DuPont Liveo™ Healthcare Grade Silicones

Eric Reynolds – Technical Service

Liveo

Agenda

- DuPont Liveo™ Healthcare Silicones
- Liveo™ Manufacturing/Quality Controls
- Silicones in Healthcare
- Liveo™ Silicone Elastomers
- Liveo™ Siliconization Products
- Liveo™ Silicone Skin Adhesives

Liveo™ Healthcare Grade Silicones

1943 — DOW CORNING

2016 — DOW; DOW CORNING

2017 — DOW; DUPONT

2019 — DUPONT Specialty Products; DOW Materials Science; CORTEVA agriscience Agriculture

2020 — DUPONT; LIVEO™

2023 — DUPONT; LIVEO™; SPECTRUM PLASTICS GROUP A DuPont Business; Donatelle® A DuPont Business

80+ years of experience in silicone materials for healthcare applications

Healthcare Industries Materials Site

- Established in 1964 specifically for healthcare manufacturing
  - Thomas Township, MI
- FDA registered manufacturing site
  - Strict adherence to current Good Manufacturing Practices (cGMPs) as defined by FDA guidelines
  - Regular FDA inspections
- ISO Registered
- Products manufactured at HIMS are sold worldwide
- Dedicated to healthcare materials

Additional Manufacturing/Quality Controls

Quality Systems in place which include:

- Cleaning
- Preventing infestation
- Quality Assurance
- Incoming Inspection
- Complaint Systems
- Operating Procedures
- Test Methods
- Documentation Review
- Calibration
- Environmental monitoring
- Validation
- Training
- Cleanliness
- Specifications
- Traceability

Ten-year batch record retention

Retain samples kept shelf life +1 year

Audits available on limited basis

Product stability program

Change notification

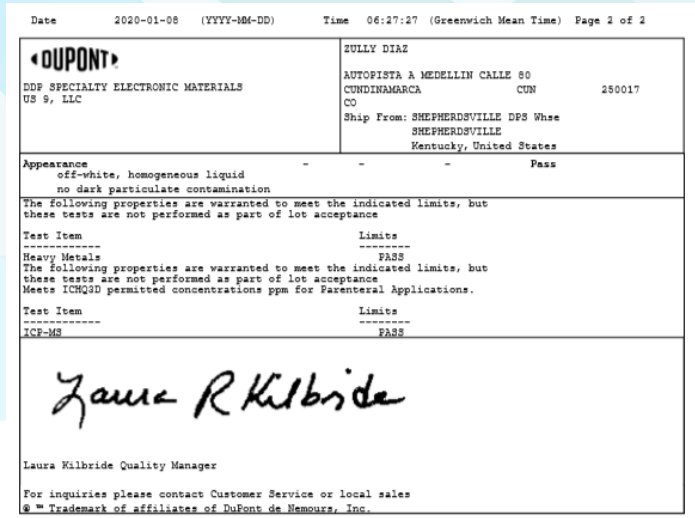
Technical/Regulatory support

Signed CoAs

ISO9001 Certified

ISO14001 Certified

ISO13485 Certified



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DDP SPECIALTY ELECTRONIC MATERIALS
US 9, LLC

ZULLY DIAZ

AUTOPISTA A MEDELLIN CALLE 80
CUNDINAMARCA CUN 250017
CO
Ship From: SHEPHERDSVILLE DPS Whse
SHEPHERDSVILLE
Kentucky, United States

Appearance	-	-	-	Pass
off-white, homogeneous liquid				
no dark particulate contamination				

The following properties are warranted to meet the indicated limits, but these tests are not performed as part of lot acceptance

Test Item	Limits
Heavy Metals	PASS

The following properties are warranted to meet the indicated limits, but these tests are not performed as part of lot acceptance
Meets ICHQ3D permitted concentrations ppm for Parenteral Applications.

