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# Needle-free injectors for medical use — Requirements and test methods

*Injecteurs sans aiguille à usage médical — Exigences et méthodes d'essai*

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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 21649 was prepared by Technical Committee ISO/TC 84, *Devices for administration of medicinal products and intravascular catheters*.

# Introduction

This International Standard applies to needle-free injectors primarily intended to administer medicinal products to humans. Because of the anticipated variation in the designs of such a broad array of devices, this International Standard is promulgated more as a “horizontal” rather than a “vertical” one. Thus, it will tend to specify the results of the design effort instead of the physical and construction requirements used as the basis for device design, so that innovation in achieving the intended purposes is not unnecessarily restricted.

Standards of this nature intentionally avoid addressing more than the most basic elements regarding the safety and performance of needle-free injector devices in humans. Any intended labelling of such devices indicating their use to deliver medicinal products into the body or into specified tissue compartments thereof (e.g., intramuscular, subcutaneous or intradermal), or for the administration of specific pharmaceutical drugs or vaccines, shall fall under the authority of national governments or supranational agencies regulating the manufacture and marketing of medical devices and pharmaceutical products. Such standards are expected to be supplemented by additional requirements and may occasionally be superseded by such regulatory authorities. Despite certain advantages for intentional interchangeability for dose chambers designed for different needle-free injection systems, as well as the potential risks of inadvertent interchangeability, these standards avoid setting forth design specifications for the uniform size, shape and interface of such dose chambers. This issue is left for future initiatives to build upon the standards promulgated herein.

The sampling plans for inspection selected for this International Standard are intended to verify the design, at a high confidence level, i.e., the manufacturer's ability to manufacture one “lot” of needle-free injectors, which conforms to the critical product attributes. The sampling plan does not replace the more general manufacturing quality systems, including lot release, which appear in standards on quality systems, e.g. the ISO 9000 series or ISO 13485.

# Needle-free injectors for medical use — Requirements and test methods

## 1 Scope

This International Standard applies to safety and performance and testing requirements for single-use and multiple-use needle-free injection systems intended for human use in clinics and other medical settings and for personal use by patients.

The dose chamber of the injection system is often disposable and intended to be replaced after either a single use or a limited number of uses. It is sometimes separable from the injection mechanism and often termed a “cartridge”, “ampoule”, “syringe”, “capsule” or “disc”. In contrast, the dose chamber also may be a permanent internal chamber designed to last through the claimed life of the device.

Excluded from this International Standard are drug delivery methods which:

— involve penetration of a part of the device itself into or through skin or mucous membranes (such as needles, tines, micro-needles, implantable slow-release drug devices);

— generate aerosols, droplets, powders or other formulations for inhalation, insufflation, intranasal or oral deposition (such as sprays, inhalers, misters);

— deposit liquids, powders, or other substances on the surface of skin or mucosal surfaces for passive diffusion or ingestion into the body (such as transdermal patches, liquid drops);

— apply sonic or electromagnetic energy (such as ultrasonic or iontophoretic devices);

— infusion systems for adding or metering medication into or through systems of artificial tubes, catheters, and/or needles which themselves enter the body.

## 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 3207:1975, *Statistical interpretation of data — Determination of a statistical tolerance interval*

ISO 3746:1995, *Acoustics — Determination of sound power levels of noise sources using sound pressure — Survey method using an enveloping measurement surface over a reflecting plane*

ISO 10993 (all parts), *Biological evaluation of medical devices*

ISO 11201:1995, *Acoustics — Noise emitted by machinery and equipment — Measurement of emission sound pressure levels at a work station and at other specified positions — Engineering method in an essentially free field over a reflecting plane*

ISO 11202:1995, *Acoustics — Noise emitted by machinery and equipment — Measurement of emission sound pressure levels at a work station and at other specified positions — Survey method* in situ

ISO 11204:1995, *Acoustics — Noise emitted by machinery and equipment — Measurement of emission sound pressure levels at a work station and at other specified positions — Method requiring environmental corrections*

ISO 14155-1:2003, *Clinical investigation of medical devices for human subjects — Part 1: General requirements*

ISO 14155-2:2003, *Clinical investigation of medical devices for human subjects — Part 2: Clinical investigation plans*

ISO 14253-1:1998, *Geometrical Product Specifications (GPS) — Inspection by measurement of workpieces and measuring equipment — Part 1: Decision rules for proving conformance or non-conformance with specifications*

IEC 60068-2-27:1987, *Environmental testing — Part 2: Tests. Test Ea and guidance: Shock*

IEC 60068-2-30:2005, *Environmental testing — Part 2-30: Tests. Test Db and guidance: Damp heat, cyclic (12 h + 12 h cycle)*

IEC 60068-2-32:1975, *Environmental testing — Part 2: Tests. Test Ed: Free fall*

IEC 60068-2-64:1993, *Environmental testing — Part 2: Test methods — Test Fh: Vibration, broad-band random (digital control) and guidance*

IEC 60601-1-1:2000, *Medical electrical equipment — Part 1-1: General requirements for safety — Collateral standard: Safety requirements for medical electrical systems*

IEC 60721-3-7:2002, *Classification of environmental conditions — Part 3-7: Classification of groups of environmental parameters and their severities — Portable and non-stationary use*

IEC 61000-4-2:2001, *Electromagnetic compatibility (EMC) — Part 4-2: Testing and measurement techniques — Electrostatic discharge immunity test*

IEC 61000-4-3:2002, *Electromagnetic compatibility (EMC) — Part 4-3: Testing and measurement techniques — Radiated, radio-frequency, electromagnetic field immunity test*

IEC 61672-1:2002, *Electroacoustics — Sound level meters — Part 1: Specifications*

GUM:1995, *Guide to the Expression of Uncertainty in Measurement (GUM). BIPM, IEC, IFCC, ISO, IUPAC, IUPAP, OIML* — First edition 1993, corrected and reprinted 1995

## 3 Terms and definitions

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

**3.1**
**intended dose**
amount (volume or mass) of medicinal product intended to be ejected at one time

**3.2**
**ejected dose**
amount (volume or mass) of medicinal product ejected at one time

**3.3**
**dose specification**
variation of dose quantities (volume or mass) — and a statistical summation of same — which the needle-free injection system will eject for one or for a range of nominal dose quantities, as annunciated by the dose indicator read by typical users of the device

**3.4**
**dose chamber**
final enclosure which holds the pharmaceutical product and has direct contact with it just prior to its administration to the patient

**3.5**
**dose indicator**
component of a needle-free injection system showing the intended dose to be delivered

NOTE Depending on the device design, such indication may or may not be apparent before the dose chamber is filled.

**3.6**
**filling device**
integral component or components of, or separate or separable accessory(ies) to, a needle-free injector which acts or assists in the transfer of medicinal product between a reservoir and a dose chamber

NOTE Needle-free injection systems in which the dose chamber is or can be pre-filled by the manufacturer of the medicinal product may function without any such filling device. When a filling device is required, it may be as simple as an adapter providing an interface between medicinal reservoir and dose chamber, (e.g., using the piston and plunger of the latter to effect the transfer), or be as complicated as a device with internal channels to actively withdraw and insert the medicinal product from and to the respective containers.

**3.7**
**injection mechanism**
components of the needle-free injection system which are designated to harness, store, prevent (as in a "safety" latch), trigger, regulate, control and transfer to the dose chamber and/or its contained medicinal product the energies required for the injection to occur

NOTE This term is not used to refer to separate accessories which transfer energy into the needle-free injector but which are separated from the needle-free injector at the time of the injection (such as a separate spring-cocking mechanism, a gas pressurizing tank, a foot pump or other separate device using electricity, muscle power or other energy source).

**3.8**
**claimed lifetime**
total number of ejections that a needle-free injection system, in normal use with recommended user maintenance and before manufacturer overhaul or refurbishment of parts, is expected to administer within its performance profile specified by the manufacturer

NOTE This number may also be expressed as a period of time (e.g. number of days, weeks, months or years) at a corresponding frequency of expected usage (e.g. number of injections per day, week, month or year).

**3.9**
**maximum and minimum dose**
volumes, masses or number of units representing the largest and smallest quantities, which the manufacturer designates the needle-free injection system is capable of ejecting by one injection

**3.10**
**reservoir**
intermediate enclosure that holds and has contact with the medicinal product immediately prior to its transfer into the dose chamber

NOTE This container is often the vial or other enclosure filled with the medicinal product by the pharmaceutical manufacturer (and termed the "primary packaging" in that industry). It may be single-dose or multi-dose, and usually requires some manipulation by the user, by an accessory filling device, or by the injector device itself to transfer the contents into the dose chamber. There may be no medicinal reservoir for those needle-free injection systems in which the dose chamber is pre-filled by the manufacturer of the medicinal product.

**3.11**
**needle-free injection system**
needle-free injector and its components and accessories that administer a medicinal product, without any part of the system penetrating the skin or mucous membranes

NOTE Such components and accessories may include:

— disposable or re-usable dose chambers;

— separable mechanisms that obtain, transfer, convert, or store energy (using hydraulic, pneumatic, mechanical, electrical, chemical or other means);

— filling devices to hold dose chambers and feed them into the injector or vessels to capture and dispose of used containers;

— instructions and educational materials for end-users.

**3.12**
**needle-free injector**
device that administers a medicinal product to a patient by using mechanical motion (such as movement of a piston or flow of a gas, but not to exclude other means) to impart kinetic energy to the medicinal product

**3.13**
**nozzle**
component of an injector through which the medicinal product is ejected

NOTE The nozzle may or may not — depending on the device design — make physical contact with the skin or other membranes of the patient.

**3.14**
**orifice**
hole at the end of the nozzle, through which the medicinal product is expelled

**3.15**
**performance profile**
manufacturer-specified set of measurable and quantitative values and tolerance intervals which describes the proper functioning of a needle-free injection system

**3.16**
**replicate**
random sequence of $V_{min}$, $V_{mid}$, and $V_{max}$

**3.17**
**unit container**
customer packaging of an individual component or needle-free injection system

## 4 Symbols and abbreviated terms

$V_{set}$ One of the 3 pre-set doses (expressed as a volume in millilitres) used in determining the uncertainty of dose for a given needle-free injector. $V_{set}$ is defined as one of the following:

a) minimum dose ($V_{set}$ = $V_{min}$) (specified in the instructions for use);

b) maximum dose ($V_{set}$ = $V_{max}$) (specified in the instructions for use);

c) midpoint dose ($V_{set}$ = $V_{mid}$) where $V_{mid}$ is defined as the injector setting closest to ($V_{min}$ + $V_{max}$)/2.

