INTERNATIONAL STANDARD

ISO 14949

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Implants for surgery — Two-part addition-cure silicone elastomers

Implants chirurgicaux — Élastomères de silicone à deux composants à réticulation par réaction d'addition

Reference number
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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 3.

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 International Standard may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

International Standard ISO 14949 was prepared by Technical Committee ISO/TC 150, *Implants for surgery*, Subcommittee SC 1, *Materials*.

Annexes A and B form a normative part of this International Standard.

Introduction

Silicones are commercially available in a variety of physical forms and formulations. Silicone-cure products often employ cure mechanisms that utilize metals, free radicals and/or atmospheric moisture. This International Standard was undertaken to describe a subset of silicones with a successful history of use in implant applications; namely, those utilizing two-part addition-cure (platinum-based) chemistry. It was developed in response to a need to standardize the raw materials, formulation, processing, characterization testing and documentation of two-part addition-cure silicone elastomers targeted as implants for surgery.

Two-part addition-cure silicone elastomer is a thermoset elastomer and is commercialized as a two-part (non-crosslinked) product. The two parts should be thoroughly mixed in a fixed ratio before shaping by extrusion, press- or injection-moulding and crosslinking at elevated temperatures.

Implants for surgery — Two-part addition-cure silicone elastomers

1 Scope

This International Standard specifies the characteristics of, and corresponding test methods for, the two-part addition-cure high consistency or liquid silicone elastomer for use in the manufacture (partially or totally) of surgical implants.

2 Normative references

The following normative documents contain provisions which, through reference in this text, constitute provisions of this International Standard. For dated references, subsequent amendments to, or revisions of, any of these publications do not apply. However, parties to agreements based on this International Standard are encouraged to investigate the possibility of applying the most recent editions of the normative documents indicated below. For undated references, the latest edition of the normative document referred to applies. Members of ISO and IEC maintain registers of currently valid International Standards.

ISO 34-1:1994, *Rubber, vulcanized or thermoplastic — Determination of tear strength — Part 1: Trouser, angle and crescent test pieces*

ISO 48:1994, *Rubber, vulcanized or thermoplastic — Determination of hardness (hardness between 10 IRHD and 100 IRHD)*

ISO 527-2:1993, *Plastics — Determination of tensile properties — Part 2: Test conditions for moulding and extrusion plastics*

ISO 3417:1991, *Rubber — Measurement of vulcanization characteristics with the oscillating disc curemeter*

ISO 6502:1999, *Rubber — Guide to the use of curemeters*

ISO 10993-1:1997, *Biological evaluation of medical devices — Part 1: Evaluation and testing*

ISO 10993-5:1999, *Biological evaluation of medical devices — Part 5: Tests for in vitro cytotoxicity*

3 Terms and definitions

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

3.1
catalyst
organometallic complex, typically containing platinum substituted by ligands made of any suitable combination of the elements carbon, hydrogen, oxygen, chlorine or silicon (with the exclusion of aromatic rings), which initiates a chemical reaction between a polymer and crosslinking agent

NOTE The catalyst may be dispersed in a silicone oligomer, polymer or mixture of these, such as $RMe_2SiO(SiMe_2O)_x(SiMeR'O)_ySiMe_2R$ where R and R′ are methyl or vinyl groups.

3.2
crosslinking agent
monomer, polymer, silicate or any combination of these, typically of the structure $R''Me_2SiO(SiMe_2O)_x(SiRMeO)_ySiMe_2R''$ where R″ is typically a methyl group or hydrogen, that on curing provides a crosswise connection to parallel polymer chains

NOTE Excess SiH is recommended (not required) before curing to ensure that the cure is total and that no residual Si-vinyl reactive entities exist, thus providing better elastomer stability.

3.3
filler
reinforcing agent
〈for the purposes of this International Standard〉 silicate or high purity amorphous silica

NOTE 1 Such agents are commercially known as fumed or precipitated silica.

