party from unintended radiation during use of the implant;	9.1 Requires markings warning of any radioactive substances.	* retained
	28.2 Requires information on radioactive substances.	* does not apply

Table A.1 *(continued)*

Essential principles, with clause numbers, of ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of this document and aspects covered
r) Information that allows either the user or the patient, or both, to be informed of any warnings, precautions, measures to be taken and limitations of use regarding the implant. This information must cover, where appropriate:	28.22 Requires warnings on precautions to avoid adverse environments.	* replacement
	28.12 Requires a warning regarding known hazards by reciprocal interference.	* retained
— either warnings, precautions or measures, or all, to be taken in the event of malfunction of the implant, or malfunction of devices used in association with the implant, or changes in implant performance that can affect safety; — either warnings, precautions or measures, or all, to be taken in regard to the exposure to reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, or temperature; — either warnings, precautions or measures, or all, to be taken in regard to the risks of interference posed by the reasonably foreseeable presence of the implant during specific diagnostic investigations, evaluations, therapeutic treatment or use (e.g. electromagnetic interference emitted by the implant affecting other equipment); — if the implant administers medicinal or biological products, any limitations or incompatibility in the choice of substances to be delivered; — either warnings, precautions or limitations, or all, related to the medicinal substance or biological material that is incorporated into the implant as an integral part of the implant; — precautions related to materials incorporated into the implant that are carcinogenic, mutagenic or toxic, or could result in sensitization or allergic reaction of the patient or user.	14.3 Requires the investigation of biocompatibility.	* retained * additional requirement

Table A.1 *(continued)*

Essential principles, with clause numbers, of ISO/TR 14283	Clauses of ISO 14708-1:2014	Clauses of this document and aspects covered
s) Warnings or precautions to be taken related to the disposal of the implant, its accessories and the consumables used with it, if any. This information must cover, where appropriate: — infection or microbial hazards (e.g. explants, needles or surgical equipment contaminated with potentially infectious substances of human origin); — environmental hazards (e.g. batteries or materials that emit potentially hazardous levels of radiation); — physical hazards (e.g. from sharps).	28.29 Requires the instructions for proper removal and disposal.	* retained
t) Date of issue or latest revision of the instructions for use and, where appropriate, an identification number.	28.25 Requires the date of issue or an indication of last revision.	* retained
5.14 Clinical evaluation		
5.14.1 For all implants, the demonstration of conformity with essential principles must include a clinical evaluation. The clinical evaluation must review clinical data in the form of any: — clinical investigation reports, — literature reports or reviews, and — clinical experience to establish that a favourable benefit-risk ratio exists for the implant.	19.4 Requires the investigation of unintended effects caused by the device.	* retained
5.14.2 Clinical investigations on human subjects must be carried out in accordance with the spirit of the Helsinki Declaration. This includes every step in the clinical investigation from the first consideration of the need and justification of the study to the publication of the results. In addition, some countries can have specific regulatory requirements for pre-study protocol review or informed consent.	19.4 Requires that any clinical investigations are conducted according to ISO 14155.	* retained

Annex B
(informative)

Rationale

B.1 General

The following notes on some of the provisions of this document are provided as an aid to understanding. The supplementary information given in this annex carry the numbers of the corresponding clauses of this document, therefore, paragraph numbering in this annex is not consecutive.

B.2 Notes on specific clauses and subclauses

6.1 This subclause clarifies the relationship between the manufacturer's stated specifications and characteristics and the *service life*.

Infusion rate accuracy is a primary safety factor and it is a well-known characteristic of some *implantable infusion pump systems* that accuracy is somewhat related to *reservoir volume* and *service life*. Device characteristics that affect *infusion rate accuracy* should be stated. The information required is important for the physician to determine the proper delivery rate and device settings.

Other ISO standards (e.g. ISO 11631) define accuracy and *repeatability* which are adopted herein for consistency. Whereas *repeatability* can be a measurable quantity stated numerically (refers to data set itself, not to a comparison between the data and true value), actual accuracy, stated against a "true" value, cannot be known. However, it is very important for the manufacturer to state exactly how accuracy was computed.

