BS EN ISO 11608-5:2012

BSI Standards Publication

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

Part 5: Automated functions (ISO 11608-5:2012)

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National foreword

This British Standard is the UK implementation of EN ISO 11608-5:2012.

The UK participation in its preparation was entrusted to Technical Committee CH/84, Catheters and syringes.

A list of organizations represented on this committee can be obtained on request to its secretary.

This publication does not purport to include all the necessary provisions of a contract. Users are responsible for its correct application.

ISBN 978 0 580 69949 8

ICS 11.040.25

Compliance with a British Standard cannot confer immunity from legal obligations.

This British Standard was published under the authority of the Standards Policy and Strategy Committee on 31 October 2012.

Amendments issued since publication

Date	Text affected

EUROPEAN STANDARD

NORME EUROPÉENNE

EUROPÄISCHE NORM

EN ISO 11608-5

October 2012

ICS 11.040.25

English Version

Needle-based injection systems for medical use - Requirements and test methods - Part 5: Automated functions (ISO 11608-5:2012)

Systèmes d'injection à aiguille pour usage médical - Exigences et méthodes d'essai - Partie 5: Fonctions automatisées (ISO 11608-5:2012)

Nadelbasierte Injektionssysteme zur medizinischen Verwendung - Anforderungen und Prüfverfahren - Teil 5: Automatisierte Funktionen (ISO 11608-5:2012)

This European Standard was approved by CEN on 29 September 2012.

EUROPEAN COMMITTEE FOR STANDARDIZATION
COMITÉ EUROPÉEN DE NORMALISATION
EUROPÄISCHES KOMITEE FÜR NORMUNG

Management Centre: Avenue Marnix 17, B-1000 Brussels

Ref. No. EN ISO 11608-5:2012: E

Foreword

This document (EN ISO 11608-5:2012) has been prepared by Technical Committee ISO/TC 84 "Devices for administration of medicinal products and intravascular catheters" in collaboration with Technical Committee CEN/TC 205 “Non-active medical devices” the secretariat of which is held by DIN.

This European Standard shall be given the status of a national standard, either by publication of an identical text or by endorsement, at the latest by April 2013, and conflicting national standards shall be withdrawn at the latest by April 2013.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. CEN [and/or CENELEC] shall not be held responsible for identifying any or all such patent rights.

This document has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association, and supports essential requirements of EU Directive.

For relationship with EU Directive, see informative Annex ZA, which is an integral part of this document.

According to the CEN/CENELEC Internal Regulations, the national standards organisations of the following countries are bound to implement this European Standard: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, Former Yugoslav Republic of Macedonia, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey and the United Kingdom.

Endorsement notice

The text of ISO 11608-5:2012 has been approved by CEN as a EN ISO 11608-5:2012 without any modification.

Annex ZA
(informative)

Relationship between this European Standard and the Essential Requirements of EC Directive 93/42/EEC on medical devices

This European Standard has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association to provide a means of conforming to Essential Requirements of the New Approach Directive 93/42/EEC on Medical Devices.

Once this standard is cited in the Official Journal of the European Union under that Directive and has been implemented as a national standard in at least one Member State, compliance with the clauses of this standard given in Table ZA.1 confers, within the limits of the scope of this standard, a presumption of conformity with the corresponding Essential Requirements of that Directive and associated EFTA regulations.

Table ZA.1 — Correspondence between this European Standard and Directive 93/42/EEC on medical devices

Clause(s)/subclause(s) of this European Standard	Essential Requirements (ERs) of Directive 93/42/EEC	Qualifying remarks/Notes
Clauses 4.1 to 4.3, all parts	1	Clause 10, all parts of ISO 11608-1 addresses pre-conditioning
Clauses 4.1 to 4.4, all parts	2	Clause 10, all parts of ISO 11608-1 addresses pre-conditioning
Clauses 4.1 to 4.3, 5, 6, all parts	3	All clauses of ISO 11608-1 are applicable
NA	4	
NA	5	
Clause 4.1 parts E and G, clause 4.3 all parts	6	
Clauses 4.2.2 and 5.1.1	7	Only 7.3 is addressed
Clause 4.1 parts D	8	Only 8.3 is addressed
Clauses 4.1 to 4.4, all parts	9	9.3 is not addressed Clause 10, all parts of ISO 11608-1 addresses pre-conditioning
Clauses 4.2.5, 4.3.3.3, 4.3.5.1, 5.1.4, 5.1.7, 5.1.8.1 and 5.2	10	All clauses of ISO 11608-1 are applicable
NA	11	
NA	12	
Clause 7	13	13.5 is not addressed Clause 5.4, part D and Q and Clause 13, all parts of ISO 11608-1 address ER 13

WARNING — Other requirements and other EU Directives may be applicable to the product(s) falling within the scope of this standard.

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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.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

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.