Test Item	Limits
ICP-MS	PASS

Laura R Kilbride

Laura Kilbride Quality Manager

For inquiries please contact Customer Service or local sales
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Silicones in Healthcare

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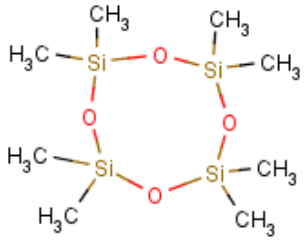
Basic Silicone Chemistry

Chemistry and Forms

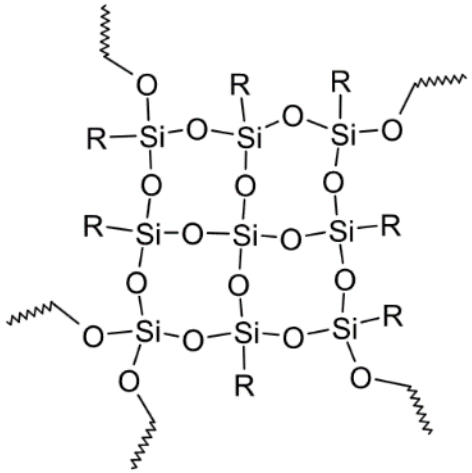
- Si - (O - Si)$_n$ - O - Si -

Polysiloxane: liquid, solid, gum

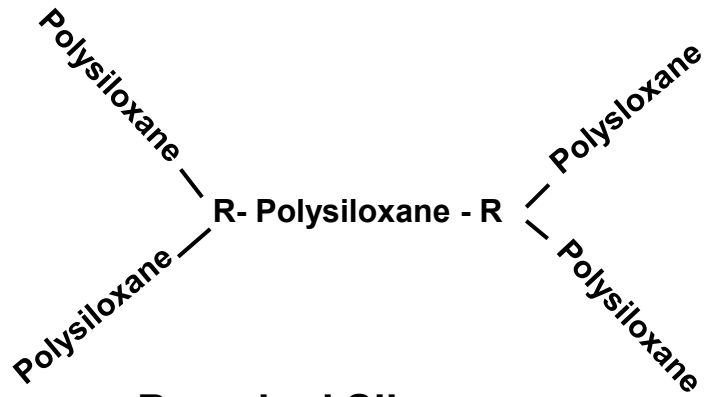


Cyclosiloxane:

above 3 SiO units, liquid



Silicone resin



Branched Siloxanes

- Elastomers
- Gels
- Adhesives
- Fluids
- Greases
- Lubricating coatings
- Hydrophobic coatings
- Wetting Agents
- Antifoams
- Solvents
- Additives
- Sealants

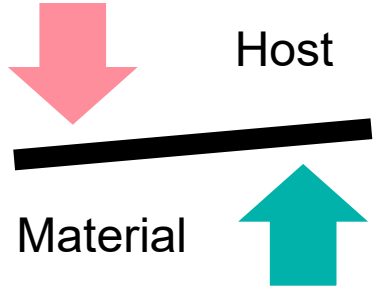
7

Why Silicones Excel in Healthcare

- Versatile and biocompatible
- Silicone elastomers/tubing
  - Easy to clean and sterilize
  - Do not support organism growth
  - Inherently flexible
  - do not include phthalates or other additives
- Silicone adhesives
  - Long-term adhesion
  - Promote easy and comfortable removal
- Silicone excipients
  - Increase compatibility; optimize effectiveness
  - Improve aesthetics & spreading – non-greasy, silky feel

Why Silicones in Healthcare

Host / Material Interactions



- Biodurability:
- Host has minimal adverse effect on material
- No material is suitable for every application…

  …but silicones have a strong history of stability in the body

  - PMDS is even added to increase the biodurability of other polymers such as polyurethane

- Biocompatibility:
- "The ability of a material to perform with an appropriate host response in a specific situation"
- No material is suitable for every application…

  …but silicones are often thought of as intrinsically biocompatible…

  … based on a long history of successful use in numerous applications

Black, J. (1992). *Biological Performance of Materials: Fundamentals of Biocompatibility.* Marcel Dekker, New York.
Remes, A., and Williams, D. F. (1992). Immune response in biocompatibility. *Biomaterials*, 13(11): 731. Colas, André; Curtis, Jim (2004). Biomaterials Science, Second Edition: An Introduction to Materials in Medicine. Elsevier, Academic Press

