Designation: F 2038 – 00

Standard Guide for Silicone Elastomers, Gels and Foams Used in Medical Applications Part I — Formulations and Uncured Materials[1]

This standard is issued under the fixed designation F 2038; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last reapproval. A superscript epsilon (ε) indicates an editorial change since the last revision or reapproval.

1. Scope

1.1 This guide is intended to educate potential users of silicone elastomers, gels and foams relative to their formulation and use. It does not provide information relative to silicone powders, fluids, and other silicones. The information provided is offered to guide users in the selection of appropriate materials, after consideration of the chemical, physical and toxicological properties of individual ingredients or by-products. This standard offers general information about silicone materials typically used for medical applications. Detail on the crosslinking and fabrication of silicone materials is found in Part II of this standard.

1.2 Fabrication and properties of elastomers is covered in the companion document, F 604, Part II. This monograph addresses only components of uncured elastomers, gels and foams.

1.3 Silicone biocompatibility issues can be addressed at several levels, but ultimately the device manufacturer must assess biological suitability relative to intended use.

1.4 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety and health practices and determine the applicability of regulatory limitations prior to use.* Users are also advised to refer to Material Safety Data Sheets provided with uncured silicone components.

1.5 Biological and physical properties tend to be more reproducible when materials are manufactured in accordance with accepted quality standards such as ANSI ISO 9001 and current FDA Quality System Regulations/Good Manufacturing Practice Regulations.

2. Referenced Documents

2.1 *ASTM Standards:*

D 1566 Standard Terminology Relating to Rubber[2]

F 813 Standard Practice for Direct Contact Cell Culture Evaluation of Materials for Medical Devices [3]

2.2 *Sterility Standards:*[4]

ANSI/AAMI ST41 Good Hospital Practice: Ethylene Oxide Sterilization and Sterility Assurance

ANSI/AAMI ST50 Dry Heat (Heated Air) Sterilizers

ANSI/AAMI ST29 Recommended Practice for Determining Ethylene Oxide in Medical Devices

ANSI/AAM1 ST30 Determining Residual Ethylene Chlorohydrin and Ethylene Glycol in Medical Devices

AAMI 13409-251 Sterilization of Health Care Products—Radiation Sterilization—Substantiation of 25kGy as a Sterilization Dose for Small or Infrequent Production Batches

AAMI TIRS-251 Microbiological Methods for Gamma Irradiation Sterilization of Medical Devices

2.3 *Quality Standards*[5]*:*

ANSI/ASQC Q9001 Quality Systems—Model for Quality Assurance in Design, Development Production, Installation, and Servicing

21 CFR 820 Quality System Regulation (current revision)

21 CFR 210 Current Good Manufacturing Practice in Manufacturing, Processing, Packing or Holding of Drugs; General (current revision)

21 CFR 211 Current Good Manufacturing Practice for Finished Pharmaceuticals (current revision)

3. Terminology

3.1 Additional pertinent definitions can be found in standard D 1566.

3.2 *Definitions:*

3.2.1 *silicone polymer*—polymer chains having a backbone consisting of repeating silicon-oxygen atoms where each silicon atom bears two organic groups. The organic groups are typically methyl, but can be vinyl, phenyl, fluorine, or other organic groups.

3.2.2 *cyclics and linears*—low molecular weight volatile cyclic siloxane species are referred to using the "D" nomenclature which designates the number of Si-O linkages in the material (usually D_4-D_{20}); species from D_7 to D_{40}(or more) may be called "macrocyclics". Linears are straight chain oligomers that may be volatile or of higher molecular weight,

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[2] *Annual Book of ASTM Standards*, Vol. 09.01

[3] *Annual Book of ASTM Standards*, Vol. 13.01

[4] Available from the American National Standards Institute, 11 West 42nd St., 13th Floor, New York NY 10036.

[5] Available from the Superintendent of Documents, U.S. government Printing Office, Washington, DC 20402.

depending on chain length; they are designated by "M" and "D" combinations, where "M" is R_3Si-O, and D is as explained above; "R" is usually methyl. (For example, MDM is $(CH_3)_3SiOSiOSi(CH_3)_3$). Low molecular weight species are present in silicone components to varying degrees depending on process and storage. The levels of macrocyclics that can be removed from silicone polymers by vacuum, high temperature stripping, or oven post-cure is dependent on the conditions used.

3.2.3 *catalyst*—a component of a silicone elastomer formulation that initiates the crosslinking reaction when the material is vulcanized.

