INTERNATIONAL STANDARD

ISO 14708-4

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Implants for surgery — Active implantable medical devices —

Part 4: Implantable infusion pumps

Implants chirurgicaux — Dispositifs médicaux implantables actifs —

Partie 4: Pompes d'infusion en implant

Reference number
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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.

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

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

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

ISO 14708-4 was prepared by Technical Committee ISO/TC 150, *Implants for surgery*, Subcommittee SC 6, *Active implants*.

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

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

— *Part 2: Cardiac pacemakers*

— *Part 3: Implantable neurostimulators*

— *Part 4: Implantable infusion pumps*

Introduction

This part of ISO 14708 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 14708-1:2000, hereinafter referred to as ISO 14708-1. The requirements of this part of ISO 14708 take priority over those of ISO 14708-1.

An implantable infusion pump is a device that delivers either a constant flow rate or a variable flow 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.

This part of ISO 14708 is relevant to all parts and accessories of implantable infusion pumps, including catheters, refill kits, direct access port kits, programmers and related software. Not all parts or accessories might be intended to be totally or partially implanted, but there is a need to specify some requirements of non-implantable parts and accessories if they could affect the safety or performance intended by the manufacturer.

Requirements for physiologic sensing functions of implantable infusion pumps are not included in this edition of this part of ISO 14708 but might be considered in future editions.

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

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

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

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

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

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

Implants for surgery — Active implantable medical devices —

Part 4: Implantable infusion pumps

1 Scope

This part of ISO 14708 is applicable to active implantable medical devices intended to deliver medicinal substances to site-specific locations within the human body.

This part of ISO 14708 is also applicable to some non-implantable parts and accessories of the devices as defined in Clause 3.

The tests that are specified in this part of ISO 14708 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 part of ISO 14708 is not intended to apply to non-implantable infusion systems. However, it does apply to devices intended to be used as trial systems because of their close affiliation with implantable infusion pumps.

2 Normative references

The following referenced documents are indispensable for the application of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 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*

IEC 60601-1:2005, *Medical electrical equipment — Part 1: General requirements for basic safety and essential performance*

IEC 60601-1-2:2007, *Medical electrical equipment — Part 1-2: General requirements for basic safety and essential performance — Collateral standard: Electromagnetic compatibility — Requirements and tests*

IEC 61000-4-3:2002, *Electromagnetic compatibility (EMC) — Part 4–3: Testing and measurement techniques — Radiated, radio-frequency, electromagnetic field immunity test*

ANSI/AAMI PC69:2000, *Active implantable medical devices — Electromagnetic compatibility — EMC test protocols for implantable cardiac pacemakers and implantable cardioverter defibrillators*

3 Terms and definitions

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

3.101
implantable infusion pump
active implantable medical device intended for delivery of a medicinal substance to a specific location within the human body

NOTE For purposes of this part of ISO 14708, an implantable infusion pump can be a single article, or a system consisting of a set of components and accessories which interact to achieve the performance intended by the manufacturer. Not all of these components or accessories might be required to be partially or totally implanted, e.g. programmers and trial systems.

3.102
pump gear
implantable part of an implantable infusion pump containing the fluid reservoir, energy source and, in some cases, control electronics

3.103
fluid path
internal surfaces of the implantable infusion pump which are in direct contact with a medicinal substance

3.104
outlet port
port where fluid enters the delivery catheter

3.105
refill access port
port allowing access to the fluid reservoir

3.106
direct access port
port allowing access to the delivery catheter

3.107
internal volume
fluid volume extending from the reservoir to the outlet port

3.108
reservoir volume
fluid volume of the reservoir that can be discharged while maintaining infusion accuracy within specifications

3.109
residual volume
fluid volume that cannot be removed from the pump gear

3.110
projected service life
period after implantation when the implantable infusion pump remains within stated specifications and characteristics

3.111
stability interval
calculated maximum interval between two subsequent reservoir refills to assure stability of the medicinal substance

3.112
infusion accuracy
how close the true (actual) infusion rate is to the specified rate

3.113
repeatability
value below which the absolute difference between two successive test results obtained with the same implantable infusion pump with the same infusate under the same conditions can be expected to lie, with a probability of 95 %

NOTE 1 A more qualitative way of looking at repeatability is the ability to consistently deliver the same results over time (e.g. infusion rate). Repeatability is a metric independent of accuracy.

NOTE 2 A method for calculating repeatability is given in Annex B of ISO 11631:1998 [9].

3.114
minimum rate
lowest rate selectable by the user

3.115
intermediate rate
rate specified by the manufacturer as typical for the implantable infusion pump

NOTE The rate specified might depend on the application.

3.116
maximum rate
highest rate selectable by the user

3.117
bolus
discrete quantity of liquid that is delivered in a short time

3.118
essential performance
performance necessary to achieve freedom from unacceptable risk

NOTE For guidance on essential performance concepts see IEC 60601-1.