ISO 11608-5 was prepared by Technical Committee ISO/TC 84, *Devices for administration of medicinal products and intravascular catheters*.

ISO 11608 consists of the following parts, under the general title *Needle-based injection systems for medical use — Requirements and test methods*:

— *Part 1: Needle-based injection systems*

— *Part 2: Needles*

— *Part 3: Finished containers*

— *Part 4: Requirements and test methods for electronic and electromechanical pen-injectors*

— *Part 5: Automated functions*

Introduction

This part of ISO 11608 is applicable to needle-based injection systems with automated functions (NIS-AUTO), primarily intended to administer medicinal products to humans. Because of the anticipated variation in the designs of NIS-AUTOs, this part of ISO 11608 is promulgated more as a “horizontal” than a “vertical” standard. Thus, it tends to specify the results of the design effort instead of the physical and construction requirements used as the basis for NIS-AUTO design, so that innovation in achieving the intended purposes is not unnecessarily restricted.

This part of ISO 11608 intentionally avoids addressing more than the most basic elements regarding the safety and performance of NIS-AUTOs in humans. Any intended labelling of such NIS-AUTOs indicating their use to deliver medicinal products into the body or into specified tissue strata thereof (e.g. intramuscular, subcutaneous or intradermal), or for the administration of specific pharmaceutical drugs or vaccines, falls under the authority of national governments or supranational agencies regulating the manufacture and marketing of medical NIS-AUTOs and pharmaceutical products.

This part of ISO 11608 is expected to be supplemented by additional requirements and might occasionally be superseded by such regulatory authorities. Despite certain advantages for intentional interchangeability for containers designed for different auto-injection systems, as well as the potential risks of inadvertent interchangeability, this part of ISO 11608 avoids setting forth design specifications for the uniform size, shape and interface of such containers. It is left for future initiatives to build upon the specifications in this part of ISO 11608.

The sampling plans for inspection selected for this part of ISO 11608 are intended to verify the design, at a high confidence level. The sampling plan does not replace more general manufacturing quality systems, including lot release, which are addressed in standards on quality management systems, for example the ISO 9000 series or ISO 13485.

All references to “function” in this part of ISO 11608 are by definition to be construed as automated functions (see 3.4). This part of ISO 11608 does not apply to these functions if they are performed manually by the user.

INTERNATIONAL STANDARD ISO 11608-5:2012(E)

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

Part 5: Automated functions

1 Scope

This part of ISO 11608 specifies requirements and test methods for the automated functions of needle-based injection systems with automated functions (NIS-AUTO), for the administration of medicinal products in humans, including but not limited to:

a) drug product preparation (e.g. reconstitution);

b) needle preparation;

c) air removal;

d) priming;

e) dose setting;

f) actuation;

g) needle insertion;

h) injection of the medicinal product;

i) disabling the NIS-AUTO;

j) needle retraction;

k) needle shielding;

l) needle hiding;

m) sharps injury protection;

n) needle removal.

2 Normative references

The following referenced documents are indispensable for the application 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, *Needle-based injection systems for medical use — Requirements and test methods — Part 1: Needle-based injection systems*

ISO 14971, *Medical devices — Application of risk management to medical devices*

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
accessory
article or supplementary part used for convenience or safety in conjunction with a NIS-AUTO

EXAMPLES Magnifying lens to aid reading of dose setting, grip enhancer, dose counter of a NIS-AUTO.

3.2
actuation
action which initiates a NIS-AUTO function (e.g. needle insertion), triggered by the actions of the NIS-AUTO user (or by another automated function)

EXAMPLE Pressing the NIS-AUTO against the injection site.

3.3
air removal
action to remove air from the container and/or needle of the NIS-AUTO

3.4
automated function
function which does not require user initiation after actuation

NOTE A dose counter is considered an automated function if it is initiated by, for example, an automated needle retraction step, and therefore changes its state without any user interference.

3.5
injection
delivery of the dose to the intended injection depth

3.6
intended injection depth
range of injection depth to which the drug is intended to be delivered

See Figure 1.

3.7
needle-based injection system with automated functions
NIS-AUTO
injection system that delivers a medication through a needle wherein one or a series of functions are initiated by an action of the user and controlled automatically by the injection system

NOTE Accessories that perform automatic functions in combination with manual injection NIS-AUTOs are regarded as NIS-AUTO.

3.8
needle cover
cover provided over a needle in order to protect the needle from damage and users from injury prior to use of the needle

3.9
needle extension
axial distance from the patient end of the needle tip to the nearest part of the NIS-AUTO body (defining the point of contact with the patient adjacent to the injection site)

3.10
needle hiding
function which obscures the needle from the user's sight either before, during or after the injection cycle

NOTE The needle hiding function only has a visual requirement designed to reduce patient trauma in case of needle phobia. It is not subject to any physical or dimensional requirements intended to restrict access to the needle. It does not imply any increased level of safety from needle stick injuries.