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Biocompatibility

Test	Reference Include	Purpose
Cytotoxicity (Cell Culture)	• USP<87> • ISO 10993-5	To screen for extractables that will cause cell viability changes. Direct contact effects also evaluated.
Class V (Acute systemic toxicity, Acute Intracutaneous irritation)	• USP<88> • ISO 10993-11 • ISO 10993-10 • ASTM F619, F749, F750	To evaluate the potential of extractables to cause systemic toxicity or skin reactions.
Guinea Pig Skin Sensitization	• J.Soc. Cosmet. Chem.24: 151 (1973) • ISO 10993-10; ASTM F2147	To assess the allergenic potential of a material or its extracts
Hemolysis	• ASTM F756	To assess ability of material or extracts to lyse red blood cells.
Ames (Mutagenicity/Genotoxicity)	• ISO 10993-3 • Mut Res 31:347 (1975)	To assess ability of material or extracts to cause genetic mutations.
Pyrogen	• USP<151> • ISO 10993-11	To determine potential for material extract to cause fever.
Implantation	• USP<88> • ISO 10993-6 • ASTM F763	To determine the potential of a material to cause tissue reactions and systemic toxicity after implantation.

Silicones in Medical Applications

Historical Examples		
Methylchlorosilanes	1946	hydrolysed on glass, preserving blood from clotting for many hours
Silicones	1949	most practical substance to coat needle, syringes (also less painful)
Silicone elastomers	1946	implant for bile duct repair
	1948	artificial urethra (still reported to work 14 months later - "no evidence [… of] acting as a foreign body irritant" - De Nicola)
	1956	hydrocephalus shunt (silicone sterilization)
	1960, …	numerous implants: "Swanson" joints, drains, catheters, shunts, extra corporeal circulation tubing, gel filled implants (breast, testicular), …

Silicone Elastomers

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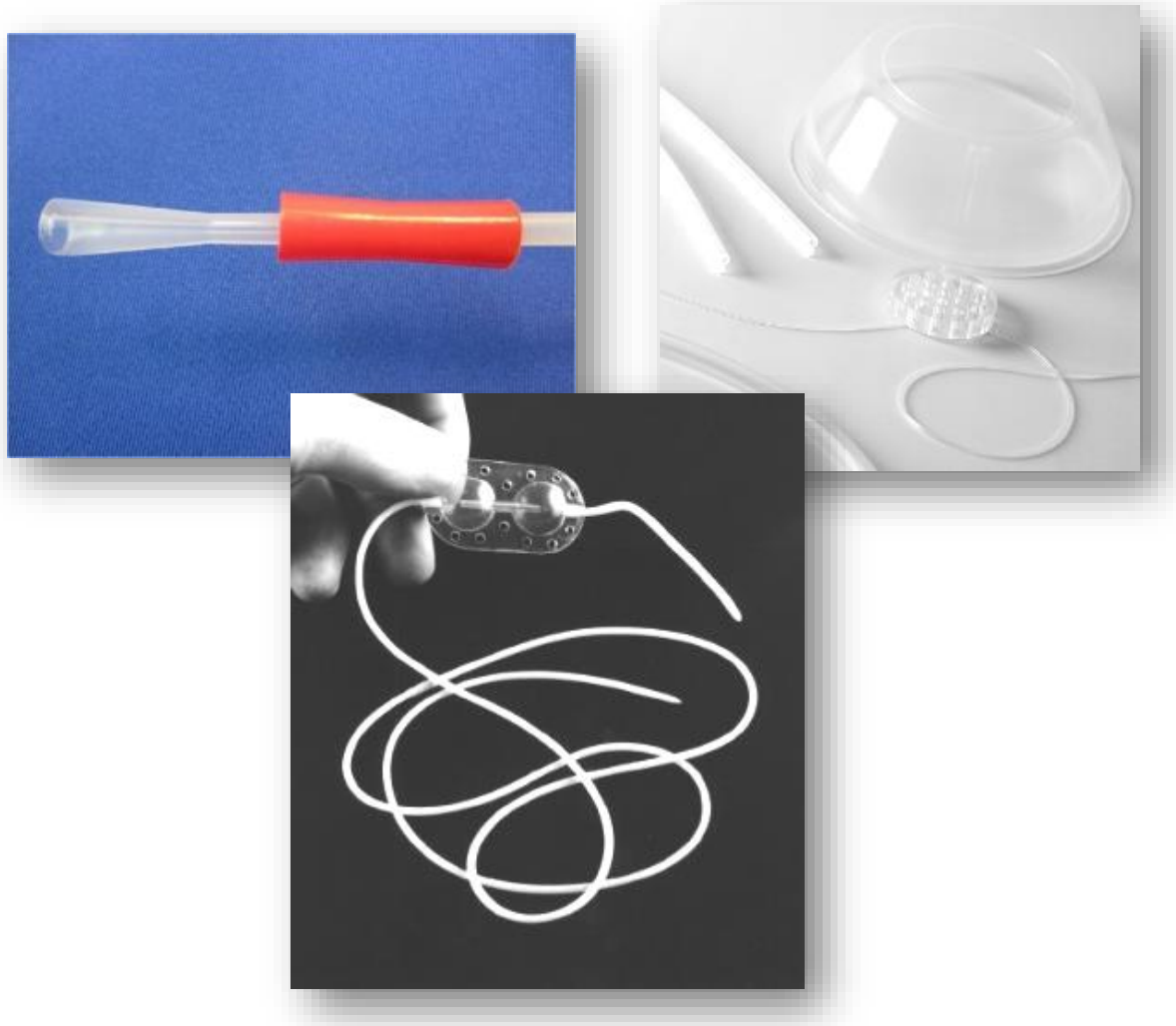
Silicone Elastomers in Medical Applications