NOTE 2 Silica can be treated with silylating agents, for example, those of the formula Me_3SiX or Me_2SiX_2 where X is a hydrolysable group, or polysiloxane oligomer of the formula $HOMe_2SiO(SiMe_2O)_p(SiMeRO)_qSiMe_2OH$ where R is a methyl or a vinyl group.

NOTE 3 Agents that impart radiopacity to the elastomer (e.g. $BaSO_4$) may have reinforcing properties.

3.4
inhibitor
compound or material that has the effect of slowing down or stopping a chemical reaction such as crosslinking

3.5
lot
batch
defined quantity of material manufactured in a single or multi-step process such that the material obtained can be considered as homogeneous

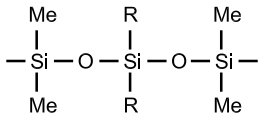
NOTE in the case of a continuous process, the term corresponds to a defined fraction of the production, characterized by its intended homogeneity.

3.6
manufacturer
company who manufactures the final medical device in question

3.7
raw materials
materials from which two-part addition-cure silicone elastomer is manufactured

3.8
silicone elastomer
synthetic rubber obtained by the crosslinking of silicone polymer chains essentially made of repeat siloxane units

EXAMPLE



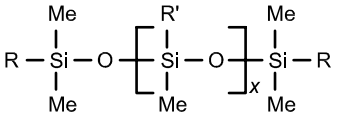
where

R is a phenyl, fluoro, hydroxyl, alkyl or other suitable organic group,

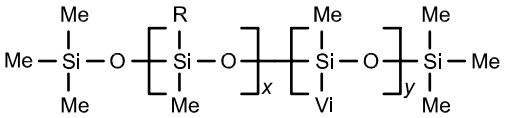
Me is $-CH_3$

3.9
silicone polymer
any polymer or combination of polymers of medium or high molecular mass of the structure $RMe_2SiO(SiMe_2O)_x(SiMeR'O)_ySiMe_2R$, where R is typically a methyl, vinyl or hydroxyl group but might also be a fluoro, phenyl or other group and where R′ is typically a methyl or vinyl group but might also be a fluoro, phenyl or other group

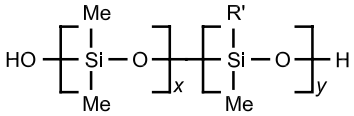
EXAMPLE 1



EXAMPLE 2



EXAMPLE 3



where

Vi is $-CH=CH_2$,

Me is $-CH_3$

both R and R′ are methyl, phenyl, fluoro or other suitable organic groups.

NOTE The definition of the polymer and its substituted groups is taken very broadly, as it is not the function of this International Standard to limit the number or the type of substituent groups present; however, for the purposes of this International Standard the definition only relates to materials with available preclinical biocompatibility data (see clause 5) and a well-established history of safe international use in implant applications.

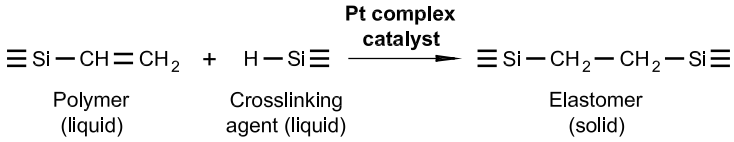
3.10
supplier
company who manufactures and/or supplies the two-part silicone elastomer used for the production of the medical device in question

3.11
treating agent
monomer, oligomer or polymer used to coat the outer surface of silica to reduce the reactivity of the silica

3.12
two-part addition-cure silicone elastomer
elastomer formed by crosslinking silicone polymer chains via an addition reaction between the vinyl functional groups of a vinyl silicone polymer and the silicon hydride of a crosslinking agent containing SiH functions

NOTE The reaction requires the presence of a catalyst, usually an organometallic complex of platinum.

EXAMPLE



where ☰ represents the remaining valencies of the Si

4 Formulation

4.1 Composition

The defined raw materials shall be used in a formulation as defined in Table 1.