3.11
insertion of needle
function which inserts the needle into the patient's skin to the intended injection depth prior to the injection of the medicinal product

3.12
needle shielding
function which covers the exposed needle before and/or after the injection cycle to reduce the likelihood of direct contact with the needle

NOTE 1 Needle shielding can reduce the risk of damage and contamination of the needle before use and can cover the needle after use.

NOTE 2 Needle shielding does not meet the requirements of a sharps injury protection feature unless it complies with ISO 23908.

3.13
priming
function that makes the dosing mechanism of the NIS-AUTO ready for actuation

3.14
retraction of needle
function which removes the needle from the target tissue to a predefined minimum needle point position inside the NIS-AUTO

3.15
risk assessment
RA
overall process comprising a risk analysis (estimation) and a risk evaluation

NOTE Adapted from ISO 14971:2007, definition 2.18.

3.16
sharps injury protection feature
function that prevents accidental sharps injury

NOTE The NIS-AUTO might provide an active or passive automated function (definitions of active and passive safety features are given in ISO 23908), distinct from needle shielding or hiding, which is designed to minimize the risks of accidental sharps injury. The NIS-AUTO cannot claim to have sharps injury protection unless it meets the requirements of ISO 23908.

3.17
target tissue
location in the body into which the medicinal product is delivered and that defines the route of administration

NOTE Parts of the body for this part of ISO 11608 can include the dermis, subcutaneous tissue and muscle.

4 Requirements

4.1 General requirements

a) The NIS-AUTO shall be designed to avoid unintended actuation.

b) The NIS-AUTO shall perform its intended automated functions when tested following pre-conditioning (including free fall) in accordance with ISO 11608-1.

EXAMPLE A NIS-AUTO that is dropped on a surface in accordance with free fall testing as described in ISO 11608-1 and that fails to perform any automated function as described in the instructions for use is deemed to have failed.

c) Completion of an automated function shall be apparent by visual and either tactile or audible means, or both, unless otherwise specified in any subclause of this part of ISO 11608, even if the sequence of operations for the NIS-AUTO consists of only one action. An automated function can be a sequence; if so, completion of the entire sequence shall be apparent to the user.

d) The NIS-AUTO shall not compromise container (drug product quality, consistency, etc.) and/or needle sterility. Devices designed to deliver more than one dose shall have an intermediate preparation step prior to delivery of each dose.

e) Where requirements do not specify forces for actuation of the automated feature/function, the appropriate force shall be determined by using a risk-based approach (consistent with ISO 14971) supported by simulated user studies that mimic actual clinical use.

NOTE The study design should be based on statistical considerations and should have clear acceptance criteria. Guidance on conducting simulated user studies can be found in IEC 62366.

f) Users shall be able to clearly distinguish between a NIS-AUTO that is unused, in use or disabled (or requiring another “setup” step before it can be used again). The NIS-AUTO shall provide visual feedback indicating clearly the state of the NIS-AUTO (i.e. unused, ready for use or disabled).

g) Manufacturers shall define the injection depth determined by the target tissue through clinical evaluation. Design verification shall demonstrate that the device is capable of delivering each dose of the medicinal product to the target tissue.

h) Where requirements in this part of ISO 11608 provide a test method without acceptance criteria, the manufacturer shall establish a specification and acceptance criteria for the automated feature/function appropriate to the intended use of the device using a risk-based approach (consistent with ISO 14971 and IEC 62366).

4.2 Preparation

4.2.1 General

The NIS-AUTO shall be designed to ensure that all preparation steps involving the NIS-AUTO are completed in the intended order or designed such that, if preparation steps are done out of sequence, continued safe and effective use of the NIS-AUTO is possible.

The NIS-AUTO shall indicate to the user that the preparation procedure has been completed. This shall be apparent to the user at least by visible means.

4.2.2 Drug product preparation (e.g. reconstitution)

Automated drug preparation shall not have an adverse impact on the drug product. Once preparation is complete, the contents of the container shall be visible to confirm the medicinal product has been properly prepared in accordance with the instructions for use, unless visibility adversely affects the drug product and/or therapy (see rationale in Annex A).

4.2.3 Needle preparation

The needle shall not be damaged by the automated feature (needle attachment, removal of needle cover, etc.). The automated needle preparation function shall not adversely affect the intended safety and performance of the NIS-AUTO. If any portion of the needle preparation (needle attachment, removal of needle cover, etc.) is automated, the NIS-AUTO shall not increase the potential of coring of any elastomeric components.

4.2.4 Air removal and/or priming

If the NIS-AUTO includes automated air removal and/or priming, the system shall still be able to deliver the pre-defined dose after the action is completed.

NOTE Air removal and priming can be combined into one step.

