

# DuPont Liveo™ Healthcare Grade Silicones

Eric Reynolds – Technical Service

Liveo

**DUPONT**™







# Agenda

- DuPont Healthcare Silicones
- Manufacturing/Quality Controls
- Introduction to Silicone Chemistry
- Silicone Elastomers
- Siliconization Products
- Silicone Skin Adhesives

# Blended history. Stronger chemistry.

1943



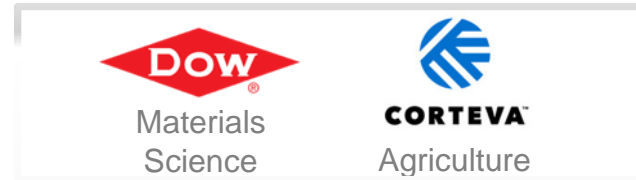
2016



2017



2019



2020



2023



 **70+** 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



Welcome to  
**HIMS**

Healthcare Industries Materials Site



# 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


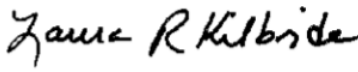
Signed CoAs

ISO9001 Certified

ISO14001 Certified

Seeking ISO13485 Certification

Date 2020-01-08 (YYYY-MM-DD) Time 06:27:27 (Greenwich Mean Time) Page 2 of 2

		SULLY DIAZ AUTOPISTA A MEDELLIN CALLE 80 CUNDINAMARCA CUN 250017 CO Ship From: SHEPHERDVILLE DPS Whse SHEPHERDVILLE Kentucky, United States	
DDP SPECIALTY ELECTRONIC MATERIALS US 9, LLC			
Appearance off-white, homogeneous liquid no dark particulate contamination		Pass	
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 Kilbride Quality Manager For inquiries please contact Customer Service or local sales © Trademark of affiliates of DuPont de Nemours, Inc.			

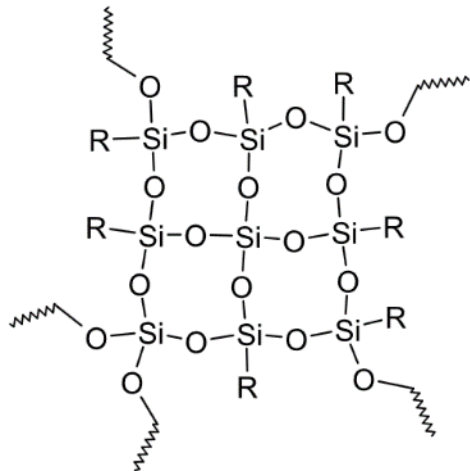
# Introduction to Silicone Chemistry

# Basic Silicone Chemistry

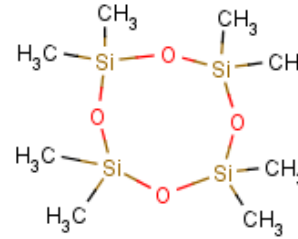
## Chemistry and Forms

- Si - (O - Si)<sub>n</sub> - O - Si -

Polysiloxane: liquid, solid, gum

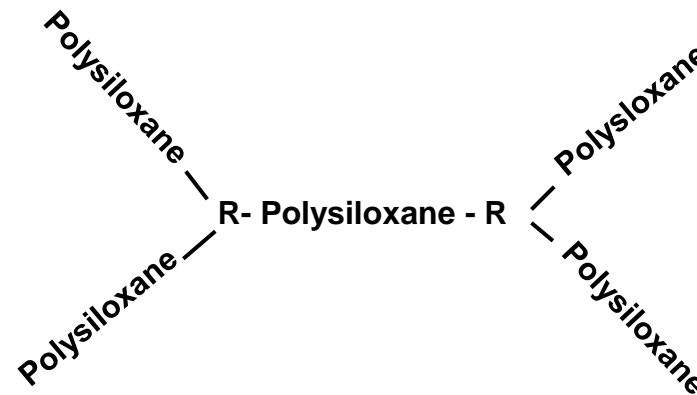


Silicone resin



Cyclosiloxane:

above 3 SiO units, liquid



Branched Siloxanes

Elastomers

Gels

Adhesives

Fluids

Greases

Lubricating coatings

Hydrophobic coatings

Wetting Agents

Antifoams

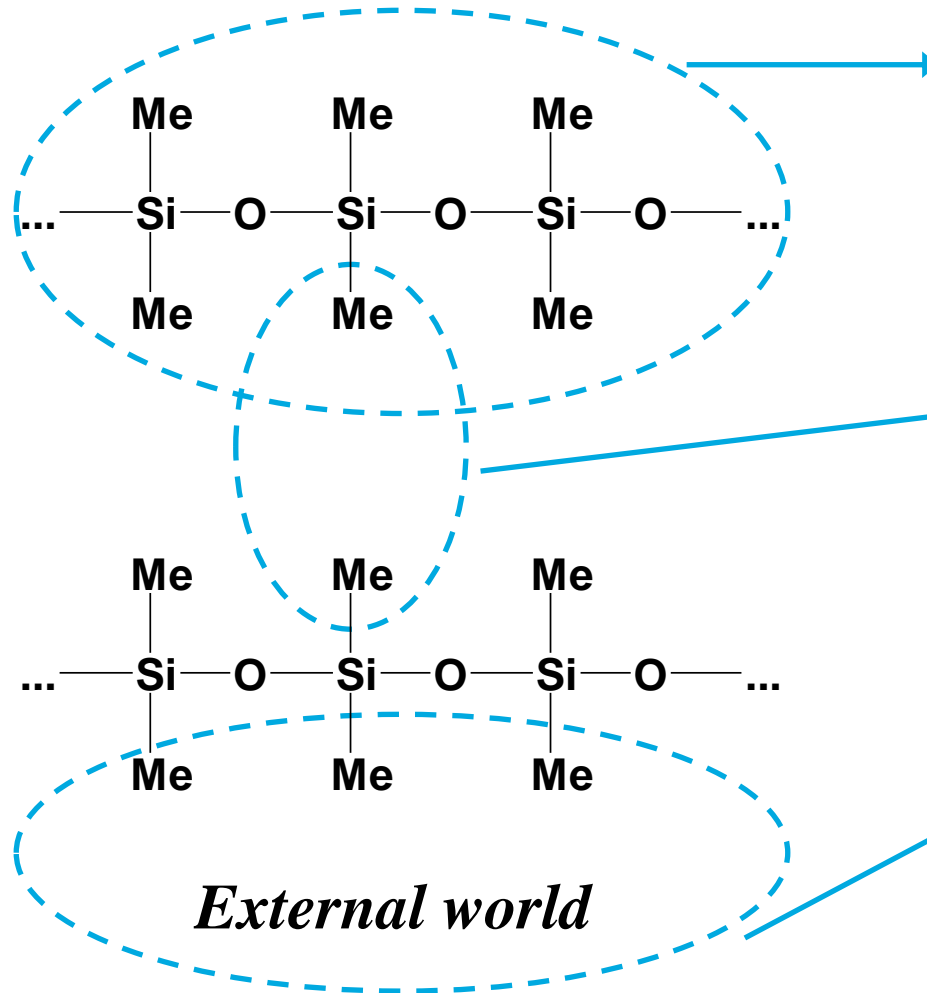
Solvents

Additives

Sealants

# Basic Silicone Chemistry

## Properties



1. Intramolecular properties:
  - strong covalent bonds
  - polar chain but flexible/hydrophobic  
(stable polymer, no stabilizers)
2. Intermolecular interactions:
  - low Me/Me interactions  
(high permeability)
  - low Tg (- 127 oC)  
(pliable at RT)
3. Interactions with living tissues:
  - low level of interactions  
(biocompatibility)



# Basic Silicone Chemistry

## Biocompatibility

Test	Reference Include	Purpose
<b>Cytotoxicity (Cell Culture)</b>	<ul style="list-style-type: none"> <li>• USP&lt;87&gt;</li> <li>• ISO 10993-5</li> </ul>	To screen for extractables that will cause cell viability changes. Direct contact effects also evaluated.
<b>Class V (Acute systemic toxicity, Acute Intracutaneous irritation)</b>	<ul style="list-style-type: none"> <li>• USP&lt;88&gt;</li> <li>• ISO 10993-11</li> <li>• ISO 10993-10</li> <li>• ASTM F619, F749, F750</li> </ul>	To evaluate the potential of extractables to cause systemic toxicity or skin reactions.
<b>Guinea Pig Skin Sensitization</b>	<ul style="list-style-type: none"> <li>• J.Soc. Cosmet. Chem.24: 151 (1973)</li> <li>• ISO 10993-10; ASTM F2147</li> </ul>	To assess the allergenic potential of a material or its extracts
<b>Hemolysis</b>	<ul style="list-style-type: none"> <li>• ASTM F756</li> </ul>	To assess ability of material or extracts to lyse red blood cells.
<b>Ames (Mutagenicity/Genotoxicity)</b>	<ul style="list-style-type: none"> <li>• ISO 10993-3</li> <li>• Mut Res 31:347 (1975)</li> </ul>	To assess ability of material or extracts to cause genetic mutations.
<b>Pyrogen</b>	<ul style="list-style-type: none"> <li>• USP&lt;151&gt;</li> <li>• ISO 10993-11</li> </ul>	To determine potential for material extract to cause fever.
<b>Implantation</b>	<ul style="list-style-type: none"> <li>• USP&lt;88&gt;</li> <li>• ISO 10993-6</li> <li>• ASTM F763</li> </ul>	To determine the potential of a material to cause tissue reactions and systemic toxicity after implantation.

