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Needle-based injection systems for medical use - Requirements and test methods - Part 3: NIS containers and integrated fluid paths (ISO/DIS 11608-3:2020)

Kanülenbasierte Injektionssysteme zur medizinischen Verwendung - Anforderungen und Prüfverfahren - Teil 3: Fertigbehälter (ISO/DIS 11608-3:2020)

Systèmes d'injection à aiguille pour usage médical - Exigences et méthodes d'essai - Partie 3: Conteneurs NIS et chemins de fluide intégrés (ISO/DIS 11608-3:2020)

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

Part 3:
NIS containers and integrated fluid paths

ICS: 11.040.25

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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).

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

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

This document was prepared by Technical Committee ISO/TC 84, *Devices for administration of medicinal products and catheters*.

This third edition cancels and replaces the second edition (ISO 11608-3:2012), which has been technically revised.

The main changes compared to the previous editions are specified in Annex B.

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 is applicable to containers (e.g. cartridges, syringes) and their integrated fluid paths intended for use with Needle-based Injection Systems (NIS) covered by the umbrella standard, ISO 11608-1. Containers may be provided pre-filled from the manufacturer (i.e. primary container closure) or empty for filling by the user (i.e. reservoir).

Prior versions focused on multi-dose pen-injector cartridges, important dimensions (e.g. inner diameter) and related attributes (e.g. disc seal eccentricity, meniscus) deemed critical for pen-injector form, fit, and function. The prior edition also included a more general discussion of "other containers" like syringes given their role in single dose NIS with automated functions (commonly referred to as auto-injectors).

The scope of the latest revision of ISO 11608 (all parts) has been expanded to include on-body delivery devices (ISO 11608-6), resulting in additional possibilities for future container types. This expansion of 11608-3 to include evolving NIS technologies requires a broader discussion of containers, integrated fluid paths, and test methods.

Given the expansion in scope of this document, test methods and dimensions specific to traditional pen-injector “Type A” cartridges have been removed and, for historical reference, that information has been preserved in informative Annex B.

There are other international and national standards, guidance materials and, in some countries, national regulations that are applicable to medical devices and pharmaceuticals; their requirements might supersede or complement this document. Developers and manufacturers of NIS are encouraged to investigate and determine if there are any other requirements relevant to the safety of their products.

ISO 11608-1 is the umbrella document of the ISO 11608 series. All other parts, including this document, are to be used in conjunction with ISO 11608-1.

Guidance on transition periods for implementing the requirements of this document is given in ISO/TR 19244.

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

Part 3: NIS containers and integrated fluid paths

1 Scope

This document specifies requirements and test methods for design verification of containers and integrated fluid paths to be used with Needle-Based Injection Systems (NIS) that fulfil the requirements of ISO 11608-1 (and other subparts as appropriate). It is applicable to single and multi-dose containers (either filled by the manufacturer [primary container closure] or by the end-user [reservoir]) and fluid paths that are integrated with the NIS at the point of manufacture.

NOTE Prefilled syringes (ISO 11040-8) are included in the scope when used with a NIS; see also scope of ISO 11608-1:20xx.

Products excluded from scope are:

— sterile hypodermic needles for single use;

— sterile hypodermic syringes for single use;

— sterile single-use syringes, with or without needle, for insulin;

— containers that can be refilled multiple times;

— containers intended for dental use;

— catheters or infusion sets that are attached or assembled separately by the user.

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 7864:2016, *Sterile hypodermic needles for single use — Requirements and test methods*

ISO 8872, *Aluminium caps for transfusion, infusion and injection bottles — General requirements and test methods*

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

ISO 10555-1:2013,[1)] *Intravascular catheters — Sterile and single-use catheters — Part 1: General requirements*

ISO 10555-5:2013, *Intravascular catheters — Sterile and single-use catheters — Part 5: Over-needle peripheral catheters*

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

1) To be published (revises ISO 10555-1:2013). Stage at time of publication ISO/PWI 10555-1:2019.

ISO 10993-17, *Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances*

ISO 11040-4, *Prefilled syringes — Part 4: Glass barrels for injectables and sterilized subassembled syringes ready for filling*

ISO 11040-5, *Prefilled syringes — Part 5: Plunger stoppers for injectables*

ISO 11040-6, *Prefilled syringes — Part 6: Plastic barrels for injectables and sterilized subassembled syringes ready for filling*

ISO 11040-8, *Prefilled syringes — Part 8: Requirements and test methods for finished prefilled syringes*

ISO 11607-1, *Packaging for terminally sterilized medical devices — Part 1: Requirements for materials, sterile barrier systems and packaging systems*

ISO 11608-1,[2)] *Needle-based injection systems for medical use — Requirements and test methods — Part 1: Needle-based injection systems*

ISO 13926-1, *Pen systems — Part 1: Glass cylinders for pen-injectors for medical use*

ISO 13926-2, *Pen systems — Part 2: Plunger stoppers for pen-injectors for medical use*

ISO 13926-3, *Pen systems — Part 3: Seals for pen-injectors for medical use*

ISO 21881:2019, *Sterile packaged ready for filling glass cartridges*

ISO 80369-7, *Small-bore connectors for liquids and gases in healthcare applications — Part 7: Connectors for intravascular or hypodermic applications*

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 terminological databases for use in standardization at the following addresses:

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

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

3.1
cartridge
container for the medicinal product which is closed on one end with a *cartridge cap* (3.2) and *disc* (3.5), and on the other end with a *plunger stopper* (3.8)

3.2
cartridge cap
component which attaches the *disc* (3.5) to the *cartridge* (3.1)

3.3
container closure integrity
CCI
adequacy of Primary Container Closure (PCC) to maintain a sterile barrier against potential contaminants until first intentional user interaction

Note 1 to entry: See definition for PCC in ISO 11608-1:20##.

