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Pen-injectors for medical use —

Part 4: Requirements and test methods for electronic and electromechanical pen-injectors

Stylos-injecteurs à usage médical —

Partie 4: Exigences et méthodes d'essai pour stylos-injecteurs électroniques et électro-mécaniques

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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 11608-4 was prepared by Technical Committee ISO/TC 84, *Devices for administration of medicinal products and intravascular catheters*.

ISO 11608 consists of the following parts, under the general title *Pen-injectors for medical use*:

— *Part 1: Pen-injectors — Requirements and test methods*

— *Part 2: Needles — Requirements and test methods*

— *Part 3: Finished cartridges — Requirements and test methods*

— *Part 4: Requirements and test methods for electronic and electromechanical pen-injectors*

Introduction

This part of ISO 11608 covers electro-mechanical driven injectors not covered by part 1 of ISO 11608. These injectors are mainly intended to administer medicinal products to humans. This part of ISO 11608 provides performance requirements regarding essential aspects of the design so that variations of such injectors are not unnecessarily restricted.

The sampling plans for inspection selected for this part of ISO 11608 are intended to verify, at a high confidence level, the manufacturer's ability to manufacture one “lot” of injectors that conforms to the critical product attributes. These sampling plans for inspection do not intend to replace the more general manufacturing quality systems practices widely used in production, e.g. the ISO 9000 series.

Materials to be used for the construction of these injectors are not specified, as their selection, to some extent, will depend upon the design, the intended use and the manufacturing process selected by the manufacturer. All materials used in these injectors which come in contact with the end-user must be non-toxic and biocompatible. In some countries, national regulations may exist and their requirements may supersede or add up to this part of ISO 11608.

In relation to specification limits and dose accuracy, the ISO directives (Part 2, A3 and A13) require that the VIM[1] and GUM[2] principles are used and incorporated in all future standards and future revisions of existing standards. The reorganization to be done in relation to this will not affect the technical content of the standards, and only the terminology shall be changed to correspond to VIM, and the principles shall be changed to correspond to GUM.

However, with this part of ISO 11608, ISO/TC 84 has decided to await the revision of the ISO 11608 series where the principles will be incorporated in all parts to conform to applicable requirements.

Pen-injectors for medical use —

Part 4: Requirements and test methods for electronic and electromechanical pen-injectors

1 Scope

This part of ISO 11608 specifies requirements and test methods for electromechanically driven injectors intended to be used with needles and with replaceable or non-replaceable cartridges. The injector may be for single-use or multiple-use. The injector system is intended to deliver medication to an end-user by self-administration or with assistance.

This part of ISO 11608 is neither applicable for needle-free injectors (as covered in ISO 21649) nor infusion pumps (as covered in IEC 60601-2-24).

This part of ISO 11608 is not applicable for devices that are capable of operating while connected to an external power supply.

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 11608-1:2000, *Pen-injectors for medical use — Part 1: Pen-injectors — Requirements and test methods*

IEC 60068-2-27:1987, *Environmental testing — Part 2: Tests. Test Ea and guidance: Shock*

IEC 60068-2-30:1980, *Environmental testing — Part 2-30: Tests — Test Db: Damp heat, cyclic (12 h + 12 h cycle)*

IEC 60068-2-64:1993, *Environmental testing — Part 2: Test methods — Test Fh: Vibration, broad-band random (digital control) and guidance*

IEC 60529:2001, *Degrees of protection provided by enclosures (IP Code)*

IEC 60601-1:1988, *Edition 2: Medical electrical equipment — Part 1: General requirements for safety* (+ AMD 1:1991 + AMD. 2: 1995)

IEC 60601-1-1:2000, *Medical electrical equipment — Part 1-1: General requirements for safety — Collateral standard: Safety requirements for medical electrical systems*

IEC 60601-1-2:2001, *Medical electrical equipment — Part 1-2: General requirements for safety — Collateral standard: Electromagnetic compatibility — Requirements and tests*

IEC 60721-3-7:1995, *Classification of environmental conditions — Part 3: Classification of groups of environmental parameters and their severities — Portable and non-stationary use*

IEC 61000-4-2:2001, *Electromagnetic compatibility (EMC) — Part 4-2: Testing and measurement techniques — Electrostatic discharge immunity test*

3 Terms and definitions

For the purposes of this document the terms and definitions given in ISO 11608-1 and the following apply.