Table 1 — General formulation for two-part addition-cure silicone elastomers

Compound	Percentage range (% mass fraction)
Silicone polymer	60 to 80
Reinforcing agent	less than 40
Crosslinking agent	1 to 5
Catalyst	$< 0{,}5$
Inhibitor	$< 1{,}0$

4.2 Raw materials assessment

Both during product development and on an audit basis (at least once a year or every tenth production lot), the supplier of the two-part addition-cure elastomer shall assess the raw materials (see 3.8) as follows.

a) Structure and functionality of polymer

The structure and functionality of the polymer(s) used shall be determined by a suitable method such as nuclear magnetic resonance spectroscopic analysis (see [2] for further information).

b) Purity of silica

The purity of the silica used shall be assessed by elemental analysis or any other suitable method, and the result should be expressed as (mg Si obtained/theoretical mass) $\times$ 100 = % mass fraction Si.

c) Structure and purity of treating agent(s)

The structure and purity of the treating agent(s) used shall be determined by a suitable method such as infrared spectroscopy (see [2] for further information).

d) Structure of the crosslinking agent(s)

The structure of the crosslinking agent(s) used shall be determined by a suitable method such as infrared spectroscopy (see [2] for further information).

e) Purity of the inhibitor

The purity of the inhibitor used shall be determined based on an appropriate analysis and shall be greater than 95 % mass fraction (see [2] for further information).

f) Structure of the inhibitor

The structure of the inhibitor used shall be determined by a suitable method such as infrared spectroscopy (see [2] for further information).

5 Biocompatibility

The biological and physical properties of the cured silicone elastomer depend largely on the formulation as contained in the two-part starting material. Processing conditions to produce silicone parts (extrusion or molding) can also impact biological and physical properties. The validation and consistency of production should be part of the quality system of the supplier. In order to ensure consistent final product properties, the manufacturer should ensure that the supplier has installed measures to control for processing and formulation parameters in accordance with ISO 9001, ISO 14969 and good manufacturing practice. In addition, process validation should include a biological assessment, since production could introduce contaminants, and the functionalities incorporated into silicone elastomers can impart biological activity.

Demonstration of biocompatibility shall be established in accordance with ISO 10993-1. Testing should be carried out at the time of material qualification and then repeated at least every 5 years to 10 years.

6 Characterization and testing

6.1 Test slab preparation

A test slab with a thickness of $(2 \pm 0{,}2)$ mm shall be prepared in accordance with ISO 34-1 and with the recommended cure schedule as well as the post-cure schedule if needed.

6.2 Identification

To analyse the cured elastomer as a silicone, the following test shall be performed on at least an audit basis: examine a slab of elastomer by infrared absorption spectrophotometry, recording the spectrum by the multiple reflection method for solids. There should be absorption maxima at approximately $(2\,962 \pm 5)\ cm^{-1}$, $(2\,906 \pm 5)\ cm^{-1}$, $(1\,260 \pm 5)\ cm^{-1}$ and $(1\,094 \pm 5)\ cm^{-1}$ to $(1\,022 \pm 5)\ cm^{-1}$.

6.3 Purity testing

6.3.1 Metal contamination

Each production lot of two-part addition-cure silicone elastomer shall be tested for metal contamination. The cured elastomer shall be tested and comply with the following specification on metal impurities. If one of these metals comprises part of a formulation component (for example $BaSO_4$), it shall not be tested as an impurity.

— $Al \leqslant 200 \times 10^{-6}$

— $P, Ti, Fe \leqslant 50 \times 10^{-6}$

— Na, Mg, Ca $\leqslant 100 \times 10^{-6}$

— Sb, Ge, Mn, Mo, Pb, Sn, Cr, Bi, V, Ag, Co, Ni, Cu, Zr, Ba, As, Zn, Se, Cd, Hg, Tl $\leqslant 10 \times 10^{-6}$

NOTE The specification limits are per element.

6.3.2 Particulate contamination

Each production lot of two-part addition-cure silicone elastomer shall be tested, by the supplier, for particulate contamination. A 100 mm × 100 mm × 2 mm sheet of cured elastomer shall be prepared according to the recommended procedure. When observing under 10× magnification, in accordance with a suitable method, the particulate contamination shall be in compliance with particulate contamination ranges shown in Table 2.