NOTE Recommended doses as specified in the instruction for use may differ from those doses that can be set.

$V_{meas}$ The volumetric measurement value for a given $V_{set}$;

$G_{meas}$ The gravimetric measurement value for a given $V_{set}$;

$\rho$ Mass density expressed in grams per millilitre;

$p$ Probability content;

$n$ Number of needle-free injectors required for a given test;

$\bar{x}$ The sample average (based on a random sample), an estimate of the population average:

$\bar{x} = \Sigma V_{meas}/n$;

$s$ The sample standard deviation (based on a random sample), an estimate of the population standard deviation:

$$s = \sqrt{\frac{\sum \left(V_{meas} - \bar{x}\right)^2}{n-1}}$$

$k$ Tolerance Limit Factor; determined from the confidence level, probability content, $p$, and the number of measurements, $n$, conducted at each dose setting;

TP The transition point in millilitres; the volume at which the definition of the upper and lower specification limit for $V_{set}$ changes from absolute terms to relative terms:

TP = 0,2 ml;

USL Upper Specification Limit for a given $V_{set}$;

LSL Lower Specification Limit for a given $V_{set}$.

# 5 Requirements

## 5.1 General requirements

When the needle-free injector is ready for injection, there is an indication to the user that the intended dose of medicinal product is present to be delivered. The needle-free injector shall indicate the dose to be delivered.

The needle-free injector shall indicate, at least by visual means, that the device is ready for injection.

After the injection, the needle-free injector shall indicate, by visual or auditory or tactile means, that the intended dose has been expelled.

The state of the needle-free injector, when ready to deliver the dose, shall be visibly different from its state when the dose has been delivered. For multi-dose needle-free injectors, the device shall be designed so it is impossible to deliver a second dose after delivery of the first dose without a second and different operation.

The needle-free injector shall be designed to prevent or to reduce the risk of premature or inadvertent actuation of the device, and/or to prevent or mitigate any injury that might result.

The materials used in the medicinal product or test fluid path (as appropriate) and any device component likely to be in direct or indirect contact with body tissues (at the injection site) shall be demonstrated to be biocompatible in accordance with ISO 10993-1 and other relevant parts of ISO 10993.

Devices with an exposed nozzle orifice, within reach of fingertips or environmental surfaces during preparation of the device for use or upon setting it down, shall be equipped with a method of reducing the possibility of contact of the orifice and nozzle face with environmental surfaces between the time of filling and the time of actual administration of the medicinal product.

Needle-free devices that are intended for use on more than one patient shall be designed for, and shall have safety demonstrated with regard to, the potential transfer of pathogens between patients.

Components intended to be sterile shall be subjected to a validated sterilization process in accordance with applicable standards.

Needle-free injectors shall not produce sound which would exceed the current recommended exposure limits (REL) for occupational noise.

Claimed lifetime shall be determined by the manufacturer based on empirical testing. The claimed lifetime may be expressed either in terms of its total number of injections, or the period of time it may be used at specified expectations for the frequency of usage (i.e., injections per week, month or year). If the needle-free injector is designed to stop working after a limited time or number of operations, the total number of operations or time shall be adopted as the claimed lifetime.

If power to the needle-free injector is provided by an external power supply (“mains”), then electrical safety shall be obtained through normative references to IEC 60601-1-1:2000. Needle-free injectors utilizing other sources of power shall reference applicable standards.

## 5.2 Noise requirements

If it is foreseeable that the device can be fired unintentionally in open air, the C-weighted peak emission sound pressure level, $L_{\mathrm{pC\ peak}}$, produced by the needle-free injector shall not exceed 120 dB (for protection of the patient) when fired in open air.

If it is not foreseeable that the device can be fired unintentionally in open air, the C-weighted peak emission sound pressure level, $L_{\mathrm{pC\ peak}}$, produced by the needle-free injector shall not exceed 130 dB (for protection of the patient) with the injection head against a surface which imitates actual use as defined by the manufacturer.

The A-weighted single event emission sound pressure level (SEL), $L_{\mathrm{pA,\ 1s}}$ produced by the needle-free injector, with the injection head against a surface which imitates actual use as defined by the manufacturer, shall fulfil:

$$L_{\mathrm{pA,\ 1s}} < 85 - 10 \log_{10} (N/28\ 800)$$

where $N$ is the claimed maximum number of shots per 8 h period as declared by the manufacturer.

NOTE This requirement corresponds to $L_{\mathrm{EP,d}} < 85$ dB.

Where the above sound pressure levels are exceeded, a warning shall be given in the instructions for use, see 8.3 p).

## 5.3 Dose specification requirements

The dose specification of the needle-free injector shall be determined by the procedures described in 6.4.1. The specification limits for the expelled liquid dose will be ± 0,01 ml for all doses of 0,2 ml or less. For all doses more than 0,2 ml, the specification limits of the expelled dose shall be ± 5 %.

For the situation where the dose specification limits above are not relevant to the intended therapeutic use, human clinical data shall be provided to substantiate the dose specification limits claimed. In the case of refillable devices this exception shall be indicated on the unit container (see 8.2.3) and in the instructions for use (see 8.3).

## 5.4 Uncertainty of measurements and conformance with specifications

The uncertainty of measurements shall be evaluated and expressed by the laboratory performing the test in accordance with Guide to the Expression of Uncertainty in Measurement (GUM).

The conformance with specification is proven in accordance with ISO 14253-1.

Conformance with specification is proven when the result of a measurement falls within the tolerance zone of the characteristic of a needle-free injector.

## 5.5 Performance profile requirements

**5.5.1** There shall be an established performance profile.

**5.5.2** The performance profile shall define the properties and tolerance intervals of the device required for consistent, reliable delivery of the medicinal product to the targeted tissues.

NOTE The performance profile and results may include one or more of the following parameters: pressure, force, volume, mass, velocity, time, distance, movement, depth or dispersion of penetration, and stream cross-section or silhouette, among others.

**5.5.3** The performance profile of the needle-free injector shall be verified by clinical data from studies conducted in accordance with ISO 14155-1 and ISO 14155-2 and good clinical practice (GCP) using the same needle-free injector or a needle-free injector demonstrated to have an equivalent performance profile. The performance profile of a device shall be correlated to the desired clinical “end-point” of successfully delivering one or more representative drugs, vaccines or other medicinal products.

NOTE The performance profile is derived from tests that do not use human subjects (i.e. preclinical, e.g. bench procedures or laboratory animal studies) which in the development phase of the device have been correlated with high predictive value to human (clinical) studies. Such studies would have demonstrated successful delivery of the intended medication(s) to the target tissues, achieving therapeutic bioavailability or pharmacokinetics, or reaching another appropriate endpoint in humans. The purpose of the performance profile is to ensure that each new unit or batch will perform in an equivalent manner to the predicate device tested in clinical studies during its development and initial registration/licensure. With this “bridge” between physical or animal testing and prior demonstration of clinical effect, newly-manufactured devices — including those which may differ somewhat due to subsequent design refinements — are presumed to also successfully deliver the intended medication to humans if they satisfy the established performance profile.

**5.5.4** Sufficient details of the test methodology shall be specified to permit independent verification of the performance profile.

NOTE Regulatory provisions may require the details of the test methodology to be made available to regulatory authorities so that the procedures can be evaluated and repeated by regulatory bodies.

## 5.6 Test requirements

### 5.6.1 Needle-free injectors subjected to standard, cool and hot atmospheres and after claimed lifetime testing

When tested in accordance with 6.2.2:

— the needle-free injectors shall have an uncertainty of dose within the limits specified in 5.3, when subjected to standard, cool and hot atmospheres;

— none of the needle-free injectors shall have visual defects after being subjected to standard, cool and hot atmospheres except for broken dose chambers that are obvious to the user;

— the needle-free injectors shall have a performance profile within the limits specified by the manufacturer after being subjected to standard, cool and hot atmospheres;

— none of the needle-free injectors shall have visual defects after being subjected to claimed lifetime testing except for broken dose chambers that are obvious to the user;

— the needle-free injectors shall have an uncertainty of dose within the limits specified in 5.3 after being subjected to claimed lifetime testing;

— the needle-free injectors shall have a performance profile within the limits specified by the manufacturer after being subjected to claimed lifetime testing.

Needle-free injectors with pre-filled non-replaceable dose chambers that have lower and/or higher acceptable operating temperatures than those specified in this International Standard shall be subjected to the test at these acceptable temperatures.These acceptable operating temperatures shall be stated in the instructions for use.

Needle-free injectors designed for a single actuation shall be excluded from claimed lifetime testing.

### 5.6.2 Needle-free injectors subjected to a dry heat storage atmosphere

When tested in accordance with 6.2.3:

— none of the needle-free injectors shall have visual defects after being subjected to a dry heat storage atmosphere except for broken dose chambers that are obvious to the user;

— the needle-free injectors shall have an uncertainty of dose within the limits specified in 5.3, after being subjected to a dry heat storage atmosphere;

— the needle-free injectors shall have a performance profile within the limits specified by the manufacturer after being subjected to a dry heat storage atmosphere.

Needle-free injectors with pre-filled non-replaceable dose chambers with a lower acceptable storage temperature shall be subjected to the test at the acceptable temperature, and this acceptable temperature shall be stated in the instructions for use.

### 5.6.3 Needle-free injectors subjected to a cold storage atmosphere

When tested in accordance with 6.2.4:

— none of the needle-free injectors shall have visual defects after being subjected to a cold storage atmosphere except for broken dose chambers that are obvious to the user;

— the needle-free injectors shall have an uncertainty of dose within the limits specified in 5.3, after being subjected to a cold storage atmosphere;

— the needle-free injectors shall have a performance profile within the limits specified by the manufacturer after being subjected to a cold storage atmosphere.

Needle-free injectors with pre-filled non-replaceable dose chambers with a higher acceptable storage temperature shall be subjected to the test at the acceptable temperature, and this acceptable temperature shall be stated in the instructions for use.

### 5.6.4 Needle-free injectors subjected to a cyclical atmosphere

When tested in accordance with 6.2.5:

— none of the needle-free injectors shall have visual defects after being subjected to a cyclical atmosphere except for broken dose chambers that are obvious to the user;

— the needle-free injectors shall have an uncertainty of dose within the limits specified in 5.3, after being subjected to a cyclical atmosphere;

— the needle-free injectors shall have a performance profile within the limits specified by the manufacturer after being subjected to a cyclical atmosphere.

Needle-free injectors with a pre-filled non-replaceable dose chamber shall not be required to fulfil the requirements of this sub-clause.

