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Sterile packaged ready for filling glass cartridges

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National foreword

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Sterile packaged ready for filling glass cartridges

Cartouches en verre préremplissables sous emballage stérile

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Foreword

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This document was prepared by Technical Committee ISO/TC 76, *Transfusion, infusion and injection, and blood processing equipment for medical and pharmaceutical use.*

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Introduction

In the last few years, following the more and more urgent request for ready for filling containers, packaging manufacturers managed to offer to the pharmaceutical industry containers already washed and sterilized. This category of products was born about 30 years ago with the appearance on the market of ready for filling syringes.

Only recently, the sterilized sub-assembled ready for filling syringes have been standardized by ISO 11040-4 and ISO 11040-7, including the corresponding packaging system. These two International Standards define the performance requirements of the glass syringes and the related test methods, as well as the ready for filling packaging system for these syringes, also including the test methods.

ISO 13926-1 specifies the design, dimensions, materials, performance and test methods for glass cylinders used with pen-injectors for medical use.

Due to the increasing market presence of syringes ready for filling and the associated advantages of this product for the pharmaceutical industry, the suppliers of packaging materials have started to develop such systems of this type for cartridges.

The availability of two packaging configurations makes ready for filling glass cartridges suitable for use both in clinical trials and in mass production. Nest and tub configuration has been conceived to be used usually with automated filling machines, while tray configuration is usually suitable for small batches filled manually or by means of semi-automated filling machines.

This duality of packaging configurations calls for a standardization of the production processes, materials quality and analytical methods when launching these products on the market, in order to avoid conceiving too highly customized processes.

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Sterile packaged ready for filling glass cartridges

1 Scope

This document specifies the characteristics of sterile and ready for filling empty glass cartridges for injectable preparations, including the minimum requirements of materials, packaging systems and analytical test methods.

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 720, *Glass — Hydrolytic resistance of glass grains at 121 °C — Method of test and classification*

ISO 8871-1, *Elastomeric parts for parenterals and for devices for pharmaceutical use — Part 1: Extractables in aqueous autoclavates*

ISO 10993-7, *Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals*

ISO 11138 (all parts), *Sterilization of health care products — Biological indicators*

ISO 11140 (all parts), *Sterilization of health care products — Chemical indicators*

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

ISO 11608-3:2012, *Needle-based injection systems for medical use — Requirements and test methods — Part 3: Finished containers*

ISO 13926-1:2018, *Pen systems — Part 1: Glass cylinders for pen-injectors for medical use*

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

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

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

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

3.1
cap
component which attaches the *disc* (3.3) to the cartridge

[SOURCE: ISO 11608-3:2012, 3.1]

3.2
customer
business entity which purchases sterile ready for filling cartridges and conducts further processing or filling as appropriate

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3.3
disc
component which seals the end of the container opposite the *plunger* (3.9)

[SOURCE: ISO 11608-3:2012, 3.5]

3.4
filling volume
90 % of the brimful capacity

[SOURCE: United States Pharmacopoeia Convention, USP <660>]

3.5
insert liner
foil to cover and protect the cartridges

3.6
manufacturer
business entity which performs or is otherwise responsible for the manufacturing of the cartridges ready to be filled by the *customer* (3.2)

3.7
nest
plastic plate with a defined hole pattern for the placing of the cartridges

[SOURCE: ISO 11040-7:2015, 3.4, modified — "suspension of the syringe bodies" was replaced with "placing of the cartridges".]

3.8
packaging system
combination of the *sterile barrier system* (3.13) and *protective packaging* (3.10)

[SOURCE: ISO 11139:2018, 3.192]

3.9
plunger
elastomeric component which seals the back end of cartridge

3.10
protective packaging
configuration of materials designed to prevent damage to the *sterile barrier system* (3.13) and its contents from the time of their assembly until the point of use

[SOURCE: ISO 11139:2018, 3.219]

3.11
protective bag
plastic bag or sealing around the *tub* (3.15) or the *tray* (3.14)

[SOURCE: ISO 11040-7:2015, 3.6, modified — "tray" was added as an additional configuration.]

3.12
sealing lid
microbial barrier material for sealing the *tub* (3.15) or the *tray* (3.14)

[SOURCE: ISO 11040-7:2015, 3.7, modified — "tray" was added as an additional configuration.]

