

THE USE OF IMPLANTABLE SILICONE IN MEDICAL DEVICES



THE GROWTH IN DEMAND FOR MEDICAL-GRADE SILICONE

After more than 50 years of using silicone rubber in medical implants, the number of applications for the material's use in both short- and long-term implantable medical devices just keeps growing. With its long track record of biocompatibility, medical-grade silicone is being used in a range of implantable devices with critical functions, such as defibrillators, heart pumps and surgical reconstructive components.

In using silicone in implantable devices, sourcing the silicone is only the first step in ensuring its purity. Medical device manufacturers need to understand how the silicone is handled and processed in the production of molded parts to ensure its quality.

This e-book provides an overview of the **characteristics** of implantable silicone, its **uses** in medical devices, the compounding and molding **processes** involved, the **science** behind medical-grade silicone, and the overriding importance of **patient safety**.

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THE RISE OF SILICONE USE IN IMPLANTABLE DEVICES

The first use of silicone as a material implanted in the human body for medical treatment is said to date back to 1946, when surgeon Dr. Frank Lahey used silicone for bile duct repair. Since the early success with experiments with such uses as tubing for urethra replacements and hydrocephalus shunts, silicone has been employed in a wide variety of medical applications and implantable devices, such as orthopedic joint implants, pacemakers, and neurostimulators.

Silicone's biocompatibility and stability when implanted within the human body for short-term or long-term applications have made it a highly popular material for medical devices.

In the 1990s, silicone breast implants were blamed for causing medical issues and lawsuits were filed against silicone suppliers, which led the United States Food and Drug Administration (FDA) to halt the use of silicone in long-term implants for years and resulted in the bankruptcy filing of one of silicone's pioneers, Dow Corning. However, after numerous clinical studies failed to detect a causal link between silicone and secondary health issues, the use of implantable silicone quickly made a comeback. Silicone's biocompatibility and stability when implanted within the human body for short-term or long-term applications have made it a highly popular material for medical devices.

According to market researchers The Freedonia Group, "U.S. demand for biocompatible materials is forecast to increase 4.9 percent annually to \$5.6 billion in 2018. Reflecting quality, performance, and cost advantages in a broad range of applications, synthetic polymers will remain the dominant-selling product group." In its report, Biocompatible Materials, Freedonia forecasts, "Engineered resins – especially thermoplastic elastomer, silicone, sulfone, and polyketone materials – will command the fastest revenue and volume growth based on quality and safety advantages in high value-added catheters and implants."

DIFFERENCES IN MEDICAL-GRADE AND IMPLANTABLE SILICONE MATERIALS

Manufacturers of medical-grade silicone have advanced the science of silicone formulation and testing to meet stringent regulations and biocompatibility standards, allowing silicone to be incorporated into the most advanced device technologies for medical treatment.

For long-term implantable devices, the U.S. Food and Drug Administration requires that the silicone be tested and supported with biological, physical and chemical testing to be considered for use in the human body for more than 29 days. In practice, implantable silicone may last inside the human body for a lifetime. Only a handful of suppliers offer long-term implantable silicone. NuSil, which is considered the industry leader, along with Applied Silicone, work directly with OEMs and the network of fabricators to ensure the correct silicone is chosen for any given application.

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According to Julie Harber, NuSil's senior technical sales representative for its medical implant line of silicone, what differentiates medical-grade silicone for long-term implants, short-term implants or skin contact applications are the differences in the level of testing and support.

She explains that medical grade silicones are manufactured under strict quality standards that follow ISO 9001 and are either directly or indirectly regulated by the FDA.

Biocompatibility Testing

After the lawsuits involving silicone breast implants, NuSil worked with the FDA to develop master access files (MAFs) of test results, which are now used by medical device manufacturers when making a regulatory submission for a device that incorporates NuSil silicone. The MAF contains information on how the silicone is formulated, processed and controlled for quality, as well as the results of mechanical, chemical and biological testing. NuSil has more than 500 MAFs on file with the FDA, which can support biocompatibility of the materials. However, medical device manufacturers are still required to test the device as a whole.

In 2013, the FDA issued draft guidance on changes to testing standards in ‘Use of International Standard ISO 10993, ‘Biological Evaluation of Medical Devices Part 1: Evaluation and Testing.’ According to an article in *MDDI Medical Device and Diagnostic Industry News*, author Thor Rollins states, “The new draft guidance document is the most expansive presentation of standards affecting the medical device industry in 18 years.” He highlights the guidance that the FDA does not approve individual materials but only final devices. “Often, medical device manufacturers test raw materials for biocompatibility, assuming that they can apply the results directly to the final device. While this approach can be successful, manufacturers must also evaluate the impact of the production process on the materials. For example, how do mold-release agents or sterilization methods such as gamma radiation affect the biocompatibility of the final device? Just because a raw material is biocompatible does not necessarily mean that the device itself will also be biocompatible.”



THE TYPES OF SILICONE MATERIALS AND ADDITIVES IN IMPLANTABLE DEVICES

Silicone rubber is formulated in liquid or gum stock and may be combined with additives specific to the function of the implantable device. The molding firm's engineers and chemists will advise on the specific formulation of silicone and any additives that may be required.

Advantages of Silicone

Due to its unique properties, silicone is frequently used in medical devices to:

- Provide insulation from electrical current
- Protect sensitive components of an implantable device, such as pacemaker leads, from corrosive bodily fluids
- Offer flexibility and long-term durability for implantable devices that must conform to the body, such as catheters and shunts

Also key to silicone's functionality is its ability to operate in temperatures ranging from $-55\text{ }^{\circ}\text{C}$ to $+230\text{ }^{\circ}\text{C}$, which also allows it to stand up to steam sterilization (autoclaving).

Types of Silicone

The primary types of silicone used in implantable devices are:

- Liquid silicone rubber (LSR)
- High consistency silicone rubber (HCR or gum stock)

The type of silicone used depends on the type of component being manufactured and the best molding process for the part. Liquid silicone rubber is used in liquid injection molding to create parts of high strength and flexibility. The cure time is considerably less than gum stock silicone, which reduces production costs. HCR or gum stock silicone is used in transfer molding to achieve specifications such as complex shapes or thin walls.

Additives

Additives may be mixed in by either silicone suppliers or by silicone molding firms, including:

- Pigments, including custom Pantone colors
- Desiccants to address issues with moisture
- Antimicrobial agents
- Radiopaque tracers such as barium sulfate for detection by x-rays

Transparent silicone is also available, which is fabricated for high-refractive index and optically clear applications such as implantable lenses.

Batch Consistency and Quality

In evaluating the additives to silicone used in implantable components, OEMs will want to ensure that the additive is properly measured and weighed as it is added to ensure uniform mixing. Molding firms should employ advanced technology in their silicone mixing and molding operations, including computer-operated and controlled production, custom automated assembly, and automated measuring machinery to ensure homogeneity, quality, and batch-to-batch consistency and tracing.

LONG-TERM AND SHORT-TERM IMPLANTABLE SILICONE APPLICATIONS

Flexan estimates that implantable silicone represents only a fraction of the total amount of medical-grade silicone used in medical devices. Because of the amount of testing and the level of purity required, implantable silicone can cost 10 to 15 times as much as standard medical-grade silicone, but implantable silicone is critical for certain devices, especially those categorized as Class III.

Because of the proven quality of silicone manufactured in the U.S., medical device OEMs and their suppliers will often specify U.S. medical-grade silicone even for overseas production.

Silicone in Class II and III Medical Devices

<p>Class III – Long-Term Implantable Devices</p> <ul style="list-style-type: none"> • 30 days to indefinite use • Implantable silicone required 	<p>Devices that save lives or prevent death, such as defibrillators, heart pumps, and surgical reconstructive components</p>
<p>Class II - Short-Term Implantable Devices</p> <ul style="list-style-type: none"> • 29 days or less • Medical-grade silicone required 	<p>Temporary implants and surgical instruments that come in contact with skin, bodily fluids, bone and tissue, such as over-molded surgical blades, electrosurgical devices, catheters, and diagnostic guide wires</p>
<p>Class II – Disposables</p> <ul style="list-style-type: none"> • One-time use • Medical-grade silicone required 	<p>Devices designed for single use but which come in contact with skin or body tissues, such as suture sleeves, disposable components for medical devices, optically clear ophthalmic lenses for use during eye surgery, and orthopedic devices</p>

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CLEANROOM MANUFACTURING TO ISO STANDARDS

Manufacturing silicone-molded components to meet cleanliness standards is a critical process that begins with the materials themselves and ends with the packaging. In production and handling, cleanrooms are essential to avoiding contamination.

Silicone molding cleanrooms are designed and operated to meet ISO standard 14644, which classifies cleanrooms according to measurements of particulates of different sizes, from 0.1 micron to 5 microns, per cubic foot of air. Class III implant-grade and Class II short-term implantable and disposable medical devices typically require at least a Class 7 (10,000) cleanroom and some as stringent as Class 5 (100).

Keeping a cleanroom manufacturing environment to ISO standards requires both good design and technology and good operating practices. Cleanrooms are designed to control contaminants, which require the right room configuration and a combination of airflow and HEPA filtration to capture airborne particulates.

Raw Material Handling

In cleanroom production, one of the most important steps is to avoid contaminants in the raw materials themselves. Although medical-grade silicone is a proven material in medical device manufacturing, the handling and preparation of silicone and other materials prior to molding must be done in the cleanest section of the cleanroom.

Cleaning and Molding

Manufacturing processes, by their very nature, generate particulates. Therefore, each component must be cleaned after the molding process is complete, which also is conducted in a high-level cleanroom environment.

It should be noted that cleaning is not the same as sterilization. Silicone molders will wash the component before packaging and shipping. OEMs typically sterilize the component themselves and then test whether the component meets their specified contamination levels. The cleaner the silicone molded part shipped from the molder, the more likely that sterilization will be effective and the device will meet FDA and international standards.



ISO 14644-1 Cleanroom Standards

CLASS	maximum particles/m ³						FED STD 209E equivalent
	≥0.1μm	≥0.2μm	≥0.3μm	≥0.5μm	≥1μm	≥5μm	
ISO 1	10	2.37	1.02	0.35	0.083	0.0029	
ISO 2	100	23.7	10.2	3.5	0.83	0.029	
ISO 3	1,000	237	102	35	8.3	0.29	Class 1
ISO 4	10,000	2,370	1,020	352	83	2.9	Class 10
ISO 5	100,000	23,700	10,200	3,520	832	29	Class 100
ISO 6	1.0x10 ⁶	237,000	102,000	35,200	8,320	293	Class 1,000
ISO 7	1.0x10 ⁷	2.37x10 ⁶	1,020,000	352,000	83,200	2,930	Class 10,000
ISO 8	1.0x10 ⁸	2.37x10 ⁷	1.02x10 ⁷	3,520,000	832,000	29,300	Class 100,000
ISO 9	1.0x10 ⁹	2.37x10 ⁸	1.02x10 ⁸	35,200,000	8,320,000	293,000	Room Air

IMPLANTABLE SILICONE MOLDING PROCESSES

Silicone molding is used to produce precision components for both implantable and disposable medical devices.

Silicone may be used to:

- mold a complete implantable part
- mold a component of an implantable device, or
- overmold a part of the device or the exterior of the device

Silicone Molding Processes

Molding engineers will work with the OEM's engineers to determine the optimal molding process, tool design, and manufacturing controls for the application, in keeping with the OEM's material preferences and plans for manufacturing and assembly, as well as expected production volume.

The main molding processes are:

- Liquid Injection Molding
- Transfer Molding
- Compression Molding
- Micromolding
- Overmolding



Liquid Injection Molding

Process

The liquid silicone rubber injection molding process delivers two-part liquid silicone directly into a mixer, which is then injected into the mold cavity. This completely closed process minimizes human interaction and avoids contamination. The fully automated process is best suited for high-volume production, although it can be adapted to lower volumes if needed.

Applications

Liquid silicone rubber injection molding is best suited for medium to high volume production runs. Low production runs require frequent material changes and start-ups, which erodes the efficiency of LIM.

Transfer Molding

Process

Silicone rubber transfer molding is used for both low and high volumes and offers shorter set-up time. In transfer molding, a hydraulic ram displaces rubber through the gates and sprues into the cavities.

Applications

Transfer molding is the process used for silicone gumstock applications to address such needs as complex shapes and thin walls. Transfer molding also is often employed for overmolding of metal and plastic inserts.

Compression Molding

Process

When silicone components are produced using compression molding, the rubber is physically placed into the cavities where the closing action of the mold completes the fill.

Applications

Silicone rubber compression molding is widely used for medical device components but requires more labor and longer curing times than Liquid Injection Molding.

Micromolding

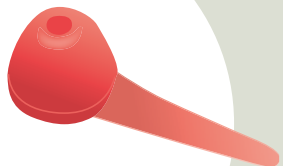
Process

Silicone micromolding is used to produce the smallest components, with the ability to hold tolerances within the micron range, even for the most complex features. Precise tooling with edge, fan, and/or microgates allows precise control of even the most challenging geometries.

Applications

Silicone rubber micromolding is employed in:

- Components for minimally invasive surgical tools
- Valves, seals, and soft tips
- Microsensory and microfluidics products
- Overmolding



Overmolding

Bonding silicone rubber to metal and other substrates

Process

The bonding of silicone rubber to components made of various substrates is a complex process, which uses either insert molding or overmolding, depending on the application. The molding process must ensure that the mold design will locate, orient, and hold the insert in the exact position throughout the molding cycle.

The main reasons for overmolding an insert are to:

- Insulate the component from an electrical current passing through the insert
- Protect the component from mechanical wear and tear
- Simplify the design and assembly by combining multiple parts into one component
- Applying a bonding agent or adhesive

Substrate materials include:

- Titanium alloys
- Stainless steel alloys
- Engineered plastics

Applications

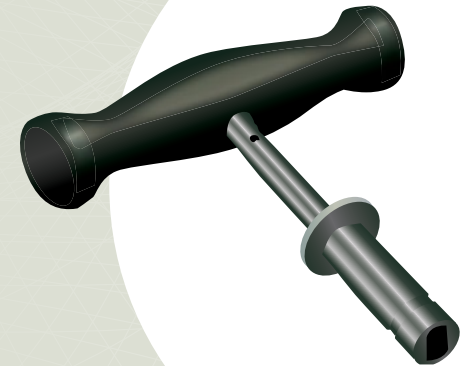
- Surgical blades
- Orthopedic handles
- Wire insulators

The quality of the chemical bond is ensured by various steps, such as:

- Degreasing and cleaning
- Abrading
- Chemical etching

- PEEK thermoplastic
- Ceramics
- Nylon

- Encapsulated housings
- Conducting/insulating barriers



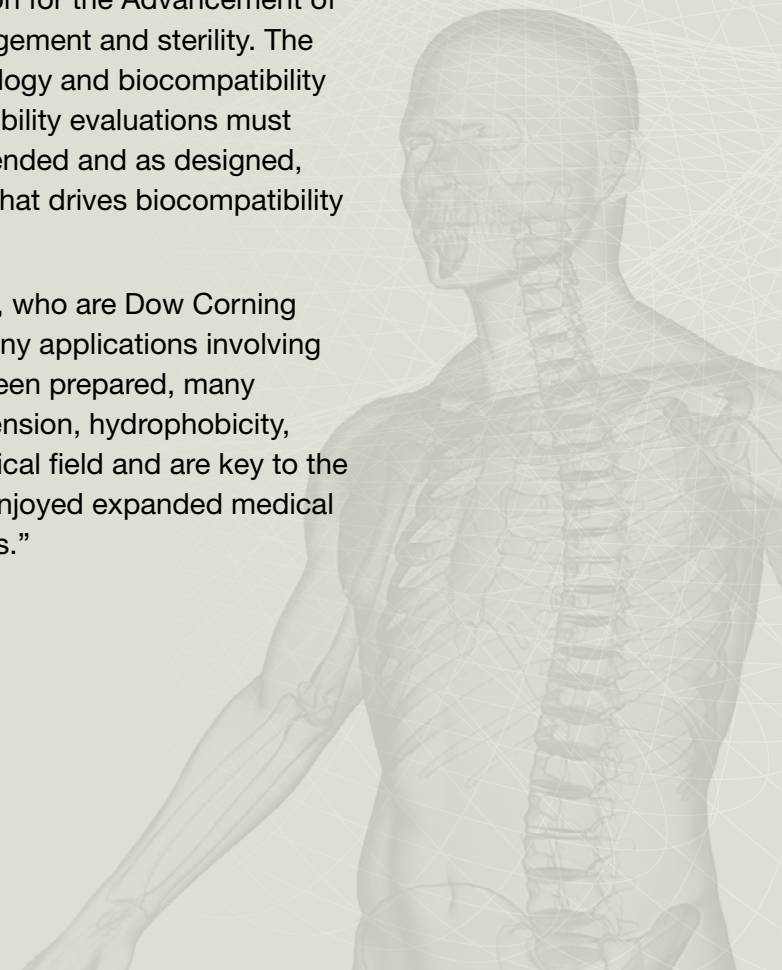
SILICONE AND PATIENT SAFETY

The attention given to the science and technology of implantable silicone stems from the imperative of the safety of the patient when in short- or long-term contact with an implantable device.

Patient safety must be the overarching consideration that drives biocompatibility evaluations.

In a forum between representatives of the FDA and industry members of the Association for the Advancement of Medical Instrumentation, panelists addressed the issues of biocompatibility, risk management and sterility. The report on the S3 Challenge 2014 stated, “Edward Reverdy, director of corporate toxicology and biocompatibility services at Boston Scientific Corporation, began with the key question that biocompatibility evaluations must answer: ‘Are the device materials interacting with a patient going to work safely, as intended and as designed, without causing risk or hazard?’ Patient safety must be the overarching consideration that drives biocompatibility evaluations.”

In “Medical Applications of Silicones” from the book Biomaterials Science, the authors, who are Dow Corning researchers, write, “Silicone’s chemical stability and elastic nature are beneficial for many applications involving long-term implantation.” Their report concludes, “A variety of silicone materials have been prepared, many possessing excellent properties including chemical and thermal stability, low surface tension, hydrophobicity, and gas permeability. These characteristics were the origin of silicone’s use in the medical field and are key to the materials’ reported biocompatibility and biodurability. Since the 1960s silicones have enjoyed expanded medical application and today are one of the most thoroughly tested and important biomaterials.”



This ebook was developed by Flexan

ABOUT FLEXAN

We offer contract manufacturing services for your end-to-end medical device outsourcing needs. We provide services for silicone and thermoplastic components and devices, including: development assistance, process design and development, molding/over-molding, extrusion, secondary operations, assembly and packaging. We offer global manufacturing options with capacity to support your growth. As an organization, we think and operate as an extension of your manufacturing environment with a rigorous focus on quality, lean six sigma and delivery.

For more information about FLEXAN visit flexan.com or call **224-543-0003**.

¹ Biocompatible Materials: US Industry Study with Forecasts for 2018 and 2023, December 2014, The Freedonia Group, Cleveland, OH

² How the New FDA Biocompatibility Testing Guidance Could Affect You, MDDI online, by Thor Rollins, March 18, 2014

³ Biomaterials Science, 2nd Edition, Elsevier, Inc., Medical Applications of Silicones, by André Colas and Jim Curtis