#### 5.6.5 Needle-free injectors subjected to free fall

When tested in accordance with 6.2.6:

— none of the needle-free injectors with replaceable dose chambers shall have visual defects after being subjected to free fall except for broken dose chambers that are obvious to the user;

— none of the needle-free injectors with non-replaceable dose chambers shall have visual defects after being subjected to free fall except for broken dose chambers that are obvious to the user;

— the needle-free injectors shall have an uncertainty of dose within the limits specified in 5.3, after being subjected to free fall;

— the needle-free injectors shall have a performance profile within the limits specified by the manufacturer after being subjected to free fall.

#### 5.6.6 Needle-free injectors subjected to vibration and shock

When tested in accordance with 6.2.7:

— none of the needle-free injectors shall have visual defects after being subjected to vibration and shock except for broken dose chambers that are obvious to the user;

— the needle-free injectors shall have an uncertainty of dose within the limits specified in 5.3, after being subjected to vibration and shock;

— the needle-free injectors shall have a performance profile within the limits specified by the manufacturer after being subjected to vibration and shock.

Needle-free injectors with limited conditions for vibration and shock shall be subjected to the test at the acceptable conditions, and these acceptable conditions shall be stated in the instructions for use.

#### 5.6.7 Needle-free injectors with electrical components subjected to electromagnetic compatibility (EMC)

##### 5.6.7.1 General

The requirements given in 5.6.7.2 and 5.6.7.3 are requirements substituting those specified in IEC 60601-1-2 as the latter standard covers requirements for electro-medical appliances in general only, and it does not address specific devices such as needle-free injectors.

NOTE 1 The tests specified in 5.6.7.2 and 5.6.7.3 are based on the requirements given in the collateral standard IEC 60601-1-2:2001. In that standard, EMC references are given to the IEC 61000-4-1 (IEC 61000-4-2, Edition 1.1:1999 and IEC 61000-4-3, Edition 1.1:1998 in particular). The span of the sweep in that standard covers all the frequencies of mobile communication systems.

NOTE 2 These requirements apply only to needle-free injectors with electronic components.

#### 5.6.7.2 Electrostatic discharge

When tested in accordance with 6.2.8:

— none of the needle-free injectors shall have visual defects after being subjected to electrostatic discharge levels;

— the needle-free injectors shall have an uncertainty of dose within the limits specified in 5.3, after being subjected to electrostatic discharge levels;

— the needle-free injectors shall have a performance profile within the limits specified by the manufacturer after being subjected to electrostatic discharge levels.

#### 5.6.7.3 Radiated radio frequency (RF) fields

When tested in accordance with 6.2.8:

— none of the needle-free injectors shall exhibit erroneous indications during the radio frequency sweep;

— none of the needle-free injectors shall have visual defects after being subjected to the radiated frequency fields;

— the needle-free injectors shall have an uncertainty of dose within the limits specified in 5.3, after being subjected to radiated radio frequency fields;

— the needle-free injectors shall have a performance profile within the limits specified by the manufacturer after radiated radio frequency fields.

## 6 Test methods

### 6.1 General

Each device shall provide only one replicate to the pool of data from which the uncertainty of dose is calculated.

Each of the required dose sizes (i.e., $V_{min}$, $V_{mid}$ and $V_{max}$) shall be evaluated separately in calculating uncertainty of dose. A single needle-free injector and dose chamber can be used to evaluate one $V_{min}$, $V_{mid}$ and $V_{max}$ dose for a given test.

For a fixed-dose device, a replicate consists of one dose.

NOTE 1 Only one replicate is contributed to the pool of data for each dose size, to ensure both inter- and intra-device variability are captured in the measurement.

NOTE 2 To satisfy the different testing requirements of Clause 5, the same group of injectors can be used for the different tests specified in 6.2.3 to 6.2.8.

If needle-free injectors are re-used, it is not required to perform test evaluations (uncertainty of dose, performance profile and visual inspection) after each test procedure specified in 6.2.3 to 6.2.8. In such cases, the test evaluations shall be performed after the last test to which the re-used needle-free injector has been subjected.

NOTE 3 If this final performance assessment produces a failure, the manufacturer may be unable to determine at which point in the testing series the failure occurred.

Unless otherwise specified, all tests and test evaluations shall be performed at standard atmosphere conditions (as defined in 6.3.2).The repeatability and reproducibility of the test apparatus should be no greater than 20 % of the permitted tolerance band for any given set of measurements.

The needle-free injector is prepared in accordance with the instructions for use.

The needle-free injector shall be operated either manually or automatically, in a way that simulates operation by the end-user, as described in the instructions for use.

## 6.2 Test procedures

### 6.2.1 General

Using the probability content levels of 0,950 (95 %) and 0,975 (97,5 %), the two-sided statistical tolerance interval for a given test and $V_{set}$ can be calculated.

The manufacturer shall select a number of devices to test, denoted $n$, appropriate for the tests specified in 6.2.2 to 6.2.8 — recognizing that the target $k$ value will increase as the sample size selected decreases.

**Table 1 — Confidence and probability content requirements for uncertainty of dose**

| **Minimum confidence** | **Minimum probability content,** $p$ | **Examples of number of devices to test,** $n$ | **Corresponding target,** $k$ **for each** $n$ (from Annex A) |
|---|---|---|---|
| 0,95 | ($p$ = 0,975) | 60<br>30<br>25<br>20<br>15 | 2,670<br>2,921<br>3,015<br>3,154<br>3,386 |
| 0,95 | ($p$ = 0,950) | 60<br>30<br>25<br>20<br>15 | 2,335<br>2,555<br>2,638<br>2,760<br>2,965 |

NOTE 1 Number of devices $n$ in Table 1 are provided as an example only.

NOTE 2 The sampling plans for inspection selected for this International Standard 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 International Standards on quality systems, e.g. the ISO 9000 series or ISO 13485.

**Table 2 — Test requirements for needle-free injectors**

| Confidence | Content $p$ | Sub-clause | Descriptions | Dose chamber replaceable | Pre-filled dose chamber non-replaceable | Empty dose chamber non-replaceable |
|---|---|---|---|---|---|---|
| 0,95 | ($p$ = 0,975) | 5.6.1 [a] | Standard, cool, hot, lifetime | x | x [b] | x |
| | | 5.6.2 | Dry heat storage | x | x [c] | x |
| | | 5.6.3 | Cold storage | x | x [d] | x |
| 0,95 | ($p$ = 0,950) | 5.6.4 | Cyclical atmosphere | x | — | x |
| | | 5.6.5 [e] | Free fall | x | x | x |
| | | 5.6.6 [f] | Vibration, shock | x | x | x |
| | | 5.6.7.1 [g] | Electrostatic | x | x | x |
| | | 5.6.7.2 [g] | RF fields | x | x | x |

[a] Single-use needle-free injectors are excluded from claimed lifetime testing. In addition, a new single-use injector shall be used for all of the other tests in 6.2.2.

[b] Needle-free injectors with pre-filled non-replaceable dose chambers that claim different acceptable operating temperatures than specified in this International Standard shall be subjected to the test at those acceptable temperatures, which shall be stated in the instructions for use.

[c] Needle-free injectors with pre-filled non-replaceable dose chambers with a lower acceptable storage temperature shall be subjected to the test at the acceptable temperature.

[d] Needle-free injectors with pre-filled non-replaceable dose chambers with a higher acceptable storage temperature shall be subjected to the test at the acceptable temperature.

[e] When free fall testing needle-free injectors with non-replaceable dose chambers, a sufficient number of devices shall be tested to ensure that $n$ devices are available for uncertainty of dose testing.

[f] Needle-free injectors that cannot satisfy the requirements of vibration and shock testing described in this International Standard shall be subjected to such testing at the acceptable conditions, which shall be stated in the instructions for use.

[g] Needle-free injectors without electronic components shall be exempt from electromagnetic compatibility testing.

### 6.2.2 Needle-free injectors subjected to standard, cool and hot atmospheres and claimed lifetime test

Subject $n$ new needle-free injectors to the standard atmosphere specified in 6.3.2 and test for uncertainty of dose in accordance with 6.4.1.

Determine the performance profile in accordance with the manufacturer's specification.

Subject the same needle-free injectors to the cool atmosphere specified in 6.3.3 and determine the uncertainty of dose at these conditions in accordance with 6.4.1.

Determine the performance profile at these conditions in accordance with the manufacturer's specification.

Subject the same needle-free injectors to the hot atmosphere specified in 6.3.4 and determine the uncertainty of dose at these conditions in accordance with 6.4.1.

Determine the performance profile at these conditions in accordance with the manufacturer's specification.

Determine the claimed lifetime of the injector in compliant use before overhaul/refurbishment of parts.

Subject the same needle-free injectors above, to the standard atmosphere specified in 6.3.2.

NOTE 1 The manufacturer may decide to select a smaller $n$ for the lifetime testing than that chosen for the previous tests. However, a corresponding target $k$ would result from this different $n$.

Subject $n$ needle-free injectors tested above to the claimed lifetime testing (simulate manual use in accordance with the instructions for use) as follows:

a) remove the cap permanently if it has no influence on the safety of the needle-free injectors;

b) insert or fill the dose chamber;

c) prepare the needle-free injector for injection;

d) expel a dose of an amount which is anticipated to represent the worst case;

e) repeat b) to d) until 1,5 × the number of injection strokes of the claimed lifetime (in accordance with the manufacturers product file) is reached.

NOTE 2 Recommended user-maintenance tasks, e.g., lubrication or replacement of “o-rings” or other user-replaceable components, may be performed at their recommended intervals during the lifetime testing.

Visually inspect the needle-free injectors in accordance with 6.4.2. If the dose chamber is broken to the extent that it is obvious to the user, replace the dose chamber. If the dose chamber is non-replaceable and is broken to the extent that is obvious to the user, exclude the needle-free injector from further testing.

Determine the uncertainty of dose in accordance with 6.4.1.

Determine the performance profile in accordance with the manufacturer's specification.

### 6.2.3 Needle-free injectors subjected to dry heat storage atmosphere

Subject $n$ new needle-free injectors to the dry heat storage atmosphere specified in 6.3.5.

Visually inspect the needle-free injectors in accordance with 6.4.2. If the dose chamber is broken to an extent that is obvious to the user, replace the dose chamber. If the dose chamber is non-replaceable and is broken to an extent that is obvious to the user, exclude the needle-free injector from further testing.

Subject the remaining needle-free injectors to the standard atmosphere specified in 6.3.2.

Determine the uncertainty of dose in accordance with 6.4.1.

Determine the performance profile in accordance with the manufacturer's specification.

### 6.2.4 Needle-free injectors subjected to cold storage atmosphere

Subject $n$ new needle-free injectors to the cold storage atmosphere specified in 6.3.6.

