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Needle-based injection systems for medical use — Requirements and test methods —

Part 2:
Double-ended pen needles

Systèmes d'injection à aiguille pour usage médical — Exigences et méthodes d'essai —

Partie 2: Aiguilles à deux extrémités pour stylos-injecteurs

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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.

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).

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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 84, *Devices for administration of medicinal products and catheters*, in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/TC 205, *Non-active medical devices,* in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

This third edition cancels and replaces the second edition (ISO 11608-2:2012), which has been technically revised.

The main changes are as follows:

— terminology for ‘needles’ was updated throughout the document and in the title of the document to ‘double-ended pen needles’ in order to more precisely describe the subject of the document;

— where possible, references to other parts of ISO 11608 (all parts) have been made instead of repeating the content in this document (for example, conditions for preconditioning). Additionally, changes have been made to align with ISO 11608-1 (e.g. sample sizes and test case matrix) ;

— content within this document has been reorganized to create a separate clause for symbols and abbreviated terms, to delineate needle tube requirements, double-ended pen needle requirements and requirements for functional compatibility with needle-based injection systems (NISs), to group the test method sections into defined sections;

— new figures have been added to more precisely illustrate the dimensions of the double-ended pen needle and test gauge referred to in this document;

— requirements for biocompatibility and pyrogenicity introduced and acceptance criteria for flow rate through the needle have been added;

— testing requirements necessary to establish functional compatibility between a specific NIS and a specific double-ended pen needle were revised to include dose delivery and needle hub removal force testing;

— new annexes have been introduced which provide an example method for testing needle bond force (Annex B) and additional background for the requirements in this document (Annex C).

A list of all parts in the ISO 11608 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

This document covers sterile double-ended needles intended for single use in conjunction with needle-based injection systems (e.g. pen injectors). These needles are often referred to as pen needles.

The devices described in this document are designed to be used with the devices described in ISO 11608-1 and ISO 11608-3. This document is intended to be used in conjunction with ISO 11608-1.

The first edition of this document, i.e. ISO 11608-2:2000, introduced the concept of interchangeability and the labelling designations "Type A" (i.e., interchangeable) and "non-Type A" for needles and container closure systems. Since its promulgation, experience has shown that the complexity of these systems makes it very difficult to ensure functional compatibility as defined in the different clauses of this document, particularly when products are made by different manufacturers and the design is not verified as a system. Based on this experience, it is believed that the Type A designation does not represent adequate guidance to the user in making decisions on the compatibility of needles and container closures with specific needle-based injection systems (NIS). As such, the labelling designation "Type A" has been removed.

The second edition of this document, i.e. ISO 11608-2:2012, addressed functional compatibility of the system through testing in accordance with Clause 11 (functional compatibility testing is in Clause 9 in this document). Flow rate was introduced as a new parameter. The sampling plans for inspection selected for this document and outlined in ISO 11608-1 are intended to verify the design, at a high confidence level. The sampling plan does not replace the more general manufacturing quality systems, including lot release, which appear in quality management systems, e.g. ISO 9001 or ISO 13485.

This document refers to ISO 11608-1 for dose accuracy requirements for functional compatibility and includes requirements for double-ended pen needle device adapted from ISO 7864:2016 and new requirements for cleanliness (as part of the freedom from defects requirement), biocompatibility and pyrogenicity testing. After the experience gained through testing for functional compatibility with the second edition of this document, the testing approach was reassessed to ensure that the appropriate tests were included. Following a rigorous review of anonymized dose accuracy data generated by manufacturers over several years, assessing the relationship of dose accuracy and the flow rate through the pen needle, it was determined that there is no relationship between the pen needle flow rate and dose accuracy. This further supports the understanding that the primary contributors to dose accuracy in the NIS system are the NIS and the cartridge.

The needle provides the fluid path from the cartridge to the subcutaneous tissue and its influence on dose accuracy is mainly affected by the correct position of the needle bevel inside the cartridge, a possible leakage and indirectly over the injection force and injection time by the flow rate. The inner diameter has an influence on the time that is needed to deliver the entire volume but not directly to the precision of the dosage. Additionally, a prescribed holding time may be specified in the NIS IFU, which provides for completion of dose delivery during expansion and or relaxation of soft parts within the NIS and cartridge. Therefore, the testing requirements necessary to establish functional compatibility between a specific NIS and a specific pen needle were revised in this edition to include dose delivery and needle hub removal force testing. Dose delivery may be demonstrated either through dose accuracy testing or through confirmation of dose delivery, which includes demonstrating that the needle bevel is positioned inside the cartridge, visual verification that the dose is expelled and inspection for absence of leakage at the base of the non-patient end of the cannula.

Needle-based injection systems for medical use — Requirements and test methods —

Part 2: Double-ended pen needles

1 Scope

This document specifies requirements and test methods for single-use, double-ended, sterile needles intended to be used with some needle-based injection systems (NISs) that use a non-integrated double-ended needle according to ISO 11608-1.

This document is not applicable to the following:

— needles for dental use;

— pre-attached syringe needles;

— hypodermic needles;

— needles intended for different routes of administration (e.g. intravenous, intrathecal, intraocular);

— materials that form the medicinal product contact surfaces of the primary container closure.

However, while this document is not intended to directly apply to these needle products, it does contain requirements and tests methods that can be used to help design and evaluate them.

NOTE Needles provided by the manufacturer integrated into the fluid path or container are covered in ISO 11608-3, and hypodermic needles provided separately are covered in ISO 7864.

