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

Part 6: On-body delivery systems

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Foreword

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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 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*.

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

ISO 11608 has traditionally addressed hand-held needle-based injection systems (NISs) which are intended for parenteral administration by injection of medicinal products through a needle to humans. These injections are performed manually, through exertion of force by the user, or automatically through use of an internal power source through a needle into the patient's tissue[1)].

The user typically places the hand-held NIS at the injection site and holds the NIS in place until the injection has completed. The intended use and medicinal product delivery requirements of some medicinal products may make manual manipulation and stabilization of a hand-held NIS during the medicinal product delivery process impractical or impossible, and may result in an incomplete dose, missed dose, or user injury. For example, it may not be appropriate for users to hold a NIS in place for an extended period of time required by the volume or viscosity of the medicinal product, or patient discomfort.

Delivery systems which are affixed to the body of the user, eliminate some of the risks associated with delivery of medicinal product through a traditional NIS. This document provides a consistent method for evaluating the unique requirements and risks associated with these systems, herein referred to as "on-body delivery systems" (OBDS).

Like ISO 11608-1 and ISO 11608-5, this document is developed more as a "horizontal" than "vertical" one, to accommodate anticipated variation in the designs. Thus, it will tend to specify the results of the design effort instead of the physical and construction requirements used as the basis for OBDS design, so that innovation in achieving the intended purposes is not unnecessarily restricted.

NISs governed by ISO 11608 are defined as "hand-held" or "on-body" delivery systems (OBDSs). By hand-held, patients control and stabilize the NIS at the injection site during administration of a discrete volume. Delivery times for this type of NIS would, therefore, be limited to avoid instability and the potential for injection site trauma. For NISs with larger delivery volumes or physical properties requiring a longer time to deliver, OBDS might be more practical. The OBDS would likely exist as either "body-worn" (directly anchored to the body, e.g. using adhesive) or "patient-worn" (indirectly anchored, e.g. catheter attached to OBDS contained in a back-pack or pocket). In either configuration, the time or speed employed to deliver a discrete volume would be based upon tolerability or convenience rather than clinical relevance (e.g. medication efficacy) as would be the case with insulin patch pumps or traditional infusion pumps (e.g. IEC 60601-2-24:2012 Ed 2.0, ISO 28620:2010) associated with continuous delivery (e.g. insulin). However, while this document is not intended to directly apply to these pump products, it does contain requirements and tests methods that can be used to help design and evaluate them.

This document only addresses the basic safety and effectiveness of the product and manufacturers may, through risk assessments, identify additional requirements due to the unique nature of their specific system or application. 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 standards on quality systems, e.g. ISO 9001 or ISO 13485.

There can be legal or regulatory requirements that take precedence over the requirements in this document.

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

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

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1) Although technically a device using a soft cannula is not "needle-based", the cannula is placed by a needle and can be included in this classification.

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

Part 6: On-body delivery systems

1 Scope

This document specifies requirements and test methods for On-Body Delivery Systems (OBDS), which are body-worn or patient-worn NISs for single patient use, intended for subcutaneous, intramuscular or intradermal delivery of a discrete volume (bolus) of medicinal product, through needles or soft cannulas, incorporating pre-filled or user-filled, replaceable or non-replaceable containers.

NOTE 1 Although technically a device using a soft cannula is not "needle-based", the soft cannula is placed by a needle and can be included in this classification.

NOTE 2 Some requirements and methods are already established and included in other parts of the ISO 11608 series. To ensure consistency, these requirements will not be repeated in this document, but referenced.

Infusion pumps which are not body or patient worn, or those that are designed for continuous delivery at a specific rate required to achieve and/or maintain a desired plasma medicinal product concentration, are excluded from this document and may be covered by IEC 60601-2-24 (if electronic) or ISO 28620 (if non-electronic). However, while this document is not intended to directly apply to these pump products, it does contain requirements and tests methods that can be used to help design and evaluate them.

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

ISO 11608-3[3], *Needle-based injection systems for medical use - Requirements and test methods - Part 3: NIS containers and fluid paths*

ISO 11608-4[4], *Needle-based injection systems for medical use - Requirements and test methods - Part 4: Needle-based injection systems containing electronics*

ISO 11608-5[5], *Needle-based injection systems for medical use - Requirements and test methods - Part 5: Automated functions*

3 Terms and definitions

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

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

3) To be published (revises ISO 11608-3:2012). Stage at time of publication: ISO/DIS 11608-3:2020.