4 Symbols and abbreviated terms

This clause of ISO 14708-1 and the following applies.

DUT device under test

5 General requirements for non-implantable parts

This clause of ISO 14708-1 applies.

6 Requirements for particular active implantable medical devices

Additional subclauses:

6.101 Implantable infusion pump characteristics

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

NOTE 1 Minimum environmental conditions for atmospheric pressure are specified in Clause 25.

Infusion accuracy shall be stated for all selectable rates (including bolus rates) over a range of reservoir volumes. Constant flow implantable infusion pump accuracy shall be stated for the specified infusion rate of the pump over a range of reservoir volumes.

The manufacturer shall provide a plot of infusion accuracy versus reservoir volume. For variable rate pumps the plot shall contain curves for minimum rate, maximum rate, and one or more intermediate rates.

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

NOTE 2 Accuracy is a commonly used term and might include the effects of systematic and random errors. Although it is convenient to combine all these errors under the heading “accuracy”, it is still a qualitative term.

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 shall be confirmed by inspection of test procedures and results provided by the manufacturer, supported by the manufacturer’s calculations as appropriate.

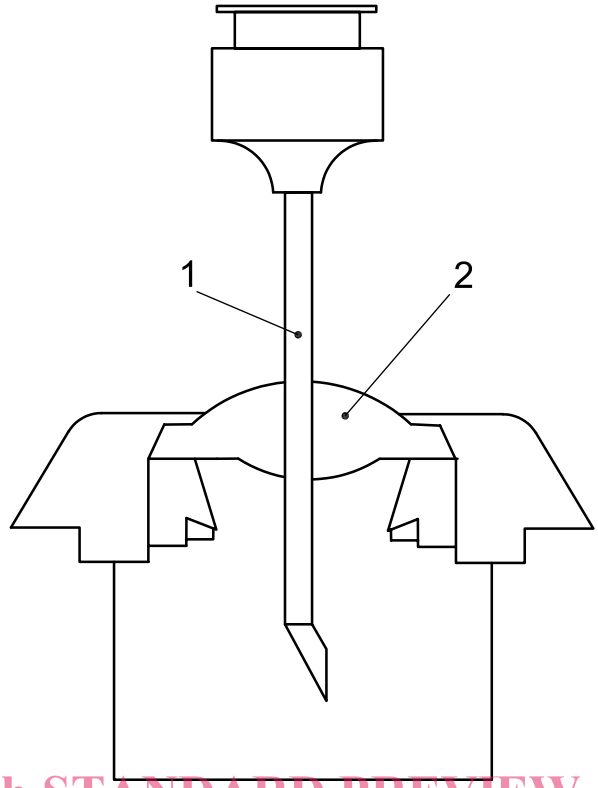
6.102 Septum puncture test

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

— Test: The DUT shall be conditioned at 37 °C ± 1 °C for not less than 12 h to achieve thermal equilibration. Each implantable 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 101.

  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 or 276 kPa. The septum’s exposed surfaces shall be examined for air bubble leakage for 1 min.

Compliance shall be confirmed if the access port life conforms to the manufacturer’s specified limits. The maximum number of punctures recommended by the manufacturer shall be stated (see 28.8).



Key

1 needle
2 septum

Figure 101 — Septum puncture test

7 General arrangement of the packaging

This clause of ISO 14708-1 applies.

8 General markings for active implantable medical devices

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

Additional subclauses:

8.101 If special handling measures have to be taken during transport, the transport packaging shall be marked accordingly (see for example ISO 780 [1] or ISO 15223 [2]).

Compliance shall be checked by inspection.

8.102 The permissible environmental conditions for transport shall be marked on the outside of the transport packaging.

Compliance shall be checked by inspection.

9 Markings on the sales packaging

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

9.4

Addition:

Specific additional information shall be provided for the following components:

a) Pump gear

— reservoir volume;

— infusion flow rate for constant flow pump;

— any additional information and relevant characteristics, as necessary, to identify the device.

b) Catheter

— length (in centimetres);

— any additional information and relevant characteristics, as necessary, to identify the device.

c) Refill kit

— any information and relevant characteristics, as necessary, to identify the device.

d) Direct access port kit

— any information and relevant characteristics, as necessary, to identify the device.

10 Construction of the sales packaging

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

10.3

Amendment:

The test is replaced by 7.1.3 b) of IEC 60601-1:2005.

NOTE Removable stickers (e.g. temporary stickers used in the manufacturing process) that provide supplementary information exceeding the information specified in Clause 9, need not be subjected to this test.

11 Markings on the sterile pack

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

Additional subclause:

11.101 The sterile pack shall bear specific additional information for the following components:

a) Pump gear

— reservoir volume;

— infusion flow rate for constant flow pumps;

— any additional information and relevant characteristics, as necessary, to identify the device.

b) Catheter

— length (in centimetres);

— any additional information and relevant characteristics, as necessary, to identify the device.

c) Refill kit

— any additional information and relevant characteristics, as necessary to identify the device.

d) Direct access port kit

— any additional information and relevant characteristics, as necessary to identify the device.