Today

From Class I devices to Class III devices

- Thermal stability
- Chemical stability
- Electrical insulation
- High gas permeability
- Good drug permeability
- Hydrophobicity
- Biocompatibility
- Biodurablity



Silicone Elastomer Product Forms

HCR and LSR

High Consistency Rubber (HCR)

High Initial Viscosity

- Slower curing
- Good uncured strength
- Good for simple geometries

Cross-link density per area is lower than LSR

- Greater polymer flexibility when cured

Liquid Silicone Rubber (LSR)

Low Initial Viscosity

- Fast curing
- Poor uncured strength
- Good for detailed geometries

Cross-link density per area is higher than HCR

- Less polymer flexibility when cured

Liveo™ Silicone Elastomer Product Forms

HCR / LSR Overview

High Consistency Rubber (HCR)

20-80 Shore A options

Cure Type:

- Platinum Catalyzed
- Peroxide Initiated

Typical Applications for HCRs

- Extrusion
- Calendaring
- Compression Molding

Liquid Silicone Rubber (LSRs)

20-70 Shore A options

Cure Type:

- Platinum catalyzed

Typical Applications

- Liquid Injection Molding (LIM)
- Transfer Molding

It’s not a liquid in the relative sense.

It’s not easy to mix by hand, at least homogeneously

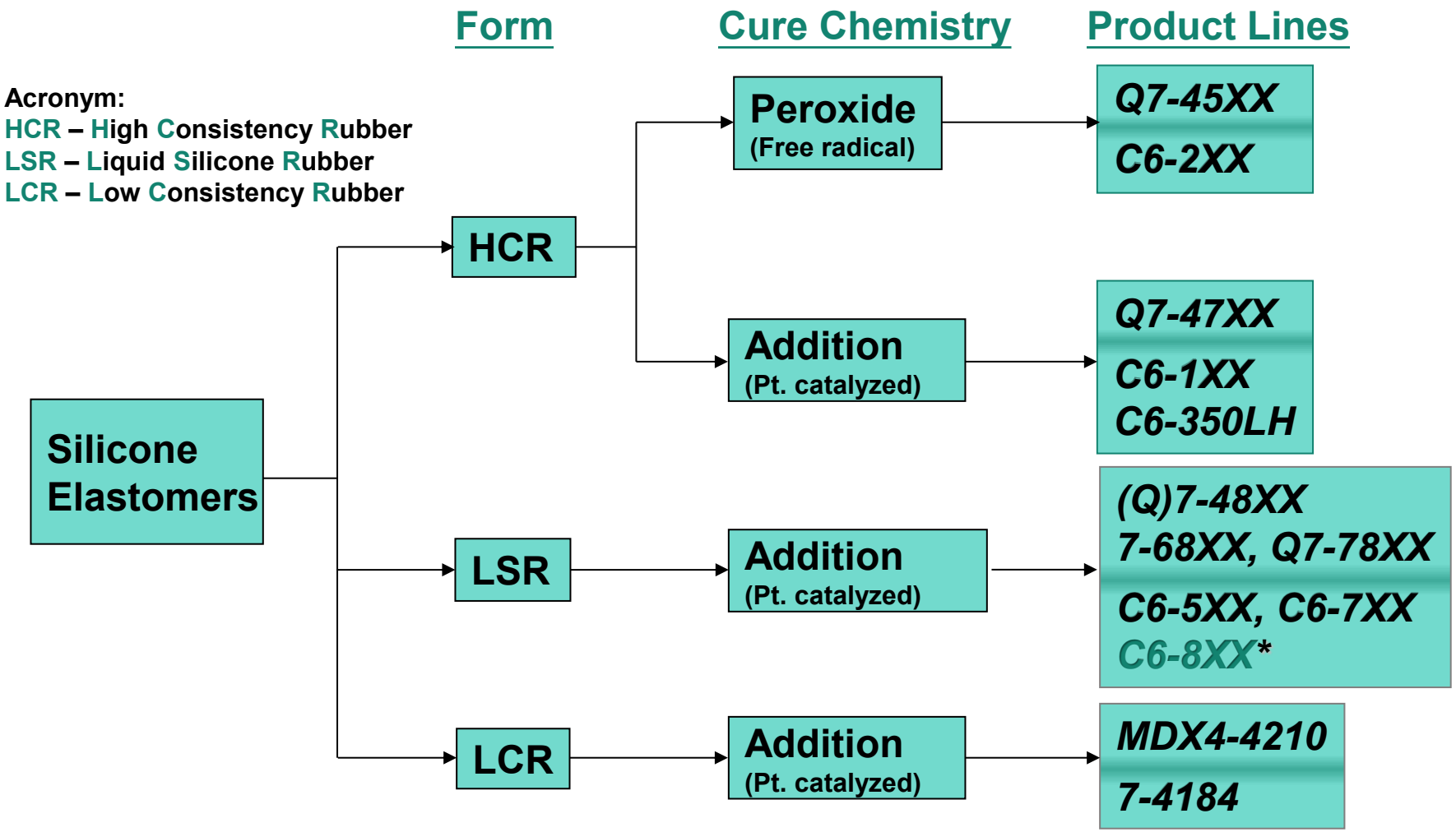
Liveo™ Silicone Elastomer Product Series

