INTERNATIONAL STANDARD

ISO 22413

Second edition
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Transfer sets for pharmaceutical preparations — Requirements and test methods

Ensemble de transfert pour préparations pharmaceutiques — 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 22413 was prepared by Technical Committee ISO/TC 76, *Transfusion, infusion and injection equipment for medical and pharmaceutical use*.

This second edition cancels and replaces the first edition (ISO 22413:2007), of which the scope was enhanced by introducing further product groups like transfer sets with integrated Luer connectors and particle filters. In that framework the following major changes were introduced:

— the Introduction was amended by h) and j);

— the Normative references were updated;

— the Figures in 3.1 were updated;

— 5.11 and 8.10 on the physical requirements and testing for Luer connector were added;

— 5.12 and 8.11 on the physical requirements and testing for filter for particles were added.

Introduction

Transfer sets for pharmaceutical preparations transmit fluids from one container to another. The transfer sets mix fluids or dissolve dry substances and are used in combination with infusion and injection containers.

The transfer sets consist either of two piercing devices or of a piercing device in combination with a Luer connector, which may be connected with each other in different ways. Transfer sets may have a housing.

Examples of different designs:

a) two piercing devices connected to each other (similar to piercing devices of infusion containers);

b) a metal cannula, bevelled on both sides or a combination of a) and b);

c) metal cannulae mostly having a hub or a grip plate in the middle to be fixed to the plastic part;

d) plastic piercing devices directly connected to a grip plate, or held by a tube at a distance to allow a higher hydrostatic pressure;

e) piercing devices with an additional ventilation channel that may end in the other tip or outside;

f) piercing devices also with an air filter;

g) piercing devices with housings serving, among other things, as a guide and a fixation on the connected containers for a secure, injury-free and contactless application;

h) piercing device in combination with a Luer connector;

i) piercing device in combination with a Luer connector and a particle filter.

Transfer sets for pharmaceutical preparations — Requirements and test methods

1 Scope

This International Standard applies to sterilized single use transfer sets that are used for pharmaceutical preparations.

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 594-1, *Conical fittings with a 6 % (Luer) taper for syringes, needles and certain other medical equipment — Part 1: General requirements*

ISO 594-2, *Conical fittings with 6 % (Luer) taper for syringes, needles and certain other medical equipment — Part 2: Lock fittings*

ISO 7864:1993, *Sterile hypodermic needles for single use*

ISO 8362 (all parts), *Injection containers and accessories*

ISO 8536 (all parts), *Infusion equipment for medical use*

ISO 15223-1, *Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied — Part 1: General requirements*

ISO 15747, *Plastic containers for intravenous injections*

ISO 15759, *Medical infusion equipment — Plastics caps with inserted elastomeric liner for containers manufactured by the blow-fill-seal (BFS) process*

3 Design and designation

3.1 Design

The designs of the individual components are given in Figures 1 to 7. The drawings serve as an illustration of possible transfer sets. Other designs are acceptable.

The Key for Figures 1 to 7 is to be found on page 3.