Visually inspect the needle-free injectors in accordance with 6.4.2. If the dose chamber is broken to an extent that is obvious to the user, replace the dose chamber. If the dose chamber is non-replaceable and is broken to an extent that is obvious to the user, exclude the needle-free injector from further testing.

Subject the remaining needle-free injectors to the standard atmosphere specified in 6.3.2.

Determine the uncertainty of dose in accordance with 6.4.1.

Determine the performance profile in accordance with the manufacturer's specification.

### 6.2.5 Needle-free injectors subjected to a cyclical atmosphere

Subject $n$ new needle-free injectors to the cyclical atmosphere specified in 6.3.7.

Visually inspect the needle-free injectors in accordance with 6.4.2. If the dose chamber is broken to an extent that is obvious to the user, replace the dose chamber. If the dose chamber is non-replaceable and is broken to an extent that is obvious to the user, exclude the needle-free injector from further testing.

Subject the remaining needle-free injectors to the standard atmosphere specified in 6.3.2.

Determine the uncertainty of dose in accordance with 6.4.1.

Determine the performance profile in accordance with the manufacturer's specification.

### 6.2.6 Needle-free injectors subjected to free fall

#### 6.2.6.1 General

Unpack and prepare the needle-free injectors according to the instructions for use with a new dose chamber. When an injector is part of a larger system, only the injector shall be tested. Coupled holders (glass), containing medicinal products, can be removed.

The free fall test shall be performed using a free fall system as specified in IEC 60068-2-32.

The test surface shall be smooth, hard, rigid and made of steel of 3 mm thickness backed by wood of between 10 mm and 19 mm thickness.

#### 6.2.6.2 Needle-free injectors with replaceable dose chamber

Subject new needle-free injectors to the standard atmosphere specified in 6.3.2 and continue as described below.

Fill the dose chamber and put on the cap.

Drop each needle-free injector 3 times by free fall in accordance with the conditions specified in IEC 60721-3-7:2002 Class 7M3, from one of the following heights:

— 1 000 mm for needle-free injectors with a mass of less than 1 kg;

— 500 mm for needle-free injectors with a mass of more than 1 kg and less than 10 kg;

— 250 mm for needle-free injectors with a mass of more than 10 kg

on to the test surface, once horizontally and twice vertically, the needle-free injector being rotated 180° between the 2 vertical drops. The needle-free injector shall be dropped in a non-turbulent way.

If a dose chamber breaks such that it is obvious to the user, replace the dose chamber and continue until all 3 drops have been performed.

Visually inspect the needle-free injectors in accordance with 6.4.2. If the dose chamber is broken to an extent that is obvious to the user, replace the dose chamber.

Determine the uncertainty of dose in accordance with 6.4.1.

Determine the performance profile in accordance with the manufacturer's specification.

#### 6.2.6.3 Needle-free injectors with non-replaceable dose chamber

Subject new needle-free injectors to the standard atmosphere specified in 6.3.2 and continue as described below.

Fill the dose chamber and put on the cap.

Drop each needle-free injector 3 times by free fall in accordance with the conditions specified in IEC 60721-3-7:2002 Class 7M3, from one of the following heights:

— 1 000 mm for needle-free injectors with a mass less than 1 kg;

— 500 mm for needle-free injectors with a mass more than 1 kg and less than 10 kg;

— 250 mm for needle-free injectors with a mass more than 10 kg

on to the test surface, once horizontally and twice vertically, the needle-free injector being rotated 180° between the 2 vertical drops. The needle-free injector shall be dropped in a non-turbulent way.

Visually inspect the needle-free injectors in accordance with 6.4.2. If the dose chamber is broken to an extent that is obvious to the user, exclude the needle-free injector from further testing.

Determine the uncertainty of dose of $n$ needle-free injectors.

Determine the performance profile of $n$ needle-free injectors, in accordance with the manufacturer's specification.

### 6.2.7 Needle-free injectors subjected to vibration and shock

Place the needle-free injectors in a safety case or pouch for transport according to the instructions for use. When an injector is part of a larger system, the whole system shall be tested. Coupled holders (glass), containing medicinal products, can be removed. Commence the test as follows.

Subject the needle-free injectors to vibration in accordance with IEC 60068-2-64.

Subject the needle-free injectors to the conditions specified in IEC 60721-3-7:2002 Class 7M3, as follows:

— acceleration spectral mass density 3 $m^2/s^3$, frequency interval 10 Hz to 200 Hz;

— acceleration spectral mass density 1 $m^2/s^3$, frequency interval 200 Hz to 500 Hz;

— vibrate the injectors in a vertical direction and in two other directions perpendicular to one another in a horizontal plane.

The vibration time shall be 1 h.

NOTE 1 Needle-free injectors that cannot satisfy the requirements of vibration and shock testing described in this International Standard shall be subjected to such testing at the acceptable conditions, which shall be stated in the instructions for use.

NOTE 2 For clarification: The test described above is applicable to electrical and non-electrical devices (there are no other vibration standards available for non-electrical devices). IEC 60721-3-7 specifies requirements for portable devices. Class 7M3 is selected because its description of transportation of the device.

NOTE 3 IEC 60068-2-64 describes the test equipment for the vibration test.

Subject the needle-free injectors to the shock test in accordance with IEC 60068-2-27.

Subject the needle-free injectors to the conditions specified in IEC 60721-3-7:2002, Class 7M3, as follows:

— to a shock response spectrum Type I: 300 $m/s^2$;

— to a schock shock response spectrum Type II: 1 000 $m/s^2$.

The number of shocks shall be 50 positive and 50 negative.

For intensive transportation of equipment over heavy surfaces, the Type I shock test should be over a number of 100 shocks positive and 100 negative.

NOTE 4 For clarification: the test described above is applicable to electrical and non-electrical devices (there are no other shock standards available for non-electrical devices).

IEC 60721-3-7 specifies requirements for portable devices; Class 7M3 is selected because its description of transportation of the device; IEC 60068-2-27 describes the test equipment for the shock test; the shock response test Type I represents transport of the device in its packaging; the shock response test Type II represents the device in use (without packaging).

Visually inspect the needle-free injectors in accordance with 6.4.2.

— For needle-free injectors with replaceable dose chambers, if the dose chamber is broken to an extent that is obvious to the user, replace the dose chamber.

— For needle-free injectors with non-replaceable dose chambers, if the dose chamber is broken to an extent that is obvious to the user, exclude the needle-free injector from further testing.

Determine the uncertainty of dose in accordance with 6.4.1.

Determine the performance profile in accordance with the manufacturer's specification.

### 6.2.8 Needle-free injectors with electrical components subjected to electromagnetic compatibility (EMC) testing

Test the needle-free injectors for exposure to electrostatic discharge and radiated fields (RF) as follows.

Place $n$ needle-free injectors with the dose chambers on a metal reference plane as specified in IEC 61000-4-2:2001.

Apply contact discharges of ($\pm$ 2, $\pm$ 4 and $\pm$ 8) kV to conductive accessible parts and coupling planes.

Apply air discharges of ($\pm$ 8, $\pm$ 10, $\pm$ 12 and $\pm$ 15) kV to non-conductive accessible parts.

The number of discharges at each level and polarity shall be 10, with a time interval of 1 s between the individual discharges.

Test the same needle-free injectors in accordance with IEC 61000-4-3:2002 (TEM cells or GREM cells may be used as described in Annex D).

As stated in IEC 61000-4-3:2002, the requirement for field uniformity shall be fulfilled in the area corresponding to the unit under test.

Test the same needle-free injectors at the 10 V/m level (unmodulated carrier) in the frequency range of (26 to 2 000) MHz.

The test signal shall be AM modulated with 1 kHz sinusoidal and to a modulation depth of 80 %.

Perform the test in each of the three axes of the needle-free injector.

Visually inspect the needle-free injectors in accordance with 6.4.2. If the dose chamber is broken to an extent that is obvious to the user, replace the dose chamber.

Determine the uncertainty of dose in accordance with 6.4.1.

Determine the performance profile in accordance with the manufacturer's specification.

### 6.2.9 Noise testing

#### 6.2.9.1 Environment for testing noise

Any environment that meets the qualification requirements of ISO 3746:1995 Annex A may be used.

NOTE In practice this means a normally furnished room with a volume exceeding 30 $m^3$.

#### 6.2.9.2 Instrumentation

The instrumentation system, including the microphone and cable, shall meet the requirements of a type 1 or type 2 instrument specified in IEC 61672-1. When measuring high peak emission sound pressure levels the microphone and the entire instrumentation system shall have the capability of handling linear peak levels exceeding the C-weighted peak levels by at least 10 dB.

NOTE If ISO 11201 is used a type 1 instrument is required.

#### 6.2.9.3 Measurement procedure

The minimum requirement is to determine emission sound pressure levels at the specified positions around the needle-free injector in accordance with ISO 11202 and ISO 11204 which are the survey methods. In case of dispute the more accurate ISO 11201 shall be used.

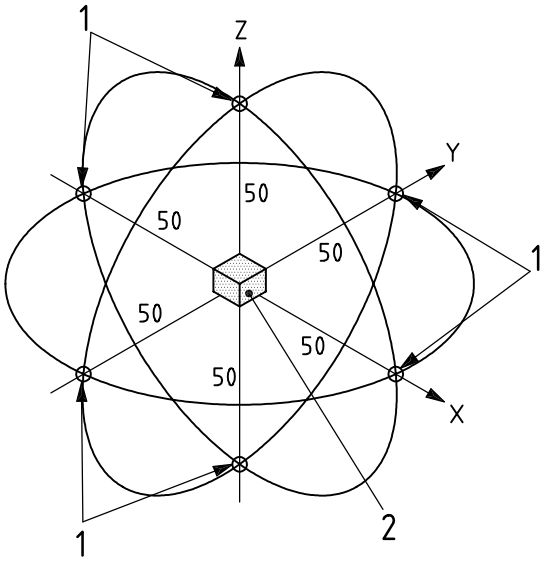
Use six microphone positions around the needle-free injector as shown in Figure 1. Place the main sound emitting part of the needle-free injector at the origin of the measuring coordinate system in its normal operating orientation in such a way that the main axis of the needle-free injector coincides with the axis of the measuring system. The device shall be tested with the injection head against a surface which imitates actual use as defined by the manufacturer.

Measure the peak sound pressure level, $L_{\text{pC peak}}$, and the single event sound pressure level, $L_{\text{pA, 1s}}$, for at least 3 impulses (event, cycles) in each position. Repeat the measurement procedure at each microphone position.

For $L_{\text{pC peak}}$ the highest value recorded at any of the microphone positions is the result.