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 9626:2016, *Stainless steel needle tubing for the manufacture of medical devices — Requirements and test methods*

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

ISO 10993-11, *Biological evaluation of medical devices — Part 11: Tests for systemic toxicity*

ISO 11608-1:2022, *Needle-based injection systems for medical use — Requirements and test methods — Part 1: Needle-based injection systems*

ISO 11608-3:2022, *Needle-based injection systems for medical use — Requirements and test methods — Part 3: Containers and integrated fluid paths*

3 Terms and definitions

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

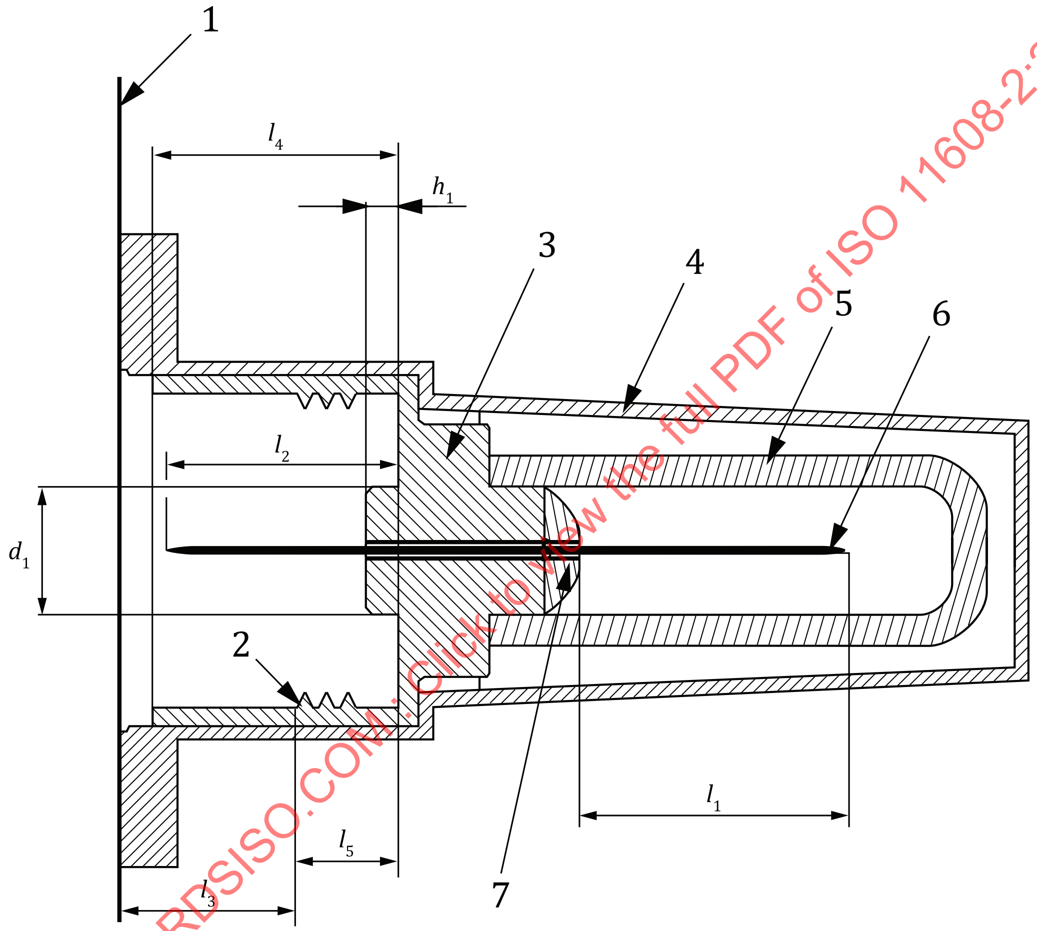
ISO and IEC maintain terminology databases for use in standardization at the following addresses:

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

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

3.1
double-ended pen needle
single-use, double-ended, sterile needles with attachment system specific for some NISs which use a non-integrated needle

Note 1 to entry: See Figure 1.



Key

1	*seal* (3.2)	l_1	patient-end needle length
2	means of needle assembly attachment	l_2	cartridge-end needle length
3	needle hub	l_3	distance from the surface of the seal to the underside of the thread
4	needle container	l_4	depth of the needle hub
5	needle shield (if included)	l_5	distance from the underside of the thread to the surface of the hub base
6	needle tube	h_1	needle hub union length
7	jointing medium (if used)	d_1	diameter of needle hub union

Figure 1 — Example presentation of double-ended pen needle assembly

3.2
seal
removable barrier which maintains the sterility of the needle inside the needle container

3.3
unit packaging
needle container, together with the *seal* (3.2) forming the packaging of the device, that maintains the sterility of the needle

3.4
user packaging
device or collection of devices in their respective *unit packaging* (3.3) provided to the user

4 Symbols

$\alpha_{1,\mathrm{min}}$	Angular distance
λ	Average wavelength of the visual light
C	Calibration constant (used for calculating flow rate using the Extended Hagen–Poiseuille equation)
d_{max}	Maximum allowable dislocation
D_{pupil}	Diameter of the pupil of the eye, where the light is deflected
D_{out}	Nominal outside diameter of the needle tube, expressed in millimetres
$D_{\mathrm{out,hub}}$	Outer diameter of the needle tube at the hub (for tapered needles)
$D_{\mathrm{out,tip}}$	Outer diameter of needle tube at the first full diameter from the tip (for tapered needles)
Q	Flow rate
ρ	Density of the fluid
Q_{min}	Minimum flow rate
U	Resolution of the eye
ΔP	Pressure difference
r	Inner radius (equal to ½ of the inner diameter)
η	Viscosity of the test fluid
V_{high}	Dose pre-set as ≥90 % of the NIS maximum dosage (expressed as a volume, in millilitres)
V_{low}	Dose pre-set as ≤10 % of the NIS maximum dosage (expressed as a volume, in millilitres)

NOTE V_{low} can be set as equal to the minimum dosage of the NIS.

5 Requirements

5.1 Needle tube requirements

5.1.1 General

The following requirements relate to the needle tube component included in the double-ended pen needle device.

5.1.2 Needle tubing materials

The needle tubing shall be made of tubing materials specified in ISO 9626:2016, Clause 4.

5.1.3 Tubing characteristics

The tubing characteristics used in needles shall meet the requirements of ISO 9626:2016, Clause 5.

5.2 Double-ended pen needle requirements

5.2.1 General

The following requirements relate to the double-ended pen needle device. Testing shall be performed using samples that have been exposed to all manufacturing processes, including sterilization, if applicable.

5.2.2 Biocompatibility

Biocompatibility of the pen needle shall be established in accordance with ISO 10993-1 (see also ISO 11608-1:2022, Annex C).

5.2.3 Dimensions for double-ended pen needle assembly

Dimensions of the double-ended pen needle assembly shall be in accordance with Table 1 (the dimensions are shown in Figure 1).

Table 1 — Dimensional requirements of double-ended pen needle

Measurements	Dimensions mm
l_1	specified length ±1,25
l_2	5,7 to 7,0
l_3	<6,0
l_4	<7,5
l_5	<3,7
h_1	0 to 1,0
d_1	0 to 3,0

Needle manufacturers shall consider the risks of not delivering to the target tissue (e.g. specified length appropriate for the target tissue) and of the cartridge end of the double-ended pen needle assembly interfering with delivery of the medicinal product (e.g. bevel not clearing septum, too much dead space in cartridge) when setting the specifications in accordance with Table 1.

