



***CONSIDERATIONS FOR MOVING FROM  
INDUSTRIAL TO MEDICAL MOLDING***

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## **INTRODUCTION**

The fabrication of silicone elastomer into finished useful objects by such ways as extrusion, calendaring, and molding, etc. has been carried out to varying degrees since the 1950's. Although these first applications for silicones were typically for industrial uses, silicone quickly found a home in the healthcare market. Since the 1960's silicones have been widely used in the manufacture of medical devices, medical device components, and medical tubing. This is due to the inherent biocompatibility of silicone materials. They have found uses in a number of life enhancing and critical care applications. As a result, the pieces and parts used in these medical applications have typically commanded a higher price than those used in more industrially oriented applications. Larger profit margins enjoyed by the traditional medical molders do come at a cost. Medical molders have to operate to a more stringent set of regulatory requirements. As a result of this, they tend to have different material, manufacturing, and finishing considerations.

Today's healthcare market is intensely competitive, and lately the target of intense cost containment pressures. Healthcare original equipment manufacturers (OEMs) and fabricators take on a considerably higher degree of risk than their counterparts on the industrial side. Not only do healthcare OEMs and fabricators have to deal with quality system audits; OEMs must face the real possibility of audits from the Food and Drug Administration, where consequences for non-compliance include severe fines and the potential for shut-down. Fabricators face audits from their customers and it is not unusual for these audits to consume two or more days per month of a quality manager's time. These issues coupled with the complexities of matching the appropriate silicone materials to the appropriate applications are enough to deter some companies from entering into the healthcare market. This paper will attempt to answer some basic questions involved with entry into healthcare fabrication, as well as, provide some guidance on what might be expected should a company choose this path.

## **HEALTHCARE REGULATORY PRACTICES**

For a few specific applications in the healthcare market, use of industrial silicone materials is totally acceptable. These applications would include such things as wound drain bulbs and devices where the nature of patient contact is skin only. For applications where the device or device component will be implanted in the patient, used in the fluid path to the patient or used in the manufacture of pharmaceutical drugs, industrial grade silicone materials are seldom formulated or manufactured for these applications and almost never tested appropriately. In the United States, two of the more widely used standards that provide for guidance in describing appropriate testing for medical device and medical device components are the United States Pharmacopoeia (USP) and the ISO 10993 Standard.

In the broadest sense, healthcare devices and device components can be divided into two main categories: long-term implant which is used to describe devices that are intended to be used for periods 30 days or longer; and short-term implant or those devices intended

for use no longer than 29 days. The ISO 10993-1 standard further subdivides the short-term category into limited (exposures no longer than 24 hours) and prolonged (exposure greater than 24 hours but less than 30 days). (Based on these standards, it is the responsibility of healthcare OEMs and fabricators to choose the most appropriate raw material for the devices that they design and/or manufacture.)

The USP, a non-profit organization, was initially established to institute a set of standards that could be used by pharmaceutical manufacturers to assist them in providing high quality medicines to their consumers. The USP is considered to be one of the most technologically advanced and respected pharmacopeia's in the world. For medical devices and medical device components, the USP testing that is almost always referenced is USP Class VI testing. Class VI testing refers to a battery of testing that was designed to evaluate plastics and elastomeric materials for potential uses in drug packaging components. The specific testing is called out in part 88 of the USP and consists of a four part evaluation involving animal testing of extracts of the control and test materials in saline, vegetable oil, alcohol, and polyethylene glycol. A material that elicits a response that is considered to be less than or equal to that of the control is considered a pass and that material can claim Class V status under the USP guidelines. USP Class VI testing consists of Class V testing plus a rabbit intra-muscular implantation test of at least five days in duration. Again, the test article is compared to a control and is considered to have passed only if it elicits a response considered less than or equal to that of the control.

It is important to point out that although USP Class VI testing is widely used and accepted throughout the United States in the healthcare industry, the testing should be construed as the minimum necessary for a raw material to be considered in medical applications. USP Class VI testing does not meet the requirements of the ISO 10993-1 guidelines, which is what the FDA currently uses for medical device approval. It is also important to point out to fabricators with plans for expansion outside the U.S. that the Class VI guidelines are not sufficient for raw material approval and further testing will be required.

The ISO 10993-1, as mentioned previously, divides medical device applications into three main exposure categories. Depending upon the nature and duration of contact, a series of tests are recommended. It is important to point out that ISO 10993-1 only provides direction as to the type of testing that should be considered for device approval. It should in no way be considered as evidence that any of the recommended testing has been carried out. Guidelines for the tests that are recommended by ISO 10993-1 can be found in the subsequent parts of the standard.