Table 2 — Particulate contamination

Particle size µm	Number of particles
$\geqslant$ 400	none
399 to 300	maximum 2
299 to 200	maximum 4
199 to 100	maximum 4

6.3.3 Cytotoxicity

Each production lot shall be cured and tested for cytotoxicity in accordance with ISO 10993-5. No cytopathic effects shall be induced around the material tested, or throughout the culture.

6.3.4 Substances soluble in hexane

The determination of substances soluble in hexane shall be undertaken in accordance with the method described in annex A. This test shall be performed on production lots, at least on an audit basis.

The residue, after extraction and evaporation, shall not exceed a mass fraction of 3 %.

6.3.5 Determination of volatile matter

The determination of the volatile matter shall be undertaken in accordance with the method described in annex B. This test shall be performed on production lots, at least on an audit basis.

The volatile matter shall not exceed a mass fraction of 2,0 %.

6.4 Cure rate

The supplier shall test each production lot of two-part addition-cure silicone elastomer for its cure rate in accordance with ISO 3417 and ISO 6502. The sample shall be prepared in accordance with the supplier's recommended procedure. The cure rate shall be measured at the supplier's recommended cure temperature using a suitable rheological technique, for example, oscillating disk rheometry. Using rheological techniques, the time needed to reach 90 % of the final torque shall be part of the product specifications.

NOTE An oscillating rheometer capable of measuring the torque being developed in the mixed material during the transition from its liquid state to its elastomeric state may be used.

6.5 Physicomechanical properties and characterization

Each production lot of addition-cure silicone elastomer shall be tested for its mechanical properties after cure. The test slab shall be prepared in accordance with the supplier's recommended procedure.

The cure schedule (time and temperature) shall be specified as well as the post-cure schedule if needed.

The supplier shall indicate the following mechanical characteristics, which shall be measured in accordance with ISO 527-2, ISO 34-1 and ISO 48 as appropriate:

— elongation at break (%);

— tensile strength at break (MPa);

— modulus at 100 % elongation (MPa);

— tear strength, die B (kN/m);

— hardness (IRHD);

— relative density, or specific gravity (kg/m^3).

7 Documentation

7.1 Data sheet

The supplier shall provide, upon request and for each type of two-part addition-cure silicone elastomer, a data sheet including at least the following information:

a) the raw material supplier’s name, address and telephone number;

b) the product reference;

c) the recommended procedure and conditions to store the non-crosslinked material in its original unopened container and the shelf-life expected under these conditions;

d) the recommended cure procedure, including the recommended mixing procedure with ratio of part A to part B, the recommended cure schedule (time and temperature) and recommended post-cure schedule if needed;

e) the range of properties, with defined specification limits and test methods, including cure/post-cure conditions;

f) the recommended sterilization methods, including the method(s) that is (are) not recommended;

g) any known restriction of use and/or statement about applications that are not recommended;

h) the biological and physical properties of the cured silicone elastomer, including conditions of sample preparation. Biological properties should be addressed by supplying compatibility test data summaries;

i) the time needed to reach 90 % of the final torque shall be part of the product specification (see ISO 3417).

7.2 Certificate of analysis

For each production lot of addition-cure silicone elastomer, the supplier shall provide a certificate of analysis that lists the results of the testing performed in accordance with the specifications and requirements listed in clause 6 of this International Standard, and a statement that: “This two-part addition-cure silicone elastomer meets the requirements for qualification testing as described in ISO 14949, *Implants for surgery — Two-part addition-cure silicone elastomers*”.

Annex A
(normative)

Determination of substances soluble in hexane

A.1 Objective

The “Substances soluble in hexane” test is described in summary in the European Pharmacopoeia [1] and allows the determination of hexane extractables in silicone elastomer.

This annex provides a more detailed standardized quantitative procedure (adapted from the European Pharmacopoeia text) in order to ensure reproducible and comparable results.

A.2 Principle

The extraction of substances soluble in hexane from cured material (silicone elastomer) is carried out using reflux condensation, and the results reported as the percent mass fraction of residue.