The procedure detail for determining delivery accuracy is predicated on the test set-up being validated for the measurements required. Due to the small delivery volumes required for measurement, errors within the test set-up and *implantable infusion pump system* preparation can be significant if the procedures are not fully validated. It is therefore necessary to examine the manufacturer's validation procedure of the test set-up and test methods used to establish the delivery accuracy of an *implantable infusion pump system*. Media, such as distilled water, may be used for testing as long as equivalency to actual intended drug use is shown.

It is necessary for the manufacturer to establish appropriate life tests to ensure reliability of the device over the *service life*. These tests may utilize accelerated testing for *implantable infusion pump system* activations and *reservoir* fills to establish the expected performance over time. These tests may be conducted on samples representative of the final device as long as there is appropriate justification that the parameters being evaluated are not affected by the use of these samples.

6.2 Access port septum, such as those used for refilling the *reservoir* or allowing direct access to the delivery catheter, are critical components, as failure of the septum would cause the *reservoir* to empty or fluid to leak into the tissues surrounding the implanted *pump*. The septum puncture test is intended to provide a standardized method of providing data in order to evaluate septum reliability.

8.3 This requirement extends labelling for handling during transport, to all parts, including implantable parts. Electrically powered non-implantable parts are covered by the requirements of Clause 5.

8.4 This requirement extends labelling for environmental conditions during transport, to all parts, including implantable parts. Electrically powered non-implantable parts are covered by the requirements of Clause 5.

14.2 Since the *fluid pathway* is in indirect contact with body fluids, via the delivery of a medicinal substance, it is included in the intent of this subclause.

14.3 *Fluid pathway* materials might have a chance of indirect contact with body fluids; as a precaution these materials also need to be assessed for biocompatibility.

14.5 Generally recognized procedures should be utilized to establish the stability of a medicinal substance within the *implantable infusion pump system.* It is the responsibility of the manufacturer to develop stability indicating assays or provide the necessary documentation to support the *pump* refill interval established in the event that testing was conducted by a third party.

17.1 It is generally accepted[7] that a localized temperature of 39 °C does not cause tissue damage. ISO 14708-1 requires <2 °C rise above the normal surrounding body temperature of 37 °C. The committee understands that the actual "normal surrounding body temperature" is influenced by several factors including the location of the implant and the environment and therefore changed to the 39 °C limit. For the purpose of design verification of a device to meet this subclause, the manufacturer can develop a test method and justify the initial starting temperature of the device based on its intended location in the body and other relevant factors.

CEM43 is a generally accepted method to normalize the impact of temperature and time on tissue for temperatures in the range of 39 °C and 57 °C.[8] Reference [9] demonstrates that the CEM43 values that represent the damage thresholds is different depending on the tissue type. Because the research is generally based on the observation of damage, values below these thresholds might be safe but the margin of this safety cannot be determined. Reference [9] therefore concludes that a CEM43 value of <2 is a safe value for any tissue. This is likely to be very conservative and van Rhoon, et al. recognizes this and recommends higher CEM43 under certain conditions and for various tissue types. The subclause 17.1 requires further analysis for CEM43 values >2 including, for example:

— the margin to the maximum values in Table 1,

— whether the heating events are repeating or a single event,

— medical assessment of the impact of the possible tissue damage and prognosis for the patient, and

— other controls.

The extent of damage to tissue due to heat is dependent on a number of factors including the duration of the exposure and the temperature experienced during the exposure. Reference [10] describes a mathematical model that unifies temperature and the cumulative duration of exposure into a single value equivalent to CEM at 43 °C for 1 min. For example, 10CEM43 is equivalent to 10 min of exposure at 43 °C. General consensus is that the units for CEM43 are minutes.

The CEM43 model approximates the nonlinear relationship of tissue damage by using two linear relationships with a break point at 43 °C.

The formula for CEM43 for a constant temperature is given by Formula (B.1):

$$CEM43 = tR^{(43-T)} \tag{B.1}$$

where

T is the temperature of the tissue in °C;

R is 0,25 for T < 43 °C and 0,5 for $T \geq 43$ °C;

t is the cumulative duration of the heating event, in minutes.