The dimensions of the means of attachment part of the double-ended pen needle (see Figure 1, dimension 2) shall be such that the needle fits and functions with the NIS for which it is intended. Pen needles shall fit the test gauge specified in 8.2.

Pen needles can be deliberately designed not to fit the test gauge described in 8.2 and not to meet the dimensional requirements given in Table 1. In such cases, a dedicated test gauge for the specific design shall be created in order to perform the tests in Clause 9. In addition, the remaining requirements, other than those in 5.2.3, shall apply. In cases where the dimensional requirements of 5.2.3 are not met, the needle labelling shall list the NIS(s) and accessories for which it has been designed and tested.

5.2.4 Needle points

When visually inspected by normal or corrected to normal vision under magnification of 2,5x and at environmental lighting conditions of ≥750 lx needle points shall appear sharp and free from feather edges, burrs and hooks.

NOTE The resolution of the human eye is approximately 5 µm. Considering a safety factor of 10, burrs of around 0,05 mm can be detected using the inspection conditions above. Where the criteria are lower than 0,05 mm, alternate inspection conditions can be used (see Annex C).

The needle point at the cartridge end shall be designed so as to minimize coring and fragmentation when penetrating the cartridge septum. Test according to the procedure specified in ISO 11608-3:2022, 5.2.

5.2.5 Freedom from defects

When inspected by normal or corrected-to-normal vision without magnification and at environmental lighting conditions of ≥750 lx and from a reading distance of between 30 cm and 70 cm, the double-ended pen needle shall meet the following requirements:

a) the outer surface of the tubing shall be smooth and free from defects;

b) lubricant shall not be visible as droplets of fluid on the outside surface of the needle tube;

c) the surface of the needle tube (patient end and cartridge end) shall appear free from particles and extraneous matter.

5.2.6 Flow rate through the needle

5.2.6.1 Non-tapered needle flow rate

For non-tapered needles, the flow rate through the needle shall demonstrate patency of the lumen, determined by either method a) or method b):

a) Measure the flow rate of water through the needle in accordance with Annex A to determine the minimum flow rate through the needle, in ml/min (expressed to a tenth of a ml/min). The measured flow rate shall be made available on request.

   The flow rate measured for each gauge size shall not be less than 80 % of an unprocessed needle tube of equivalent outer diameter and length having a minimum inner diameter in accordance with ISO 9626 when tested under the same pressure, or shall not be less than 80 % of the minimum flow rate as calculated based on the Extended Hagen–Poiseuille equation, presented in C.3.5, which has the following dependency: $Q=Q(r,l,\eta,\rho,\Delta p,C)$

   When acceptance criteria are based upon the Extended Hagen-Poiseuille equation, the validity of the equation shall be ensured when calculating the theoretical flow rate. See C.3.5 for details about the validity of the equation.

b) Demonstrate that a stainless steel stylet of the appropriate diameter selected from the diameters given in Table 2 shall pass through the needle.

It is recommended to use method a) for needles with designated metric sizes below 0,30 mm and hence no stylets are listed in Table 2 for designated metric sizes below 0,30 mm.

Table 2 — Size of stylet to test patency of lumen

Designated metric size of needle mm	Needle Gauge	Outer diameter of stylet mm			
		for needle of regular walled tubing	for needle of thin-walled tubing	for needle of extra-thin-walled tubing	for needle of ultra-thin-walled tubing
0,30	30	0,11	0,13	0,15	0,19
0,33	29	0,11	0,15	0,19	0,21
0,36	28	0,11	0,15	—	—
0,40	27	0,15	0,19	—	—
0,45	26	0,18	0,23	—	—
0,50	25	0,18	0,23	—	—
0,55	24	0,22	0,27	—	—
0,60	23	0,25	0,29	0,30	—
0,70	22	0,30	0,35	0,37	—
0,80	21	0,40	0,42	0,44	—
0,90	20	0,48	0,49	0,50	—
1,10	19	0,58	0,60	0,68	—
1,20	18	0,70	0,73	0,83	—

5.2.6.2 Tapered needle flow rate

For tapered needles, the patency of lumen shall be verified by measuring the flow rate of water through the needle in accordance with Annex A to determine the minimum flow rate through the needle, in ml/min (expressed to a tenth of a ml/min). The measured flow rate shall be made available on request.

The flow rate measured for each gauge size shall not be less than 80 % of an unprocessed needle tube with minimum inner diameter at both the tip and hub corresponding to their respective designations from ISO 9626, when tested under the same pressure.

5.2.7 Bond between hub and needle tube

The union of the hub and needle tube shall withstand at least the minimum force specified in Table 3 at standard atmosphere and following preconditioning in accordance with Clause 7 in dry heat, cold storage, damp heat and cyclical atmospheres when tested in accordance with 9.1. The minimum force shall be based on the metric size designation of the needle. For tapered needles, the minimum force given in Table 3 shall be determined by the outer diameter of the needle tube at the hub ($D_{out\text{-}hub}$).

Table 3 — Minimum force for bond between hub and needle tube

Designated metric size of needle mm	Needle gauge	Minimum force N
0,18	34	11
0,20	33	
0,23	32	
0,25	31	
0,30	30	
0,33	29	22
0,36	28	
0,40	27	
0,45	26	
0,50	25	
0,55	24	34
0,60	23	
0,70	22	40
0,80	21	44
0,90	20	54
1,10	19	69
1,20	18	

NOTE Table adapted from ISO 7864:2016, Table 2, with gauge from 9626:2016, Table 1.

5.2.8 Dislocation of measuring point at patient end

Dislocation of the cannula point (d_{max}) at the patient end shall be in accordance with:

$$d_{max} = 0{,}07 \times l_1 + 0{,}3$$

where

d_{max} is maximum allowable dislocation, expressed in millimetres;

l_1 is patient-end needle length (see Figure 1), expressed in millimetres.

when tested in accordance with 9.2.

5.2.9 Ease of assembly

Attachment of the needle to the NIS shall be possible without removing the needle from its opened unit packaging, when tested in accordance with 9.3.

5.2.10 Sterility

The needle in its unit packaging shall have been subjected to a validated sterilization process, e.g. in accordance with ISO 11135 or ISO 11137-1.