A.3 Sample preparation

A.3.1 General

Two cases shall be considered:

— non-cured elastomer (non-processed);

— cured elastomer already processed (tubing, etc.).

A.3.2 Non-cured elastomer

The material shall be cured in order to obtain a slab of homogeneous thickness of $(2{,}0 \pm 0{,}2)$ mm which allows physical testing (tear strength, for instance, in accordance with ISO 34).

Conditions used for curing (temperatures, time, pressure, post-cure) having direct influence on results shall be recorded and given with results.

Once cured, the slab shall be cut into 5 mm $\times$ 5 mm pieces, observing the experimental precautions given in A.6.

The sample geometry has a direct influence on the test results; therefore it is recommended to follow the dimensions above for comparison. If another geometry is chosen, it shall be reported in the results.

A.3.3 Already processed “cured” elastomer

In the case of tubing or another processed material, it is recommended that the sample dimensions be identical to those indicated above. In all cases the dimensions shall be reported.

A.4 Reagents

All reagents shall be of at least “reagent grade” or “for analysis” purity.

A.4.1 n-Hexane

A.4.2 Isopropanol, for material and bench cleaning.

A.5 Apparatus and glassware

The following apparatus and glassware should be used:

A.5.1 25 ml **volumetric pipettes**, class A.

A.5.2 Six **500 ml glass flasks** capable of withstanding a maximum temperature of 450 °C.

A.5.3 500 ml flasks with ground glass fittings.

A.5.4 100 ml glass volumetric flasks.

A.5.5 100 ml glass beakers.

A.5.6 Condensers.

A.5.7 Sintered glass filter funnel (porosity 4).

A.5.8 Vacuum filtration flask.

A.5.9 Vacuum pump for filtration.

A.5.10 Electrothermal glass flask heater.

A.5.11 Thermostatted water bath, heated to a temperature of 100 °C under a hood.

A.5.12 Ventilated oven at 100 °C to 105 °C.

A.5.13 Cork rings for glass flasks.

A.5.14 Desiccator containing silica gel with indicator.

A.5.15 Polytetrafluoroethylene (PTFE) cutting surface and film.

A.5.16 Scalpel or other apparatus which can cut out evenly pieces of 5 mm × 5 mm.

A.6.17 Analytical balance (precision 0,1 mg).

A.6 Experimental precautions

The usual safety recommendations apply and the following precautions shall be taken:

— if there is dust on the material before sample cutting, rinse with deionized water and dry delicately with absorbent paper and with high purity nitrogen flux;

— clean carefully the material and bench used to cut the elastomer;

— using a wash bottle, rinse glassware with isopropanol;

— rinse glassware with hexane before drying;

— evenly rinse condensers with hexane;

— regenerate the desiccating agent as soon as the indicator changes colour.

A.7 Procedure

A.7.1 Number of experiments

The experiment shall be carried out in triplicate; i.e. three refluxes shall be performed.

A.7.2 Extraction

Cut the material evenly into pieces of approximately 5 mm × 5 mm.

In each glass flask rinsed with n-hexane, load 2,0 g (accurately weighed) of the material and 100 ml of n-hexane (by graduated cylinder). Apply PTFE film to the glass fittings.

Boil this mixture gently under a reflux condenser for 4 h.

Stopper each glass flask and place them on cork rings.

Cool the flasks for 1 h with the condensers still connected.

A.7.3 Filtration

Filter the contents of each flask rapidly through a glass filter funnel (porosity 4). Rinse each glass flask and sintered glass filter three times with about 5 ml of n-hexane. Collect the filtrate into a 100 ml volumetric flask. Add n-hexane to the mark and mix.

A.7.4 Evaporation

About 2 h before evaporation, put 100 ml beakers (previously tared and identified with permanent marker) in a ventilated oven at 100 °C to 105 °C for 1 h. Allow to cool in a desiccator for 1 h.

Using a volumetric pipette, transfer 25 ml of solution from each flask prepared according to A.7.3 into each of three of the 100 ml beakers. Place the beakers in a boiling water bath, evaporate for about 1 h and dry the beakers containing the residue in a ventilated oven at 100 °C to 105 °C for 1 h. Cool the beakers in a desiccator for 1 h.

A.7.5 Weighing

Remove the beakers containing residue, one by one, from the desiccator. Weigh each beaker using the analytical balance.

A.8 Calculation

Calculate the percent residue in each beaker using the following equation:

$$\% \text{ residue} = (m_r - m_t) \times 400/m_i$$

where

m_t is the mass of the empty beaker;

m_r is the mass of the beaker + residue;

m_i is the initial mass of elastomer.

Record:

a) the individual results;

b) the average of the three experiments;

c) the standard deviation;

d) the relative standard deviation.

A.9 Specification

The residue, expressed as a percentage (mass fraction), shall be $\leqslant$ 3 %.

Annex B
(normative)

Determination of volatile matter

B.1 Objective

This annex describes a quantitative technique for the determination of volatile matter in silicone elastomer.

This standardized procedure was adapted from the European Pharmacopoeia monograph [1] but in more detailed terms in order to obtain reproducible and comparable results.

B.2 Principle

The volatile matter in the cured material is determined by drying, heating and weighing.

B.3 Sample preparation

The procedure given in A.3 shall be followed.

B.4 Reagent

B.4.1 **Isopropanol**, of at least “reagent grade” or “for analysis” purity, for material and bench cleaning.

B.5 Apparatus and glassware

B.5.1 **Aluminium dishes**, diameter 86 mm, height 25 mm.

B.5.2 **Desiccators** containing silica gel with indicator.

B.5.3 **Scalpel** or other apparatus which can evenly cut pieces of 5 mm × 5 mm.

B.5.4 **Ventilated oven** set at 200 °C.

B.5.5 **Analytical balance,** precision 0,1 mg.

B.6 Experimental precautions

The usual safety recommendations and the following experimental precautions shall be taken:

— clean carefully the material and bench used to cut the elastomer;

— regenerate the desiccating agent as soon as the indicator changes colour.

B.7 Procedure

B.7.1 Number of experiments

The experiment shall be carried out in triplicate.

B.7.2 Drying of elastomer samples

Cut about 30 g of material into pieces approximately 5 mm × 5 mm. Distribute about 10 g uniformly (i. e. avoiding adhesion of pieces) in each of three aluminium dishes and put the dishes in a desiccator for 48 h.

B.7.3 Drying of dishes

The next day, place three tared empty aluminium dishes in the oven at 200 °C for 4 h followed by 1 h in a desiccator.

B.7.4 Oven heating of elastomer samples

After 48 h desiccation, transfer 10 g of precisely weighed material (from B.7.2) into each of the dried, empty dishes (from B.7.3), then place these dishes in an oven at 200 °C for 4 h, followed by 1 h in a desiccator.

B.7.5 Weighing

Remove the dishes, one by one, from the desiccator. Weigh each dish using the analytical balance.

B.8 Calculation

Calculate the percent volatile matter for each dish, using the following equation:

$$\%\ \text{volatile matter} = \left[m_{\text{i}} - \left(m_{\text{f}} - m_{\text{t}}\right)\right] \times 100/m_{\text{i}}$$

where

m_{t} is the mass of the empty dish,

m_{i} is the initial mass of elastomer,

m_{f} is the mass of the dish + material.

Record:

a) the individual results;

b) the average of the three experiments;

c) the standard deviation;

d) the relative standard deviation.

B.9 Specification

The volatile matter content of the silicone elastomer, expressed as % mass fraction, shall be $\leqslant$ 2 %.

Bibliography

[1] *European Pharmacopoeia,* Section 3.1.9 Materials used for containers fabrication and containers, Monograph: Silicone elastomer for closures and tubing, 3rd edn. 2000

[2] *The Analytical Chemistry of Silicones*, A. Lee Smith (ed.), Wiley & Sons, 1991, ISBN 0-471-51624-4

[3] ISO 9001:2000, *Quality management systems — Requirements*

[4] ISO 14969:1999, *Quality systems — Medical devices — Guidance on the application of ISO 13485 and ISO 13488*

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