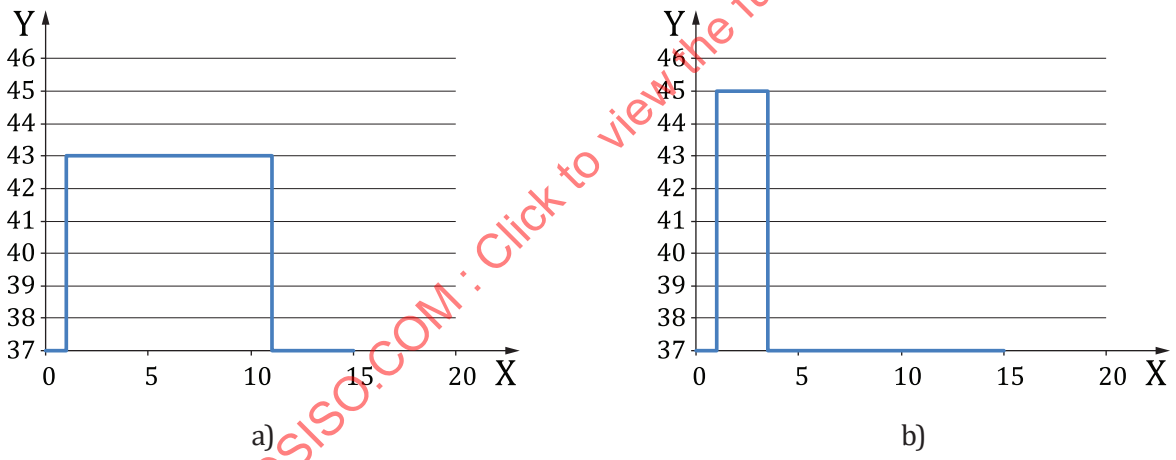
Formula (B.1) is valid for temperatures between 39 °C and 57 °C.

Evaluating the CEM43 formula at different temperatures and a constant duration yields the values shown in Table B.1.

Table B.1 — Evaluating CEM43 formula at different temperatures

Temperature °C	Duration min	CEM43
40	10	0,156 25
41	10	0,625
42	10	2,5
43	10	10
44	10	20
45	10	40
46	10	80
47	10	160
48	10	320
49	10	640
50	10	1 280
51	10	2 560
52	10	5 120
53	10	10 240

In the case of constant temperature for the duration of exposure, a plot of the temperature versus time would be a rectangle and its CEM43 value can be calculated using Formula (B.1).



Key

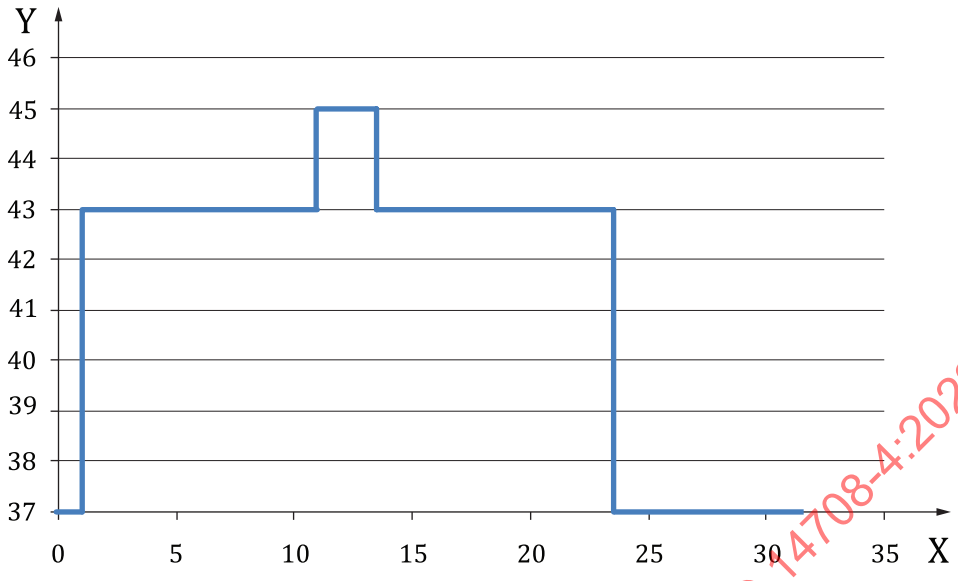
X time in min

Y temperature in °C

Figure B.1 — Two examples of the same CEM43 result with different exposure times

The examples in Figure B.1 both yield a 10CEM43; the first chart shows 10 min exposure at 43 °C while the second is 2,5 min at 45 °C.