5.2.11 Pyrogenicity

The pen needle shall be non-pyrogenic, demonstrated by fulfilling the following requirements for endotoxin-mediated pyrogenicity and material-mediated pyrogenicity:

a) the pen needle device shall not exceed the lesser of 0,5 EU/ml (endotoxin units) or 20 EU per device when tested, for example, in accordance with relevant pharmacopeia such as US Pharmacopeia <161>;

b) the pen needle device shall conform to ISO 10993-11 for material-mediated pyrogenicity.

5.3 Functional compatibility with NISs

5.3.1 General

When the labelling claims that the needle is compatible with a NIS, the following functional compatibility requirements shall be fulfilled:

a) dose delivery in accordance with 5.3.2 to confirm integrity of a clinically relevant fluid pathway;

b) needle removal torque as specified in 5.3.3.

when tested in accordance with the test methods for functional compatibility provided in 9.4.

Bracketing and matrixing of needle sizes, flow rates or other parameters may be applied, if justified.

NOTE 1 Bracketing and matrixing is typically only appropriate within a given needle manufacturer, with consideration of the geometry of the needle hub.

NOTE 2 Dose accuracy of the combination NIS, cartridge and needle is mainly driven by the NIS and the cartridge. The needle provides the fluid path from the cartridge to the subcutaneous tissue and its influence on dose accuracy is mainly affected by the correct position of the needle bevel inside the cartridge, a possible leakage, and indirectly, over the injection force and injection time by the flow rate. The inner diameter has an influence on the time which is needed to deliver the entire volume but not directly to the precision of the dosage. Additionally, a prescribed holding time can be specified in the NIS IFU, which provides for completion of dose delivery during expansion and or relaxation of soft parts within the NIS and cartridge.

5.3.2 Dose delivery

5.3.2.1 General

The needle and the NIS shall deliver the doses set verified by either

a) dose accuracy as specified in 5.3.2.2, or

b) confirmation of dose delivery as specified in 5.3.2.3.

The sample quantity requirements specified in 9.4.1 shall apply.

5.3.2.2 Dose accuracy

When the dose accuracy testing specified in 9.4.2.2 is selected for verification of dose delivery, the accuracy requirements in ISO 11608-1:2022, 7.4.2, shall apply.

5.3.2.3 Confirmation of dose delivery

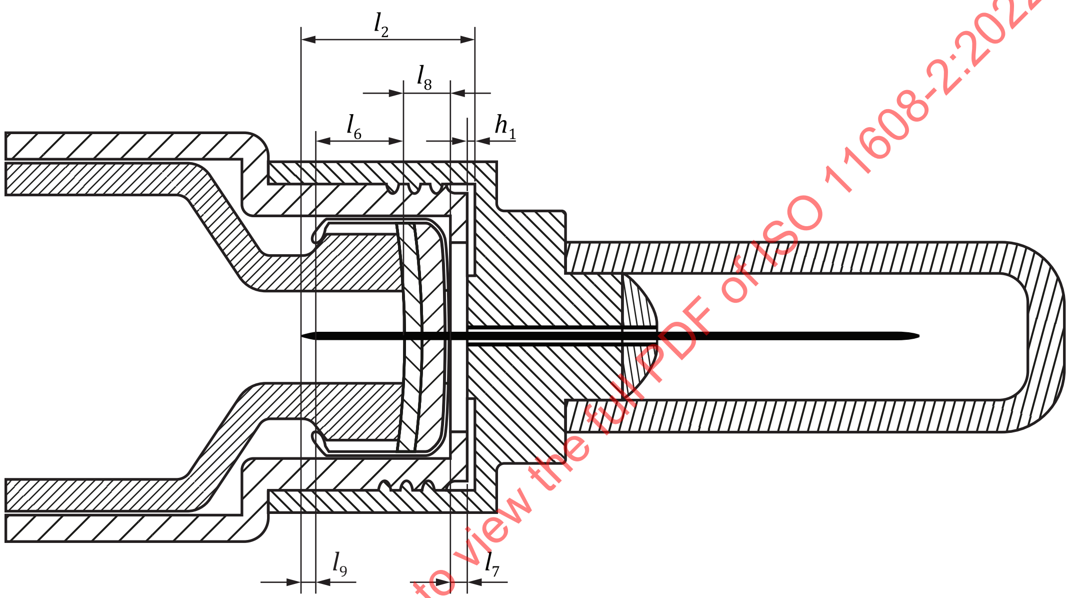
When the qualitative confirmation of dose delivery approach is selected for verification of dose delivery, the following shall apply:

a) When tested in accordance with the method specified in 9.4.2.3, fluid shall be expelled from the NIS and confirmed visually.

b) When tested in accordance with the method specified in 9.4.2.3, the needle when detached from the NIS following expelling a dose shall not have visible fluid present at the base of the non-patient end of the cannula (see intersection of l_2 and h_1 in Figure 1).

c) The needle bevel shall be positioned behind the septum (l_6 > 0 mm) inside the cartridge when the pen needle is applied to the NIS with a torque of (0,07 ± 0,01) Nm. An example for positioning of the needle bevel inside the cartridge is illustrated in Figure 2. For calculations, see Annex C.

Verification of this requirement can be based on calculations of worst case (e.g. taking into account impact by tolerance, impact by deformation of the septum due to friction between needle and septum). The calculations may differ for alternative designs, including other means of cartridge support in the cartridge holder (e.g. cartridge shoulder).



Key

l_2 cartridge-end needle length

l_6 gap between bevel and septum

l_7 bottom thickness of cartridge holder

l_8 thickness of septum

l_9 length of bevel cut

h_1 needle hub union length

As there can be additional influences on dimensions, such as due to crimping processes, it is recommended to measure the dimension l_7 and l_8 for the NIS that the manufacturer intends to claim conformance to in order to determine l_6.

Figure 2 — Example of positioning of needle bevel inside the cartridge

5.3.3 Needle removal torque

The needle hub peak removal torque shall be determined for the combination of the needle and the NIS with which compatibility is sought. Testing shall be performed in accordance with 9.4.3.

The needle hub peak removal torque shall be less than 0,100 Nm. If the needle has no thread, applicable assembly and disassembly testing shall be adapted to the corresponding requirements:

a) if three or more needles result in a peak (removal) torque of 0,100 Nm or more, the test is rejected;

b) if zero, one or two needles result in a peak (removal) torque of 0,100 Nm or more, the test results are accepted.

