
Pen-injectors for medical use —

Part 1:

**Pen-injectors — Requirements and test
methods**

Stylos-injecteurs à usage médical —
Partie 1: Stylos-injecteurs — Exigences et méthodes d'essai
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Foreword

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

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 3.

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 part of ISO 11608 may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

International Standard ISO 11608-1 was prepared by Technical Committee ISO/TC 84, *Medical devices for injections*.

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*

Annex A of this part of ISO 11608 is for information only.

Introduction

This part of ISO 11608 covers pen-injectors primarily intended for human use. It provides performance requirements regarding essential aspects, so that variations of design are not unnecessarily restricted.

The devices described in this part of ISO 11608 are designed to be used with devices described in ISO 11608-2 and ISO 11608-3.

It is recognized that interchangeability of the components (pen-injector, needle and cartridge) is desirable for some medicinal products and to be avoided for other medicinal products, and that future design may change the current concepts. Therefore, ISO 11608-2 and ISO 11608-3 encourage interchangeability by establishing certain specific requirements for interchangeable needles (Type A) and interchangeable cartridges (Type A) respectively.

Performance requirements are imposed on both Type A (interchangeable) and non-Type A needles and cartridges. Additional dimensional requirements are imposed on Type A needles and cartridges and hereby indirectly on pen-injectors intended for either Type A needles and/or Type A cartridges.

Information as to whether the components are interchangeable (Type A) or not should be given on the unit container.

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 pen-injectors that conforms to the critical product attributes. The sampling plans for inspection do not replace the more general manufacturing quality systems that appear in standards on quality systems, e.g. the ISO 9000 series.

Materials to be used for the construction are not specified, as their selection to some extent will depend upon the design, the intended use and the process of manufacture by individual manufacturers. All materials should be resistant to the medicinal product intended to be injected with the pen-injector.

In some countries national regulations exist, and their requirements may supersede or complement this part of ISO 11608.

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Pen-injectors for medical use —

Part 1:

Pen-injectors — Requirements and test methods

1 Scope

This part of ISO 11608 specifies requirements and test methods for pen-injectors intended to be used with needles and with replaceable or non-replaceable prefilled cartridges.

This part of ISO 11608 is also applicable to pen-injectors which are not electrically driven, but are equipped with electronic components.

This part of ISO 11608 is not applicable to high-pressure injectors and electrically driven injectors.

2 Normative references

The following normative documents contain provisions which, through reference in this text, constitute provisions of this part of ISO 11608. For dated references, subsequent amendments to, or revisions of, any of these publications do not apply. However, parties to agreements based on this part of ISO 11608 are encouraged to investigate the possibility of applying the most recent editions of the normative documents indicated below. For undated references, the latest edition of the normative document referred to applies. Members of ISO and IEC maintain registers of currently valid International Standards.

ISO 11608-2:2000, *Pen-injectors for medical use — Part 2: Needles — Requirements and test methods.*

ISO 11608-3:2000, *Pen-injectors for medical use — Part 3: Finished cartridges — Requirements and test methods.*

IEC 60068-2-6:1995, *Environmental testing — Part 2: Tests. Test Fc: Vibration (sinusoidal).*

IEC 60068-2-6:1995, *Corr. 1.*

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

IEC 60068-2-30, *Amendment No. 1:1985.*

IEC 61000-4-2:1999, *Electromagnetic compatibility (EMC) — Part 4-2: Testing and measurement techniques — Electrostatic discharge immunity test.*

IEC 61000-4-3:1998, *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 part of ISO 11608, the following terms and definitions apply.

The nomenclature of some components of pen-injectors is illustrated in Figure 1.

3.1

pen-injector

medical device intended for parenteral administration by injection of medicinal products from a multidose cartridge

NOTE The doses may be pre-set by manufacturer or user.

3.2

connector

mechanical arrangement allowing the connection between the needle and the cartridge

3.3

cartridge

primary container for the medicinal product

3.4

injection mechanism

mechanism which performs the parenteral injection of the pre-set dose

3.5

release mechanism

mechanism which initiates the parenteral injection of the pre-set dose

3.6

injection stroke

that portion of a parenteral injection involving movement of the injection mechanism following initiation by the release mechanism

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NOTE It does not include the subsequent relaxation of the system components required for the complete injection of the pre-set dose.