In practice, the temperature is likely to vary in value for the duration of exposure. In this case, the CEM43 value can be calculated by the summation of the CEM43 values for a series of rectangles, each with a known duration and temperature. The example in Figure B.2 shows such a profile which results in a 30CEM43. It consists of an initial temperature exposure of 43 °C for 10 min followed by 2,5 min at 45 °C and then another 43 °C for 10 min.



Key

X time in min

Y temperature in °C

Figure B.2 — Example showing a 30CEM43 time and temperature profile

By sampling the temperature at known time intervals and using the above approach, the CEM43 value for a given temperature profile can be calculated by Formula (B.2):

$$\mathrm{CEM43} = \sum_{i=1}^{n} t_i \times R^{(43-T_i)} \tag{B.2}$$

where

t_i is the i-th time interval in minutes;

T_i is the average temperature of the tissue in degrees Celsius during the interval t_i;

R is 0,25 for $T < 43$ °C and 0,5 for $T \geq 43$ °C;

n is the number of samples taken during the heating duration.

Formula (B.2) is valid for temperatures between 39 °C and 57 °C.

NOTE This method is used in Reference [9].

Single fault conditions were removed from the requirements of 17.1 because single fault conditions are already evaluated as part of 19.3. See rationale for 19.3 for more details on how to address harm related to heat under single fault failure.

19.3 As 19.3 is responsible for assessing risks from failures, it was decided for this document that all requirements requiring assessment of single fault failures would be moved to 19.3. One such requirement was originally found in 17.1 for protection from harm caused by heat. This rationale is to remind that although 17.1 does not address single fault conditions, harm related to heat under single fault conditions still needs to be evaluated in 19.3. The following explains an example of how this could be executed using the concept of components with high-integrity characteristics, that could also be used for other types of effects from single fault failures.

First, identify components, through the risk management process, that would need to be considered to ensure that patient is protected from harm caused by heat under single fault conditions. Acceptance

criteria from 17.1 can be used to determine the acceptability of the risk under single fault conditions. It is possible that certain component failures might not meet the requirement of 17.1 and for which further risk control is not practicable.

Considering ISO 14971:2019, 7.4: "If the residual risk is not judged acceptable using the criteria established in the risk management plan and further risk control is not practicable, the manufacturer may gather and review data and literature to determine if the medical benefits of the intended use outweigh the residual risk," it could be possible for the manufacturer to justify the risk with components that are considered as possessing high-integrity characteristics.

The first step to determine a component with high-integrity characteristics is to conduct a risk analysis to find those characteristics that are required to be maintained. Having done this, the appropriate component can be selected. Reference can be made to IEC or ISO component standards as part of the determination of the characteristics required.

Testing of component with high-integrity characteristics are only part of the required determination of suitability. Since a particular component with high-integrity characteristics has to function as intended or a hazard is likely to occur, additional considerations include as appropriate:

— continuous surveillance as part of the manufacturing process and also after assembly into the end product;

— particular characteristics of the device concerned;

— lot testing;

— calibration;

— control of manufacturing defects;

— maintenance;

— projected *service life* of the *implantable infusion pump system*;

— use of relevant component standards;

— failure mode characteristics;

— environmental conditions;

— anticipated misuse of the *implantable infusion pump system*;

— interaction with other equipment.

It would not be expected from the manufacturer to test the single component fault condition of a component with high-integrity characteristics (such as required by 17.1), provided that all the aspects identified to ensure the high-integrity characteristics components are met and implemented by the manufacturer.

For example, certain faults from a battery, like an internal short, could result in unacceptable risk and risk controls to prevent this once the device is implanted would not be practicable. In this particular case, the battery selected for this function would require to be a component with high-integrity characteristics, which is defined as a component where one or more characteristics ensure that its function is fault-free in relation to the safety requirements of this document during the projected *service life* of the *implantable infusion pump system* in normal use and reasonably foreseeable misuse.

19.5 The *pump reservoir* and catheter contain materials which could affect the stability and efficacy of the medicinal substance. All device materials in the *fluid pathway* of the *implantable infusion pump system* which are exposed to a medicinal substance need to be characterized for their suitability in the design. The characterization should consider the potential for changes of physical characteristics of the materials and the potential for material degradation from exposure to a medicinal substance over time. Any leachable or degradation product identified should be assessed for their effect on the