6 Sampling

Table 4 summarizes test requirements for double-ended pen needles devices intended to be used with NISs.

Table 5 summarizes test requirements when demonstrating functional compatibility between double-ended pen needles and NISs.

Each test case can have more than one characteristic (e.g. needle removal force plus others) that needs to be tested. The sample size here is for each characteristic to be tested, although multiple characteristics can be tested on the same set of samples, and potentially at the same time.

Other sample sizes may be chosen. However, if smaller than the recommended sample size, it shall be justified that the sample size is appropriate for the risk associated with the characteristic.

Either dose accuracy or confirmation of dose delivery methods may be used to satisfy the dose delivery requirement (5.3.2).

Table 4 — Test case matrix – Double-ended pen needles

Double-ended pen needle test case (with reference to subclauses)		Probability content	Recommendations for variable data (normal distribution or converted)			Recommendations for attribute data
			Number of measurements *n*	Two-sided target *k*	One-sided target *k*	Number of measurements *n*
Dimensions for double-ended pen needles (5.2.3)		0,95	20	2,760	2,396	60
Needle points (5.2.4)		0,95	N/A	N/A	N/A	60
Freedom from defects (5.2.5)		0,95	N/A	N/A	N/A	60
Flow rate through the needle (5.2.6)		0,95	60	N/A	2,022	60
Bond between hub and needle tube, (5.2.7):	no preconditioning (Clause 8)	0,95	20	N/A	2,396	60
	preconditioning in dry-heat (7.1)	0,95	20	N/A	2,396	60
	preconditioning in cold storage (7.1)	0,95	20	N/A	2,396	60
	preconditioning in damp heat atmosphere (7.1)	0,95	20	N/A	2,396	60
	preconditioning in a cyclical atmosphere (7.2)	0,95	20	N/A	2,396	60
Dislocation of measuring point at patient end (5.2.8)		0,95	20	2,760	2,396	60
Ease of assembly (5.2.9)		0,95	N/A	N/A	N/A	60

Table 5 — Test case matrix – Functional compatibility between double-ended pen needle and NIS

Functional compatibility case (with reference to Clauses)		NIS System designation				Probability content	Recommendations for variable data (normal distribution or converted)			Recommendations for attribute data
		A	B	C	D		Number of measure-ments n	Two-sided target *k*	One-sided target *k*	Number of measure-ments n
Dose delivery (5.3.2) - test either con-firmation of dose delivery or dose accu-racy:	Dose accuracy (5.3.2.2)	X	X	X	X	0,975	30[a]	2,921	2,608	120[a]
	Confirmation of dose delivery (5.3.2.3)	X	X	X	X	0,975	N/A	N/A	N/A	120[b]
Needle removal torque (5.3.3)		X	X	X	X	0,898 76	N/A	N/A	N/A	60 (2 failures are al-lowed)

[a] For variable dose NIS, the number of measurements is for each dose level, V_{low} and V_{high}

[b] For variable dose NIS, the total number of measurements should include 100 V_{low} measurements and 20 V_{high} measurements, which make up the 120 total measurements. The V_{high} measurements shall be obtained using a minimum of 5 unique cartridges, which is aligned with ISO 11608-1:2022, Table F.1 for systematic failures at 50,0 % probability.

7 Preconditioning of needles

7.1 Preconditioning in a dry-heat, cold storage and damp heat atmosphere

Place needles within unit packaging in each test chamber according to atmospheric conditions as specified in ISO 11608-1:2022, Tables 5, 6 and 7.

7.2 Preconditioning in a cyclical atmosphere

Place the needle within its unit packaging in a test chamber. Carry out conditioning in accordance with ISO 11608-1:2022, 10.3.5.

8 Standard atmosphere and test apparatus

8.1 Standard test atmosphere

Unless otherwise specified, measurements shall be performed in the standard atmosphere according to ISO 11608-1:2022, Table 4.

8.2 Test gauge

The test gauge shall be made out of hardened steel, e.g. W1. The dimensions shall be given in millimetres and shall be in accordance with Figure 3.