3.1
drive system
electromechanical mechanism responsible for expelling the dose

3.2
pen-injector
pen-injector with an electromechanical drive system

4 Symbols and abbreviated terms

See Clause 4 of ISO 11608-1:2000.

5 General requirements

See Clause 5 of ISO 11608-1:2000.

6 Test conditions

6.1 Standard atmosphere

See 6.1 of ISO 11608-1:2000.

6.2 Cool atmosphere

See 6.2 of ISO 11608-1:2000.

6.3 Hot atmosphere

See 6.3 of ISO 11608-1:2000.

7 Preconditioning of pen-injectors

7.1 Preconditioning in dry heat atmosphere

See 7.1 of ISO 11608-1:2000.

7.2 Preconditioning in cold storage atmosphere

See 7.2 of ISO 11608-1:2000.

7.3 Preconditioning in cyclical atmosphere

See 7.3 of ISO 11608-1:2000.

7.4 Preconditioning by free fall

See 7.4 of ISO 11608-1:2000.

7.5 Preconditioning by vibration

Instead of the vibration test as described in 7.5 of ISO 11608-1:2000, the following applies.

— Unpack and prepare 5 pen-injectors according to the instructions for use with a new cartridge.

— Place the pen-injectors in the box or pouch for transport as instructed by the manufacturer.

— Subject the pen-injectors to vibration in accordance with IEC 60068-2-64.

— Subject the pen-injectors to the conditions specified in IEC 60721-3-7:1995 Class 7M3, as follows:

  — acceleration spectral density 3 m^2/s^3, frequency range 10 Hz to 200 Hz;

  — acceleration spectral density 1 m^2/s^3, frequency range 200 Hz to 500 Hz;

  — vibrate the pen-injectors in a vertical direction and in two other directions perpendicular to one other in a horizontal plane.

The vibration time shall be 1 h.

NOTE Injectors with limited conditions for vibration shall be subjected to the test at acceptable conditions, and these acceptable conditions shall be stated in the instructions for use.

7.6 Preconditioning by shock

Subject the same 5 pen-injectors as used in 7.5 to the shock test in accordance with IEC 60068-2-27.

Subject the pen-injectors to the conditions specified in IEC 60721-3-7:1995 Class 7M3, as follows:

— to a shock response spectrum Type I: 300 m/s^2;

— to a shock response spectrum Type II: 1 000 m/s^2.

The number of shocks shall be 50 positive and 50 negative.

The shock response test Type II represents the device in use (without packaging).

7.7 Preconditioning for the influence of fluid leakage

The purpose of this test is to evaluate the influence of liquid that leaks from the cartridge (back-leakage) or leaks from a broken cartridge into the pen-injector.

— Remove the cartridge holder and pour the contents of one cartridge of the medicinal product into the pen-injector at the most likely point of entry.

— Using appropriate safety equipment, shake the pen-injector in all directions by hand for 30 s.

— Allow the medicinal product to drain from the original point of fluid entry, for 10 min.

— Attach a new cartridge, run a self test and monitor any messages (if applicable).

— Store the pen-injector in a horizontal orientation according to the instructions for use, for 24 h.

— Expel all medicinal product from the cartridge by injections and monitor the self test and any error messages (if applicable).

— Replace the used cartridge with a new one.

— Store the pen-injector in a horizontal orientation according to the instructions for use, for 96 h.

— Expel all medicinal product from the cartridge by injections and monitor the self test and any error messages (if applicable).

An error that is obvious to the lay user is allowed if it does not influence any safety aspects.

7.8 Preconditioning for dust test according to IEC 60529

The purpose of this test is to determine the influence of dust on the mechanics and on the electronics of the pen-injector: IP-5 test protection test of enclosures (dust test).

The measuring method for dust protection IP5X shall be in accordance with IEC 60529 (standard atmosphere). The test shall be carried out with one pen-injector and inserted cartridge.

After the test:

— the pen-injectors shall be cleaned thoroughly as described in the instructions for use;

— a visual inspection according to Clause 13 and a functional inspection according to Clause 14 shall be performed.

An error that is obvious to the lay user is allowed if it does not influence any safety aspects.

7.9 Preconditioning for damp heat test according to IEC 60068-2-30

Carry out test Ca, “Damp heat, steady state” as indicated in IEC 60068-2-30:1980.