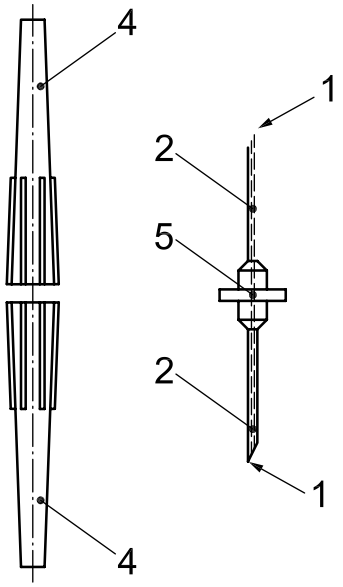


Figure 1 — Transfer set with one channel

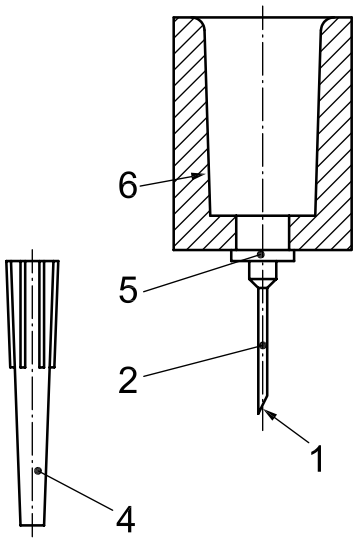


Figure 2 — Transfer set with one channel in combination with a Luer connector

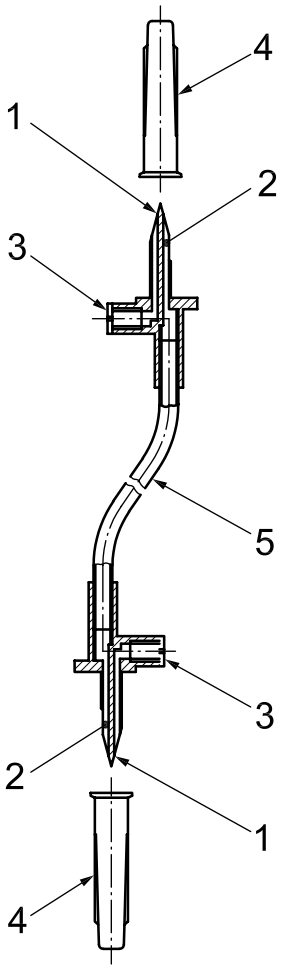


Figure 3 — Transfer set with an air inlet/air outlet

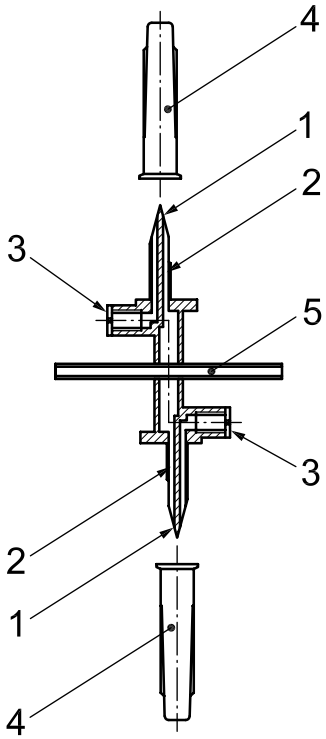


Figure 4 — Alternative transfer set with an air inlet/air outlet

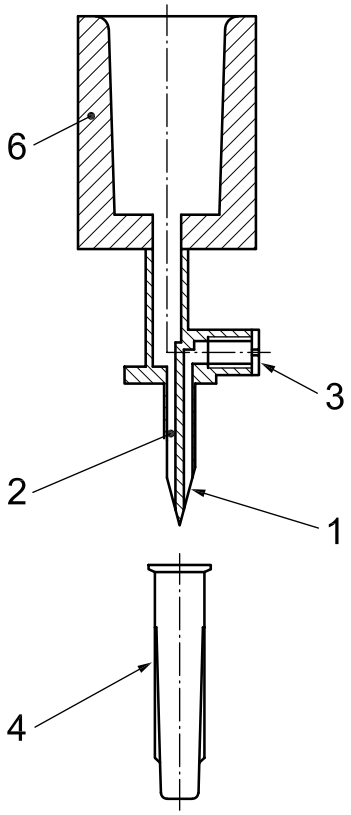


Figure 5 — Transfer set with an air inlet/air outlet in combination with a Luer connector

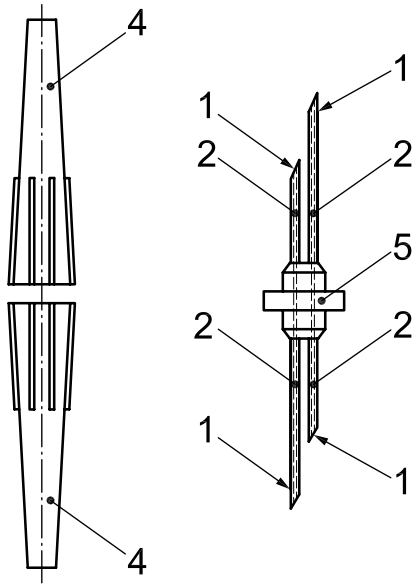


Figure 6 — Transfer set with two channels

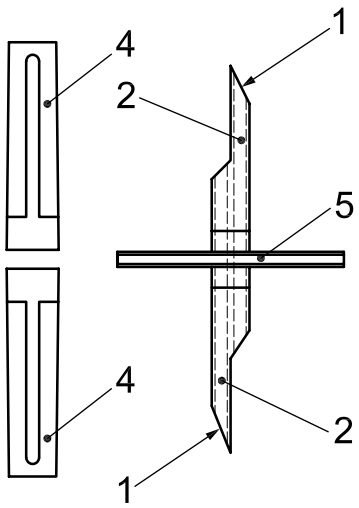


Figure 7 — Alternative transfer set with two channels

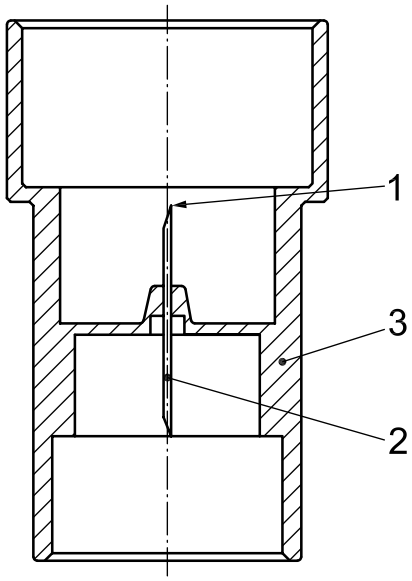
Key for Figures 1 to 7

1 piercing device
2 channel
3 channel with air filter for ventilation, optionally lockable
4 protective cap