## **QUALITY SYSTEMS/OEM REQUIREMENTS**

A fabricator looking to secure contract-manufacturing jobs from large healthcare OEMs must operate under some type of quality system, or at the absolute minimum, some quality system guidelines. Typically, an ISO 9000 or QS 9000 system should be considered for entry into healthcare contract manufacturing. When long-term (>30days)

implant medical devices and medical device components are being considered, it may be necessary to implement Good Manufacturing Practices (GMPs) or medical device Quality System Requirements (QSRs).

Some of the key benefits of a quality system are written procedures and a high degree of traceability. For the most part, healthcare is an industry that has difficulty managing change and must in some cases, be able to provide documented proof that changes of any kind did not occur during the manufacturing process. Although it will be atypical for the Food and Drug Administration to audit a healthcare fabricator, the chances of an audit for a healthcare OEM increase considerably. If and when such an audit happens at an OEM, respective fabricators can almost certainly expect that they will be contacted for support.

Ultimately, the decision as to whether or not a fabricator needs a quality system to fabricate medical devices or components is up to the OEM that will be placing the work. Typically, the average healthcare fabricator is ISO 9002 registered, ISO 9001 if they offer design services. With this said however, fabricators that are QS 9000 registered should not be considered at a disadvantage; this is because most, if not all, of the elements covered under ISO are also part of QS 9000 quality systems. Fabricators can expect that healthcare OEMs will perform some type of audit of their quality system before any work gets placed. This audit can be as simple as a phone conversation or a form that the OEM requires to be filled out. The more conservative healthcare OEMs may even send a representative from their quality department to perform an in-person, in-depth audit.

## **CLEAN ROOM CONSIDERATIONS**

A properly maintained clean room, or at the very least clean area, is another consideration for fabricators looking to participate in the healthcare market. Clean rooms are classified based on either Federal Standard 209E or ISO standard 14644, parts one and two. These standards specify the allowable number of particles that can be present per cubic foot of air in the clean room. For example, a class one hundred thousand clean room would mean that there could be no more than 100,000 particles greater than 0.5 microns in size per cubic foot of air.

Care should be taken during the planning stages of clean room set-up, as it is important to know exactly what class of clean room that you will require. Installation of a clean-room that would be considered more than necessary for the applications that you will be pursuing can turn out to be very costly in terms of initial construction and day-to-day operation. Typically the lower class clean rooms are required for long-term implant fabrication, class 10,000 and lower as a general rule of thumb.

For more information on clean room construction, equipment, and monitoring services, a search of the World Wide Web should provide a number of suitable choices. For standards pertaining to contamination control and monitoring, the Institute of Environmental Sciences and Technology can be consulted.

## **SILICONE MATERIAL SELECTION**

One of the most difficult and sometimes confusing decisions that a potential healthcare fabricator will have to make, when given the choice by the OEM, is the selection of appropriate silicone material. For the most part, the healthcare OEM will choose the material that the medical device or component is to be made from. Occasionally, the OEM might list similar silicone products from a few different materials suppliers and in some instances, especially for new medical devices, OEMs will allow or even encourage the fabricator to choose an appropriate silicone material. When a fabricator is given the chance to choose the material and supplier that they will work with, it's a choice that should not be taken lightly. Even though the manufacture of a medical device may be entirely contracted to healthcare fabricators, the OEM remains the fabricator of record and thus takes on any liabilities that may be associated with the finished device. As a result, healthcare OEMs tend to have little patience for fabricators that make poor material/supplier decisions.

When given the opportunity by a healthcare OEM, the first group of decisions that must be made are those that relate to the physical properties of a silicone material. Typically the OEM will share with the fabricator the specific physical properties that they feel the material must possess or, at the very least, the details of the intended application. If the latter happens to be the case, silicone material suppliers typically have individuals (Technical Service Representatives in the case of Dow Corning) that can assist you in identifying the most appropriate product for the application. These individuals can also assist you with product information sheets for the material(s) as well as samples if necessary.

Once the appropriate silicone material(s) are identified from the standpoint of physical performance and characteristics, the next step is to narrow the list down even further based on the biological testing that is necessary for the intended application of the device or component. As alluded to previously, for short-term implant applications ( $\leq 29$  day) in the United States, USP Class VI tested material should be considered as the absolute minimum.

It is important to point out that different raw materials suppliers define USP Class VI testing differently. As mentioned previously, strict interpretation of the USP Class VI requirements would call for USP Class V extractables testing and rabbit, intramuscular implantation test for a time period of at least five days in duration. Upon successful completion of these tests, a material can be claimed as USP Class VI. Due to the inherent costs associated with the implantation part of this testing, several raw material suppliers will only run implant testing for period of between five and ten days. Per the wording in the USP standard this is totally acceptable but it should raise some questions both in the minds of the healthcare OEMs and healthcare fabricators.