For $L_{\text{pA, 1s}}$ the logarithmic mean average of the measured SEL-levels is the result.

Dimensions in centimetres




**Key**

1 microphone

2 needle-free injector

**Figure 1 — Microphone positions**

## 6.3 Test conditions

### 6.3.1 General

Unless otherwise specified, test measurements shall be performed at standard atmosphere conditions as specified in 6.3.2.

### 6.3.2 Standard atmosphere

A standard atmosphere shall be defined as:

— Temperature: from 18 °C to 28 °C;

— Relative humidity: from 25 % RH to 75 % RH;

after having been subjected to storage for at least 4 h in this atmosphere.

### 6.3.3 Cool atmosphere

The needle-free injectors are placed in a test chamber for at least 4 h in the following cool atmosphere:

— Temperature: 5 °C ± 3 °C.

### 6.3.4 Hot atmosphere

The needle-free injectors are placed in a test chamber for at least 4 h in the following hot atmosphere:

— Temperature: 40 °C ± 2 °C;

— Relative humidity: 50 % RH ± 10 % RH.

### 6.3.5 Dry heat storage atmosphere

The needle-free injectors are placed in a test chamber for at least 96 h in the following dry heat atmosphere:

— Temperature: 70 °C ± 2 °C;

— Relative humidity: 50 % RH ± 10 % RH.

### 6.3.6 Cold storage atmosphere

The needle-free injectors are placed in a test chamber for at least 96 h in the following cold atmosphere:

— Temperature: −40 °C ± 3 °C.

### 6.3.7 Cyclical atmosphere

The needle-free injectors are placed in a test chamber. Conditioning in accordance with IEC 60068-2-30 is carried out as follows:

— Variant 1 [see IEC 60068-2-30:1980, Figure 2 a)];

— Upper temperature: 55 °C ± 2 °C;

— 6 cycles.

NOTE The relevant clauses of IEC 60068-2-30:1980 are: Clause 3: Testing chamber, Clause 6: Conditioning and Clause 8: Recovery.

## 6.4 Test evaluations

### 6.4.1 Uncertainty of dose

#### 6.4.1.1 General

The substance to be tested for uncertainty of dose assessment shall be either the medicinal product intended to be used with the injector, or a representative substance of appropriate viscosity, mass density or other applicable properties. Devices not labelled to inject a specific medicinal product shall be tested across a representative range of substances described by the aforementioned physical properties.

Uncertainty of dose is determined by selecting and testing a number of needle-free injectors. The number of needle-free injectors depends upon the dose chamber and accuracy requirements for a given test. Assuming that the test results are normally distributed and that each measurement is independent, the following method enables accuracy result to be used as the basis for determining a statistical tolerance interval for 3 dose settings (the minimum, midpoint and maximum dose settings for a given needle-free injector), i.e. an interval such that there is a fixed probability (confidence level) that the interval will contain at least a proportion ($p$, probability content) of the true population from which the sample is taken. The statistical tolerance interval is two-sided, and the limits of the interval are called “statistical tolerance limits” or “natural limits of the process”.

To pass the requirement of uncertainty of dose, there shall be a 95 % confidence that at least $p$ of all doses delivered will fall between the proposed upper and lower specification limits for the 3 dose settings.

The two-sided statistical tolerance interval is calculated using the average ($\bar{x}$) plus or minus the standard deviation of the sample values, $s$, multiplied by a tolerance limit factor, $k$:

The two-sided statistical tolerance = $\bar{x} \pm (k \times s)$

The factor, $k$, is determined based upon the confidence level (95 %), probability content, $p$, and the number of measurements, $n$, taken for each of the 3 dose settings. ISO 3207:1975, Table 8, lists the tolerance limit factors for the construction of two-sided statistical tolerance intervals when the true population mean and standard deviation are not known. Annex A contains a more comprehensive two-sided tolerance limit for the 95 % confidence level.

#### 6.4.1.2 Accuracy assessment

If $V_{set} \leqslant$ TP, then:

USL = $V_{set}$ + 0,01 ml;

LSL = $V_{set}$ – 0,01 ml.

If $V_{set} >$ TP, then:

USL = $V_{set} + (5 \times V_{set})/100$;

LSL = $V_{set} - (5 \times V_{set})/100$.

A needle-free injector population satisfies the requirements when, for a given $V_{set}$, the following expressions are fulfilled:

$\bar{x} + (k \times s) \leqslant$ USL;

$\bar{x} - (k \times s) \geqslant$ LSL.

#### 6.4.1.3 Gravimetric conversion

All doses ($V_{set}$ or $G_{set}$) delivered are recorded gravimetrically ($G_{meas}$, expressed in grams). For solution-based systems, these recordings are converted to volumes ($V_{meas}$) by using the mass density ($\rho$, expressed in grams per millilitre) for the test fluid. The following equation can be used to convert gravimetric measurements to volumetric:

$$V_{meas} = G_{meas}/\rho$$

### 6.4.2 Visual inspection

Visually inspect the performance (e.g. stored data, settings, dose or indications) of each needle-free injector that has electronic components.

Markings on each needle-free injector (words, characters, numbers, symbols, quantity/volume scales, grid lines and index marks, among others) shall remain visible and easily legible by normal vision, or vision corrected to normal, at environmental lighting conditions of (215 $\pm$ 20) lux.

Inspect each needle-free injector for significant defects under normal, or corrected to normal vision. Defects in electronic parts leading to non-functioning are permitted if the non-functioning is obvious to the user.

The inspection should in particular include checking for significant defects such as:

— displaced parts;

— non-intact marking;

— cracks in the body and/or component of the needle-free injector;

— the fixation between the different parts of the body of the needle-free injector.

## 7 Test report

Each report of the testing performed in accordance with this International Standard shall at least include the following information:

a) a reference to this International Standard, i.e. ISO 21649:2006;

b) identification of the needle-free injector tested;

c) identification of the test system used;

d) identification of the test substance used;

e) the test results;

f) details of any deviation from this International Standard;

g) specification of test system;

h) the name and address of the test facility;

i) the date of the test;

j) indication of re-use of needle-free injectors for testing in accordance with 6.1.

# 8 Information supplied by the manufacturer

## 8.1 General

The needle-free injector shall be accompanied by sufficient information to use it safely, taking into account the training and knowledge of the potential users, and to identify the manufacturer.

Instructions for use shall be included in the unit container.

## 8.2 Marking

### 8.2.1 General

Any marking on the needle-free injector, which is essential for the safe use of the device, shall be visible, easily legible and indelible after being subjected to the test conditions specified in 6.3.7. Any marking on the unit container which is essential for the safe use of the needle-free injector shall be visible and legible. This shall be checked by visual inspection by normal, or corrected-to-normal, vision at environmental lighting condition of (215 ± 20) lx.

### 8.2.2 Marking on the needle-free injector

The marking on the needle-free injector shall at least comprise the following particulars:

a) name or trade name of the manufacturer;

NOTE A trademark or logo may be sufficient to identify the manufacturer.

b) details necessary for the user to identify the needle-free injector;

c) batch code, the lot number or the serial number preceded by an appropriate symbol.

### 8.2.3 Marking on the unit container

The marking on the unit container shall at least comprise the following particulars:

a) name and address of the manufacturer;

b) details necessary for the user to identify the needle-free injector;

c) content of the unit container;

d) information on the type of medicinal product(s) intended to be injected by means of the needle-free injector;

e) batch code, lot number or the serial number preceded by an appropriate symbol;

f) any special storage and/or handling conditions;

g) expiry date, if any (year and month expressed e.g. as YYYY-MM, e.g. 2004-12);

h) the dose specification limit, if different from that specified in 5.2.

## 8.3 Instructions for use

The instructions for use shall at least contain information on the following particulars:

a) the information required in 8.2.3 except that the information regarding expiry date, if any, lot number, batch code or serial number can be omitted;

b) any warnings and/or precautions to be taken; e.g. that the needle-free injector shall not be used for injections if it is obvious to the user that it does not function correctly, or that the device shall not be fired without its cartridge in place or without being loaded with medicinal product (dry firing), if this would result in damage or improper functioning of the device;

c) any risks associated with its normal use;

d) if the device shall be installed with or connected to other medical devices or equipment in order to operate as required for its intended purpose, sufficient details of its characteristics in order to identify the correct devices or equipment to use in order to obtain a safe combination;

e) information on the appropriate process to allow re-use of the needle-free injector, including dose chamber replacement, cleaning and disinfection;

f) details on any preparation needed before the needle-free injector can be used, e.g.:

   — the need to prime before each injection;

   — how to assemble/disassemble the product and replace the dose chamber;

g) description of the method of use, e.g. setting the dose, reading the scales, contact pressure, device orientation, contact angle with injection site, injection procedure as step-by-step operation;

h) the time to wait before removing the needle-free injector from the injection site;

i) the dose setting interval;

j) if acceptable storage temperatures are other than those specified in 6.3.5 and 6.3.6 (+70 °C and −40 °C), the acceptable temperature interval for storage of the needle-free injector without medicinal product;

k) any special storage requirements;

l) type of replaceable batteries and their number, if used;

m) description of special features;

n) whether the needle-free injector is designed so that it does not allow a larger dose to be set than left in the medicinal reservoir;

o) details allowing the medical staff to brief the user on any contra-indications and any precautions to be taken; these details shall in particular cover precautions to be taken in the event of breakage or changes in the performance of the needle-free injector;

p) If the sound pressure levels specified in 5.2 are exceeded, a warning shall be given that precautions shall be taken to avoid ear damage, e.g. that the device shall not be used close to the ear or that ear protection is required.