# Silicones in Medical Applications

Historical Examples		
<b>Methylchlorosilanes</b>	1946	hydrolysed on glass, preserving blood from clotting for many hours
<b>Silicones</b>	1949	most practical substance to coat needle, syringes (also less painful)
<b>Silicone elastomers</b>	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

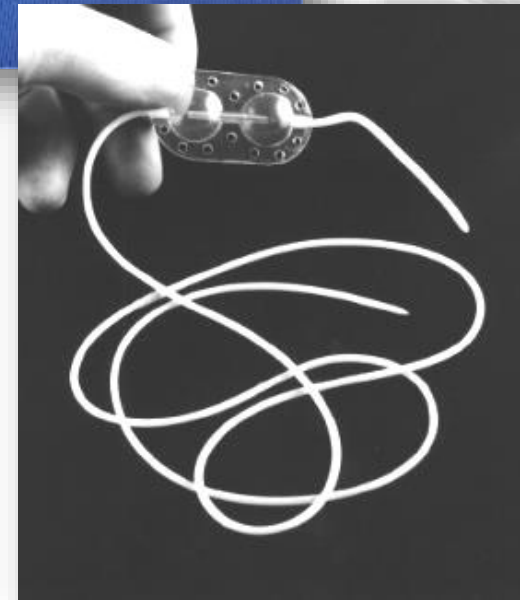
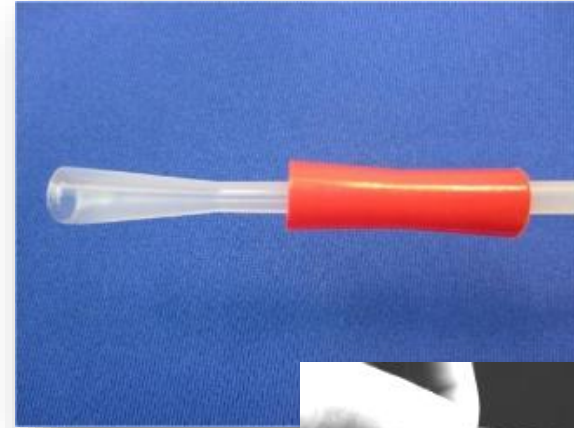