4) To be published (revises ISO 11608-4:2006). Stage at time of publication: ISO/DIS 11608-4:2020.

5) To be published (revises ISO 11608-5:2012). Stage at time of publication: ISO/DIS 11608-5:2020.

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 http://www.iso.org/obp

3.1
body-worn OBDS
OBDS (3.5) that is directly adhered to the skin

3.2
dose delivery profile
plot of the volumetric output of the device against unit time throughout the duration of the delivery

Note 1 to entry: See Annex B.

3.3
leakage
escape of medicinal product from the device, other than from the patient end of the fluid path during delivery

3.4
needle (cannula) extension
axial distance from the patient end of the needle tip to the nearest part of the OBDS body (defining the point of contact with the patient adjacent to the injection site)

Note 1 to entry: See ISO 11608-5:20##, Figures C.1 to C.7 for 90-degree insertion and less than 90-degree insertion.

3.5
on-body delivery system
OBDS
delivery system, which is affixed to the body of the user that actively delivers medicinal product, and includes the medicinal product container and components for administration through a needle or soft cannula

Note 1 to entry: OBDS allows for “hands-free” drug delivery and does not prevent free patient movement or ambulation during use.

3.6
occlusion
blockage or closing of fluid path of *OBDS* (3.5) during drug administration that is not part of the intended use

3.7
patient tolerability
level to which pain, discomfort and other effects experienced during use of the device are accepted by patients

3.8
patient worn injector
body-worn device that is attached over or under patient’s clothes, but not directly adhered to the skin

Note 1 to entry: This type of injector is attached to the patient through tubing and a catheter.

4 Requirements

4.1 General

The general requirements specified in ISO 11608-1:20##, 5.1 apply.

4.2 Risk assessment

The requirements in ISO 11608-1:20##, 5.3 apply.

NOTE For OBDS, an assurance case (for example, developed using recommendations such as those in AAMI TIR 38) can be used to fulfil the ISO 14971 requirement for a risk management report.

4.3 Usability engineering

The requirements specified in ISO 11608-1:20##, 5.4 apply.

4.4 Uncertainty of measurement and conformity with specifications

The requirements specified in ISO 11608-1:20##, 5.5 apply.

4.5 General design requirements

Applicable requirements specified in ISO 11608-1:20##, 5.6 apply.

4.6 Physical or mechanical requirements and test methods

4.6.1 General

Unless otherwise specified, the testing shall be performed at standard atmosphere as specified in ISO 11608-1. For OBDS, manufacturers shall determine the temperature range of the device and drug during delivery (which may be impacted by body temperature). In use testing, and testing of drug compatibility should be completed throughout that temperature range.

4.6.2 Systems comprising rigid needles

The requirements in ISO 11608-3 apply.

4.6.3 Systems comprising a soft cannula(s)

The requirements in ISO 11608-3 apply.

4.6.4 Leakage from the OBDS

The device shall be inspected for leakage when tested in accordance with ISO 11608-1, in environments and orientations representative of the expected use. Any amount of leakage observed during testing shall be assessed for its ability to impact device performance, fluid path or medicinal product sterility, or risk to humans or the environment.

Any leakage shall be addressed by risk assessment and appropriate information shall be provided to the user.

If any preconditioning creates the appearance of condensation or any other external evidence of fluid, the manufacturer shall assess and confirm that this was not medicinal product leakage.

4.6.5 Means of attachment for body-worn OBDS

The developer of the OBDS shall establish performance criteria to ensure that the means of attachment to the body is adequate to maintain a reliable medicinal product delivery pathway.

If the means of attachment uses adhesive, the following apply:

— attachment of the OBDS to the adhesive patch is adequate to maintain reliable medicinal product delivery pathway;

— if odour control, MVTR (moisture vapour transmission rate), water resistance or impermeability, absorbency or conformity have been identified requirement for the OBDS, the adhesive material should be tested for these properties.

Conduct adhesion/attachment test when used as specified in the instructions for use. Where the device shall be maintained in a specific orientation, visually confirm that the device maintains the required orientation during testing. If an adhesive is used, see Annex A, which contains suggested test methods for verifying the functional performance of an adhesive. It is up to the manufacturer to identify suitable tests from those suggested or to develop their own test.