# Annex A
(informative)

# Two-sided tolerance limit factors ($k$)

**Table A.1 — Two-sided tolerance limit factors**

| Confidence = 95 % | | | | | | | |
|---|---|---|---|---|---|---|---|
| $n$ | $p$ = 0,750 | $p$ = 0,900 | $p$ = 0,950 | $p$ = 0,975 | $p$ = 0,990 | $p$ = 0,995 | $p$ = 0,999 |
| 2 | 22,383 | 31,092 | 36,519 | 41,308 | 46,944 | 50,813 | 58,844 |
| 3 | 5,937 | 8,306 | 9,789 | 11,101 | 12,647 | 13,710 | 15,920 |
| 4 | 3,818 | 5,368 | 6,341 | 7,203 | 8,221 | 8,921 | 10,377 |
| 5 | 3,041 | 4,291 | 5,077 | 5,774 | 6,598 | 7,165 | 8,345 |
| 6 | 2,638 | 3,733 | 4,422 | 5,034 | 5,758 | 6,256 | 7,294 |
| 7 | 2,391 | 3,390 | 4,020 | 4,579 | 5,241 | 5,697 | 6,647 |
| 8 | 2,223 | 3,156 | 3,746 | 4,269 | 4,889 | 5,316 | 6,206 |
| 9 | 2,101 | 2,986 | 3,546 | 4,044 | 4,633 | 5,039 | 5,885 |
| 10 | 2,008 | 2,856 | 3,393 | 3,871 | 4,437 | 4,827 | 5,640 |
| 11 | 1,934 | 2,754 | 3,273 | 3,735 | 4,282 | 4,659 | 5,446 |
| 12 | 1,874 | 2,670 | 3,175 | 3,624 | 4,156 | 4,522 | 5,287 |
| 13 | 1,825 | 2,601 | 3,093 | 3,531 | 4,051 | 4,409 | 5,156 |
| 14 | 1,783 | 2,542 | 3,024 | 3,453 | 3,962 | 4,312 | 5,044 |
| 15 | 1,747 | 2,492 | 2,965 | 3,386 | 3,885 | 4,230 | 4,949 |
| 16 | 1,716 | 2,449 | 2,913 | 3,328 | 3,819 | 4,158 | 4,865 |
| 17 | 1,689 | 2,410 | 2,868 | 3,277 | 3,761 | 4,095 | 4,792 |
| 18 | 1,665 | 2,376 | 2,828 | 3,231 | 3,709 | 4,039 | 4,727 |
| 19 | 1,643 | 2,346 | 2,793 | 3,191 | 3,663 | 3,988 | 4,669 |
| 20 | 1,624 | 2,319 | 2,760 | 3,154 | 3,621 | 3,943 | 4,616 |
| 21 | 1,607 | 2,294 | 2,731 | 3,121 | 3,583 | 3,903 | 4,569 |
| 22 | 1,591 | 2,272 | 2,705 | 3,091 | 3,549 | 3,865 | 4,526 |
| 23 | 1,576 | 2,251 | 2,681 | 3,063 | 3,518 | 3,831 | 4,486 |
| 24 | 1,563 | 2,232 | 2,658 | 3,038 | 3,489 | 3,800 | 4,450 |
| 25 | 1,551 | 2,215 | 2,638 | 3,015 | 3,462 | 3,771 | 4,415 |
| 26 | 1,539 | 2,199 | 2,619 | 2,993 | 3,437 | 3,744 | 4,385 |
| 27 | 1,529 | 2,184 | 2,601 | 2,973 | 3,415 | 3,720 | 4,356 |
| 28 | 1,519 | 2,170 | 2,585 | 2,954 | 3,393 | 3,696 | 4,330 |
| 29 | 1,510 | 2,157 | 2,569 | 2,937 | 3,373 | 3,675 | 4,304 |
| 30 | 1,501 | 2,145 | 2,555 | 2,921 | 3,355 | 3,654 | 4,281 |
| 31 | 1,493 | 2,134 | 2,541 | 2,905 | 3,337 | 3,635 | 4,259 |
| 32 | 1,486 | 2,123 | 2,529 | 2,891 | 3,320 | 3,617 | 4,238 |
| 33 | 1,478 | 2,113 | 2,517 | 2,877 | 3,305 | 3,600 | 4,218 |
| 34 | 1,472 | 2,103 | 2,505 | 2,864 | 3,290 | 3,584 | 4,199 |
| 35 | 1,465 | 2,094 | 2,495 | 2,852 | 3,276 | 3,569 | 4,182 |

**Table A.1** *(continued)*

| Confidence = 95 % | | | | | | | |
|---|---|---|---|---|---|---|---|
| $n$ | $p$ = 0,750 | $p$ = 0,900 | $p$ = 0,950 | $p$ = 0,975 | $p$ = 0,990 | $p$ = 0,995 | $p$ = 0,999 |
| 36 | 1,459 | 2,086 | 2,484 | 2,840 | 3,263 | 3,555 | 4,165 |
| 37 | 1,454 | 2,077 | 2,475 | 2,829 | 3,250 | 3,541 | 4,149 |
| 38 | 1,448 | 2,070 | 2,466 | 2,819 | 3,238 | 3,528 | 4,134 |
| 39 | 1,443 | 2,062 | 2,457 | 2,809 | 3,227 | 3,516 | 4,119 |
| 40 | 1,438 | 2,055 | 2,448 | 2,799 | 3,216 | 3,504 | 4,105 |
| 41 | 1,433 | 2,049 | 2,440 | 2,790 | 3,205 | 3,492 | 4,092 |
| 42 | 1,429 | 2,042 | 2,433 | 2,781 | 3,196 | 3,482 | 4,080 |
| 43 | 1,424 | 2,036 | 2,425 | 2,773 | 3,186 | 3,471 | 4,068 |
| 44 | 1,420 | 2,030 | 2,418 | 2,765 | 3,177 | 3,461 | 4,056 |
| 45 | 1,416 | 2,024 | 2,412 | 2,757 | 3,168 | 3,452 | 4,045 |
| 46 | 1,412 | 2,019 | 2,405 | 2,750 | 3,160 | 3,443 | 4,034 |
| 47 | 1,409 | 2,014 | 2,399 | 2,743 | 3,151 | 3,434 | 4,024 |
| 48 | 1,405 | 2,009 | 2,393 | 2,736 | 3,144 | 3,425 | 4,014 |
| 49 | 1,402 | 2,004 | 2,387 | 2,729 | 3,136 | 3,417 | 4,004 |
| 50 | 1,398 | 1,999 | 2,382 | 2,723 | 3,129 | 3,409 | 3,995 |
| 51 | 1,395 | 1,994 | 2,376 | 2,717 | 3,122 | 3,401 | 3,986 |
| 52 | 1,392 | 1,990 | 2,371 | 2,711 | 3,115 | 3,394 | 3,978 |
| 53 | 1,389 | 1,986 | 2,366 | 2,705 | 3,108 | 3,387 | 3,969 |
| 54 | 1,386 | 1,982 | 2,361 | 2,700 | 3,102 | 3,380 | 3,961 |
| 55 | 1,383 | 1,978 | 2,356 | 2,694 | 3,096 | 3,373 | 3,953 |
| 56 | 1,381 | 1,974 | 2,352 | 2,689 | 3,090 | 3,367 | 3,946 |
| 57 | 1,378 | 1,970 | 2,347 | 2,684 | 3,084 | 3,361 | 3,939 |
| 58 | 1,376 | 1,967 | 2,343 | 2,679 | 3,079 | 3,355 | 3,932 |
| 59 | 1,373 | 1,963 | 2,339 | 2,675 | 3,073 | 3,349 | 3,925 |
| 60 | 1,371 | 1,960 | 2,335 | 2,670 | 3,068 | 3,343 | 3,918 |
| 61 | 1,369 | 1,957 | 2,331 | 2,666 | 3,063 | 3,338 | 3,912 |
| 62 | 1,366 | 1,953 | 2,327 | 2,661 | 3,058 | 3,332 | 3,905 |
| 63 | 1,364 | 1,950 | 2,324 | 2,657 | 3,053 | 3,327 | 3,899 |
| 64 | 1,362 | 1,947 | 2,320 | 2,653 | 3,048 | 3,322 | 3,893 |
| 65 | 1,360 | 1,944 | 2,317 | 2,649 | 3,044 | 3,317 | 3,887 |
| 66 | 1,358 | 1,941 | 2,313 | 2,645 | 3,039 | 3,312 | 3,882 |
| 67 | 1,356 | 1,939 | 2,310 | 2,641 | 3,035 | 3,307 | 3,876 |
| 68 | 1,354 | 1,936 | 2,307 | 2,638 | 3,031 | 3,303 | 3,871 |
| 69 | 1,352 | 1,933 | 2,304 | 2,634 | 3,027 | 3,298 | 3,866 |
| 70 | 1,350 | 1,931 | 2,300 | 2,631 | 3,023 | 3,294 | 3,861 |
| 71 | 1,349 | 1,928 | 2,297 | 2,627 | 3,019 | 3,290 | 3,856 |
| 72 | 1,347 | 1,926 | 2,295 | 2,624 | 3,015 | 3,285 | 3,851 |
| 73 | 1,345 | 1,923 | 2,292 | 2,621 | 3,011 | 3,281 | 3,846 |
| 74 | 1,344 | 1,921 | 2,289 | 2,617 | 3,008 | 3,277 | 3,841 |
| 75 | 1,342 | 1,919 | 2,286 | 2,614 | 3,004 | 3,274 | 3,837 |
| 76 | 1,341 | 1,917 | 2,284 | 2,611 | 3,001 | 3,270 | 3,832 |
| 77 | 1,339 | 1,914 | 2,281 | 2,608 | 2,997 | 3,266 | 3,828 |
| 78 | 1,337 | 1,912 | 2,278 | 2,605 | 2,994 | 3,262 | 3,824 |
| 79 | 1,336 | 1,910 | 2,276 | 2,603 | 2,991 | 3,259 | 3,820 |