	Liveo™ C6	*Liveo*™ (Q)7 BioMedical Grade
Applications	▶ Non long-term implant ▶ Suitable for medical insert ▶ Suitable for selected short-term implant (<30 days) ▶ Suitable for non –implant ▶ Food contact application • 21 CFR 177.2600 (food grade)	▶ Long-term implant (> 30 days, indemnification needed) ▶ Suitable for medical insert ▶ Suitable for selected short-term implant (<30 days) ▶ Suitable for non –implant ▶ Food contact application • 21 CFR 177.2600 (food grade)
Quality System	▶ ISO 9001 Quality Management System ▶ Produced in GMP facility*	▶ ISO 9001 Quality Management System ▶ Produced in GMP facility*
Documentation	▶ Regulatory summary ▶ Summary of Health Data	▶ Regulatory summary ▶ Summary of Health Data ▶ EU Technical File/US Drug Master File
Testing	▶USP Class V and VI ▶Select ISO 10993 • Cytotoxicity • 30-day implant • Skin sensitization ▶Select EP 3.1.9. • Volatile matter • Substance soluble in hexane (SSH)	▶USP Class V and VI ▶Select ISO 10993 • Cytotoxicity • 30-day and 90-day implant • Hemolysis • Skin sensitization • Mutagenicity/Genotoxicity • Pyrogenicity (USP) ▶Select EP 3.1.9. • Volatile matter • Substances soluble in hexane (SSH)
Other	▶ Shore A, hardness 20-70 ▶ Liveo Healthcare Industries Materials Site (HIMS) change notification policy ▶ Manufactured at HIMS (U.S.A.)	▶ Shore A, hardness 20-70 ▶ Liveo Healthcare Industries Materials Site (HIMS) change notification policy ▶ Manufactured at HIMS (U.S.A.)

* Following principles of 21 CFR 820 (medical Device Quality system Regulation/Good Manufacturing Practices)

Liveo™ Silicone Elastomer Product Line

Overall Healthcare Material Offerings



* *Product line in development*

Liveo™ Silicone Elastomer Product Lines Highlights

Developmental Product - Liveo™ C6-8XX LSR

DuPont will supply these new materials for use in traditional healthcare short-term implant and non-implant applications.