4.2.5 Dose setting

In the case of a variable dose NIS-AUTO, if designed to automatically set a dose, it shall indicate the set dose to the user by at least visual means and allow a means to adjust the set dose as appropriate.

4.3 Injection

4.3.1 Needle hiding

Needle hiding shall not interfere at any time with the NIS-AUTO intended function. If hiding the needle is required before, during or after injection, the needle shall not be visible to the user when tested in accordance with 5.1.11.1.

NOTE Post-injection needle hiding is not considered to be sharps injury protection.

4.3.2 Actuation of injection

A minimum of two manual actions shall be required in order to use the system, i.e. from locked to unlocked state/ready for injection, then press to actuate.

A multi-dose/use injection system with automated functions, once actuated, shall not allow an additional actuation without a separate and distinct action prior to a subsequent actuation.

4.3.3 Needle insertion and extension

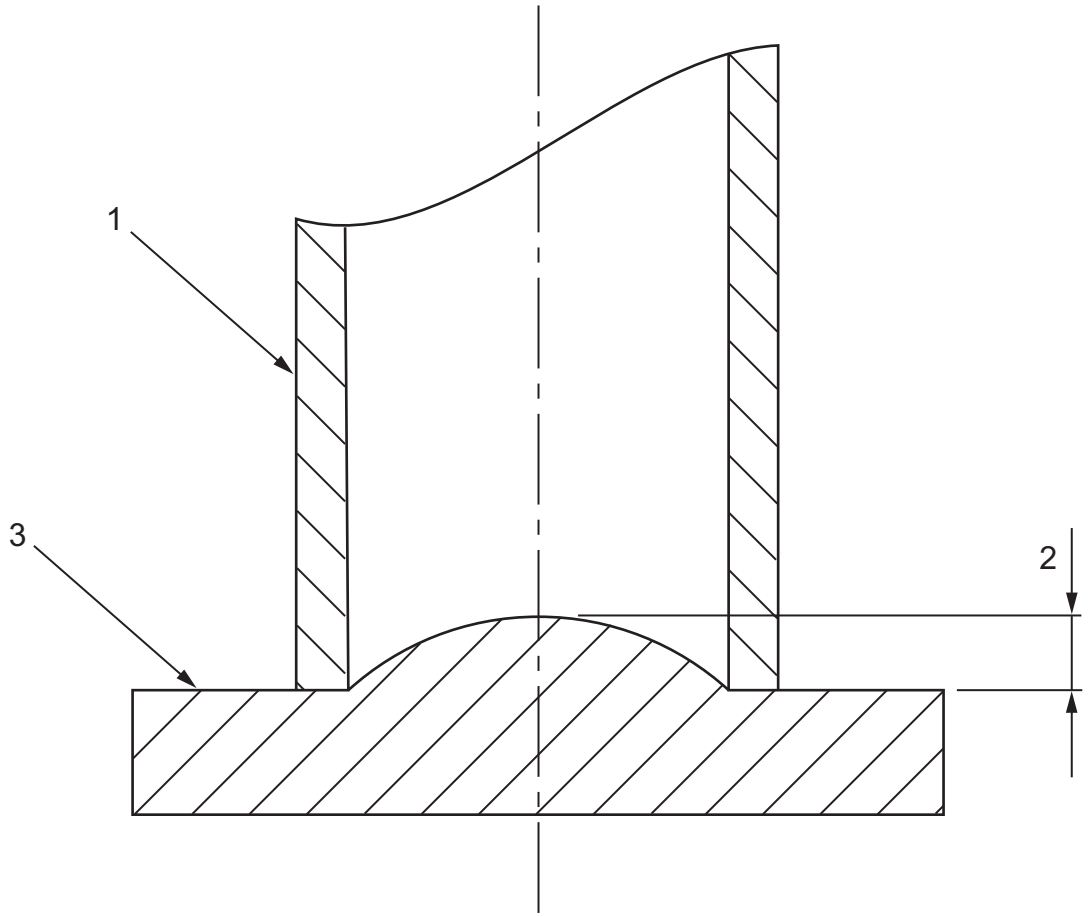
4.3.3.1 Insertion distance

Automated needle insertion shall extend the needle tip to the specified position. This shall be confirmed through measurement of the needle extension in accordance with the methods in 5.1.7.

The manufacturer shall demonstrate that the required needle extension results in needle penetration consistent with the intended use.

The minimum force against the skin required to actuate the NIS-AUTO to achieve adequate needle insertion shall be determined in order to ensure complete penetration to the intended injection depth.

An adjustment to the needle extension specification may be required for those NIS-AUTOs that, when pressed against the skin, cause skin doming (see Figure 1). Any adjustment to this specification shall be determined by the manufacturer’s risk assessment.