Compliance shall be checked by inspection.

12 Construction of the non-reusable pack

This clause of ISO 14708-1 applies.

13 Markings on the active implantable medical device

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

13.1

Amendment:

The wet rub test is replaced by 7.1.3 b) of IEC 60601-1:2005, after which the markings shall remain clearly legible.

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

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

14.2

Replacement:

Any part of the implantable infusion pump, intended in normal use to be in contact with body fluids, shall be evaluated to determine if the release of particulate matter is hazardous.

— Test: Remove the implantable part aseptically from the non-reusable pack. Immerse the implantable part in a bath of approximately 9 g/l saline solution, suitable for injection, or filtered saline or ultra-pure water, in a neutral glass container. The volume of the saline in millilitres shall be $5 \pm 0{,}5 \times$ the numerical value of the surface area of the implantable part expressed in cm^2. The container shall be covered with a glass lid and maintained at 37 °C ± 1 °C for between 8 h and 18 h, the bath being agitated throughout the period. A reference sample of similar volume shall be prepared from the same batch of saline, maintained and agitated in a similar way to the specimen. A sample of liquid from the specimen bath and from the reference bath shall be compared using apparatus suitable for measurement of particle size, such as apparatus operating on the light blockage principal [see for example method 2.9.19 of the European Pharmacopoeia, 3rd edition, 1977, (Council of Europe) [3]].

The excess average count of particles from the specimen compared to the reference sample shall not exceed the amount determined, by the manufacturer, to be hazardous. If the manufacturer does not make this determination then the excess average count shall not exceed 100 per ml greater than 5,0 µm and shall not exceed 5 per ml greater than 25 µm.

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

14.3

Addition:

This requirement also applies to the implantable infusion pump's fluid path materials (indirect contact).

Biocompatibility may be assessed in accordance with one or more parts of ISO 10993, e.g. ISO 10993-1 [4].

Additional subclause:

14.101

For implantable infusion pumps that require the medicinal substance to be periodically replenished, the manufacturer shall establish the maximum interval during which the medicinal substance will maintain a potency of at least 90 % of the initial concentration of the medicinal substance instilled into the pump's reservoir. The manufacturer shall stipulate the stability interval at body temperature for each medicinal substance claimed (see 28.8). In addition, an evaluation for the presence of potentially hazardous degradation products in the medicinal substance, for the stability interval established, shall be conducted.

Compliance shall be confirmed if records provided by the manufacturer establish that the safety and quality of the substance have been verified by analogy with the appropriate methods.

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

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

15.1

Amendment:

Clause 23 of IEC 60601-1:1988 is replaced by 9.3 of IEC 60601-1:2005 (see Clause 5).

Compliance shall be checked as specified in IEC 60601-1.

16 Protection from harm to the patient caused by electricity

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

16.1

Amendment:

Clause 19 of IEC 60601-1:1988 is replaced by 8.7 of IEC 60601-1:2005 (see Clause 5).

16.2

Addition:

If the results of a risk assessment or other means (e.g. published data, test studies, calculations) indicate that the current limit should be less than 1 µA for a particular application, then the allowable limit shall be changed so that the risk is mitigated.

17 Protection from harm to the patient caused by heat

Replacement:

No outer surface of an implantable part of the implantable infusion pump shall be greater than 2 °C above the normal surrounding body temperature, in normal operation or single-fault condition, unless the manufacturer demonstrates that a higher temperature rise is justified for a particular application.

Compliance shall be confirmed by a review of the manufacturer's documentation, including results from modelling, a design or risk assessment, test studies or other appropriate means.

NOTE Currently, some studies have shown that, depending on the location of specific tissue within the human body, a 2 °C temperature limit might be unnecessarily restrictive. Under this circumstance, the manufacturer is allowed the burden of substantiation.

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

This clause of ISO 14708-1 applies.

19 Protection from unintended effects caused by the device

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

19.2

Replacement:

If the service life (see 3.110) of the implantable infusion pump is dependent upon an implanted source of electrical energy, such as a battery, an indication shall be provided that gives an advanced notice of energy source depletion. The manufacturer shall define the expected duration of the remaining service life following this notice.

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

NOTE This subclause is also applicable to rechargeable energy sources.

19.3

Replacement:

An implantable infusion pump shall be designed so that the failure of any single component, part or (if the device incorporates a programmable electronic system) software program, shall not cause an unacceptable hazard.

— Assessment: Risk assessment and risk control shall be conducted in accordance with published standards, such as ISO 14971 [5].

Compliance shall be confirmed by a review of the risk management report or equivalent manufacturer's documents.

19.4

Amendment:

The assessment is amended to allow clinical investigations conducted in accordance with published standards, such as ISO 14155-1 or 14155-2 [6],[7].