2) To be published (revises ISO 11608-1:2012). Stage at time of publication: ISO/DIS 11608-1:2020.

3.4
fragmentation
formation of elastomeric particles which are generated when the disc is pierced by a needle, spike or other access device for filling or delivery

Note 1 to entry: Disc coring is one mechanism to generate fragments

[SOURCE: ISO 8871-5:2016, 3.2 - modified]

3.5
disc
component of a container (typically a *cartridge* (3.1)), which seals the end of the container through which the medicinal product is accessed

Note 1 to entry: E.g. disc septum or elastomeric closure.

3.6
fluid path
pathway the medicinal product follows from the container or reservoir to the targeted delivery site

3.7
medicinal product compatibility
impact of the device on the quality of the medicinal product

Note 1 to entry: Impact of medicinal product on device is covered in ISO 11608-1.

3.8
plunger stopper
component that seals one end of the container and interfaces with the delivery device

3.9
sterility assurance level
SAL
probability of a single viable microorganism occurring after sterilization

Note 1 to entry: It is expressed as the negative exponent to the base 10.

[SOURCE: ISO 11139:2018, 3.275 - modified]

3.10
sterile barrier system
system of components that provide a barrier to microbial ingress

4 Requirements

4.1 General

These requirements apply to containers or integrated fluid paths intended to be used with a NIS. When test methods and specifications are noted, they are included to assist manufacturers and suppliers in supporting compliance with design specification of the NIS in accordance with the applicable parts of ISO 11608.

Specific requirements for NIS primary container closure system components are:

a) glass syringes (including integrated needles) shall comply with applicable clauses of ISO 11040-4 and ISO 11040-8;

b) plastic syringes (including integrated needles) shall comply with applicable clauses of ISO 11040-6 and ISO 11040-8;

c) syringe plunger stoppers shall comply with applicable clauses of ISO 11040-5;

d) glass cartridges shall comply with applicable clauses of ISO 13926-1 and ISO 21881;

e) cartridge plunger stoppers shall comply with applicable clauses of ISO 13926-2;

f) cartridge discs shall comply with applicable clauses of ISO 13926-3;

g) cartridge caps shall comply with applicable clauses of ISO 8872;

h) all reservoirs provided empty to the user shall be free of droplets of fluid (lubrication) on the outside or inside surfaces when viewed under normal or corrected-to-normal vision.

4.2 Container integrity

4.2.1 Container Closure Integrity (CCI)

Container closure integrity shall be ensured until first intentional user interaction which breaks CCI.

If the NIS is manufacturer-assembled with a Primary Container Closure (PCC) to form a single integral unit, the manufacturing processes, including assembly, shall be shown to not adversely impact container closure integrity, in accordance with applicable pharmacopeia.

4.2.2 Resealability — All multi-dose cartridges or reservoirs with discs

For all cartridges or reservoirs with discs intended for multiple penetrations, after having been penetrated in accordance with the test method specified in 5.1, the penetrated discs of 20 cartridges or reservoirs shall not leak from the penetration site when the cartridge is pressurized.

The resealable disc of the cartridge or reservoir shall be punctured 1,0 times the maximum number of penetrations expected during its intended use.

4.2.3 Fragmentation (disc coring) - cartridges or reservoirs with discs

Cartridges or reservoirs that are accessed through an elastomeric disc (barrier) with a needle, spike or other access device for delivery shall not exceed six elastomeric disc fragments in the visible range (>150 µm in diameter) per 100 punctures in accordance with the method described in 5.2, collected from both coring (ejected from the needle) and fragmentation (collected from the liquid in the container or reservoir).

For multi-dose cartridges or reservoirs, each disc (barrier) shall be punctured 1.0 times the maximum number of penetrations expected during its intended use.

Risk assessment shall assess the impact of fragments on the function of the NIS to determine if additional mitigations or lowering the limit of allowed fragments are required.

NOTE The impact of any fragments on the function of the NIS can be assessed through dose accuracy testing.

4.3 Cannula requirements (as part of the fluid path)

4.3.1 Rigid needles

If the integrated fluid path contains a rigid needle, the strength of union between the needle at its connection point to the NIS shall not break when an attachment force given in ISO 7864:2016, Table 2 is applied as tension. The directions of force shall be applied as the needle would encounter during removal from the injection site.

For tapered needles, the minimum force given in ISO 7864:2016, Table 2 is determined by the outer diameter at the hub as indicated in ISO 7864:2016, Figure 1.

The performance of the rigid needle part shall fulfil the requirements in ISO 9626:2016, Clause 5 and ISO 7864:2016, 4.10.4, 4.11, 4.12 and 4.13, or an equivalent and applicable standard for tubing suited to

