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Prefilled syringes —

Part 8: Requirements and test methods for finished prefilled syringes

Seringues préremplies —

Partie 8: Exigences et méthodes d'essai pour seringues préremplies prêtes à l'emploi

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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 on 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.

The committee responsible for this document is ISO/TC 76, *Transfusion, infusion and injection, and blood processing equipment for medical and pharmaceutical use*.

ISO 11040 consists of the following parts, under the general title *Prefilled syringes*:

— *Part 1: Glass cylinders for dental local anaesthetic cartridges*

— *Part 2: Plunger stoppers for dental local anaesthetic cartridges*

— *Part 3: Seals for dental local anaesthetic cartridges*

— *Part 4: Glass barrels for injectables and sterilized subassembled syringes ready for filling*

— *Part 5: Plunger stoppers for injectables*

— *Part 6: Plastic barrels for injectables*

— *Part 7: Packaging systems for sterilized subassembled syringes ready for filling*

— *Part 8: Requirements and test methods for finished prefilled syringes*

Introduction

Historically, injectable (parenteral) liquid pharmaceutical products have been mainly provided in primary containers (i.e. ampoules and vials) which required the liquid to be transferred into a hypodermic syringe and combined with the appropriate injection needle before its final use. This procedure is not only time-consuming, but also presents a great number of possibilities for contamination and use errors.

Over the past several years, the presentation of liquid pharmaceutical products in prefilled syringes for single use, many with staked needles, is becoming more prevalent. The simplicity of use that is provided not only benefits their use in the clinical setting, but also enables these to be used by lay users in a home setting.

The standardization of the requirements for prefilled syringes has been addressed by ISO/TC 76 in two ways:

— the specification of the components of the prefilled syringe prior to filling is included in the previous parts of the ISO 11040 series;

— the requirements for the final prefilled syringe, presented to the user as a finished product, are addressed in this part of ISO 11040.

Finished prefilled syringes require marketing authorization as a drug, in some regions as a combination product or as a medical device, depending on the content and the intended use. The syringe plays a dual role in the prefilled syringe product — as a container closure system and as a delivery device. Safety, performance and usability need to be considered, as well in case of intended preassembly, copackaging or label reference for use with other devices and equipment. This part of ISO 11040 addresses the content and syringe as a system, with the intent to ensure the successful performance for its intended purpose.

There are other international and national standards and guidance publications and, in some countries, national regulations that are applicable to medical devices and pharmaceuticals. Their requirements might supersede or complement this part of ISO 11040. Developers and manufacturers of finished prefilled syringes are encouraged to investigate and determine whether there are any other requirements relevant to the safety or marketability of their products.

Prefilled syringes —

Part 8: Requirements and test methods for finished prefilled syringes

1 Scope

This part of ISO 11040 is applicable to aseptically filled or terminally sterilized finished prefilled syringes (intended for single use only) based on ISO 11040-4 or ISO 11040-6, together with ISO 11040-5, for parenteral injection preparations with focus on quality, functional performance and safety requirements, as well as relevant test methods.

Finished prefilled syringes which have undergone an additional preparation step by the user before injection (e.g. diluent syringes that have been emptied for reconstitution and in which the reconstituted drug solution has been aspirated after reconstitution) are excluded from the scope of this part of ISO 11040.

NOTE 1 This part of ISO 11040 can also be used as a guidance for other types, designs and/or sizes of prefilled syringes, e.g. dual chamber prefilled syringes.

NOTE 2 In case the finished prefilled syringes are used in a needle-based injection system, see also ISO 11608-3.

NOTE 3 Attention is drawn to applicable national or regional regulations such as Ph. Eur[1], USP[2] or JP[3].

NOTE 4 Finished prefilled syringes containing so-called borderline products, e.g. hyaluronic acid, are included in the scope of this part of ISO 11040, though they are not always regulated as a pharmaceutical product.

2 Normative references

The following documents, in whole or in part, are normatively referenced in this document and are indispensable for its application. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 11040-4:2015, *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*

ISO 23908, *Sharps injury protection — Requirements and test methods — Sharps protection features for single-use hypodermic needles, introducers for catheters and needles used for blood sampling*

ISO 80369-1, *Small-bore connectors for liquids and gases in healthcare applications — Part 1: General requirements*

ISO 80369-7, *Small-bore connectors for liquids and gases in healthcare applications — Part 7: Connectors with 6% (Luer) taper for intravascular or hypodermic applications*

1) See http://www.edqm.eu/.

2) See http://www.usp.org/.

3) See http://www.pmda.go.jp.

ISO 80369-20, *Small-bore connectors for liquids and gases in healthcare applications — Part 20: Common test methods*

ISO 7886-1:2015, *Sterile hypodermic syringes for single use — Part 1: Syringes for manual use*

IEC 62366, *Medical devices — Application of usability engineering to medical devices*

3 Terms and definitions

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

3.1
finished prefilled syringe
prefilled container closure system for parenteral injection preparations as it is marketed, including e.g. assembly of components, terminal sterilization and final packaging

3.2
manufacturer
natural or legal person holding the licence for the pharmaceutical product with responsibility for the design, manufacture, packaging, and labelling of a finished prefilled syringe, before it is placed on the market or put into service, regardless of whether these operations are carried out by that person or on that person's behalf by a third party

3.3
risk management
systematic application of management policies, procedures and practices to the tasks of analysing, evaluating, controlling and monitoring risk

[SOURCE: ISO 14971:2007, 2.22]

3.4
user
patient or health care provider (clinical personnel, doctor, or lay person) who prepares and/or uses the finished prefilled syringe

4 User requirements

4.1 Definition of intended use

The manufacturer shall define the intended use of the finished prefilled syringe. Aspects to be considered shall include the following:

— users including their health status;

— the route of administration;

— target tissue;

— additional medical devices or application aids that are used for application, e.g. needle-based injection systems, infusion tubes, reconstitution aids, sterile hypodermic needles, plunger rod/finger flange;

— characteristics of the environment during transport, storage and use;

— interactions between user, environment and prefilled syringe;

— point of use, e.g. hospital, homecare;

— frequency of application;

— criticality of medication, e.g. medication for acute care or for chronic diseases.

4.2 Risk management

Manufacturers shall follow a risk-based approach during the design, development, manufacture and life cycle of the finished prefilled syringe like exemplary described by ISO 14971. Risk management shall consider the intended use, interactions between content and container, and environmental conditions. This can result in product-specific requirements and test methods that differ from what is outlined in this part of ISO 11040.

If the prefilled syringe is intended to be used in combination with preattached, copackaged or label referenced devices and equipment, the manufacturer shall ensure that the whole combination, including the connection system, is safe, usable and does not impair the specified performances of the devices.

NOTE For filling process, see Reference [17].

4.3 Application of usability engineering

The usability of the prefilled syringe shall be considered and validated according to a process compliant with IEC 62366.

NOTE 1 For further information, see Reference [16].

NOTE 2 The instructions for use are part of the usability testing.

5 System characterization

5.1 Critical dimensions

Critical dimensions shall be defined considering the intended use of the finished prefilled syringe. Special focus shall be given to:

— interfaces with other devices (e.g. sharp injury prevention features or needle-based injection systems, needleless connection devices), components and users;

— connectivity with other devices at the point of use (e.g. IV access systems or needles);

— plunger stopper position depending on the intended use (e.g. use in needle-based injection systems).

Figure 1 includes examples on how to measure the plunger stopper position on finished prefilled syringes.