Key

1 NIS-AUTO

2 skin doming (if applicable)

3 skin

Figure 1 — Skin doming (if applicable)

4.3.3.2 Needle damage

The needle shall not be damaged by the automated feature.

4.3.3.3 Dose delivery

The sequence and timing of insertion when performed in conjunction with an automated injection shall not cause incomplete delivery of the dose to the intended injection depth.

NOTE This requirement can be verified as a separate study, or can be verified during full dose accuracy testing using the method in 5.1.9.1.

The risk assessment shall address the potential hazard to the patient of any portion of the liquid that may be delivered outside the intended injection depth.

4.3.4 Injection of the medicinal product

Each dose shall be delivered into the intended injection depth. Dose accuracy shall be confirmed through the methods given in 5.1.8.

The NIS-AUTO shall provide confirmation of completion of the automated injection in an unmistakable and clear manner. Such confirmation shall be at least a persistent visual indication. This indication shall be reset between injections for multi-dose NIS-AUTOs.

NOTE Additional tactile and/or audible indicator(s) may be included.

The instructions for use shall clearly cover the actions to be taken by the user in the event of failure of the NIS-AUTO to deliver the medicinal product.

4.3.5 Needle retraction

4.3.5.1 Completion of dose delivery

The sequence and timing of the retraction shall not cause incomplete delivery of the dose to the intended injection site.

NOTE This requirement can be verified as a separate study, or can be verified during full dose accuracy testing using the method in 5.1.9.1.

The risk assessment shall address the potential hazard to the patient of any portion of the liquid that may be delivered outside the intended injection depth.

4.3.5.2 Retraction distance

After retraction, the needle tip shall be sub-flush to the front-most part of the NIS-AUTO (defining the point of contact with the patient adjacent to the injection site) such that the retracted position ensures that the needle is completely retracted from the patient's tissue when measured in accordance with the method described in 5.1.9.2.

4.3.5.3 Communication of completion

The NIS-AUTO shall provide visible, audible or tactile indication to the user that the needle has been successfully retracted from the injection site.

4.3.6 Disabling the NIS-AUTO (single-use NIS-AUTOs or last dose from multiple-dose disposable NIS-AUTOs)

Disabling of the NIS-AUTO shall take place after either or both of the following have occurred:

a) the injection is completed;

b) the NIS-AUTO is removed from the body.

The NIS-AUTO shall not disable at any time before the NIS-AUTO has completed its intended function. After completion of the disabling function, the NIS-AUTO shall not be able to be put into a state (e.g. refilled, reloaded, reset), which will allow the NIS-AUTO to perform any subsequent injections.

If the NIS-AUTO provides automated disabling, it shall not do so until it has completed its intended use (hence, it shall not be unintentionally disabled).

4.3.7 Needle shielding

Automatic pre- and post-injection needle shielding shall not interfere at any time with the NIS-AUTO intended function. Prior to use, the feature shall resist overriding forces to prevent unintended exposure of the needle tip when tested in accordance with 5.1.11.

Once activated, after the NIS-AUTO has completed its intended use, the feature shall resist overriding forces to prevent unintended exposure to the needle tip.

Using a risk-based approach (consistent with 4.4), the manufacturer shall determine appropriate minimum overriding forces. These force values shall be obtained with the methodology outlined in Clause 5.

NOTE Post-injection needle shielding can be considered to be sharps injury protection if the NIS-AUTO meets all the requirements of ISO 23908.

4.3.8 Needle removal from the NIS-AUTO

Automatic needle removal shall not activate at any time before the NIS-AUTO has completed its intended function.

4.4 Risk analysis requirements

A system that becomes automated by the addition of a component or accessory shall be subject to risk analyses in accordance with ISO 14971.

A system that becomes automated by the addition of a component or accessory shall be subject to usability analyses and testing in accordance with IEC 62366.

The benefits of automating one or more functions shall outweigh the risk of introducing them.

5 Test methods

5.1 General

5.1.1 Test conditions

Any suitable test system can be used that enables the required accuracy (determined by calibration) and precision (determined by Gauge R&R) to be obtained. The repeatability and reproducibility (Gauge R&R) of the test apparatus shall not exceed 20 % of the allowed tolerance range for any given measurement. For destructive test measurements, the Gauge R&R shall not exceed 30 % of the allowed tolerance range. At a minimum, the Gauge R&R should cover ±2 standard deviations (thereby covering approximately 95 % of the variation).

EXAMPLE A measurement system with a measurement specification limit of ±0,01 ml (range of 0,02 ml) comes out of the Gauge R&R with a Gauge R&R/tol. range ratio of 20 %, which means that the Gauge R&R (four standard uncertainties) equals 0,02 ml/5 = 0,004 ml. The uncertainty of the measurement is ±2 standard deviations (see ISO/IEC Guide 98-3), which equals 0,002ml.