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3.7

mechanism holder

part of the body of the injector containing the injection mechanisms

3.8

selector

mechanism which allows pre-setting of a dose

3.9

increment

smallest possible difference to be selected between two dose amounts

3.10

indicator

means by which the amount of pre-set dose is shown

3.11

residual scale

graduated scale which indicates the remainder of medicinal product in the cartridge

3.12

dose accuracy

accuracy with which the pen-injector delivers a pre-set dose of medicinal products

3.13

cap

part of the pen-injector intended to protect the system

3.14**pre-setting**

procedure by which individual amounts of medicinal product can be selected for injection by the user

3.15**unit container**

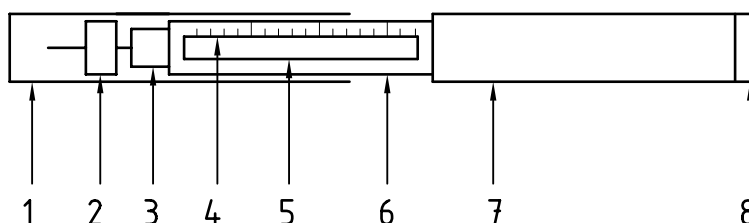
package intended for customer use

3.16**Type A**

classification of needles and cartridges for pen-injectors which fulfil certain specific requirements providing interchangeability

3.17**non-Type A**

classification of needles and cartridges which are not classified as Type A



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Key

- 1 Cap
- 2 Injection system
- 3 Connector
- 4 Residual scale
- 5 Window
- 6 Cartridge holder
- 7 Mechanism holder
- 8 Release mechanism

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Figure 1 — Schematic presentation of a pen-injector

4 Symbols and abbreviations

V_{set} One of the three pre-set doses (expressed as a volume, in millilitres) used in determining the dose accuracy for a given pen-injector. V_{set} is defined as one of the following:

- a) minimum dose ($V_{\text{set}} = V_{\text{min}}$) (specified in the instructions for use);
- b) maximum dose ($V_{\text{set}} = V_{\text{max}}$) (specified in the instructions for use);
- c) midpoint dose ($V_{\text{set}} = V_{\text{mid}}$), where V_{mid} is defined as the injector setting closest to $(V_{\text{min}} + V_{\text{max}})/2$.

NOTE Recommended doses as specified in the instruction for use may differ from those doses that can be set.

V_{meas} The volumetric measurement value for a given V_{set}

G_{meas} The gravimetric measurement value for a given V_{set}

- ρ Density, expressed in grams per millilitre
- p Probability content
- Y Number of pens required for a given test
- R Number of replicates required for a given test. A replicate is a random sequence of V_{\min} , V_{mid} , and V_{\max} . There are six possible replicates.
- n Number of measurements (V_{meas}) to be made for each V_{set}
- \bar{x} The sample mean; when based on a random sample, an estimate of the true mean:

$$\bar{x} = \sum V_{\text{meas}} / n$$

- s The sample standard deviation; when based on a random sample, an estimate of the true standard deviation:

$$s = \left[\sum (V_{\text{meas}} - \bar{x})^2 / (n - 1) \right]^{1/2}$$

- k Tolerance Limit Factor, determined from the confidence level (95 %), probability content (p) and the number of accuracy measurements (n) conducted at each dose setting

- α Absolute error (millilitres) used to define the upper and lower specification limits for a pre-set dose in absolute terms

- β Relative error (%) used to define the upper and lower specification limits for a pre-set dose in relative terms

- TP The transition point volume (millilitres) at which the definition of the upper and lower specification limits for V_{set} changes from absolute terms to relative terms:

$$TP = (100 \times \alpha) / \beta$$

- U Upper specification limit for a given V_{set}

- L Lower specification limit for a given V_{set}

5 General requirements

When the pen-injector is ready for injection, the cartridge holder shall allow visibility of the deliverable volume. It shall be possible to determine whether sufficient medicinal product remains in order to administer the maximum pre-settable dose.