**Table A.1** *(continued)*

| Confidence = 95 % | | | | | | | |
|---|---|---|---|---|---|---|---|
| $n$ | $p$ = 0,750 | $p$ = 0,900 | $p$ = 0,950 | $p$ = 0,975 | $p$ = 0,990 | $p$ = 0,995 | $p$ = 0,999 |
| 80 | 1,335 | 1,908 | 2,274 | 2,600 | 2,988 | 3,255 | 3,816 |
| 81 | 1,333 | 1,906 | 2,271 | 2,597 | 2,984 | 3,252 | 3,812 |
| 82 | 1,332 | 1,904 | 2,269 | 2,594 | 2,981 | 3,249 | 3,808 |
| 83 | 1,330 | 1,902 | 2,267 | 2,592 | 2,978 | 3,246 | 3,804 |
| 84 | 1,329 | 1,900 | 2,264 | 2,589 | 2,975 | 3,242 | 3,800 |
| 85 | 1,328 | 1,899 | 2,262 | 2,587 | 2,973 | 3,239 | 3,797 |
| 86 | 1,327 | 1,897 | 2,260 | 2,584 | 2,970 | 3,236 | 3,793 |
| 87 | 1,325 | 1,895 | 2,258 | 2,582 | 2,967 | 3,233 | 3,790 |
| 88 | 1,324 | 1,893 | 2,256 | 2,580 | 2,964 | 3,230 | 3,786 |
| 89 | 1,323 | 1,892 | 2,254 | 2,577 | 2,962 | 3,227 | 3,783 |
| 90 | 1,322 | 1,890 | 2,252 | 2,575 | 2,959 | 3,225 | 3,780 |
| 91 | 1,321 | 1,888 | 2,250 | 2,573 | 2,957 | 3,222 | 3,776 |
| 92 | 1,320 | 1,887 | 2,248 | 2,571 | 2,954 | 3,219 | 3,773 |
| 93 | 1,318 | 1,885 | 2,246 | 2,569 | 2,952 | 3,216 | 3,770 |
| 94 | 1,317 | 1,884 | 2,244 | 2,566 | 2,949 | 3,214 | 3,767 |
| 95 | 1,316 | 1,882 | 2,242 | 2,564 | 2,947 | 3,211 | 3,764 |
| 96 | 1,315 | 1,881 | 2,241 | 2,562 | 2,944 | 3,209 | 3,761 |
| 97 | 1,314 | 1,879 | 2,239 | 2,560 | 2,942 | 3,206 | 3,758 |
| 98 | 1,313 | 1,878 | 2,237 | 2,558 | 2,940 | 3,204 | 3,755 |
| 99 | 1,312 | 1,876 | 2,236 | 2,556 | 2,938 | 3,201 | 3,752 |
| 100 | 1,311 | 1,875 | 2,234 | 2,555 | 2,936 | 3,199 | 3,750 |
| 102 | 1,309 | 1,872 | 2,231 | 2,551 | 2,931 | 3,194 | 3,744 |
| 104 | 1,308 | 1,869 | 2,228 | 2,547 | 2,927 | 3,190 | 3,739 |
| 106 | 1,306 | 1,867 | 2,225 | 2,544 | 2,923 | 3,186 | 3,734 |
| 108 | 1,304 | 1,864 | 2,222 | 2,541 | 2,919 | 3,181 | 3,729 |
| 110 | 1,302 | 1,862 | 2,219 | 2,537 | 2,916 | 3,177 | 3,724 |
| 112 | 1,301 | 1,860 | 2,216 | 2,534 | 2,912 | 3,173 | 3,720 |
| 114 | 1,299 | 1,858 | 2,213 | 2,531 | 2,909 | 3,170 | 3,715 |
| 116 | 1,298 | 1,855 | 2,211 | 2,528 | 2,905 | 3,166 | 3,711 |
| 118 | 1,296 | 1,853 | 2,208 | 2,525 | 2,902 | 3,162 | 3,707 |
| 120 | 1,295 | 1,851 | 2,206 | 2,522 | 2,899 | 3,159 | 3,703 |
| 122 | 1,293 | 1,849 | 2,203 | 2,520 | 2,896 | 3,155 | 3,699 |
| 124 | 1,292 | 1,847 | 2,201 | 2,517 | 2,893 | 3,152 | 3,695 |
| 126 | 1,291 | 1,845 | 2,199 | 2,514 | 2,890 | 3,149 | 3,691 |
| 128 | 1,289 | 1,843 | 2,197 | 2,512 | 2,887 | 3,146 | 3,687 |
| 130 | 1,288 | 1,842 | 2,194 | 2,510 | 2,884 | 3,143 | 3,684 |
| 132 | 1,287 | 1,840 | 2,192 | 2,507 | 2,881 | 3,140 | 3,680 |
| 134 | 1,286 | 1,838 | 2,190 | 2,505 | 2,878 | 3,137 | 3,677 |
| 136 | 1,284 | 1,837 | 2,188 | 2,503 | 2,876 | 3,134 | 3,674 |
| 138 | 1,283 | 1,835 | 2,186 | 2,500 | 2,873 | 3,131 | 3,670 |
| 140 | 1,282 | 1,833 | 2,185 | 2,498 | 2,871 | 3,128 | 3,667 |
| 142 | 1,281 | 1,832 | 2,183 | 2,496 | 2,868 | 3,126 | 3,664 |
| 144 | 1,280 | 1,830 | 2,181 | 2,494 | 2,866 | 3,123 | 3,661 |
| 146 | 1,279 | 1,829 | 2,179 | 2,492 | 2,864 | 3,121 | 3,658 |
| 148 | 1,278 | 1,827 | 2,177 | 2,490 | 2,861 | 3,118 | 3,655 |

**Table A.1** *(continued)*

| Confidence = 95 % | | | | | | | |
|---|---|---|---|---|---|---|---|
| $n$ | $p$ = 0,750 | $p$ = 0,900 | $p$ = 0,950 | $p$ = 0,975 | $p$ = 0,990 | $p$ = 0,995 | $p$ = 0,999 |
| 150 | 1,277 | 1,826 | 2,176 | 2,488 | 2,859 | 3,116 | 3,652 |
| 152 | 1,276 | 1,825 | 2,174 | 2,486 | 2,857 | 3,114 | 3,650 |
| 154 | 1,275 | 1,823 | 2,172 | 2,484 | 2,855 | 3,111 | 3,647 |
| 156 | 1,274 | 1,822 | 2,171 | 2,483 | 2,853 | 3,109 | 3,644 |
| 158 | 1,273 | 1,821 | 2,169 | 2,481 | 2,851 | 3,107 | 3,642 |
| 160 | 1,272 | 1,819 | 2,168 | 2,479 | 2,849 | 3,105 | 3,639 |
| 162 | 1,272 | 1,818 | 2,166 | 2,477 | 2,847 | 3,102 | 3,637 |
| 164 | 1,271 | 1,817 | 2,165 | 2,476 | 2,845 | 3,100 | 3,634 |
| 166 | 1,270 | 1,816 | 2,163 | 2,474 | 2,843 | 3,098 | 3,632 |
| 168 | 1,269 | 1,815 | 2,162 | 2,473 | 2,841 | 3,096 | 3,630 |
| 170 | 1,268 | 1,813 | 2,161 | 2,471 | 2,840 | 3,094 | 3,627 |
| 172 | 1,267 | 1,812 | 2,159 | 2,469 | 2,838 | 3,092 | 3,625 |
| 174 | 1,267 | 1,811 | 2,158 | 2,468 | 2,836 | 3,091 | 3,623 |
| 176 | 1,266 | 1,810 | 2,157 | 2,466 | 2,834 | 3,089 | 3,621 |
| 178 | 1,265 | 1,809 | 2,155 | 2,465 | 2,833 | 3,087 | 3,619 |
| 180 | 1,264 | 1,808 | 2,154 | 2,464 | 2,831 | 3,085 | 3,616 |
| 185 | 1,263 | 1,805 | 2,151 | 2,460 | 2,827 | 3,081 | 3,611 |
| 190 | 1,261 | 1,803 | 2,148 | 2,457 | 2,823 | 3,077 | 3,607 |
| 195 | 1,259 | 1,801 | 2,146 | 2,454 | 2,820 | 3,073 | 3,602 |
| 200 | 1,258 | 1,798 | 2,143 | 2,451 | 2,816 | 3,069 | 3,598 |
| 205 | 1,256 | 1,796 | 2,140 | 2,448 | 2,813 | 3,065 | 3,593 |
| 210 | 1,255 | 1,794 | 2,138 | 2,445 | 2,810 | 3,062 | 3,589 |
| 215 | 1,253 | 1,792 | 2,136 | 2,442 | 2,807 | 3,059 | 3,585 |
| 220 | 1,252 | 1,790 | 2,133 | 2,440 | 2,804 | 3,055 | 3,581 |
| 225 | 1,251 | 1,789 | 2,131 | 2,437 | 2,801 | 3,052 | 3,576 |
| 230 | 1,250 | 1,787 | 2,129 | 2,435 | 2,798 | 3,049 | 3,574 |
| 235 | 1,248 | 1,785 | 2,127 | 2,432 | 2,795 | 3,046 | 3,571 |
| 240 | 1,247 | 1,783 | 2,125 | 2,430 | 2,793 | 3,043 | 3,568 |
| 245 | 1,246 | 1,782 | 2,123 | 2,428 | 2,790 | 3,041 | 3,564 |
| 250 | 1,245 | 1,780 | 2,121 | 2,426 | 2,788 | 3,038 | 3,561 |
| 255 | 1,244 | 1,779 | 2,120 | 2,424 | 2,786 | 3,036 | 3,558 |
| 260 | 1,243 | 1,777 | 2,118 | 2,422 | 2,783 | 3,033 | 3,555 |
| 265 | 1,242 | 1,776 | 2,116 | 2,420 | 2,781 | 3,031 | 3,553 |
| 270 | 1,241 | 1,775 | 2,115 | 2,418 | 2,779 | 3,028 | 3,550 |
| 275 | 1,240 | 1,773 | 2,113 | 2,416 | 2,777 | 3,026 | 3,547 |
| 280 | 1,239 | 1,772 | 2,111 | 2,415 | 2,775 | 3,024 | 3,545 |
| 285 | 1,238 | 1,771 | 2,110 | 2,413 | 2,773 | 3,022 | 3,542 |
| 290 | 1,238 | 1,770 | 2,109 | 2,411 | 2,771 | 3,020 | 3,540 |
| 295 | 1,237 | 1,768 | 2,107 | 2,410 | 2,769 | 3,018 | 3,538 |
| 300 | 1,236 | 1,767 | 2,106 | 2,408 | 2,767 | 3,016 | 3,535 |
| 310 | 1,234 | 1,765 | 2,103 | 2,405 | 2,764 | 3,012 | 3,531 |
| 320 | 1,233 | 1,763 | 2,101 | 2,402 | 2,761 | 3,008 | 3,527 |
| 330 | 1,232 | 1,761 | 2,098 | 2,400 | 2,758 | 3,005 | 3,523 |
| 340 | 1,230 | 1,759 | 2,096 | 2,397 | 2,755 | 3,002 | 3,519 |