The first point of consideration should bear greater significance for those OEMs and fabricators involved in medical devices that are to be implanted for periods greater than ten days in duration. Although arguable to a point, most pathologists would tend to agree

that an implantation test of such short duration (five to ten days) provides little overall information as to how the material will actually behave in the body. The main reason for this is that up until day 10 to 14 (depending on the animal) all that is really evident at the implantation site is the trauma of the surgery as well as some initial healing. This trauma and healing, typically present to the same degree at both the control and test article sites makes distinguishing whether or not the test material has caused a response different from control very difficult. Typically, the animal has not even had a chance to encapsulate the implant at this point, something that will occur. Based on these observations it is very feasible that although a material passes a Class VI five to ten day implantation test, it would fail a longer-term test. Taking all of this into account, OEMs and fabricators of short-term implant devices ( $\leq 29$  day) that are marketed for implantation in the body for time periods greater than two weeks may wish to choose a Class VI material with a longer-term implantation test associated with it. Dow Corning® Class VI silicone materials are one, if not the only, potential solution to such an issue.

To ensure safety and performance, Dow Corning Class VI silicone materials have passed both seven and thirty day subcutaneous and intramuscular implantation testing. Protocols for these tests meet all of the requirements called out by ISO. The seven-day time point is done for purposes of competitive comparison and as a first-check of any negative response the implants may be eliciting. The thirty-day time point is the one on which most emphasis is placed. For a Dow Corning product to be claimed as Class VI, it must successfully pass both time points of the implant test. Dow Corning has evaluated some developmental materials, similar to those of our competition, that have passed a seven-day implantation test and went on to fail the thirty-day test. The entire Dow Corning Class VI product line has successfully passed both seven and thirty-day implantation tests. Out of principal, Dow Corning will not sell products into short-term implant applications that do not pass an ISO compliant thirty-day implantation test.

## **MANUFACTURING AND FINISHING CONSIDERATIONS**

The last topic for discussion centers on manufacturing and finishing of medical devices and components. In many cases any idle manufacturing equipment that the typical industrial fabricator already has in house can be used for the manufacture of many types of healthcare products. All that may be necessary is for proper cleaning procedures to be put in place and inspection of the hydraulics system such that any leaks or weak hoses are repaired or replaced. Once you have a machine operating in a clean room environment a hydraulic fluid leak could prove to be a very expensive act to remedy. Something also to keep in mind is that hydraulic machines could limit the class of clean room that you are trying to achieve. Healthcare fabricators that are running hydraulic molding presses and/or liquid injection molding machines in the higher class clean rooms typically have the rooms set up such that the hydraulics are located outside of the room. Another option for liquid injection molding would be to consider one of the new electric machines that are available.

Another important factor that typically takes industrial molders some time for adjustment is the fact that mold release agents are typically not used in medical molding. There are

few, if any, FDA approved mold cleaners and release agents that are available for medical molding. However dilute solutions of sodium dodecyl sulfate in water (1-2%) have gained wide acceptance in the industry as a mold release agent. Also, dilute aqueous solutions of most commercially available soaps have been successfully used to clean molds. For cleaning purposes, if something stronger than a soap solution is needed, isopropyl alcohol is another widely accepted solvent for cleaning that works very well for removing mixed/milled stock from injection molding machines. There are other cleaning solvents in use at both the healthcare OEMs and fabricators. These solvents are most likely acceptable but due to the fact the uses are not wide spread, they will not be mentioned here.

Finally, it is not atypical for OEMs to ask for “flash-free”, washed parts, although these tasks are not difficult, they usually require specialized equipment and can add some additional start-up costs to an operation. With today’s available tooling technology, it is almost possible to produce flash-free parts right from the mold. When a de-flashing operation is necessary, this is typically done cryogenically although there are other means. Part washing is typically accomplished with an alcohol and water solution, typically 70% isopropyl alcohol and 30% water, but different ratios are more than acceptable. A recommendation would be that your wash solution contains at least 20% water to avoid significant swelling of the manufactured parts.

## **CONCLUSION**

A transition from industrial to medical type molding, although not easy by any means, is definitely possible as long as it is done with the proper and necessary planning. As more and more of the larger healthcare OEMs are dismantling their own internal molding capabilities in efforts to cut-costs, the opportunities for such a transition should continue to grow in the near future. For those companies interested in the transition, this paper has provided a better feel for what initial steps to consider and a basic overview of the medical molding process.

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