Testing of adhesion/attachment shall also measure performance of the device under conditions consistent with the intended use of the product, which may include exposure to typical fluids that may be encountered during use (e.g. water, personal cleaning products, deodorants, skin lotion, medical alcohols, perspiration) including the medicinal product, if appropriate. Adhesive tests may be performed on material that has undergone sterilization or aging if it is anticipated through the risk analysis that the adhesive property will be adversely affected by such conditioning. Based on risk assessment, additional evidence may be required to demonstrate the performance and safety of the means of attachment. This may include use on humans under simulated conditions of actual use (not necessarily including the actual delivery). This evidence may also need to confirm that the adhesive bond between the device and the user does not cause unacceptable tissue trauma (as defined by risk assessment) or create a bond that is too difficult for the user to remove. It is recognized that in some cases, reference to existing clinical and/or other evidence may be sufficient to demonstrate performance of the means of attachment.

NOTE 1 The factors that affect Medical Adhesive Related Skin Injuries (MARSI) are complex and related to factors that the device manufacturer can control (adhesive properties, design of patch geometry, suggested application points, etc.) and factors that the device manufacturer cannot control (patient population, removal technique, etc.)[6]. The selection of the adhesive should show due consideration for the risk of MARSI to the end user balanced against the performance requirements of the OBDS, applying risk control, where practicable.

NOTE 2 Extended wear may result in the adhesive developing a stronger bond over time which could impact the patient. This should be considered and addressed in the testing.

4.6.6 Occlusion

The potential harm to the patient of a partial or complete occlusion resulting in a reduction or cessation of delivery, or delivery of a fast bolus, shall be determined, and the risk based on the criticality of the medicinal product shall be addressed in the risk assessment. If required, appropriate control(s) (design and/or indicator, instruction for user etc.) shall be implemented which may include a mechanism for the user to determine the ongoing status of the delivery (i.e. a delivery indicator).

NOTE 1 Occlusion might lead to OBDS not meeting its primary function such as dose accuracy or delivery time. The clearance after occlusion might lead to an instantaneous fast injection that might adversely impact the patient.

NOTE 2 Delivery indication can be done by audible or tactile means or by an analogue or digital indicator.

4.7 Functional performance requirements and test methods

4.7.1 General

In addition to the conditioning specified in ISO 11608-1, manufacturers shall evaluate if simulating additional conditions to which the OBDS is subjected as worn before and/or during delivery (e.g. "normal/anticipated conditions" from ISO 11608-1) when testing primary functions is appropriate.

6) Medical Adhesives and Patient Safety: State of the Science by McNichol et al. Wound Ostomy Continence and Nursing, July/August 2013.

These additions shall be based on the risk analysis (e.g. due to the potential for extended dose delivery time and warming of the OBDS while affixed to the body). Potential conditions to consider include:

— vibration;

— temperature;

— humidity;

— atmospheric pressure;

— light exposure;

— orientation.

Each additional test shall be carried out at conditions that simulate the operation of the OBDS as described in the instructions for use.

NOTE Primary functions may be able to be assessed during the same testing protocol and on one set of samples.

4.7.2 Dosing requirements and methods

4.7.2.1 General

There are three measurements relevant to the dosing of OBDS:

— dose accuracy;

— dose delivery time; and

— dose delivery profile.

At a minimum, dose accuracy is considered a primary function. Risk assessment shall determine whether dose delivery time is considered a primary function, in accordance with ISO 11608-1.

4.7.2.2 Dose accuracy

Design verification of the required dose accuracy, determined by risk assessment, shall be performed in accordance with and shall meet the requirements specified in ISO 11608-1.

The dose accuracy (dose delivered) shall be verified by measuring the total dose delivered. Where the dose is specified as discontinuous dosing segments, each dose segment shall be measured for dose accuracy.

If the OBDS is intended to be paused or stopped by the user (i.e. delivery volume during pause = 0), then the dose accuracy testing at standard atmosphere conditions shall include this state to ensure that the accuracy of the dose delivered shall not be adversely affected by any planned interruption (pause/stop feature on device) of the dose. Based on the risk assessment, the manufacturer shall determine if assessment of the dose accuracy including the pause/stop feature is required after any additional pre-conditionings besides standard.

4.7.2.3 Dose delivery time

Dose delivery time is a measure of the time over which the total (or each if there are multiple dose segments) dose is delivered.

Design verification of the required dose delivery time, determined by risk assessment, shall be performed in accordance with ISO 11608-5.

The dose delivery time (time the prescribed dose is delivered) shall be verified by measuring the time over which the total dose is delivered. Where the dose is specified as discontinuous dosing segments, the time of the delivery of each dose segment shall be measured.