# Silicone Elastomers in Medical Applications

Today

From Class I devices to Class III devices

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



# Product Forms

## Overview

### High-consistency silicone rubber (HCRs)

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



# Product Forms

## How is an LSR Different from an HCR?

### 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

### LSR

Low Initial Viscosity

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

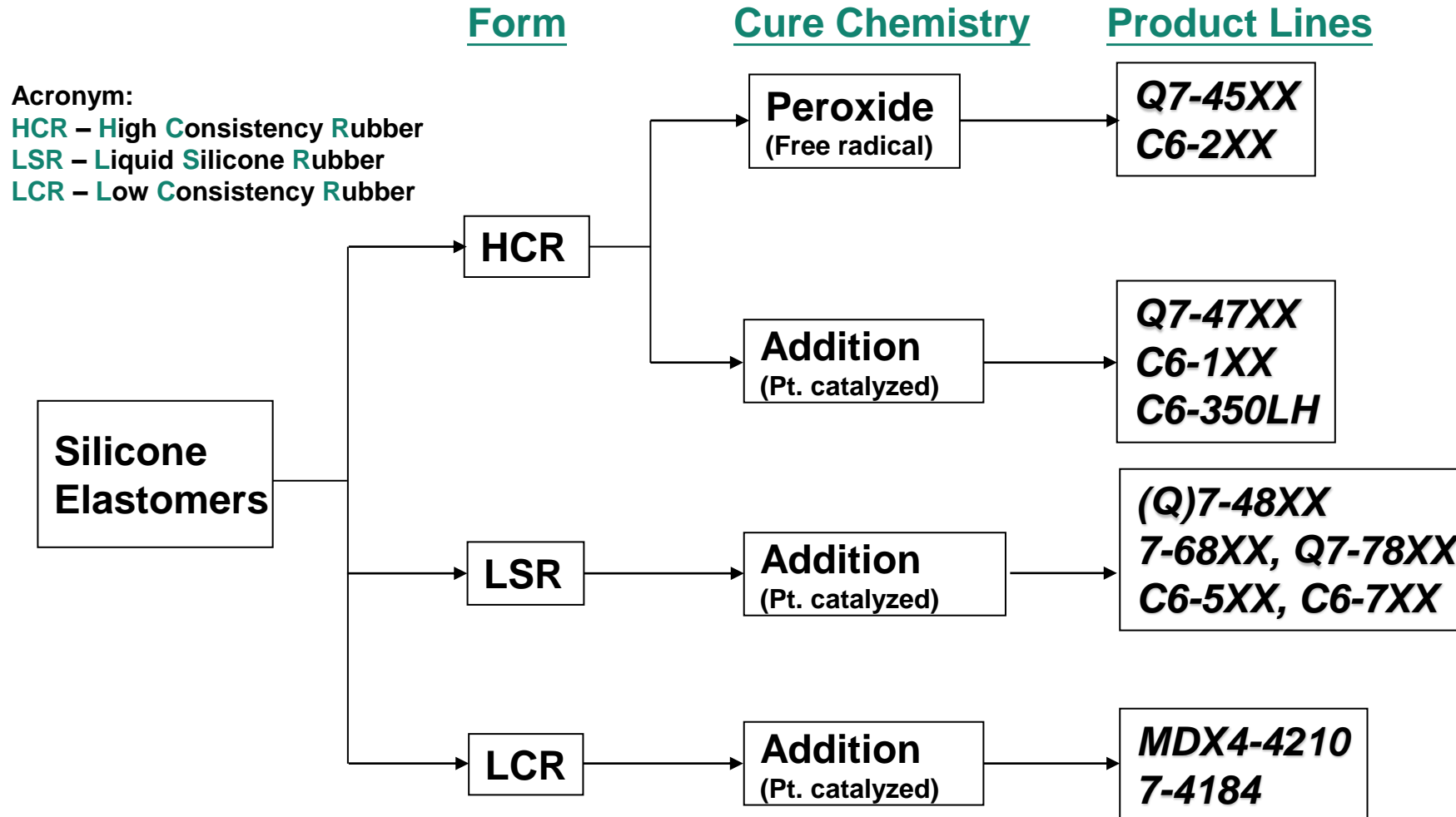
Cross-link density per area is higher than HCR