5 connection of piercing devices by hub, grip plate or tube
6 female Luer connector

3.2 Design for a transfer set with housing

The design of a transfer set with housing is given in Figure 8. The drawing serves as an illustration of a possible transfer set. Other designs are acceptable.



Key
1 piercing device
2 channel
3 housing

Figure 8 — Transfer set with housing

3.3 Designation

Example 1:

A transfer set without housing (NH) is designated by the term “Transfer set”, the number of this International Standard and the initials NH as follows:

Transfer set ISO 22413 – NH

Example 2:

A transfer set with housing (WH) is designated by the term “Transfer set”, the number of this International Standard and the initials WH as follows:

Transfer set ISO 22413 – WH

4 Material

The materials for the transfer sets and their individual components shall comply with the requirements in accordance with Clause 5. If the components come into contact with the liquid to be transferred, the chemical and biological requirements in accordance with ISO 8536-4 shall be met.

Piercing devices are manufactured from appropriate materials, e.g. metal and/or plastic.

5 Physical requirements

5.1 Particulate contamination

Transfer sets shall be manufactured under such conditions that minimize particulate contamination. All parts shall be smooth and clean. When tested in accordance with 8.1 the evaluation number of the particulate contamination shall not exceed 90.

5.2 Tensile strength

5.2.1 When tested as specified in 8.2 the transfer set shall withstand a static tensile force of not less than 15 N for 15 s.

5.2.2 When using metal piercing devices the steadiness under tensile or compressible force without breaking shall comply with the values listed in Table 2 of ISO 7864:1993.

5.3 Tightness

The transfer set shall be air-tight, no leaks of air or liquid shall occur when tested in accordance with 8.3. Sterility shall be maintained.

5.4 Free flow

When tested in accordance with 8.4 a free flow of air and/or liquid shall be ensured.

5.5 Piercing device

The piercing devices shall be suitable for penetration of the intended closure system for injection and/or infusion containers made of glass or plastic. After puncture, a free flow shall be ensured. When tested in accordance with 8.5 the surface of the piercing devices shall be smooth and free of burrs.

The maximum diameter of the piercing device shall be $\leqslant$ 6,5 mm.

5.6 Penetration force

When tested in accordance with 8.6 the penetration forces determined in Table 1 shall not be exceeded.

Table 1 — Penetration force

Type of piercing device	Penetration force N max.	Counterpart
Transfer sets with metal piercing device	10	Injection stoppers ISO 8362-2 – 20 – A (7.2.2) Hardness: 40 Shore A to 55 Shore A
Transfer sets with plastic piercing device	80	Infusion stoppers ISO 8536-2 – 32 – A (Annex B) Hardness: 40 Shore A to 55 Shore A
NOTE Freeze-drying stoppers (FD stoppers) can have tight channels at the bottom which considerably affect the penetration force.		

5.7 Fragmentation

5.7.1 The design of the piercing devices should avoid fragments being emitted during piercing.

5.7.2 If plastic piercing devices are tested in accordance with Annex A, a maximum of two fragments per ten penetrations may occur.

5.7.3 If metal piercing devices are tested in accordance with Annex B, a maximum of three fragments per 100 penetrations may occur.

5.8 Air inlet and air outlet

For transfer sets containing an air inlet device with air filter, the device shall allow venting and maintain sterility. Testing shall be effected in accordance with 8.8.

The air filter should be hydrophobic.

5.9 Protective caps

The protective caps at the end of the transfer sets shall maintain the sterility of the closure-piercing device. Protective caps should be secure but easily removable.

The protective caps shall be appropriate for the intended sterilization process.

5.10 Transfer sets with a housing

5.10.1 Transfer sets with a housing shall be designed in order to comply with the series of International Standards ISO 8362 and ISO 8536 as well as to comply with the International Standards ISO 15747 and ISO 15759.

5.10.2 The transfer sets with a housing should be designed in a manner that injury or contact with cannulae is prohibited by the housing, the protective caps or by suitable packaging.