- Short-term implant is considered anything that will reside in the body for 29 days or less. (e.g., wound drains, g-tubes)
- Insert is considered anything that is placed inside the body without any surgical incision.
- Non-implant applications (e.g., needle-less access valves)

UNDER NO CIRCUMSTANCES CAN THESE MATERIALS BE USED FOR LONG TERM IMPLANT APPLICATIONS (i.e., for Surgical Implantation ≥30 Days)

Features

- Two-part, platinum-catalyzed, heat-cured silicone elastomers
- 30-70 shore A durometer range
- Physical properties achieved as molded
- **Improved rheology for easier processing and better part to part consistently**
- **Extended mixed pot life**

Documentation & testing

- USP Class V and VI
- Select ISO 10993, including cytotoxicity (-5), 30-day implant (-6), skin sensitization (-10)
- Select European Pharmacopoeia 3.1.9, including volatile matter and substances soluble in hexane
- Manufactured in accordance with ISO 9001 standards under the principles of cGMP

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Siliconization Products

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What are the benefits of “Siliconization”?

What is **“Siliconization”**?

- Silicone materials are applied to medical parts (e.g. parenteral drug components) to **lubricate** or **hydrophobe** (water-proof) them

Siliconization **benefits** in medical and pharmaceutical applications:

- **On Glass**
  - Full drainage of the solution contained in the bottle
  - Decreased adsorption of the active
- **On Stoppers**
  - Moisture barrier at container opening
- **On Needles**
  - Reduction of penetration forces and patient pain
- **On Syringes barrel**
  - Reduction of extrusion force
- **On Urinary Catheters**
  - Reduction of risks (bacteria and incrustation)

Other suitable applications

- Process aid in assembly medical devices such as feeding parts in assembly lines
- Lubricant to perform as a mold release agent
- Lubricant/coating for medical parts, such as
  - Rubber components/stoppers
  - O-rings
  - Plastic valves
  - IV parts
  - Biopsy forceps, cutting edge
  - Cannula, Guidewires
  - Laparoscopic surgical devices
  - G.I. dilator
  - Tracheotomy kits

- Plasticizer in silicone rubber formula

How do Fluids & Dispersion compare?

	360 Fluid 100% Silicone	366 Emulsion Water Based	MDX4-4159 Solvent Dispersion
Curable coating	No	No	Yes
Dilute before use	Maybe	Yes	Yes
Apply via dip, wipe	Yes	Yes	Yes
Apply via spray	Yes	Yes	No
Sterilize coated article, not bulk	Yes	Yes	Yes
Removable from treated surface	Yes	Yes	Difficult
Use just the amount you need	Yes	Yes	Yes

Silicone Fluids

Medical vs. Industrial grade

Comparison with Pharmacopeias Monograph

Example of 1,000cSt

Characteristic	Liveo™ 360 Medical Fluid	Industrial Grade Silicone Fluid	USP Monograph Dimethicone	EP Monograph Silicone oil used as a lubricant
Identification				
Viscosity at 25°C	✓	✓	✓	✓
Infrared Absorption	✓	--	✓	✓
Colorimetric	✓	--	--	✓
Reaction of Silicates	✓	--	--	✓
Acidity	✓	✓	✓	✓
Mineral Oils	✓	--	--	✓
Phenylated Compound	.			.
Refractive Index (20°C)	✓	--	--	✓
Heavy Metals	✓	--	✓	✓
Volatile Matter/Loss on Heating	✓	✓	✓	✓
Specific Gravity	✓	✓	✓	--
Refractive Index (20°C)	✓	✓	✓	--
Bacterial Endotoxins	✓	--	✓	--
Assay	✓	--	✓	--
Appearance	✓	✓	--	--
Color APHA	✓	✓	--	--