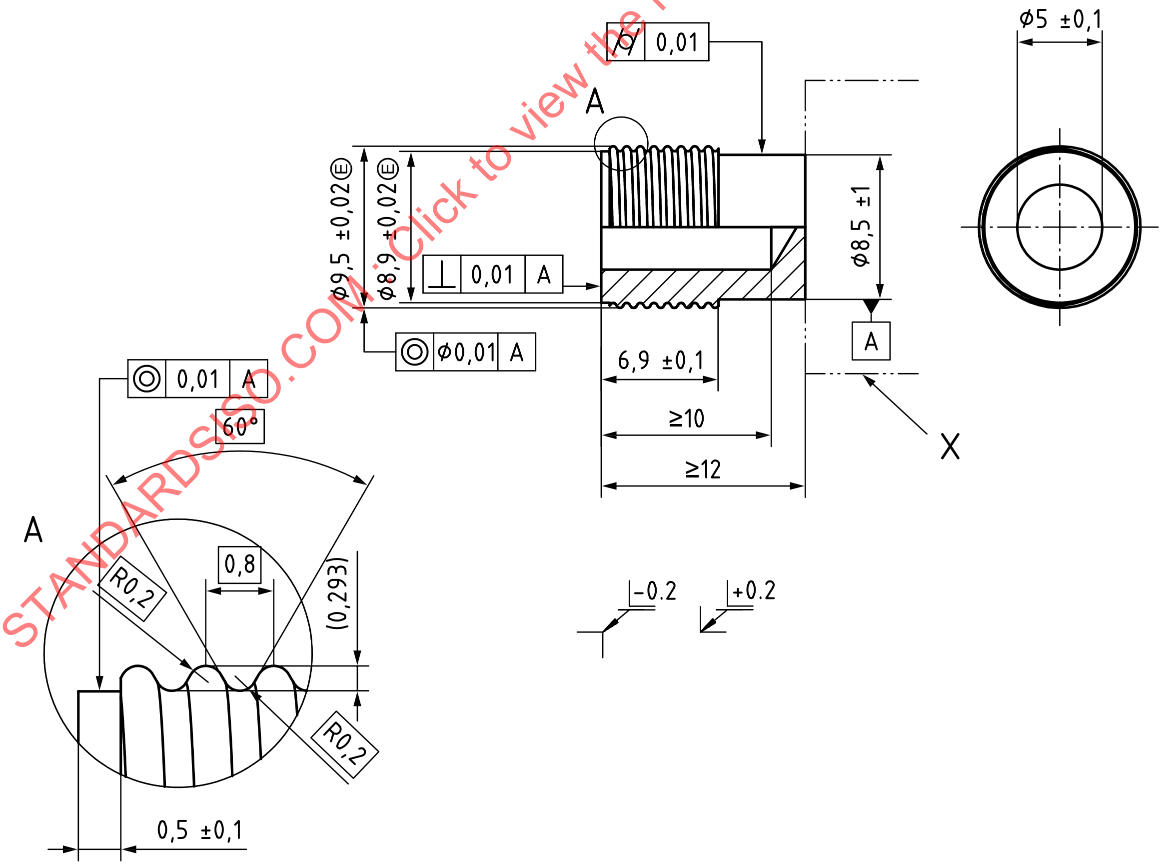


Figure 3 — Test gauge for needles

Needles may be deliberately designed with unique geometry which does not meet the dimensional requirements given in Table 1 and therefore will not fit the test gauge shown in Figure 3. In such cases, a dedicated test gauge for the specific design shall be created in order to perform the tests.

8.3 Test apparatus

All test apparatus shall conform to the requirements in ISO 11608-1:2022, 6.1.

Torque testing apparatus shall be capable of holding the needle and the NIS firmly (for needles with a thread). The apparatus shall be capable of measuring an assembly torque (clockwise direction) of (0,07 ± 0,02) Nm. The apparatus shall also be capable of measuring a removal torque (anti-clockwise direction). The apparatus shall be suitable for determining whether the peak value result conforms to the requirement.

Time keeping device, capable of timing 10 s ± 0,5 s.

9 Test methods

9.1 Bond between hub and needle tube

Select a sample size in accordance with Clause 6.

Attach the needle to a test gauge (see Figure 3). Verify that the needle is completely attached.

Grip the needle tube and apply a tension in the direction of the needle axis.

NOTE An example of a test method for determining needle bonding strengths is given in Annex B.

Repeat the needle bond strength test with new sets of needles, each preconditioned in accordance with Clause 7 at one of the conditions specified in Table 4.

9.2 Determination of dislocation of measuring point at patient end

Select a sample size in accordance with Clause 6.

Tighten the needle to the test gauge (see Figure 3) with a torque of 0,060 Nm to 0,080 Nm.

Place the test gauge upon a “V-block” that is affixed to the cross-slide of an optical comparator.

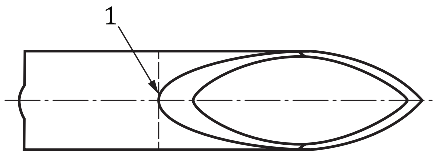
Align the top edge of the cylindrical part of the test gauge outer diameter with the x-axis of the comparator.

Move the “V-block” upwards by half the outer diameter of the test gauge.

NOTE Moving the "V-block" will align the test gauge centre line with the x-axis of the comparator.

Rotate the test gauge and the maximum dislocation (positive or negative) of the centre of the lumen at the level of the measuring point shown in Figure 4 relative to the x-axis of the comparator (dimension to be expressed to a tenth of millimetre).

Methods other than the non-contact method are acceptable to determine dislocation.



Key

1 measuring point

Figure 4 — Point on the needle for measuring dislocation

9.3 Ease of assembly

Select samples in accordance with Clause 6.

With the needle in its unit packaging, attach the needle to a test gauge (see Figure 3). Verify that the needle is completely attached without needing to remove the needle from its open unit packaging. If the needle has no thread, assembly testing shall be adapted to the corresponding requirements.

9.4 Functional compatibility with NISs

9.4.1 Sample quantity requirements

Select the test needle samples in accordance with Clause 6. Consider the following when selecting the samples:

— Dose delivery testing is performed by delivering doses through the pen needle and measuring combinations of injection cycles (in random or alternating sequence) of test replicates. Only one replicate shall be taken for each needle.

— Where the NIS to be evaluated is fixed dose, testing shall be performed using the fixed dose level. For variable dose NIS, testing shall include two dose levels, where $V_{low} \leq 10$ % of the NIS maximum dosage or equal to the NIS minimum dosage and $V_{high} \geq 90$ % of the NIS maximum dosage, in accordance with Table 5.

— The NIS, cartridge and needle combinations for removal torque testing can be the same samples used for dose delivery testing or different samples.

— An adequate supply of NIS shall be collected to complete the test. The number of NISs should be calculated prior to testing. The NIS fluid volume and the maximum NIS dosage are some of the factors that shall determine this required quantity.

— If required by the acceptance criteria and test results, additional needles and NISs can also need to be prepared and tested.

— A NIS and cartridge combination with an integrated non-replaceable container or with an integrated replaceable container should be used until the fluid is depleted in accordance with typical NIS usage guidelines, i.e., the next required full dose cannot be set and/or delivered. The test liquid shall be as specified in ISO 11608-1:2022, 6.2.

— When the volume of fluid remaining in the NIS is lower than is required for the test, a new NIS shall be used with an integrated non-replaceable container, or a new cartridge (and cartridge holder, if threaded) shall be inserted into a new NIS with replaceable container, as applicable.

9.4.2 Test procedures for testing dose delivery

9.4.2.1 General

The dose delivery requirement shall be demonstrated either through dose accuracy testing (9.4.2.2) or through confirmation of dose delivery (9.4.2.3).

9.4.2.2 Procedure for testing dose accuracy

Select a sample size in accordance with Clause 6 and consider the requirements in 9.4.1.

Dose accuracy can be measured with the needle submerged or non-submerged, with the measurement equipment in accordance with ISO 11608-1:2022, Clause 6.

Prepare the balance or measurement equipment.

Prime the NIS, as applicable, in accordance with the instructions for use.

For a variable dose NIS, select and set the first target dose.

NOTE 1 This is the V_{low} or the V_{high} dose according to a random or alternating dosing sequence.

Operate the NIS and determine the dose delivered (e.g. gravimetrically or volumetrically)..

For a variable dose NIS, perform dose accuracy for the second target dose on the NIS with new needles.

NOTE 2 This is the other dose (either the V_{low} or the V_{high}) according to a random or alternating dosing sequence.