5.11 Luer connector

Transfer sets with Luer connectors shall be designed in compliance to ISO 594-1 and ISO 594-2.

5.12 Filter for particles

Particle filter, if integrated, shall retain particles that might plug or become lodged in capillaries.

6 Chemical requirements

In accordance with ISO 8536-4.

7 Biological requirements

In accordance with ISO 8536-4.

8 Testing of physical requirements

8.1 Particulate contamination

Tested In accordance with ISO 8536-4.

8.2 Tensile strength

Expose the transfer set to be tested to a static tensile force of 15 N applied along the longitudinal axis for 15 s. Inspect whether the transfer set withstands the test force applied.

For metal piercing devices the testing of the hub of the metal cannula shall be done in accordance with Clause 13 of ISO 7864:1993.

8.3 Tightness of transfer set

Seal the transfer set at one end. Apply an internal overpressure of 50 kPa for 15 s using air at the open end, submerge it in water and determine whether air escapes.

Close the air inlet, if available, during testing.

8.4 Free flow

Visually inspect if the lumen is free of contractions.

8.5 Piercing device

Visually inspect if the surface of the piercing device is smooth and free from burrs.

Ensure the diameter complies with 5.5.

8.6 Penetration force

8.6.1 For plastic piercing devices testing shall be done in accordance with ISO 8536-2:2010, Annex B.

8.6.2 For metal piercing devices testing shall be done in accordance with ISO 8362-2:2008, 7.2.2.

8.7 Testing on fragmentation

8.7.1 For plastic piercing devices testing shall be done in accordance with Annex A.

8.7.2 For metal piercing devices testing shall be done in accordance with Annex B.

8.8 Effectiveness of air inlet and air outlet with air filter

In accordance with ISO 8536-4.

8.9 Efficiency of protective caps

Perform an efficiency test in order to determine whether the protective caps can be removed without contact with the protected parts. The protective caps shall not fall under their own weight.

8.10 Luer connector

In accordance with ISO 594-1 and ISO 594-2.

8.11 Filter for particles

Integrity of integrated particle filters has to be tested.

9 Testing of chemical requirements

In accordance with ISO 8536-4.

10 Testing of biological requirements

In accordance with ISO 8536-4.

11 Packaging

11.1 The transfer sets shall be packed individually and ready for use. A single pack shall be designed in a way that ensures packaging integrity.

11.2 The packaging material shall ensure sterilization of all included transfer sets and their sterility until the end of their shelf life.

12 Storage

12.1 The packed transfer sets should be stored at such a temperature and humidity as to ensure that shelf life is maintained.

12.2 The packed transfer sets shall be protected against the influence of direct light.

13 Labelling

13.1 Unit container

At least the following information shall be declared on the packaging, using the symbols in accordance with ISO 15223-1:

a) “Single use only”;

b) “Method of sterilization”;

c) “Batch/Lot-No.”;

d) “Expiry date – use before”;

e) “Do not use transfer set, if protective caps have fallen off or packaging has been damaged”;

f) identification block of standard designation, e.g. ISO 22413 – WH;

g) name and address of manufacturer or supplier.

13.2 Shelf or multi-unit container

The following information shall be declared on multiple packagings:

— specifications as listed under 13.1 a) to d) and 13.1 f) and g);

— storage conditions in accordance with Clause 12.

Annex A
(normative)

Testing of fragmentation of transfer sets with plastic piercing devices

A.1 General

Many medical disposables are equipped with piercing devices. These piercing devices are intended to be used to pierce closure systems, which may result in fragmentation. Fragments are particles – unintentionally generated while puncturing the closure system by means of the piercing device – which block the channel of the piercing device or may fall into the pharmaceutical preparation.

The test described below is to be used as a reference method for closure systems intended to be pierced with plastic piercing devices.

This test does not apply to piercing devices for injection stoppers.

A.2 Principle

The closure system of the containers for infusion or injection is pierced with a piercing device; the remaining fragments are collected and counted.

A.3 Apparatus

A.3.1 Ten infusion bottles, half-filled with filtered water, sealed with closure systems.

A.3.2 Devices for rinsing.

A.4 Test samples and counterparts

Table A.1 — Test samples and counterparts

Test sample	Closure system	
	Marking	Requirement
Ten transfer sets with plastic piercing devices	Infusion stopper ISO 8536-2 – 32 – A (Annex B)	Hardness: 40 Shore A to 55 Shore A

A.5 Pre-treatment

a) The plastic piercing devices are used without any pre-treatment.

b) The infusion stoppers are rinsed, sterilized and dried. Rinse twice using water at 60 °C in a glass. Sterilization is done in dry, saturated steam at (121 ± 1) °C for 30 min in an autoclave. Drying is done at a temperature of 60 °C for 60 min in a drying cabinet.

c) Sterilization serves as a simulation of the normal pre-treatment. In case of deviation due to a different method of application (e.g. sterilization by irradiation), it shall be stated in the test record.

d) The infusion bottles (A.3.1) are cleaned.