Silicone Skin Adhesives for Medical Device Applications

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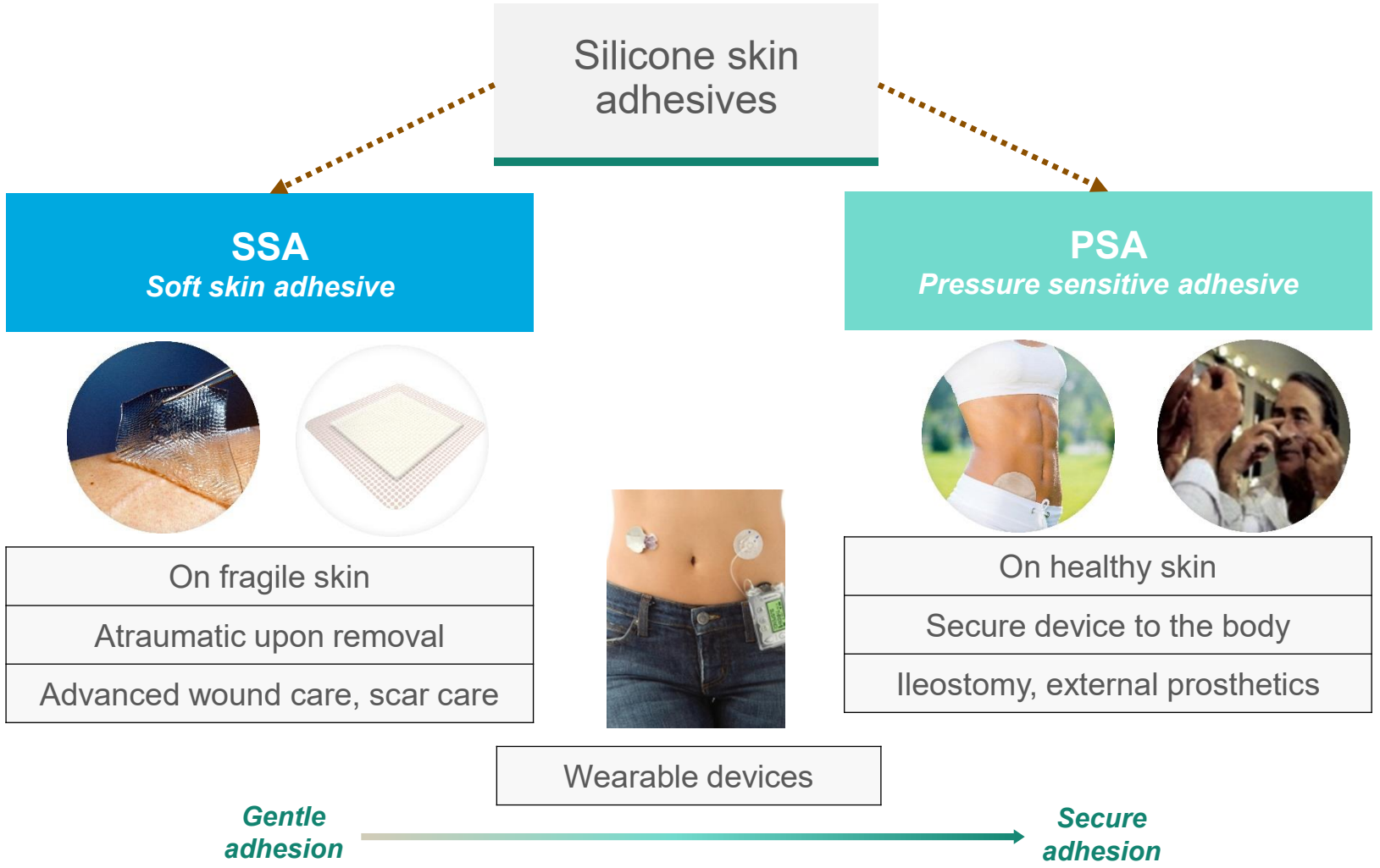
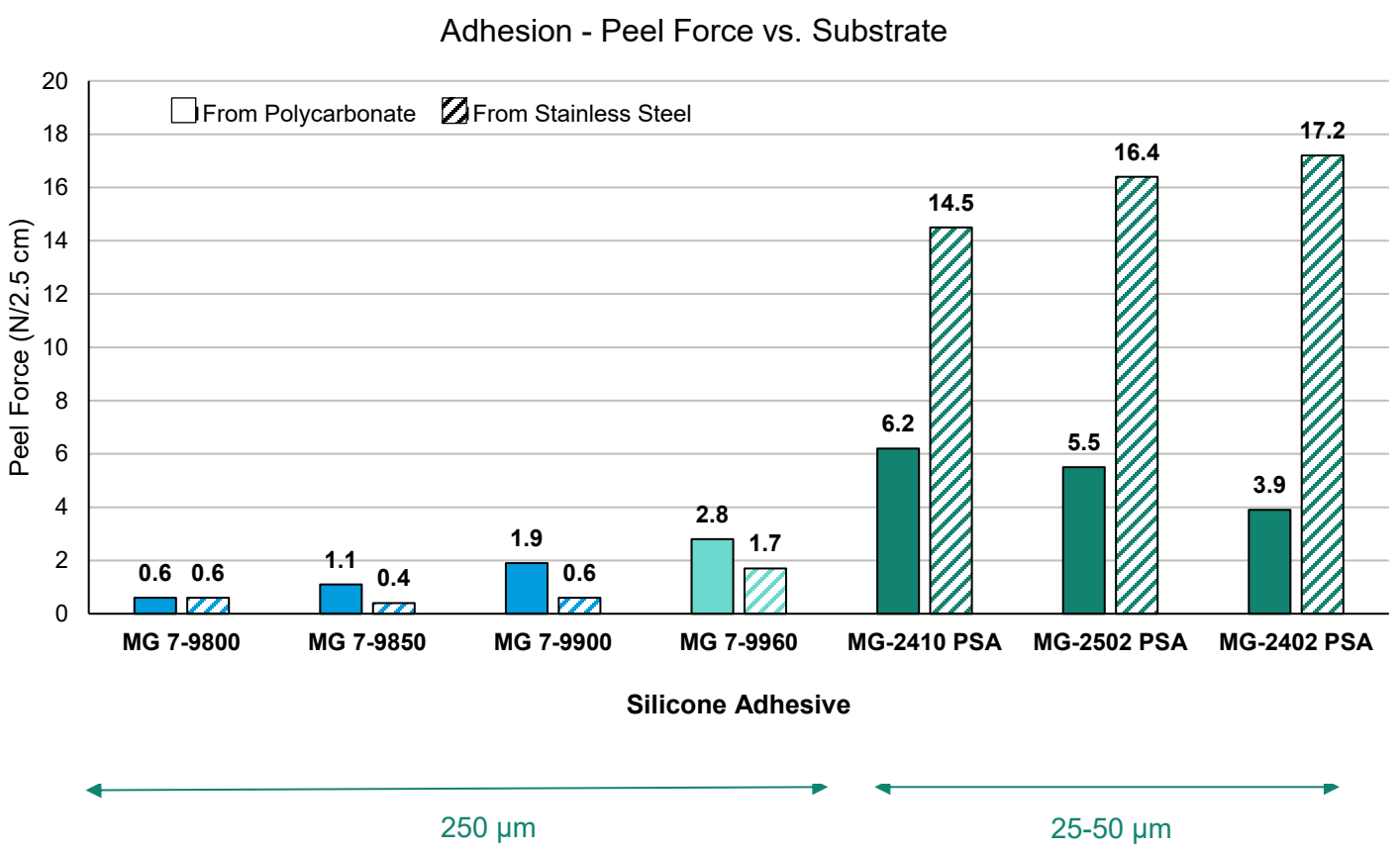
Liveo™ Silicone Skin Adhesive Technologies