NOTE Some of the requirements in this part of ISO 11608 only have one-sided limits, in which case the Gauge R&R should only be used to find the R&R standard deviation. The measurement uncertainties are calculated as 2 × R&R standard deviations.

The manufacturer shall define and describe the tests that are required to demonstrate the functionality of any and all automated functions for the system.

This shall be confirmed after pre-conditioning (to be determined during testing in accordance either with ISO 11608-1 or procedures to be specified in this part of ISO 11608).

Unless otherwise specified, all tests and test evaluations shall be performed at standard atmosphere conditions (as defined in ISO 11608-1). Consideration shall be given to the sequential operation of a NIS-AUTO when testing. Where the design of a NIS-AUTO allows operations to be performed in a sequence other than that specified, the manufacturer shall document how the risks of out-of-sequence operation have been addressed.

5.1.2 Drug product preparation (e.g. reconstitution)

The manufacturer shall confirm that the drug product prepared automatically within the NIS-AUTO, when used according to the instructions for use, meets the drug product specification. Confirmation will normally be achieved by at least visual means, according to the drug product specification.

5.1.3 Needle preparation

Automated needle preparation shall be performed according to the instructions for use. Following this, the needle tip shall be inspected, using optical magnification where appropriate to confirm that there is no obvious damage to the needle tip. The NIS-AUTO shall perform all subsequent functions within the specified parameters.

5.1.4 Air removal and/or priming

Automated air removal and/or priming shall be performed in accordance with the instructions for use. Following this, the NIS-AUTO shall still be able to deliver the specified volume of drug product specified in the requirements in accordance with ISO 11608-1.

5.1.5 Automatic dose setting and memory

Where the dose delivered is variable and may be set automatically, the values of V_{min}, V_{mid} and V_{max} used in dose accuracy assessment shall be appropriate to the range that may be set automatically.

Where the NIS-AUTO is intended to display the previously set dose, the dose displayed shall be verified as that previously set and confirmed through a subsequent dose accuracy measurement.

5.1.6 Actuation

Each of the manual steps leading to an automated injector sequence shall be undertaken according to the instructions for use and measurements made, where appropriate (for example, torque to rotate a safety lock or force to operate a button). This ensures that the initiation of each step is within the specified limits.

Where the design permits only sequential operation, the steps shall be undertaken in sequence.

Where the design permits non-sequential operation, the steps shall be undertaken in each of the possible sequences. In whichever order the steps are undertaken, the NIS-AUTO shall not start the automated injection until all of the steps are completed.

5.1.7 Needle extension

The axial distance from the patient end of the needle tip to the nearest part of the NIS-AUTO body (defining the point of contact with the patient adjacent to the injection site) shall be measured during normal operation of the NIS-AUTO. Measurement may be by mechanical, optical or other means, but shall not affect the position of the needle tip. The distance measured shall be within the specification for the NIS-AUTO.

5.1.8 Injection

Dose accuracy shall be determined according to the dose accuracy method of ISO 11608-1.

Dose accuracy testing may be modified using the method specified in 5.1.9.1 for NIS-AUTOs that combine automated insertion and/or retraction with the injection.

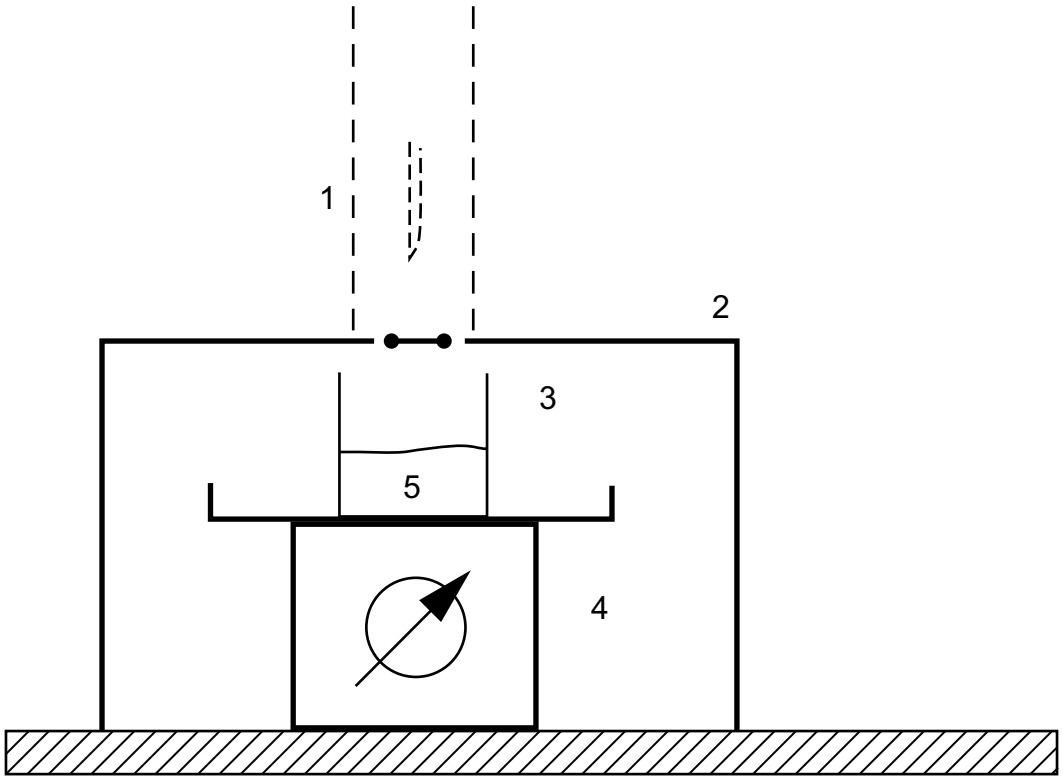
5.1.9 Needle insertion and needle retraction