3.2.4 *crosslinker or crosslinking agent*—a component of a silicone elastomer that is a reactant in the crosslinking reaction that occurs when an elastomer is vulcanized.

3.2.5 *inhibitor*—a component of a silicone elastomer added to moderate the rate of the crosslinking reaction.

3.2.6 *filler*—a finely divided solid that is intimately mixed with silicone polymers during manufacture to achieve specific properties. The fillers used in silicone elastomers are one of two types:

3.2.6.1 *reinforcing fillers*— usually have high surface areas and are amorphous in nature such as fumed or precipitated silica. Such fillers impart high strength and elastomeric physical properties to the elastomer.

3.2.6.2 *extending fillers*— typically have lower surface area and lower cost than reinforcing fillers. They include crystalline forms of silica and diatomaceous earths. While they provide some reinforcement, because they are relatively inexpensive, they are used primarily to extend the bulk of the silicone.

3.2.7 *additives*—a component of a silicone elastomer used in relatively small amounts to perform functions such as marking, coloring, or providing opacity to the elastomer.

3.2.8 *silicone base*—a uniformly blended mixture of silicone polymers, fillers, and additives which does not contain crosslinkers or catalyst.

3.2.9 *uncured elastomer*—a silicone base which contains crosslinker and/or catalyst but has not been vulcanized.

3.2.10 *silicone elastomer*—an uncured elastomer that has been subjected to conditions which cause it to become crosslinked. Elastomers may be either high consistency rubbers, low consistency rubbers, or RTVs. (see below)

3.2.10.1 *high consistency rubbers (HCRS)*—are materials which cannot be pumped by conventional pumping equipment. They normally must be processed using high shear equipment such as a two-roll mill and parts are typically fabricated using compression or transfer molding techniques.

3.2.10.2 *low consistency rubbers or liquid silicone rubbers (LSRS)*—are normally flowable materials which can be readily pumped. They can be mixed by pumping through static mixers and parts can be fabricated using injection molding techniques.

3.2.10.3 *RTVs (room temperature vulcanization)*— are one-part elastomers which cure in the presence of atmospheric moisture. Little, if any, acceleration of cure rate is realized by increasing temperature. Because cure is dependent upon diffusion of water into the elastomer, cure in depths greater than 0.25 inches (0.635 cm) is not recommended.

3.2.10.4 *gels*—are lightly crosslinked materials having no or relatively low levels of reinforcement beyond that provided by the crosslinked polymer. They are usually two-part formulations utilizing a platinum catalyzed addition cure system. The hardness of the gel can be adjusted within wide limits. The material is not usually designed to bear heavy loads but rather to conform to an irregular surface providing intimate contact. As a result, loads are distributed over a wider area. These materials may also be used to provide protection from environmental contaminants.

3.2.10.5 *foams*—are crosslinked materials which have a component added to them that generates a volatile gas as the material is being vulcanized. This results in a material with a very low density. These are usually two-part formulations utilizing a platinum catalyzed addition cure system. They conform to an irregular surface as they expand to provide intimate contact and protection from the environment but are more rigid and provide more strength than gels. Since foams are expanded elastomers, on a weight basis they are highly crosslinked relative to gels. Most cure conditions will result in a closed cell foam.

3.2.11 *lot or batch*—a quantity of material made with a fixed, specified formulation in a single, manufacturing run carried out under specific processing techniques and conditions.

3.2.12 *vulcanization*—an irreversible process in which covalent chemical bonds are formed between silicone polymer chains. During vulcanization, the material changes from a flowable or moldable compound to an elastomeric material which cannot be reshaped except by its physical destruction.

3.2.13 *types of cure*—based upon the cure chemistry employed, silicone elastomers used in medical applications fall into one of three categories: condensation cure, peroxide cure, and addition cure.

3.2.13.1 *condensation cure*—these materials liberate an organic leaving group during curing and are normally catalyzed by an organometallic compound.

one-part—material supplied ready to use in an air tight container which cures upon exposure to atmospheric moisture. The material cures from the surface down and cure depths of greater than about 0.25 inches (0.635 cm) are not practical.

two-part—material supplied in two separate containers which must be intimately mixed in the prescribed proportions shortly before use. Because they do not rely upon dispersion of atmospheric moisture into the silicone, the cure depth is not limited.

3.2.13.2 *peroxide cure*—one-part formulations vulcanized by free radicals generated by the decomposition of an organic peroxide.