The pen-injector shall be stored at a temperature of 40 °C and a RH of 93 % for 4 d. After 4 d, the pen-injectors shall be acclimated for 1 h at standard atmosphere (18 °C to 28 °C and a RH 25 % to 75 %).

After being acclimated, Clause 13 shall be carried out.

An error that is obvious to the lay user is allowed if it does not influence any safety aspects.

7.10 Preconditioning by lifetime testing

Precondition the pen-injector according to the procedure described in 9.2.3 of ISO 11608-1:2000. After each injection and priming, if required by the instructions for use, the device shall be switched off and power switched on again prior to the next life-cycle dose.

NOTE The workload of the battery may be different during this test compared to normal use because of the frequency of consecutive injections. Battery replacement or external power supplies may be necessary to achieve the requirements of 7.10.

8 Reagent and apparatus

See Clause 8 of ISO 11608-1:2000.

9 Determination of dose accuracy

9.1 Dose accuracy

9.1.1 General

See 9.1.1 of ISO 11608-1:2000.

9.1.2 Accuracy assessment (expressed in millilitres)

See 9.1.2 of ISO 11608-1:2000.

9.1.3 Example of accuracy limit calculation

See 9.1.3 of ISO 11608-1:2000.

9.1.4 Procedure

9.1.4.1 General

See 9.1.4.1 of ISO 11608-1:2000.

9.1.4.2 Accuracy requirements

See 9.1.4.2 of ISO 11608-1:2000.

9.1.4.3 Preparation and operation of pen-injectors

See 9.1.4.3 of ISO 11608-1:2000.

9.1.4.4 Random settings

See 9.1.4.4 of ISO 11608-1:2000.

9.2 Dose accuracy requirements

9.2.1 General

See 9.2.1 of ISO 11608-1:2000.

9.2.2 Dose accuracy when subjected to standard, cool and hot atmospheres

See 9.2.2 of ISO 11608-1:2000.

9.2.3 Dose accuracy and lifetime test of pen-injectors with replaceable cartridges after delivery of claimed lifetime doses

Determine the dose accuracy of an appropriate number of pen-injectors in accordance with 9.1 under the conditions specified in 7.10

9.2.4 Dose accuracy after being subjected to dry heat storage preconditioning

See 9.2.4 of ISO 11608-1:2000.

9.2.5 Dose accuracy after being subjected to cold storage preconditioning

See 9.2.5 of ISO 11608-1:2000.

10 Freedom from defects

10.1 Freedom from defects after being subjected to cyclical preconditioning

See 10.1 of ISO 11608-1:2000.

10.2 Freedom from defects after being subjected to vibration

None of the pen-injectors shall have visible defects after vibration when inspected in accordance with Clause 13.

None of the pen-injectors shall have functional defects after vibration when inspected in accordance with Clause 14.

10.3 Freedom from defects after being subjected to shock

None of the pen-injectors shall have visible defects after shock when inspected in accordance with Clause 13.

None of the pen-injectors shall have functional defects after shock when inspected in accordance with Clause 14.

10.4 Freedom from defects after being subjected to free fall

See 10.3 of ISO 11608-1:2000.

10.5 Freedom from defects after being subjected to leakage

None of the pen-injectors shall have visible defects after being subjected to leakage when inspected in accordance with Clause 13.

None of the pen-injectors shall have functional defects after being subjected to leakage when inspected in accordance with Clause 14.

10.6 Freedom from defects after being subjected to dust according to IEC 60529

None of the pen-injectors shall have visible defects after being subjected to dust when inspected in accordance with Clause 13.

None of the pen-injectors shall have functional defects after being subjected to dust when inspected in accordance with Clause 14.

10.7 Freedom from defects after being subjected to damp heat according to IEC 60068-2-3

None of the pen-injectors shall have visible defects after being subjected to damp heat when inspected in accordance with Clause 13.

None of the pen-injectors shall have functional defects after being subjected to damp heat when inspected in accordance with Clause 14.

11 Determination of electromagnetic compatibility

11.1 Electromagnetic compatibility (EMC)

11.1.1 General

See 11.1.1 of ISO 11608-1:2000.