A.6 Procedure

The infusion stoppers are placed on infusion bottles, half-filled with filtered water and sealed with a crimp cap. Each infusion stopper is pierced once with the piercing device inside the piercing area. After piercing, the plastic piercing device is rinsed out by injecting approximately 1 ml of water into the infusion bottle.

By swirling the infusion bottle with the piercing device, generated fragments are rinsed off. Crimp cap and infusion stopper are removed from the infusion bottles; the content is successively filtered through a membrane filter (0,8 µm), while the infusion bottles are swirled gently to avoid sedimentation of fragments.

A.7 Evaluation

Fragments that are visible on the membrane filter from a viewing distance of 25 cm are evaluated. The nature of the fragments is assessed using a six-fold magnifying glass.

The number of the discovered fragments for every ten punctures shall be stated.

Annex B
(normative)

Testing of fragmentation of transfer sets with metal piercing devices

B.1 General

Many medical disposables are equipped with piercing devices. These piercing devices are intended to be used to pierce closure systems, which may result in fragmentation. Fragments are particles – unintentionally generated while puncturing the closure system by means of the piercing device – which block the channel of the piercing device or may fall into the pharmaceutical preparation.

The test described below is to be used as a reference method for closure systems intended to be pierced with metal piercing devices.

This test does not apply to piercing devices for infusion stoppers.

Transfer sets have, in general, multiple piercing devices. During testing and evaluation each piercing device is to be considered separately.

B.2 Principle

The closure system of the containers for infusion or injection is punctured with a piercing device; the remaining fragments are collected and counted.

B.3 Apparatus

B.3.1 25 injection bottles, half-filled with filtered water, sealed with closure systems.

B.3.2 Device for rinsing the particles out of the cannulae, e.g. disposable syringes.

B.4 Test samples and counterparts

Table B.1 — Test samples and counterparts

Test sample	Closure system	
	Marking	Requirement
25 transfer sets with metal piercing devices	Injection stopper ISO 8362-2 – 20 – A (Annex B)	Hardness: 40 Shore A to 55 Shore A

B.5 Pre-treatment

a) The metal piercing devices are used without pre-treatment.

b) The injection stoppers are sterilized and dried. Sterilization is done in dry, saturated steam at (121 ± 1) °C for 30 min in an autoclave.

c) Sterilization serves as a simulation of the normal pre-treatment. In case of deviation due to a different method of application (e.g. sterilization by irradiation), it shall be stated in the test record.

d) Drying of the autoclaved injection stoppers is done at a temperature of 60 °C for 60 min in a drying cabinet.

e) The injection bottles (B.3.1) are cleaned so that they contain no particles that would falsify the test result.

B.6 Procedure

The injection stoppers are placed on injection bottles, half-filled with filtered water and sealed with a crimp cap. Afterwards, each injection stopper is punctured four times with the metal piercing device at different places of the piercing area. After the fourth puncture any fragment is removed from the piercing device by rinsing or puncturing. After a total of 100 punctures the crimp caps of the bottles are removed and the content is filtered through a membrane filter (0,8 µm).

Testing is performed in accordance with ISO 7864:

— four punctures per piercing device × 25 piercing devices result in 100 punctures;

— four punctures per stopper × 25 stoppers result in 100 punctures.

Due to statistical reasons or because of technical facts (e.g. for transfer sets with a housing) the number of test samples may be increased up to 100 and the numbers of punctures for each test sample may be decreased to 1. That means that one puncture per piercing device × 100 punctures result in 100 punctures.

B.7 Evaluation

Fragments that are visible on the membrane filter from a viewing distance of 25 cm are evaluated. The nature of the fragments is assessed using a six-fold magnifying glass.

The number of the discovered fragments for every 100 punctures shall be stated.

Bibliography

[1] DIN 13097-4, *Hypodermic needles — Part 4: Point geometry, requirements and testing*

[2] EN 1707, *Conical fittings with a 6 % (Luer) taper for syringes, needles and certain other medical equipment — Lock fittings*

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

[4] ISO 8871 (all parts), *Elastomeric parts for parenterals and for devices for pharmaceutical use*

[5] Pharmacopoeia Europaea (Ph. Eur.)

[6] United States Pharmacopeia (USP)

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