- Less polymer flexibility when cured



# Silicone Elastomer Product Line

## Overall Healthcare Material Offerings



# Liveo™ Elastomer Product Series

	Liveo™ C6	Liveo™ BioMedical Grade
Applications	<ul style="list-style-type: none"> <li>▶ Non long-term implant</li> <li>▶ Suitable for medical insert</li> <li>▶ Suitable for selected short-term implant (&lt;30 days)</li> <li>▶ Suitable for non –implant</li> <li>▶ Food contact application                             <ul style="list-style-type: none"> <li>• 21 CFR 177.2600 (food grade)</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>▶ Long-term implant (&gt; 30 days, indemnification needed)</li> <li>▶ Suitable for medical insert</li> <li>▶ Suitable for selected short-term implant (&lt;30 days)</li> <li>▶ Suitable for non –implant</li> <li>▶ Food contact application                             <ul style="list-style-type: none"> <li>• 21 CFR 177.2600 (food grade)</li> </ul> </li> </ul>
Quality System	<ul style="list-style-type: none"> <li>▶ ISO 9001 Quality Management System</li> <li>▶ Produced in GMP facility*</li> </ul>	<ul style="list-style-type: none"> <li>▶ ISO 9001 Quality Management System</li> <li>▶ Produced in GMP facility*</li> </ul>
Documentation	<ul style="list-style-type: none"> <li>▶ Regulatory summary</li> <li>▶ Summary of Health Data</li> </ul>	<ul style="list-style-type: none"> <li>▶ Regulatory summary</li> <li>▶ Summary of Health Data</li> <li>▶ EU Technical File/US Drug Master File</li> </ul>
Testing	<ul style="list-style-type: none"> <li>▶ USP Class V and VI</li> <li>▶ Select ISO 10993                             <ul style="list-style-type: none"> <li>• Cytotoxicity</li> <li>• 30-day implant</li> <li>• Skin sensitization</li> </ul> </li> <li>▶ Select EP 3.1.9.                             <ul style="list-style-type: none"> <li>• Volatile matter</li> <li>• Substance soluble in hexane (SSH)</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>▶ USP Class V and VI</li> <li>▶ Select ISO 10993                             <ul style="list-style-type: none"> <li>• Cytotoxicity</li> <li>• 30-day and 90-day implant</li> <li>• Hemolysis</li> <li>• Skin sensitization</li> <li>• Mutagenicity/Genotoxicity</li> <li>• Pyrogenicity (USP)</li> </ul> </li> <li>▶ Select EP 3.1.9.                             <ul style="list-style-type: none"> <li>• Volatile matter</li> <li>• Substances soluble in hexane (SSH)</li> </ul> </li> </ul>
Other	<ul style="list-style-type: none"> <li>▶ Shore A, hardness 20-70</li> <li>▶ Liveo Healthcare Industries Materials Site (HIMS) change notification policy</li> <li>▶ Manufactured at HIMS (U.S.A.)</li> </ul>	<ul style="list-style-type: none"> <li>▶ Shore A, hardness 20-70</li> <li>▶ Liveo Healthcare Industries Materials Site (HIMS) change notification policy</li> <li>▶ Manufactured at HIMS (U.S.A.)</li> </ul>

