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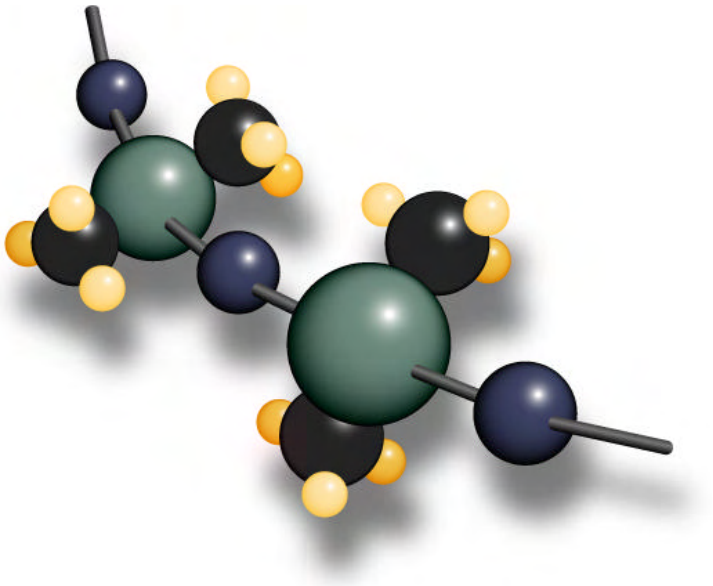

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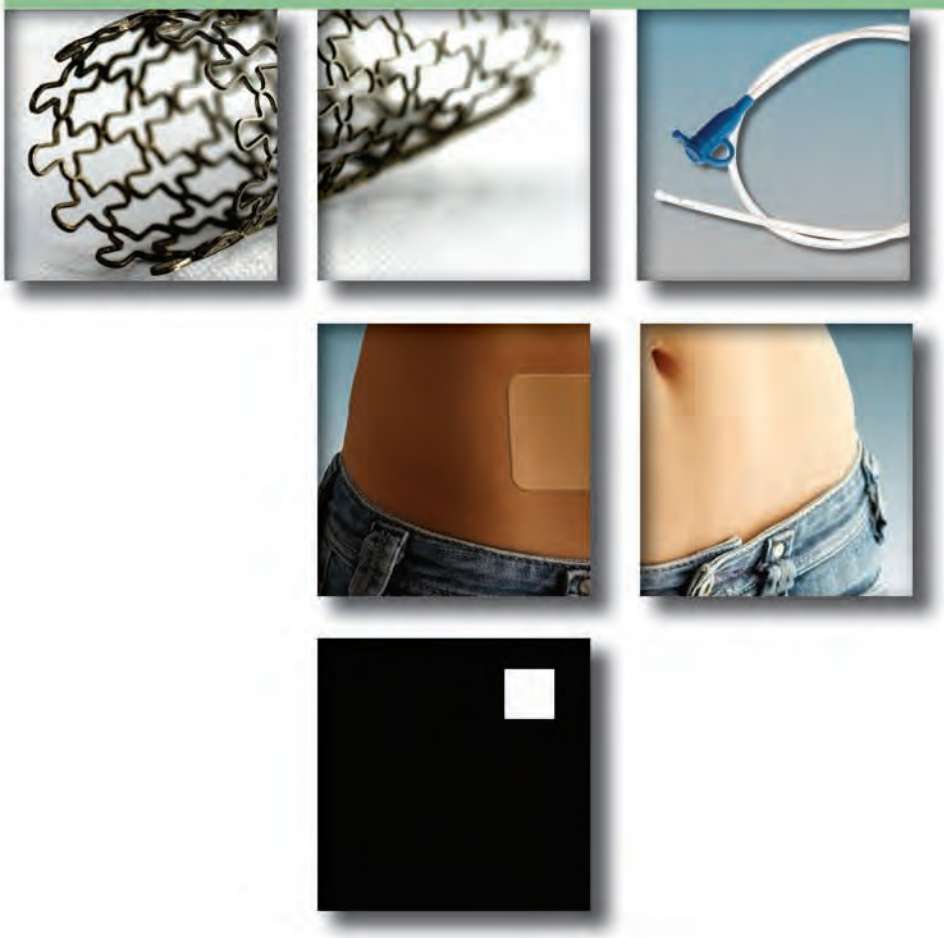
NuSil SILICONE TECHNOLOGY

Creative Partners in a Material World

Drug Delivery Materials Selection Guide



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As the global leader in the formulation, manufacture and regulatory support of silicones for the healthcare industry, NuSil Technology offers multiple solutions for combination product designers and engineers. For over 30 years, NuSil has developed a reputation for high-quality products, value-added customer service, and comprehensive regulatory support for silicones supplied to the drug delivery and combination medical device industry.

COMBINATION PRODUCT CHALLENGES

Designers and engineers looking to combine an API into a silicone matrix for combination devices may be faced with a variety of challenges. These challenges may include:

- Preserving mechanical properties of the device
- Compatibility of silicone cure chemistry and API stability
- Maintaining process-ability with fabrication method (molding, extruding, etc.)
- Verifying content uniformity of API in silicone
- Achieving prescribed dose delivery rate and end point

Once a candidate API is selected for an application, engineers must identify a partner that can address these challenges by providing a drug delivery silicone system. This system must allow for the production of combination devices featuring controlled release rates tested per GLP and manufactured in accordance with Pharmaceutical cGMP.

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COMBINATION PRODUCT SOLUTIONS

NuSil offers a complete product line of silicone systems for use in drug delivery. Additionally, NuSil is capable of formulating, validating, manufacturing, testing and providing regulatory support for a custom product designed to achieve customer-defined, application-specific physical, mechanical and elution properties.

Core Competencies and Resources:

- **Material Design**
  - **Chemistry** – Experts in formulating silicone from the manufacture of raw materials to the delivery of finished goods.
  - **Custom Formulation** – Custom silicone formulations designed with required cure profiles to accommodate environmental sensitivities of APIs.
  - **Compounding** – Extensive experience compounding APIs into silicones

- **Controlled Manufacturing Facilities** – Class 100,000 - 10,000 clean room facilities dedicated to API compounding and packaging.

- **Testing** – Comprehensive analytical capabilities utilizing validated test methods to certify drug elution rates, content uniformity, and drug degradation in accordance with GLP and analytical requirements of a pharmaceutical component.

- **Regulatory Support** – Drug Master File (DMF) submissions with U.S. FDA and international regulatory authorities.

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MATERIAL DESIGN

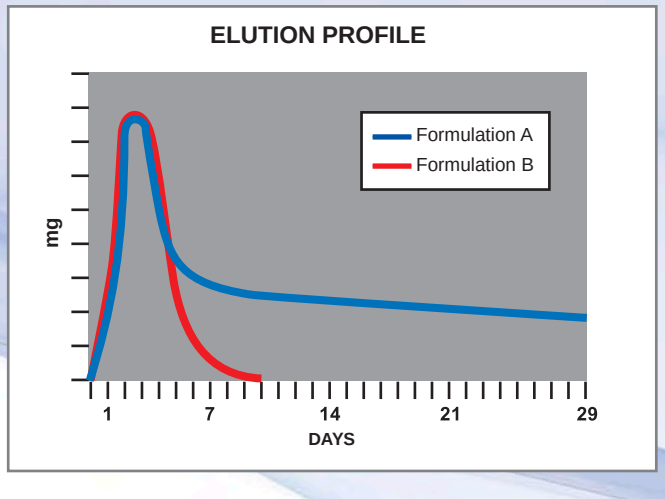
Chemistry

NuSil is a vertically integrated silicone formulator. We design and manufacture our own polymers, crosslinkers, catalysts, cyclics and silanes to produce Fluids, Gels, Adhesives and Elastomers. This competency allows us to adjust silicone properties in order to optimize process-ability, mechanical characteristics and/or drug elution rates.

Custom Formulation

NuSil is capable of formulating silicone elastomers with a variety of excipient compounds and other additives to achieve a targeted drug release profile. Custom formulations are designed to ensure the stability and integrity of the API within its certified shelf-life.

The following elution profile models two distinctively different API release rates – each of which can be achieved by modifying the silicone:API formulation in order to deliver the specified API elution rate.



Compounding

NuSil has years of experience handling APIs and compounding with a wide variety of excipients at scales ranging from 50ml kits to 55 gallon drums.

CONTROLLED MANUFACTURING FACILITIES

NuSil has invested in multiple facility expansions to accommodate the growing demand for silicones compounded with APIs. Located at NuSil's global headquarters in Carpinteria, CA, these facilities are environmentally controlled up to Class 10,000 and registered with the United States FDA and the California Department of Public Health as drug manufacturing establishments.

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TESTING

In accordance with GLP and the analytical requirements of a pharmaceutical component, NuSil's in-house laboratories can perform the following verification analysis on each lot of a custom formulation:

- Identity Testing
- Mechanical & Chemical
- Elution Rate

As part of the validation of each custom formulation, NuSil's in-house laboratories can perform the following qualification tests:

- Content uniformity
- API degradation
- Shelf life stability

NuSil's validated elution test methods quantify API elution rates from a cured silicone matrix. Elution rates can be measured in various liquid media which model end use environment.

Using state-of-the-art analytical equipment, NuSil is able to identify and assay a wide range of API compounds eluted from cured silicones. NuSil can qualitatively and quantitatively report API purity and stability.

REGULATORY SUPPORT

NuSil maintains Drug Master Files (DMFs) with the United States FDA, and other international regulatory authorities. NuSil's DMFs provide agency reviewers access to NuSil's proprietary product formulations, manufacturing processes, and material testing data.

NuSil is committed to providing our customers with the required regulatory submissions and knowledge to allow for successful device approval.

Quality System in Accordance with:

- ISO 9001-certified since 1994
- 21 CFR Part 210/211 cGMP for Finished Pharmaceuticals
- ICH Q7 GMP for Active Pharmaceutical Ingredients
- IPEC GMP for Pharmaceutical Excipients

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Product Name	Comments	Cure System	Appearance	Viscosity	Work Time	Cure Time	Specific Gravity	Durometer	Tensile	Elongation
Unrestricted Drug Delivery Silicones										
DDU-310	**Fluid**	Non-Curing	Translucent	-	-	-	0.97	-	-	-
DDU-4330	**Low Consistency Elastomer**	Platinum	Translucent Gray	115,000	-	Cure: 3 minutes @ 150°C Post Cure: 1 hour @ 150°C. Stabilized for a minimum of 3 hours	1.09	25 (Type A)	700	525%
DDU-4340	**Low Consistency Elastomer**	Tin-Alkoxy	Gray to Tan	-	9 min	30 minutes @ 23°C (73°F). Stabilize for 24 hours minimum @ ambient temp. and humidity	1.14	50 (Type A)	550 (3.8)	175%
DDU-4351	**Gel**	Tin-Alkoxy	Translucent	10,000	40 min	30 minutes @ 23°C (73°F). Stabilize for 24 hours @ ambient temp and humidity	0.98	75 (000)	70 (0.50)	120%
DDU-4630	**HCR** Plasticity: 75 mil (1.9 mm)	Platinum	Translucent, pale tan	-	2.5 hours	10 minutes @ 116°C. Stabilized for a minimum of 24 hours	1.11	35 (Type A)	1500 (10.3)	1000%
Restricted Drug Delivery Silicones										
DDR-1370	**Pressure Sensitive Adhesive:** Non Volatile Content: 65%; Release Force: 11 ppi (1.9kN/m); Blunt Probe Test: 1.5 lbs	Non-Curing	Translucent	1,450	-	-	-	-	-	-
DDR-4355	**Gel** Penentration: 5mm	Platinum	Transparent	15,000	-	3 hours @ 60°C (140 °F)	-	-	-	-

Properties tested on a lot-to-lot basis. Do not use the typical properties shown in this table as a basis for preparing specifications.
Please contact NuSil Technology for assistance and recommendations in establishing particular specifications.

UNRESTRICTED DRUG DELIVERY SILICONES

NuSil Technology's unrestricted materials may be considered for long-term implant applications (greater than 30 days). It is the responsibility of the device manufacturer to determine the safety and efficacy of the device and the materials used in that device.

RESTRICTED DRUG DELIVERY SILICONES

NuSil Technology's restricted materials may be considered for use in short-term implant applications (29 days or less) or for external applications. It is the responsibility of the device manufacturer to determine the safety and efficacy of the device and the materials used in that device.

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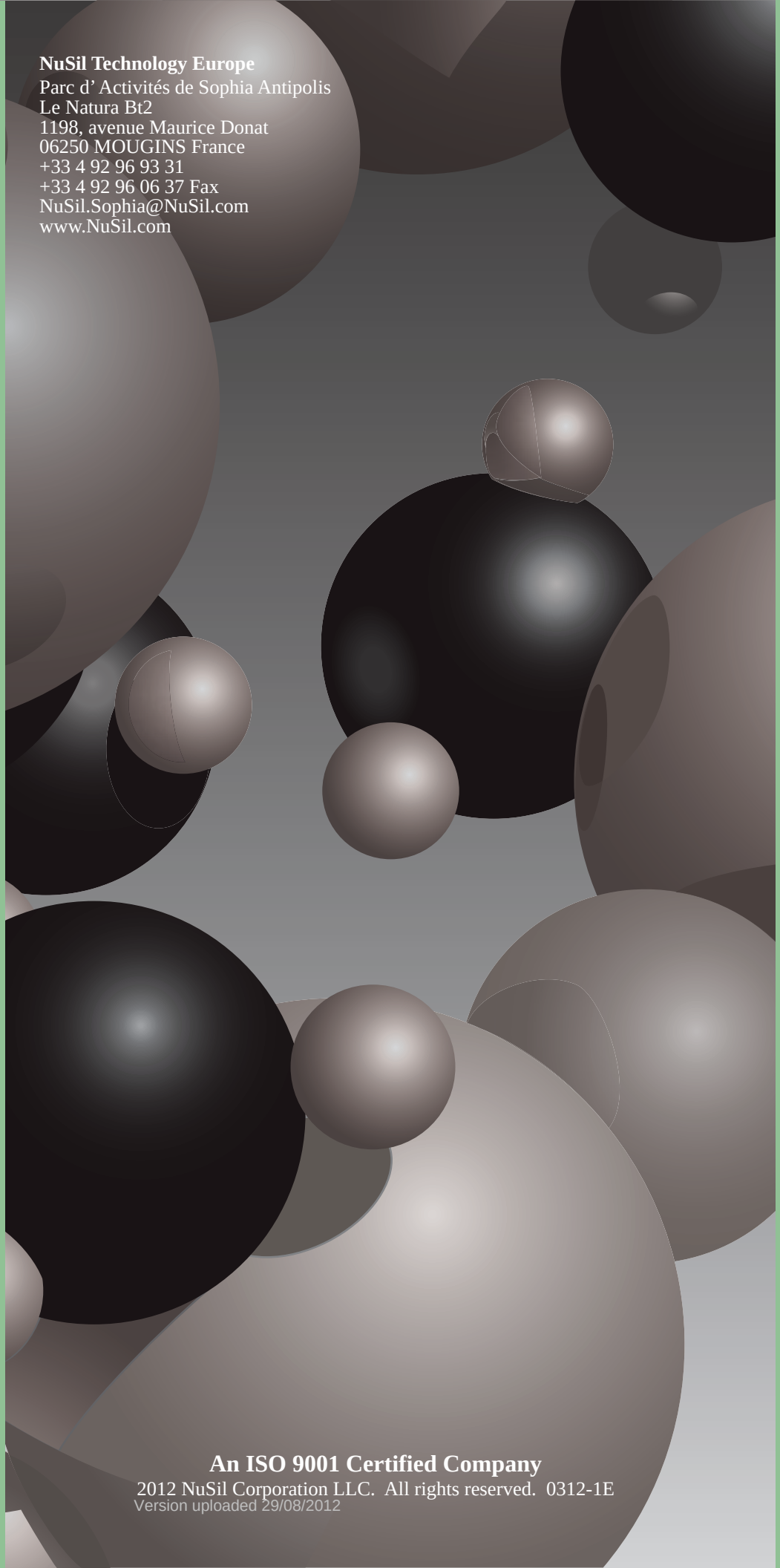

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