11.1.2 Exposure to electrostatic discharge

The pen-injector is placed on a metal reference plane as specified in IEC 61000-4-2. This plane is provided with an insulating layer to prevent discharges to the plane. Contact discharges of (± 2, ± 4 and ± 8) kV shall be applied to conductive accessible parts and coupling planes. Air discharges of (± 8, ± 10, ± 13 and ± 15) kV shall be applied to non-conductive accessible parts. The number of discharges at each level and polarity shall be 10 with a time interval of minimally 1s between the individual discharges. Charge accumulation by successive test discharges shall be avoided, for example, by using an air ionizer between the test discharges (see 60601-1-2 and IEC 61000-4-2).

The following checks shall be carried out:

— a final check of the accuracy according to Clause 9;

— a visual inspection according to Clause 13 (for the applicable parts only);

— a final functional check according to Clause 14.

An error that is obvious to the lay user is allowed if it does not influence any safety aspects.

NOTE The stated discharge values are more conservative than what is described in 60601-1-2 due to the potentially more extreme electrostatic conditions associated with ambulatory or home use of these devices.

11.1.3 Exposure to radiated fields (RF)

See 11.1.3 of ISO 11608-1:2000.

11.2 Electrostatic discharge

See 11.2 of ISO 11608-1:2000.

11.3 Radiated radio frequency (RF) fields

See 11.3 of ISO 11608-1:2000.

12 Electrical safety

12.1 Electrical safety for medical devices

The standard for systems IEC 60601-1-1 shall be applicable if the pen-injector is coupled to non-medical equipment (an ordinary PC for example).

12.2 Electrical safety for systems

12.2.1 The pen-injector shall be tested according to the applicable clauses of IEC 60601-1.

12.2.2 It is not in the line of IEC 60601-1 to place a symbol for either type B, or type BF or type CF on a pen-injector, as this symbol could confuse the private user of the pen-injector (the user does not need to know about the IEC 60601-1 standard). It is probably in line with IEC 60601-1 to classify a pen-injector in its documentation as “internally powered” (no symbol for this on the pen-injector).

If the pen-injector is part of a system, the relevant symbol (B, BF or CF) shall be placed on the pen-injector according to IEC 60601-1-1. In this situation, the importance of the IEC 60601-1-1 compensates for the disadvantage that the private user gets confused by a symbol.

13 Visual inspection

See Clause 12 of ISO 11608-1:2000 with the following addition.

An error that is obvious to the lay user is allowed if it does not influence any safety aspects.

14 Functional inspection

14.1 General

The following shall be carried out:

— a check on the proper working of the button and segments of the display;

— a check on the working of any audible feedback (if applicable);

— acceptance of a new cartridge (if applicable);

— actual displayed parameters or warning/error messages.

An error that is obvious to the lay user is allowed if it does not influence any safety aspects.

14.2 Replaceable cartridge

See 13.1 of ISO 11608-1:2000.

14.3 Nonreplaceable cartridge

See 13.2 of ISO 11608-1:2000.

14.4 Accuracy

See 13.3 of ISO 11608-1:2000.

15 Test report

See Clause 14 of ISO 11608-1:2000.

16 Information supplied by the manufacturer

16.1 General

See 15.1 of ISO 11608-1:2000.

16.2 Marking

16.2.1 General

See 15.2.1 of ISO 11608-1:2000.

16.2.2 Marking on the injector

See 15.2.2 of ISO 11608-1:2000.

16.2.3 Marking on the unit container

See 15.2.3 of ISO 11608-1:2000.

16.3 Instructions for use

See 15.3 of ISO 11608-1:2000 with following additional points:

a) a complete view of the information on the display;

b) a list of alarms/error messages;

c) a warning that under certain circumstances the specified accuracy may not be maintained (if applicable);

d) the time for which the electronic display is retained following switch off;

e) a specification of the maximum drug volume that may be expelled under SINGLE FAULT CONDITIONS;

f) warnings against:

   1) the hazards of explosions when used under critical environmental conditions (e.g., medically used rooms, gas concentrations);

   2) excessive temperatures and other safety hazards;

   3) how to handle if the pen-injector becomes wet (e.g. broken cartridge).

Bibliography

[1] VIM: *International vocabulary of basic and general terms in metrology*

[2] GUM: *Guide to the expression of uncertainty in measurement*

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[7] IEC 61000-4-1:2000, *Electromagnetic compatibility (EMC) — Part 4-1: Testing and measurement techniques — Overview of IEC 61000-4 series*

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