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

# Siliconization Products



# 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?

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

# Silicone Fluids

## Medical vs. Industrial grade

### Comparison with Pharmacopeias Monograph

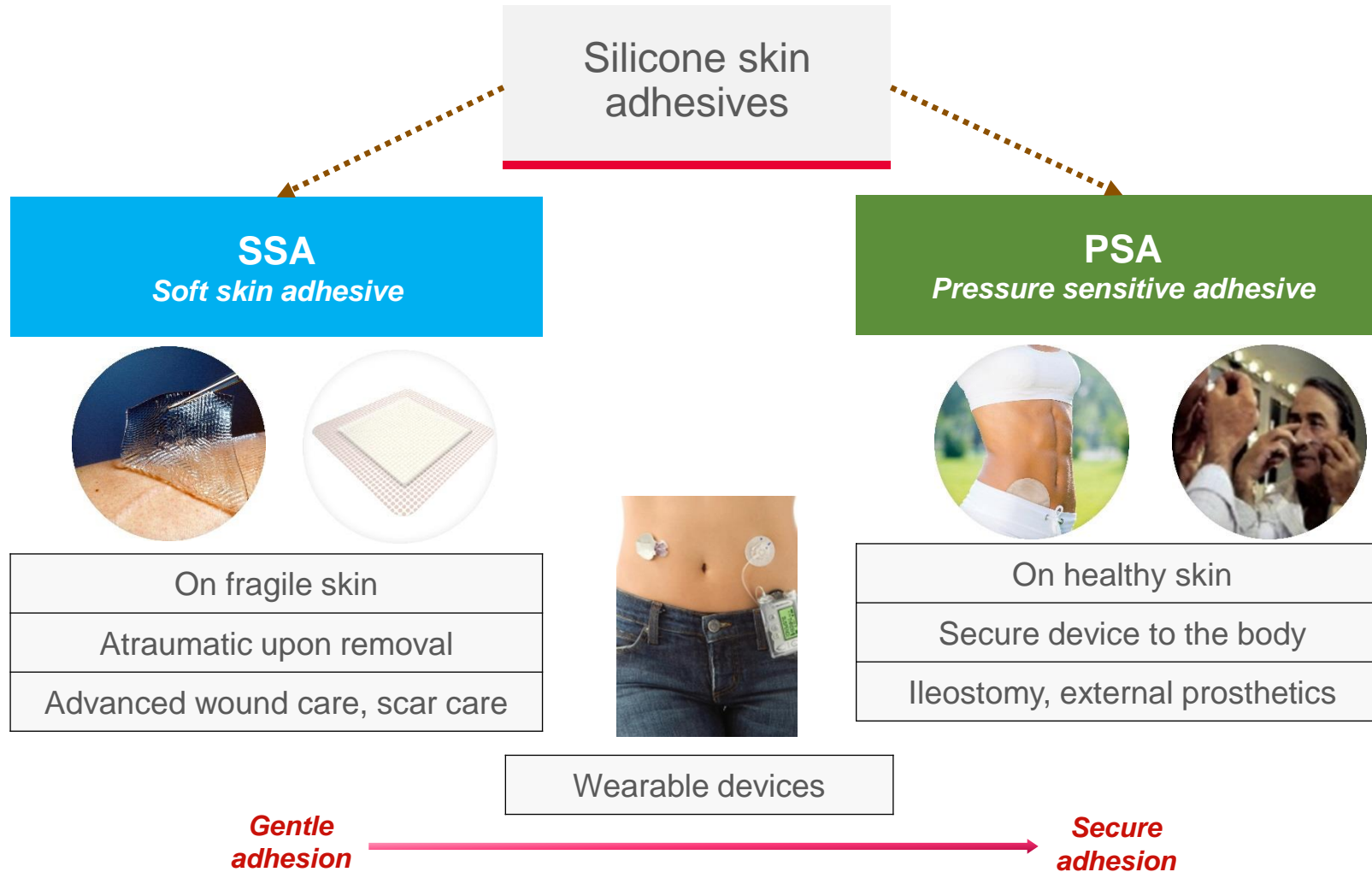
#### Example of 1,000cSt

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

# Silicone Skin Adhesives for Medical Device Applications

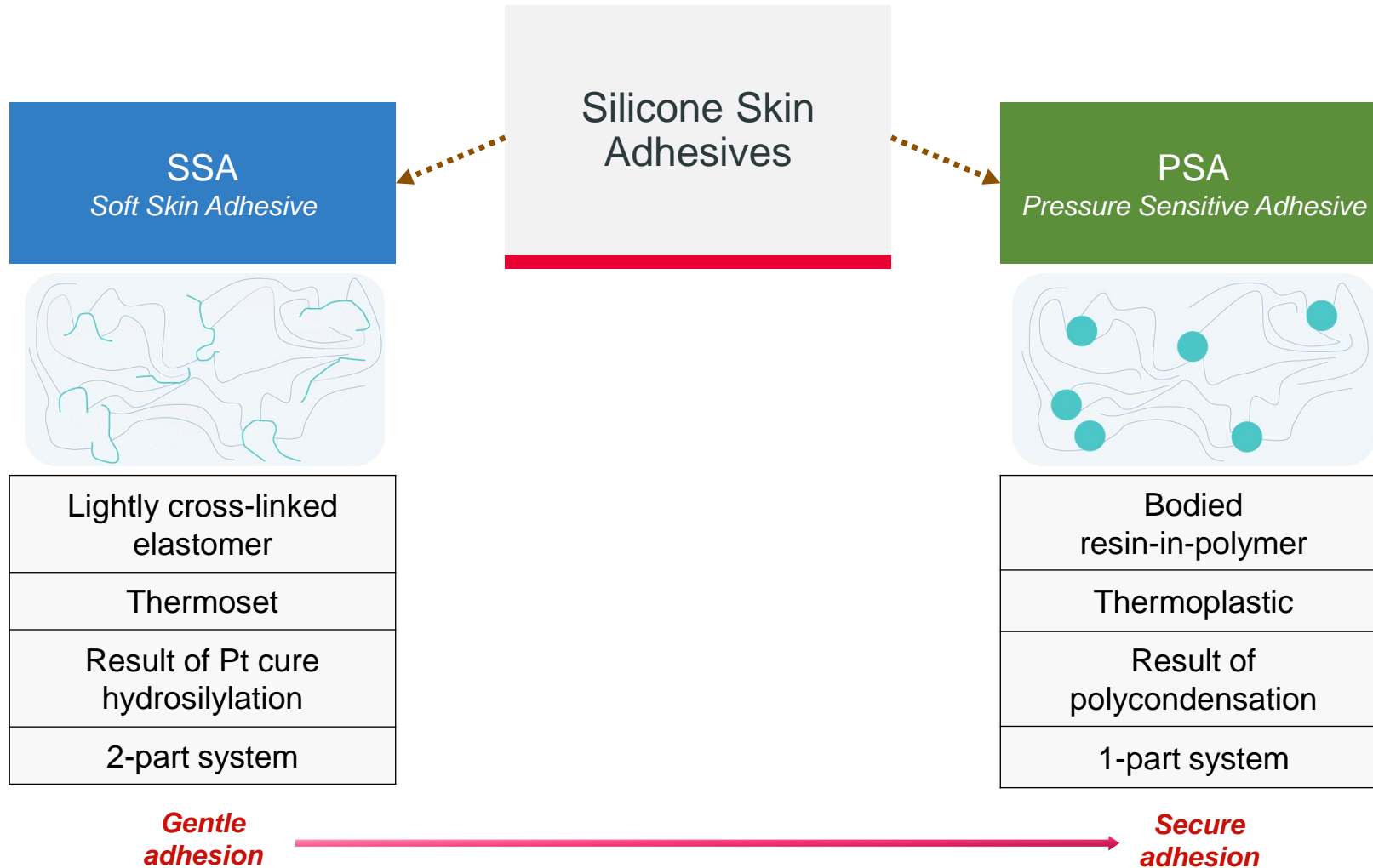