3.13
sterile barrier system
minimum package that prevents ingress of microorganisms and allows aseptic presentation of product at the point of use

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3.14
tray
plastic container with optional supports to accommodate individual cartridges

3.15
tub
plastic container to accommodate the filled *nest* (3.7)

[SOURCE: ISO 11040-7:2015, 3.11]

4 Quality system

4.1 General

The testing hereunder described shall be carried out within a formal quality system.

NOTE ISO 15378 contains requirements for a suitable quality management system for primary packaging materials for medicinal products.

4.2 Testing

4.2.1 Any suitable test system can be used, when the required accuracy (calibration) and precision (gauge repeatability and reproducibility) can be obtained. In case the gauge is applied, repeatability and reproducibility of the test apparatus shall be no greater than the range documented in test method precision and bias statements or as established by industry round robin studies.

4.2.2 The sampling plans used for the selection and testing of sterile ready for filling cartridges or components thereof shall be based upon statistically valid rationale at all process steps.

NOTE Examples of suitable sampling plans are given in ISO 2859-1 and ISO 3951 (all parts).

4.2.3 Unless agreed otherwise, testing shall be performed at ambient laboratory conditions.

5 Process description and requirements

5.1 Washing

5.1.1 Washing is the process intended to reduce particle, lubricant or any other contamination on the bulkware cartridges after converting process steps.

5.1.2 Water used for final rinsing shall meet the specifications of water for injection (WFI) (see USP and/or Ph.Eur).

5.2 Drying

Drying is an optional step to guarantee the absence of rinsing water after washing if heating is not applied. The air shall be filtered using a filter with a pore size of maximum 0,22 µm.

5.3 Lubrication

The inner surface of the cartridges can be lubricated. Limit values of the amount of lubricant and the required glide forces are subject to agreement between the manufacturer and the customer. Lubrication of the inner surface of the cartridges is applied in order to improve gliding properties. This is usually done by siliconization, with silicone emulsion followed by heat treatment.

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Annex D specifies a suitable test method for the determination of the quality and consistency of the lubrication using a glide force test.

5.4 Capping and crimping

5.4.1 Cartridges can optionally, upon customer request, be pre-capped with selected rubber formulations. The rubber material that can be in contact with the injectable product shall meet applicable requirements of ISO 8871-1. For additional regional or national requirements of pharmacopoeias, see type I or type II requirements of Ph. Eur. 3.2.9, USP <381>.

5.4.2 The closure system shall provide an appropriate liquid leakage resistance when tested in accordance with Annex F.

5.5 Plunger insertion

If required by the customer, as option of capping and crimping, plunger insertion can be performed by the manufacturer. The rubber constituent shall meet applicable requirements of ISO 8871-1. For additional regional or national requirements of pharmacopoeias, see type I or type II requirements of Ph. Eur. 3.2.9, USP <381> and JP 7.03 that is applicable to volumes > 100 ml.

5.6 Packaging

5.6.1 Non-sterile glass cartridges already washed, shall be packed in plastic trays or nest and tub configuration as agreed between the manufacturer and the customer. See Annex H.

5.6.2 For packaging systems for sterilized ready for filling cartridges, see Clause 7.

5.7 Sterilization

5.7.1 Sterilized ready for filling cartridges shall be sterilized according to a sterility assurance level (SAL) of 10^{-6}, using a suitable validated sterilization method (see e.g. ISO 11135, ISO 17665-1, ISO 11137 (all parts) or ISO 14937).

5.7.2 The sterilization process shall not compromise the product safety and performance. Sterilization compatibility of sterile barrier systems and packaging systems is assessed following the requirements in ISO 11607-1.

NOTE Sterility testing is subject to national or regional pharmacopoeias, see the methods given in Ph. Eur., 2.6.1, USP <71> and JP 4.06.

For ethylene oxide sterilization the requirements for residuals of ISO 10993-7 apply. See also Reference [20].

6 Requirements for glassware

6.1 General

Cartridges shall be produced from glass with characteristics such as to be adequate to contain products for injection.

6.2 Material

6.2.1 The material shall be colourless (cl) or amber (br) glass of the hydrolytic resistance grain class HGA 1 in accordance with ISO 720.

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