- Used for many years in medical and pharmaceutical applications, especially in advanced wound care and transdermal drug delivery systems
- Recognized for quality; versatility; and aptitude to offer atraumatic removal, repositionability, reliable long-lasting adhesion and comfortable wear
- Designed to provide suitable adhesion performance for the application, plus improved patient compliance

Adhesive Properties – Peel Force

Silicone PSAs have higher peel force than silicone SSAs



TEST PRINCIPLE

Measure the force required to remove an adhesive layer from the adherent / substrate such as stainless steel or polycarbonate substrates

Higher force value indicates greater ability to hold device

Texture Analyzer TA XT Plus 180°peel

Samples construction

Adhesive coated on polyester film at defined thickness

Typical Properties of PSAs

Biocompatibility to adhesive solids

Tests	Results
Cytotoxicity (in-vitro)	No cytopathic effects
Irritation (USP intra-cutaneous test from USP biological reactivity)	Non-irritating
Sensitization	Non-sensitizing
USP Systemic Toxicity/USP biological reactivity	No difference between control and test material (30 and 90 days)
90-Day implant	Equivalent response between control and test material (30 and 90 days)
USP Pyrogen test	Met test requirements for absence of pyrogens

Summary

- DuPont™ Liveo™ uses the diversity of silicone chemistry to provide a variety of material solutions for the healthcare and medical device industry.
- The quality systems and controls at DuPont's dedicated healthcare manufacturing site help ensure material is suitable to be called "healthcare grade".
- Multiple grades and forms of silicone elastomers to provide the appropriate solution for diverse device applications.
- Siliconization products in multiple product forms for lubrication or hydrophobing purposes.
- A spectrum of silicone skin adhesives target all level of skin attachment needs.