# DuPont™ Liveo™ Silicone Skin Adhesive technologies



- 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

# A range of silicone skin adhesives – Chemical structure

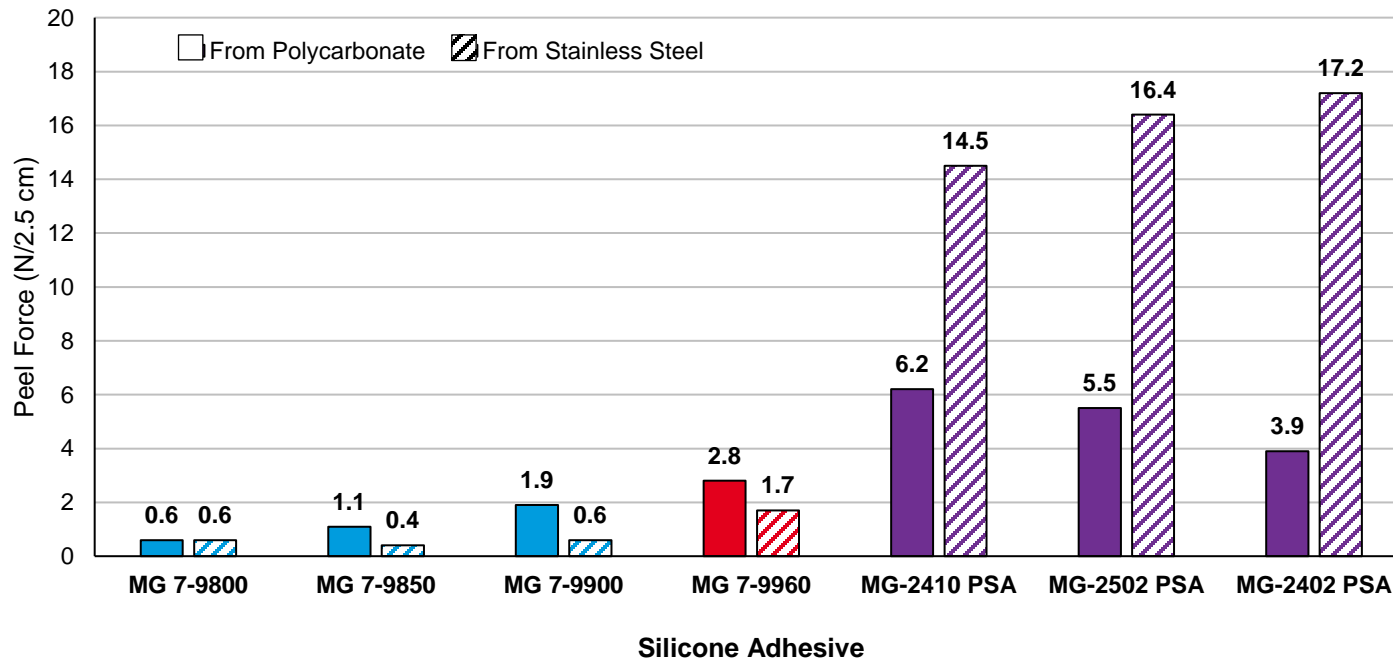




# Adhesive Properties – Peel Force

Silicone PSAs have higher peel force than silicone SSAs

Adhesion - Peel Force vs. Substrate



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.





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