The pen-injector shall be designed such that it is able to deliver the labelled volume from the cartridge for which it is designed.

The pen-injector shall be designed such that the last dose delivered from a cartridge satisfies requirements for dose accuracy.

The pen-injector shall indicate the pre-set dose.

The pen-injector shall indicate, at least by visual means, that it is ready for injection. There shall be an indication of the pre-setting procedure by tactile or audible means, or both.

The state of the pen-injector, when ready to deliver a dose, shall be different to its state when the dose has been delivered. The difference shall be visible.

The pen-injector shall indicate, by visual, audible or tactile means or any combination of these, that the injection stroke has been completed.

If the pen-injector is designed for variable doses, it shall be so designed that it is impossible to deliver a second dose after delivery of the first dose without a second pre-setting.

The pen-injector shall be so designed that it:

- does not allow a larger dose to be pre-set than is left in the cartridge; or
- does not allow dose delivery if the pre-set amount exceeds the amount of medicinal product left in the cartridge; or
- indicates the amount of medicinal product delivered; or
- indicates the amount of medicinal product not delivered of the pre-set dose.

The pen-injector shall be designed to function with a needle fulfilling the specifications of ISO 11608-2.

If the pen-injector is designed to function with a single-compartment cartridge, it shall be designed to function with a cartridge fulfilling the specifications of ISO 11608-3.

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6 Test conditions

6.1 Standard atmosphere

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Unless otherwise specified, measurements shall be performed in the following atmosphere:

- temperature: from 18 °C to 28 °C;
- relative humidity: from 25 % RH to 75 % RH;

after having been subjected to storage for at least 4 h in this atmosphere.

6.2 Cool atmosphere

The assembled pen-injector with the cartridge and needle is placed in a test chamber for at least 4 h in the following cool atmosphere:

- temperature: (5 ± 3) °C.

6.3 Hot atmosphere

The assembled pen-injector with the cartridge and needle is placed in a test chamber for at least 4 h in the following hot atmosphere:

- temperature: (40 ± 2) °C;
- relative humidity: (50 ± 10) % RH.

7 Preconditioning of pen-injectors

7.1 Preconditioning in dry heat atmosphere

The pen-injector without the cartridge and needle is placed in a test chamber for at least 96 h in the following hot atmosphere:

- temperature: $(70 \pm 2) ^\circ\text{C}$;
- relative humidity: $(50 \pm 10) \% \text{RH}$.

7.2 Preconditioning in cold storage atmosphere

The pen-injector without the cartridge and needle is placed in a test chamber for at least 96 h in the following cold atmosphere:

- temperature: $(-40 \pm 3) ^\circ\text{C}$.

7.3 Preconditioning in cyclical atmosphere

The pen-injector with the cartridge and without the needle is placed in a test chamber. Conditioning in accordance with IEC 60068-2-30 is carried out as follows:

- variant 1 (see IEC 60068-2-30, Figure 2a);
- upper temperature: $(55 \pm 2) ^\circ\text{C}$; and
- 6 cycles.

NOTE The relevant clauses of IEC 60068-2-30:1980 are: clauses 3, 6 and 8.

7.4 Preconditioning by free fall

Prepare the pen-injector according to the instructions for use with a new cartridge and proceed as follows:

- a) Pen-injectors with replaceable cartridges
 - 1) Expel the air.
 - 2) Take off the needle and put on the cap.
 - 3) Drop each pen-injector three times by free fall from a height of 1 000 mm onto the test surface (see 8.3), once horizontally and twice vertically, the pen-injector being rotated 180° between the two vertical drops. Care shall be taken that the pen-injector is released in a non-turbulent way.
 - 4) If a cartridge breaks such that it is obvious to the user, replace the cartridge and continue until all three drops have been performed.
- b) Pen-injectors with non-replaceable cartridges
 - 1) Expel the air.
 - 2) Take off the needle and put on the cap.
 - 3) Drop the pen-injectors by free fall from a height of 1 000 mm onto the test surface (see 8.3) in accordance with i), ii) and iii), as follows: