Biological Evaluation of:

Silicone Liners and Sleeves

Contents

Biocompatibility evaluation carried out by (names, job titles and qualifications):
- Mattia Rampazzo, Product Manager. Over 10 years-experience as product manager; experience in preparation of 4 technical files compliant to the MDR2017/745, including 3 Clinical Evaluations.
- Deanna Lopedito, Quality & Regulatory Manager. 10+ years in handling medical device requirements for Class I devices manufactured by Alps South, LLC.

Author: Mattia Rampazzo

Date: 07/24/2025
Release: 01

1. General information

Device Group:	Silicone liners and Silicone Sleeves
Ref. nr:	See STED11 Basic Characteristics
Intended use:	The prosthetic liner serves as an interface between the prosthetic socket and the amputee's residual limb. The prosthetic sleeve helps maintain suspension by creating an airtight seal at the top of the prosthetic socket without restricting circulation
Lifetime claimed:	Liners: 12 months, depending on the user's activity level. Discontinue the use in case of signs of wear or deterioration. Ultraseal liner: 6 months, depending on the user's activity level. Discontinue the use in case of signs of wear or deterioration. Sleeves: 3 months, depending on the user's activity level. Discontinue the use in case of signs of wear or deterioration.
Storage conditions:	Store in a cool dry place, protected from light, moisture, heat, oxygen, ozone and any chemicals.

2. Categorization according ISO 10993-1:2009, chapter 5

Although the liner is removed nightly for hygiene, the same device is reapplied daily. ISO 10993-1 (§5.2.3) states that for repeated-use devices the cumulative contact time shall be considered. The cumulative exposure exceeds 30 days; therefore, the device is categorized as Surface Device – Intact Skin – Long-term (> 30 days). This categorization drives the selection of biological endpoints evaluated in this report.

Nature of body contact	**Duration of contact**		
	(A) < 24h	(B) 24h - 30d	(C) > 30d
Does not contact body directly of indirectly	Does not apply		
Surface-contacting devices:			
a) Skin: *e.g. electrodes, external prostheses, fixation tapes, compression bandages, etc.*			X
b) Mucosal membranes: *e.g. contact lenses, urinary catheters, intravaginal devices, endotracheal tubes, etc.*	Does not apply		
c) Breached or compromised surfaces: *e.g. dressings, healing devices and occlusive patches for ulcers, burns, etc.*	Does not apply		
External communicating devices:			
a) Blood path, indirect: *e.g. solution administration-, extension-, transfer sets and blood administration sets*	Does not apply		
b) Tissue/bone/dentin: *e.g. laparoscopes, arthroscopes, draining systems, dental cements, etc.*	Does not apply		
c) Circulating blood: *e.g. intravascular catheters, temporary pacemaker electrodes, oxygenators, dialysers*	Does not apply		
Implant devices:			
a) Tissue/bone: *e.g. orthopaedic pins, plates, drug supply devices, neuromuscular sensors*	Does not apply		
b) Blood: *pacemaker electrodes, artificial arteriovenous fistulae, heart valves, vascular grafts*	Does not apply		

3. Test selection

Following selection applies: (Highlight)

Body contact		**Contact Duration** **A** = Limited **B** = Prolonged **C** = Permanent	Cytotoxicity	Sensitization	Irritation or intra-cutaneous reactivity	Systemic toxicity (acute)	subchronic toxicity (Subacute toxicity)	Genotoxicity	Implantation	Haemo-compatibility	USP Classification[1]
Surface Devices	Skin	A	X	X	X						I
		B	X	X	X						I
		C	X	X	X						I
	Mucosal membrane	A	X	X	X						I
		B	X	X	X						III
		C	X	X	X		X	X			V
	Breached or compromised surfaces	A	X	X	X						III
		B	X	X	X						V
		C	X	X	X		X	X			VI
Externally Communicating Devices	Blood Path, indirect	A	X	X	X	X				X	IV
		B	X	X	X	X				X	V
		C	X	X		X	X	X		X	VI
	Tissue / Bone / Dentin	A	X	X	X						IV
		B	X	X	X	X	X	X	X		VI
		C	X	X	X	X	X	X	X		VI
	Circulating Blood	A	X	X	X	X				X	IV
		B	X	X	X	X	X	X	X	X	VI
		C	X	X	X	X	X	X	X	X	VI
Implant Devices	Tissue / bone	A	X	X	X						VI
		B	X	X	X	X	X	X	X		VI
		C	X	X	X	X	X	X	X		VI
	Blood	A	X	X	X	X	X		X	X	VI
		B	X	X	X	X	X	X	X	X	VI
		C	X	X	X	X	X	X	X	X	VI

Source ISO 10993:-1:2009, Annex A, Table A.1

[1] United States Pharmacopoeia classification

4. Available standards[2]

ISO 10993 consists of the following parts, under the general title Biological evaluation of medical devices:

- Part 1: Evaluation and testing within a risk management process
- Part 2: Animal welfare requirements
- Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity
- Part 4: Selection of tests for interactions with blood
- Part 5: Tests for in vitro cytotoxicity
- Part 6: Tests for local effects after implantation
- Part 7: Ethylene oxide sterilization residuals
- Part 9: Framework for identification and quantification of potential degradation products
- Part 10: Tests for irritation and skin sensitization
- Part 11: Tests for systemic toxicity
- Part 12: Sample preparation and reference materials
- Part 13: Identification and quantification of degradation products from polymeric medical devices
- Part 14: Identification and quantification of degradation products from ceramics
- Part 15: Identification and quantification of degradation products from metals and alloys
- Part 16: Toxicokinetic study design for degradation products and leachables
- Part 17: Establishment of allowable limits for leachable substances
- Part 18: Chemical characterization of materials
- Part 19: Physico-chemical, morphological and topographical characterization of materials (Technical Specification)
- Part 20: Principles and methods for immunotoxicology testing of medical devices (Technical Specification)

Biological Risks	Acceptable EN-ISO Standard	Acceptable ISO Standard
Cytotoxicity	EN ISO 10993-5:2009	idem
Sensitization	EN ISO 10993-10:2023	ISO 10993-10:2021
Irritation	EN ISO 10993-10:2023	ISO 10993-10:2021
Acute Systemic Toxicity	EN ISO 10993-11:2009	ISO 10993-11:2006
Subchronic Toxicity	EN ISO 10993-11:2009	ISO 10993-11:2006
Genotoxicity	EN ISO 10993-3:2014	idem
Implantation	EN ISO 10993-6:2009	ISO 10993-6:2007
Haemocompatibility	EN ISO 10993-4:2009	ISO 10993-4:2002, incl. Amd 1:2006
Chronic Toxicity	EN ISO 10993-11:2009	ISO 10993-11:2006
Carcinogenicity	EN ISO 10993-3:2014	idem
Reproductive	EN ISO 10993-3:2014	idem
Biodegradation	EN ISO 10993-9:2021	ISO 10993-9:2019
Other:		
Ethylene oxide sterilization residuals	EN ISO 10993-7:2008/AC:2009	idem
Sample preparation	EN ISO 10993-12:2021	idem
Degradation Polymeric	EN ISO 10993-13:2010	idem
Degradation Ceramics	EN ISO 10993-14:2009	ISO 10993-14:2001
Degradation Metals	EN ISO 10993-15:2023	ISO 10993-15:2019
Toxicokinetic study	EN ISO 10993-16:2010	Idem
Limits for leachable substances	EN ISO 10993-17:2023	Idem
Chemical characterization	EN ISO 10993-18:2020, EN ISO 10993-18:2020/A1:2023	ISO 10993-18:2020

[2] Source: http://ec.europa.eu/growth/single-market/european-standards/harmonised-standards/medical-devices/index_en.htm

5. Physical effects

Physical effects of the device are considered (if they impact the biocompatibility) according to ISO 10993-19.

	Information:
Porosity	
Classical	Non-porous (closed-cell elastomer)
Connectivity	
Scaffolds	
Morphology	
Crystallinity	Amorphous elastomer
Amorphous	
Multiple phases	
Hard/soft surfaces	
Surface energy/charge	
Hydrophobic	Literature & material datasheet; no surface charge
Hydrophylic	
Protein adsorption	
Protein repulsion	
Abrasion resistance	
Stability of treated surface	Internal wear testing shows no visible particle shedding; no incident reported for over 20 years
Surface friction	Material surface mechanically treated to reduce the friction on the skin. Internal test showed that the mechanically treated material has a low coefficient of static friction (1/5 of regular non treated silicone)
Topography	
Surface chemical mapping	Material is molded with a smooth finish; no abrasion complaints for over 20 years
Roughness (smooth, pitted, grooved, irregular terrain, textured)	
Particles	
Size	Does not apply
Size distribution	
3D shape	
Shape and Form	
Shape and Form	
Swelling	
Water absorption	Minimal, no impact on material charcterization
Solvent absorption	None reported
Shape change	No shape changes due to swelling

The reviewed parameters either pose no biological hazard or are adequately controlled and supported by >20 years of clinical use. Therefore, no additional ISO 10993-19 testing is required.

6. Manufacturing

List of manufacturing steps, see separate flowchart in STED.

7. Material characterization

Material characterization shall be performed according ISO 10993-18.

See report: None

The material composing the subject device and that comes in contact with intact skin has been in commerical use for over 20 years with millions of units sold; Post Market Information and Literature Search performed during the Clinical Evaluation confirm its safe use.
Therefore, no additional ISO 10993-18 testing is required

Within the scope of this biocompatibility evaluation, the raw material intended for direct contact with the patient's skin has been rigorously assessed. The relevant Safety Data Sheets (SDSs) were critically reviewed to identify potential hazards and undesirable biological effects, with particular emphasis placed on toxicological endpoints.
The results of the raw-material assessment are presented in Chapter 8.

8. Risk Management

In a separate document (according EN ISO 14971:2019), the manufacturer established, documents and maintains throughout the life-cycle an ongoing process for identifying hazards associated with a medical device, estimating and evaluating the associated risks, controlling these risks, and monitoring the effectiveness of the controls. This process includes the following elements:
– risk analysis;
– risk evaluation;
– risk control;
– production and post-production information.

Based on the risk management process described in ISO 14971, the biological evaluation of medical devices and their materials comprises the following elements.

Risk evaluation on materials

ALPS Silicone is available in 2 formulations. Materials used in each formulation are listed in the chart below.

Material	Silicone Pro	OptiSil
Silicone Elastomer	X	X
Silicone Fluid	X	X
White Colorant		X

Material	Content (ranking)*	Acute dermal toxicity	Skin corrosion/irritation	Skin sensitization
Silicone Elastomer	1	Not classified for acute toxicity based on available data	No data available	No data available
Silicone Fluid	2	Prolonged skin contact is unlikely to result in absorption of harmful amounts. Typical for this family of materials.LD50, Rabbit, > 2,000 mg/kg No deaths occurred at this concentration.	Based on product testing: Brief contact is essentially nonirritating to skin	Did not cause allergic skin reactions when tested in guinea pigs
White Colorant	3	No data available	Based on available data, the classification criteria are not met	Due to lack of data the classification is not possible

**Actual concentration is withheld as a trade secret*

Raw material assessment does not bring any new or unknown risks.

9. Literature review

A review and evaluation of the literature is essential for justification and planning of any biological evaluation of a material or a medical device. The aim of such a review is to determine scientific background for the biological evaluation.
It also provides essential information for assessing risks/benefits and achieving the ethical conduct of the planned evaluation as required by ISO 10993-2.
sufficient.

A literature review is performed of any biological evaluation of a material or a medical device. See STED118 Clinical Evaluation Report.

10. Evaluation

Test conducted

SILICONE PRO Formulation

- ANSI/AAMI/ISO 10993-10:2010/ (R) 2014 – Biological evaluation of medical devices – Part 10 Tests for irritation and skin sensitization.
  Ref. Geneva Laboratories Proc. No: CL1024M
  - Test Report #JN19H0511
  - Date: 9/19/2019
  - Primary Irritation Index = 0
  - Test Article Response Category was = negligible

- ANSI/AAMI/ISO 10993-5:2009 (R)2014 – Biological evaluation of medical devices for in vitro cytotoxicity
  Ref. Geneva Laboratories Proc. No. CC1003
  - Test Report # JN19H0510
  - Date: 8/27/2019

Results: Test article is considered non-cytotoxic and meets ISO acceptance criteria of no more than Grade 2

Further assessment

- Raw materials assessment

One of the two silicone formulations underwent laboratory testing. No laboratory testing is deemed necessary for the remaining formulation, as justified by the raw materials assessment, the clinical evaluation report and over 20 years of safe clinical use.

No additional testing required.

11. Conclusion

A full ISO 10993 and ISO 14971 assessment confirms the Gel liners and Gel sleeves are biocompatible for long-term skin contact.

Cytotoxicity skin irritation and skin sensitization have been evaluated by laboratory tests.

Chemical and toxicological risks were addressed through Raw materials assessment, Clinical Evaluation Report, and over 20 years of safe clinical use

Residual risks are negligible; therefore, no additional biological testing is required.