Complete the other required test replicates using new needles with the same NIS and cartridge, as required by the NIS fluid volume size using a test schedule (e.g. random or alternating high and low volume settings for variable dose NIS).

Convert all mass readings to volume, using the appropriate density for the test liquid and environmental conditions in accordance with ISO 11608-1:2022, 7.2.1.

9.4.2.3 Procedure for dose delivery confirmation

The procedure for dose delivery confirmation includes two elements:

a) visual confirmation that fluid is expelled; and

b) visual inspection for absence of leakage.

Select a sample size in accordance with Clause 6 and consider the requirements in 9.4.1.

Prime the NIS, as applicable, in accordance with the instructions for use.

For a variable dose NIS, select and set the target dose.

NOTE This is the V_{low} or the V_{high} dose according to a random dosing sequence.

Operate the NIS and visually confirm that fluid was expelled.

Remove the needle and inspect the base of the needle at the non-patient end of the cannula of the samples by normal or corrected-to-normal vision without magnification and at environmental lighting conditions of ≥750 lx for any leakage of test liquid.

Complete the other required test replicates using new needles with the same NIS and cartridge, as required by the NIS fluid volume size using a testing schedule (see Clause 6), ensuring to include at least 5 cartridge samples in the measurements for V_{high}, as defined in Table 5.

9.4.3 Procedure for testing needle hub removal torque

Select a sample size in accordance with Clause 6 and consider the requirements in 9.4.1.

Load the associated cartridge into the reusable NIS, as applicable.

For NISs with integrated non-replaceable containers, the fluid is within the NIS itself and no cartridges are to be loaded.

Insert the test needle or NIS into the needle hub torque test apparatus.

Combine the test needle with the NIS with an application torque of (0,07 ± 0,01) Nm. Record the peak assembly (torque-on) measured result for each test needle and confirm that the peak torque is between 0,06 Nm to 0,08 Nm.

Start the 10 s timer. Allow the assembly to rest for at least 10 s.

Unscrew the pen needle threaded hub from the NIS and record the peak (torque-off) removal torque result.

10 Packaging

Each needle shall be sealed in its unit packaging. One or more unit packages shall be contained in the user packaging.

The materials used in the unit packaging shall not have a detrimental effect on the contents. The materials and design of this container shall ensure:

a) maintenance of the sterility of the contents under normal handling and storage;

b) minimal risk of contamination of the contents during removal from the container;

c) that when the seal is removed there is no interference with the subsequent assembly of the needle and NIS;

d) adequate protection of the contents during normal handling, transit and storage;

e) that the container cannot be resealed once it has been opened and that there is evidence of the container having been opened.

11 Information supplied with the needle(s)

11.1 General

The needle shall be accompanied by information that is sufficient for its safe use, taking into account the training and knowledge of potential users. Instruction for use should be included in the user packaging (see 11.3).

If the needle is provided with both a needle container and a needle shield, a warning shall be given in the instructions for use and/or on the user packaging regarding the need to remove both the needle container and needle shield before injection, for example the following text and illustration given in Figure 5 can be given:

Warning — Remove both the needle container and the needle shield before an injection. If both the needle container and the needle shield are not removed before use, the medication or dose might not be injected, which can result in harm.

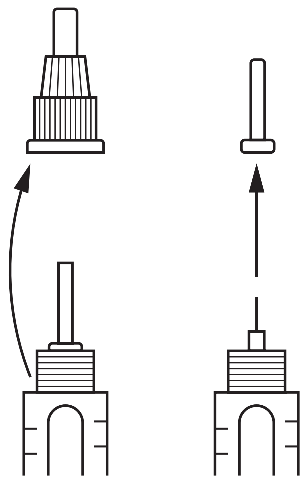


Figure 5 — Representative example image for warning regarding the need to remove both the needle container and needle shield before injection

11.2 Marking

11.2.1 Marking on the unit packaging

In addition to the requirements in ISO 11608-1, the marking on the unit packaging shall comprise at least the following particulars:

a) details necessary for the user to identify the needle, including the designated metric size, in accordance with the following expression:

$$D_{out} \times l_1$$

where

D_{out} is the nominal outside diameter of the needle tube, expressed in millimetres;

l_1 is the nominal length of the needle tube, expressed in millimetres.

EXAMPLE 0,33 mm x 12,7 mm.

b) For tapered pen needles, details necessary for the user to identify the needle, including the designated metric size, shall be provided in accordance with the following expression:

$$\left(D_{out\text{-}tip} / D_{out\text{-}hub}\right) \times l_1$$

where

$D_{out\text{-}tip}$ is the designated metric size of the needle tube at the first full diameter from the tip (measuring point 1, at the end of the bevel geometry as shown in Figure 4) expressed in millimetres;

$D_{out\text{-}hub}$ is the designated metric size of the needle tube at the hub side, measured at the first full diameter from the top of the hub or from the top of the jointing medium, if used, expressed in millimetres;

l_1 is the nominal length of the needle tube, expressed in millimetres (see Figure 1).

c) the word “sterile” or the symbol ISO 7000-2499 and method of sterilization (symbols ISO 7000-2500, ISO 7000-2501, ISO 7000-2502 and ISO 7000-2503, as appropriate):

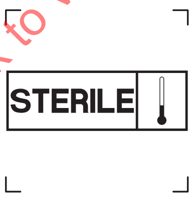
ISO 7000-2499:

ISO 7000-2500:

ISO 7000-2501:

ISO 7000-2502:

ISO 7000-2503:



11.2.2 Marking on the user packaging

In addition to the requirements in ISO 11608-1, the marking on the user packaging shall comprise at least the following particulars:

a) information on the NISs with which the needle assembly is intended to be used and which have been confirmed as functionally compatible with the needle in accordance with 5.3;

NOTE Compatibility testing is specified in 9.4.

b) the words “for single use” or the symbol ISO 7000-1051;

c) the word “sterile” or the appropriate symbol [see 11.2.2 c)].

11.3 Instructions for use

In addition to the requirements in ISO 11608-1, the instructions for use, where given, shall contain information on the attachment of the needle to the NIS, if the attachment procedure differs from that given in the instructions for use of the NIS.

Annex A
(normative)

Determination of flow rate through needle

A.1 Principle

The water flow through a sample needle is measured using an appropriate calibrated and qualified flow meter, or an apparatus such as the one outlined in Figure A.1, combined with a calibrated scale.