5.1.9.1 Dose accuracy

Using the dose accuracy method specified in 5.1.8, a membrane shall be placed over the measurement container flush with the surface around the opening of the NIS-AUTO (shown in Figure 2).

The volume of drug delivered before penetration of the membrane and after extraction from the membrane shall be excluded from the calculation of dose accuracy. The membrane shall not allow any liquid to flow into the measurement container other than that through the needle and shall not adversely affect the needle insertion or retraction.

For uses of the injector whereby the risk assessment determines that the intended injection site starts at a depth greater than skin level, the position of the membrane shall be adjusted accordingly away from the end of the injector.



Key

1 NIS-AUTO
2 membrane and hood (not connected to scale)
3 beaker
4 scale
5 liquid

Figure 2 — Example of the dose accuracy test set-up

Other methods are permitted. One alternative might be a two-staged approach: using high-speed photography, confirm that expression of the full dose begins and ends within a pre-specified percentage (based on the intended injection depth) of the needle extension. For example, with a 10 mm needle extension, a 30 % allowance would require that fluid expression begin and end with the needle extended at least 7 mm. Then satisfy standard dose accuracy requirements as given in ISO 11608-1.

5.1.9.2 Retracted position

The NIS-AUTO shall be operated according to the instructions for use. At the end of the retraction function the axial distance from the needle tip to the front-most part of the NIS-AUTO body (defining the point of contact with the patient adjacent to the injection site) shall be measured.

5.1.10 Disabling the NIS-AUTO

The disabled NIS-AUTO shall be subjected to the conditions specified for normal actuation and the actuation force (where appropriate) shall be increased to at least two times the specified maximum for normal actuation. The NIS-AUTO shall not perform any part of its normal actuation.

The NIS-AUTO shall not perform any part of its disabled functionality.

The same NIS-AUTO shall then be subjected to free fall in a non-turbulent way from a height of 1 000 mm onto a 3-mm-thick hard, smooth steel surface backed with wood of minimum thickness of 10 mm, in the following positions:

a) horizontally;

b) vertically on one end;

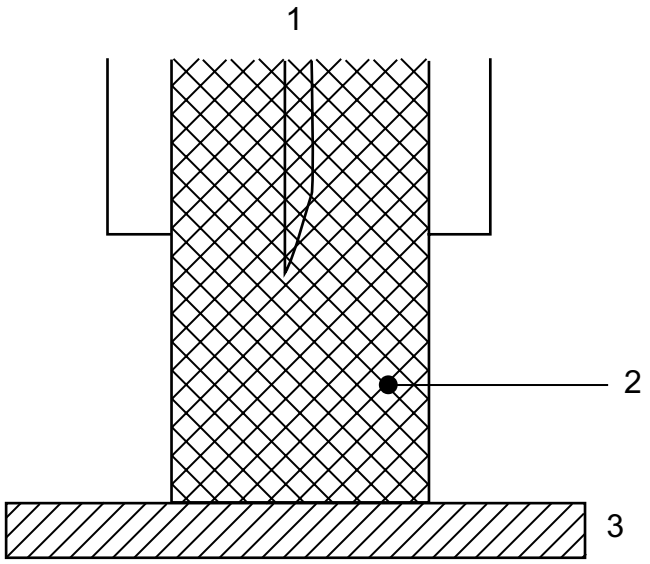
c) vertically on the opposite end to b).

The NIS-AUTO shall not perform any part of its disabled functionality during any of these falls.

5.1.11 Pre- and post-injection needle hiding and shielding

5.1.11.1 Needle hiding

The test method shall be conducted in such a way that the feature that hides the needle prevents visibility of the needle through the material (e.g. opaque or non-transparent material). The visibility of the needle through the opening for needle travel, before and after injection, is shown in Figure 3.