**Table A.1** *(continued)*

| Confidence = 95 % | | | | | | | |
|---|---|---|---|---|---|---|---|
| $n$ | $p$ = 0,750 | $p$ = 0,900 | $p$ = 0,950 | $p$ = 0,975 | $p$ = 0,990 | $p$ = 0,995 | $p$ = 0,999 |
| 350 | 1,229 | 1,757 | 2,094 | 2,395 | 2,752 | 2,999 | 3,515 |
| 360 | 1,228 | 1,756 | 2,092 | 2,392 | 2,749 | 2,996 | 3,512 |
| 370 | 1,227 | 1,754 | 2,090 | 2,390 | 2,747 | 2,993 | 3,509 |
| 380 | 1,225 | 1,752 | 2,088 | 2,388 | 2,744 | 2,990 | 3,505 |
| 390 | 1,224 | 1,751 | 2,086 | 2,386 | 2,742 | 2,988 | 3,502 |
| 400 | 1,223 | 1,749 | 2,084 | 2,384 | 2,739 | 2,985 | 3,499 |
| 425 | 1,221 | 1,746 | 2,080 | 2,379 | 2,734 | 2,979 | 3,493 |
| 450 | 1,219 | 1,743 | 2,077 | 2,375 | 2,729 | 2,974 | 3,486 |
| 475 | 1,217 | 1,740 | 2,073 | 2,371 | 2,725 | 2,969 | 3,481 |
| 500 | 1,215 | 1,737 | 2,070 | 2,368 | 2,721 | 2,965 | 3,476 |
| 525 | 1,213 | 1,735 | 2,067 | 2,364 | 2,717 | 2,961 | 3,471 |
| 550 | 1,212 | 1,733 | 2,065 | 2,361 | 2,713 | 2,957 | 3,466 |
| 575 | 1,210 | 1,731 | 2,062 | 2,358 | 2,710 | 2,953 | 3,462 |
| 600 | 1,209 | 1,729 | 2,060 | 2,356 | 2,707 | 2,950 | 3,458 |
| 625 | 1,208 | 1,727 | 2,058 | 2,353 | 2,704 | 2,947 | 3,455 |
| 650 | 1,207 | 1,725 | 2,056 | 2,351 | 2,702 | 2,944 | 3,451 |
| 700 | 1,204 | 1,722 | 2,052 | 2,347 | 2,697 | 2,939 | 3,445 |
| 750 | 1,202 | 1,719 | 2,049 | 2,343 | 2,692 | 2,934 | 3,439 |
| 800 | 1,201 | 1,717 | 2,046 | 2,339 | 2,688 | 2,930 | 3,434 |
| 850 | 1,199 | 1,715 | 2,043 | 2,336 | 2,685 | 2,926 | 3,430 |
| 900 | 1,198 | 1,712 | 2,040 | 2,333 | 2,682 | 2,922 | 3,426 |
| 950 | 1,196 | 1,711 | 2,038 | 2,331 | 2,679 | 2,919 | 3,422 |
| 1000 | 1,195 | 1,709 | 2,036 | 2,328 | 2,676 | 2,916 | 3,418 |
| 1500 | 1,186 | 1,697 | 2,022 | 2,312 | 2,657 | 2,895 | 3,394 |
| ∞ | 1,150 | 1,645 | 1,960 | 2,241 | 2,576 | 2,807 | 3,291 |

# Annex B
(informative)

# Examples of accuracy limit calculations and random settings

## B.1 Example of accuracy limit calculation

In the following, an example of calculation (volumes expressed in millilitres) is given.

If $V_{set}$:

$V_{min}$ = 0,02 ml;

$V_{mid}$ = 0,16 ml;

$V_{max}$ = 0,30 ml;

and: TP = 0,2 ml

then:

for $V_{min} \leqslant$ TP USL = (0,02 + 0,01) ml = 0,030 ml;

LSL = (0,02 − 0,01) ml = 0,010 ml;

for $V_{mid} \leqslant$ TP USL = (0,16 + 0,01) ml = 0,170 ml;

LSL = (0,16 − 0,01) ml = 0,150 ml;

for $V_{max} >$ TP USL = 0,30 ml + (5 × 0,30 ml)/100 = 0,315 ml;

LSL = 0,30 ml − (5 × 0,30 ml)/100 = 0,285 ml.

## B.2 Random settings

For a given test, uncertainty of dose is evaluated by delivering and measuring $V_{set}$ in combinations of injection cycles or replicates (random sequences of the 3 preset doses, $V_{set}$). A random sequence of 3 preset doses can occur in six possible ways ($R_1$, $R_2$, $R_3$, $R_4$, $R_5$ and $R_6$):

$R_1$: $V_{min}$, $V_{mid}$, $V_{max}$;

$R_2$: $V_{min}$, $V_{max}$, $V_{mid}$;

$R_3$: $V_{mid}$, $V_{min}$, $V_{max}$;

$R_4$: $V_{mid}$, $V_{max}$, $V_{min}$;

$R_5$: $V_{max}$, $V_{min}$, $V_{mid}$;

$R_6$: $V_{max}$, $V_{mid}$, $V_{min}$.

# Annex C
(informative)

## Correspondence between ISO/IEC standards and EN standards

| ISO/IEC | EN | Title |
|---|---|---|
| ISO 10993-1:2003 | EN ISO 10993-1:2003 | Biological evaluation of medical devices — Part 1: Evaluation and testing |
| ISO 11201:1995 | EN ISO 11201:1995 | Acoustics — Noise emitted by machinery and equipment — Measurement of emission sound pressure levels at a work station and at other specified positions — Engineering method in an essentially free field over a reflecting plane |
| ISO 11202:1995 | EN ISO 11202:1995 | Acoustics — Noise emitted by machinery and equipment — Measurement of emission sound pressure levels at a work station and at other specified positions — Survey method *in situ* |
| ISO 11204:1995 | EN ISO 11204:1995 | Acoustics — Noise emitted by machinery and equipment — Measurement of emission sound pressure levels at a work station and at other specified positions — Method requiring environmental corrections |
| ISO 14155-1:2003 | EN ISO 14155-1:2003 | Clinical investigation of medical devices for human subjects — Part 1: General requirements |
| ISO 14155-2:2003 | EN ISO 14155-2:2003 | Clinical investigation of medical devices for human subjects — Part 2: Clinical investigation plans |
| ISO 14253-1:1998 | EN ISO 14253-1:1998 | Geometrical Product Specifications (GPS) — Inspection by measurement of workpieces and measuring equipment — Part 1: Decision rules for proving conformance or non-conformance with specifications |
| IEC 60068-2-27:1987 | EN 60068-2-27:1993 | Environmental testing. Part 2: Tests. Test Ea and guidance: Shock |
| IEC 60068-2-30:2005 | EN 60068-2-30:1999 (based on IEC 1980 document) | Environmental testing — Part 2-30: Tests — Test Db: Damp heat, cyclic (12 h + 12 h cycle) |
| IEC 60068-2-32:1975 | EN 60068-2-32:1993 | Basic environmental testing procedures — Part 2: Tests — Test Ed: Free fall |
| IEC 60068-2-64:1993 | EN 60068-2-64:1994 | Environmental testing — Part 2: Test methods — Test Fh: Vibration, broad-band random (digital control) and guidance |
| IEC 60721-3-7:2002 | EN 60721-3-7:1995 | Classification of environmental conditions — Part 3-7: Classification of groups of environmental parameters and their severities — Portable and non-stationary use |
| IEC 61000-4-2:2001 | EN 61000-4-2:2001 | Electromagnetic compatibility (EMC) — Part 4-2: Testing and measurement techniques — Electrostatic discharge immunity test |
| IEC 61000-4-3:2002 | EN 61000-4-3:2002 | Electromagnetic compatibility (EMC) — Part 4-3: Testing and measurement techniques — Radiated, radio-frequency, electromagnetic field immunity test |
| IEC 61672-1:2002 | EN 61672-1:2003 | Electroacoustics - Sound level meters — Part 1: Specifications |

# Annex ZA
(informative)

# Relationship between this International Standard and the Essential Requirements of EU Directive 93/42/EEC

By agreement between ISO and CEN, this CEN annex is included in the DIS and the FDIS but will not appear in the published ISO standard.

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

Once this standard is cited in the Official Journal of the European Communities under that Directive and has been implemented as a national standard in at least one Member State, compliance with the normative 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 International Standard and Directive 93/42/EEC**

| Clause(s)/sub-clause(s) of this International Standard | Essential requirements (ERs) of Directive 94/42/EEC | Qualifying remarks/Notes |
|---|---|---|
| 5.1 | 7.1, 8.1, 8.3, 8.4, 12.7.3, 12.8.1, 12.8.2 | |
| 5.3 | 12.8 | |
| 5.4 | 10, 12.8, 12.9 | |
| 5.5 | 1, 2, 3, 4, 6 | |
| 5.6.1 | 4, 9.2, 10.1, 12.8.1 | |
| 5.6.2 | 5 | |
| 5.6.3 | 5 | |
| 5.6.4 | 5 | |
| 5.6.5 | 4, 12.7.1 | |
| 5.6.6 | 4, 12.7.1, 12.7.2 | |
| 5.6.7 | 9.2, 12.5 | |
| 6.1, 6.2 | 1, 3, 4, 5 | General conditions for performing tests |
| 6.2.2 | 4, 9.2 | |
| 6.2.3 | 5 | |
| 6.2.4 | 5 | |
| 6.2.5 | 5 | |
| 6.2.6 | 4, 9.1, 12.7.1 | |
| 6.2.7 | 4, 9.2, 12.7.1 | |
| 6.2.8 | 9.2 | |
| 6.3 | 4, 5 | |
| 6.4.1 | 3, 4, 12.8 | |

| Clause(s)/sub-clause(s) of this International Standard | Essential requirements (ERs) of Directive 94/42/EEC | Qualifying remarks/Notes |
|---|---|---|
| 6.4.2 | 3, 4, 5, 10.2, 12.9, 13.1, 13.2 | |
| 7 | All applicable ERs | Report on tests |
| 8.1 | 13.1 | |
| 8.2 | 13.1, 13.3, 13.4, 13.5 | |
| 8.3 | 13.6 | |

**WARNING — Other requirements and other EU Directives may be applicable to the products falling within the scope of this International Standard.**

# Bibliography

[1] ISO 7886-1:1993, *Sterile hypodermic syringes for single use — Part 1: Syringes for manual use*

[2] ISO 9000:2005, *Quality management systems — Fundamentals and vocabulary*

[3] ISO 11134:1994, *Sterilization of health care products — Requirements for validation and routine control — Industrial moist heat sterilization*

[4] ISO 11135:1994, *Medical devices — Validation and routine control of ethylene oxide sterilization*

[5] ISO 11137:1995, *Sterilization of health care products — Requirements for validation and routine control — Radiation sterilization*

[6] ISO 13485:2003, *Medical devices — Quality management systems — Requirements for regulatory purposes*

[7] ISO 15223:2000, *Medical devices — Symbols to be used with medical device labels, labeling and information to be supplied*

[8] IEC 60601-1-2:2001, *Medical electrical equipment — Part 1-2: General requirements for safety — Collateral standard: Electromagnetic compatibility — Requirements and tests*

[9] IEC 61000-4-1:2000, *Electromagnetic compatibility (EMC) — Part 4-1: Testing and measurement techniques — Overview of IEC 61000-4 series*

[10] IEC 61000-4-2:1999, *Electromagnetic compatibility (EMC) — Part 4-2: Testing and measurement techniques — Electrostatic discharge immunity test*

[11] IEC 61000-4-3:1998, *Electromagnetic compatibility (EMC) — Part 4-3: Testing and measurement techniques — Radiated, radio-frequency, electromagnetic field immunity test*

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