NOTE This method is adapted from ISO 7864:2016, Annex C.

A.2 Materials

Pen needle samples shall be selected in accordance with Clause 6.

Distilled or other purified water.

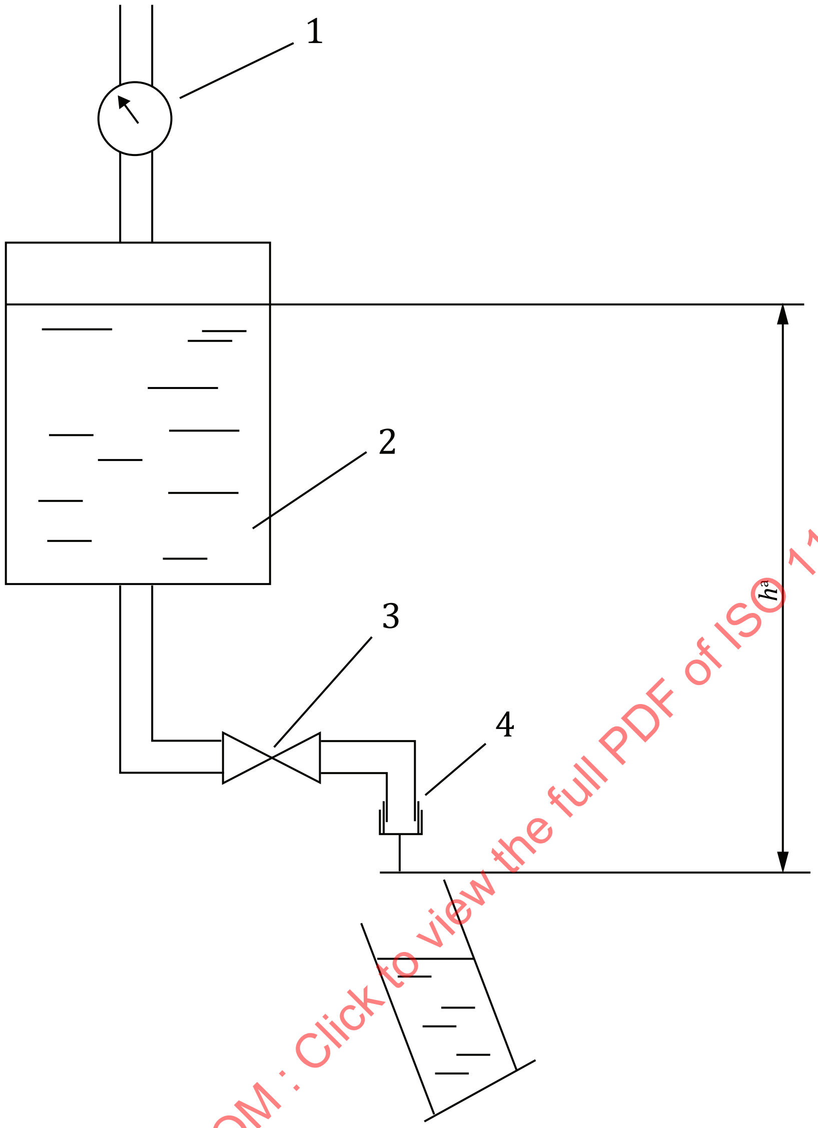
A.3 Apparatus

Test fixture (see Figure A.1), upon which the sample needle is mounted, combined with a calibrated and qualified flow meter or a calibrated scale.

Water tank, to which the test fixture is connected, pressurized to (1,1 ± 0,01) bar using compressed air.

NOTE The pressure 1,1 bar is considered to best mimic the average user situation.

Timekeeping device, with measurement uncertainty of ±0,25 s maximum.



Key

1 pressure gauge
2 distilled water
3 ON/OFF valve
4 needle interface
h
a Maximum 100 mm.

Figure A.1 — Example of test equipment

A.4 Test procedure

Fill the water tank with water at (23 ± 2) °C and connect or screw the test needle into the test fixture that is connected to the water tank.

If using a flow meter, let the water flow through the needle for at least 15 s and record the flow rate.

If using a balance and a timekeeping device, let the water flow through the needle for at least 15 s and collect the efflux in a suitable vessel. Record the time of the flow of the water.

Determine the volume by weighing the mass of the efflux, assuming that the density of water equals 1,000 g/ml.

NOTE The tolerances on temperature, pressure and time keeping have been chosen taking into account what is commonly achieved, although it is recognized that they contribute differently to the overall tolerance.

A.5 Test analysis

If the time of flow and volume were recorded, calculate the flow rates obtained from each sample in millilitres per minute by dividing the volume by the time period that the measurement was made.

Determine the minimum flow rate (expressed to a tenth of a ml/min), which at least 0,95 (95 %) of all needles will exceed at a confidence level of 0,95 (95 %), by using the formula:

$$Q_{\text{min}} = \bar{x} - k \times s$$

where

Q_{min} is the minimum flow rate;

$\bar{x}$ is the mean of the flow rates;

k 2,022 (k-factor from Table 4);

s is the standard deviation of the flow rates.

Annex B
(informative)

Needle bonding strength test method

B.1 Principle

The test is used to assess the bonding strength between the needle tube and the needle hub.

It is mainly designed to verify whether the applied needle bonding system is appropriate for the needle to withstand a tensile force as determined by the designated metric size of the needle.

B.2 Materials

Sterilized needles, sample size as determined for the intended test program, see Clause 6.

B.3 Apparatus

Universal tensile and compression testing machine complying with the following:

— load cell appropriate for the force to be measured;

— test speed of (50 ± 5) mm/min;

— sampling rate as appropriate for this testing purpose.

Test fixture holding the needle allowing the needle to be aligned with the lower gripper.

Needle tube gripper device with gripper jaws designed to avoid slippage.

B.4 Preparation and preservation of test samples

Testing is made at ambient laboratory conditions, unless otherwise specified.

B.5 Procedure

Insert the test sample vertically positioned on the testing machine.

Set the load cell to "zero". Ensure that no significant pre-load is applied when the grippers are closed.

Grip the needle in such a manner to avoid slippage.

Apply a test speed of (50 ± 5) mm/min at an appropriate sampling rate (data points per second).

Start the test.

Stop the test once the needle is clearly removed from the hub, or the hub or needle tube is broken.

Record the maximum load (N). This corresponds to the needle bonding force.