Key

1 NIS-AUTO (before or after injection)

2 example of a needle hiding feature

3 test surface

Figure 3 — Example of needle hiding test set-up

5.1.11.2 Needle shielding

If the NIS-AUTO includes a lock-out feature, it shall withstand a minimum load as determined from the risk assessment (at least two times its actuation force), which shall be applied to the surface around the opening of the NIS-AUTO using a flat plate. The plate dimensions shall be larger than the NIS-AUTO profile so that the application of the force onto the surface around the opening is entirely within the plate. Under the application of this load, the needle tip shall not touch the flat plate.

5.2 Dose specification requirements

The dose accuracy of the NIS-AUTO shall be determined by the procedures described in ISO 11608-1.

5.3 Uncertainty of measurements and conformance with specifications

Unless otherwise specified, the tests shall be performed in the standard atmosphere as specified in ISO 11608-1.

6 Test report

In addition to the requirements specified in ISO 11608-1, the test report shall include the following:

a) reference to this International Standard, i.e. ISO 11608-5:2012;

b) identification of the automated function(s);

c) pre-defined pass and fail criteria for the automated function and statement of whether these are met.

7 Information to be supplied by the manufacturer

Information shall be included in accordance with ISO 11608-1.

Annex A
(informative)

Rationale for requirements

A.1 General

This annex contains rationale statements for some of the requirements in this part of ISO 11608. It is included to provide additional information to the user.

A.2 Preparation

A.2.1 General

Since NIS-AUTOs that are covered by this part of ISO 11608 have one or more automated functions, 4.2.1 helps to ensure that the user cannot inadvertently initiate steps out of sequence if that order is important to the proper and safe functioning of the NIS-AUTO.

A.2.2 Drug preparation (e.g. reconstitution)

Since the user does not have the ability to control drug preparation (e.g. reconstitution) for the NIS-AUTO (and the manufacturer cannot ensure proper drug preparation through training), 4.2.2 requires the manufacturer to ensure that the automated function carries out such preparation in an appropriate and consistent manner.

Visibility of drug product might not be needed if, for example:

a) the drug is photosensitive;

b) the therapy would be affected by the user checking for the integrity of the drug (e.g. emergency drug).

A.2.3 Needle preparation

The term “needle preparation” includes any preparatory steps the user might be required to perform prior to initiation of any automated steps, e.g. attaching the needle or removing the cover.

Automated needle preparation is an improvement on manual needle preparation, so this should be verified or a rationale given as to how it is improved.

A.2.4 Dose setting

Subclause 4.2.5 describes automated dose setting of a previously set dose, rather than the utilization of post-injection memory on the NIS-AUTO.

In addition, 4.2.5 specifies that the user is able to adjust the dose if an automated feature suggests a dose for the user.

A.3 Injection

A.3.1 Actuation of injection

Subclause 4.3.2 is included for user safety, by eliminating or reducing the potential for inadvertent actuation and triggering of any kind of automated NIS-AUTO.

In addition, in the special case of a multi-dose or multi-use NIS-AUTO, this requirement is intended to reduce or eliminate the potential for inadvertent second (or subsequent) actuations without an explicit user-initiated step between each subsequent actuation.

A.3.2 Needle insertion and extension

Since NIS-AUTOs that fall within the scope of this part of ISO 11608 control the extent to which the needle is inserted into the patient by limiting the amount the needle is extended from the NIS-AUTO, 4.3.3 requires that automated needle insertion and extension be tested in order to ensure the intended insertion distance is met and the dose is delivered to the intended part of the body.

A.3.3 Injection of the medicinal product

Since NIS-AUTOs covered by this part of ISO 11608 might automate the injection of the medicinal product, 4.3.4 requires that the user should be provided with some persistent means of confirmation when this function has occurred.

A.3.4 Needle retraction

Subclause 4.3.5 addresses the retraction of the needle from the injection site.

It mandates that any automated needle retraction take place after the injection of the medicinal product has been completed.

A.3.5 Disabling the NIS-AUTO (for single use NIS-AUTOs or after the last dose from multi-dose disposable NIS-AUTOs)

Subclause 4.3.6 addresses both single-use NIS-AUTOs, and the end of life of a multi-dose or multi-use NIS-AUTO. It is not applicable to each individual injection of such a multi-dose NIS-AUTO.

The purpose of 4.3.6 is to ensure that the NIS-AUTO cannot be unintentionally disabled.

A.3.6 Needle shielding

Subclause 4.3.7 does not cover needle stick injury protection. These requirements are given in ISO 23908.

A.3.7 Needle removal from the NIS-AUTO

Further requirements can be found in ISO 23908.

A.4 Risk analysis requirements

ISO 14971 and IEC 62366 are cited in 4.4 to re-emphasise that they are normative references and that they might require more (or less) than is specified in this part of ISO 11608.

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[3] ISO 9000, *Quality management systems — Fundamentals and vocabulary*

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