3.2.13.3 *addition cure*—two-part elastomers which must first be mixed together and then cure by addition of a silylhydride to a vinyl silane in the presence of a platinum catalyst.

3.2.14 *dispersion*—an uncured silicone elastomer dispersed in a suitable solvent to allow application of a thin layer of elastomer to a substrate by either dipping or spraying.

4. Significance and Use

4.1 This standard is intended to provide guidance for the

specification and selection of silicone materials for medical device applications.

4.2 Silicone manufacturers supplying materials to the medical device industry should readily provide information regarding non-proprietary product formulation to their customers either directly, or through the US FDA master file program.

5. Formulation

5.1 Elastomers, gels, and foams shall be manufactured using formulations containing combinations of the following raw materials.

5.1.1 *silicone polymer*—any polymer of medium or high molecular weight of the structure shown in Fig. 1 where R is a methyl, an unsaturated alkyl group or a hydroxy group, R is generally a methyl or an unsaturated alkyl group but may also be a phenyl, trifuoropropyl, or other hydrocarbon radical, and x and y are integers greater than or equal to zero. At least 2.0 alkenyl groups must exist per chain if R is not a hydroxy group.

5.1.2 *catalyst*—an organometallic complex of platinum or tin bonded to ligands made of any suitable combination of elements such as carbon, hydrogen, oxygen, fluorine and silicon.

5.1.2.1 *platinum*—this catalyst may be dispersed in a silicone polymer of the structure shown in Fig. 1 having a viscosity low enough that the resulting dispersion is easily pourable. Platinum catalysts can be used in the range of 5 to 20 ppm of active platinum but typically are present at about 7.5 ppm.

5.1.2.2 *tin*—one-part condensation cure formulations will typically contain from 0.1 to 0.5 wt percent of an organotin compound. Two-part condensation cure formulations will typically contain from 0.5 to 2.0 weight percent organotin compound. The ligands attached to tin will be some combination of alkyl groups, alkoxy groups, or the anions of a carboxylic acid.

5.1.3 *Crosslinker or crosslinking agent*—

5.1.3.1 *Two-part, addition cure formulation*—the crosslinker is a polymer of the structure shown in Fig. 2 where R is generally a methyl or a hydrogen group such as to provide at least 2.0 SiH groups per chain and x and y are integers greater than or equal to zero. In order to avoid chain extension, the functionality of either the vinyl-containing polymer or the SiH-containing crosslinker must be at least 3.0.

Because of the limitless possibilities for the structure of both the crosslinker and the functional (vinyl containing) polymer, it would be meaningless to define a weight range for the level of crosslinker in a formulation. However, the amount of crosslinker will typically be sufficient to provide a stoichiometric excess of SiH groups over the amount of unsaturated alkyl groups when the 2 components (parts) of the addition cure silicone elastomer are mixed together in the manufacturer's recommended ratio.

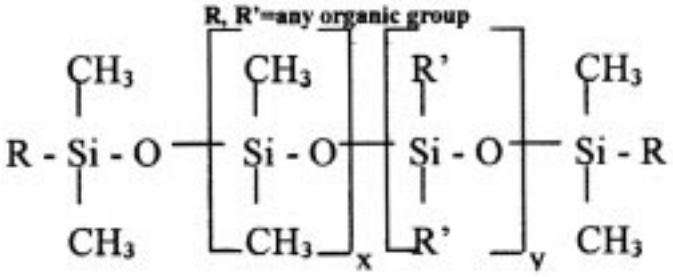

FIG. 1

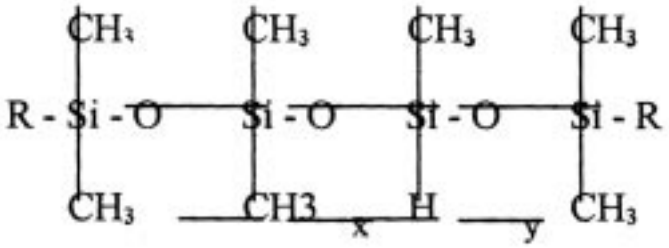

FIG. 2

5.1.3.2 *One-part RTVs and two-part addition cure formulations*—the crosslinker may be an organosilane monomer of the general formula:

$$R_xSi(OR')_{4-x} \quad (1)$$

where:

R = organic group excluding phenyl
OR' = hydrolyzable group such as alkoxy, acetoxy, ketoximo, etc.

5.1.3.3 *Peroxide vulcanized elastomers*— organic peroxides comprise a third type of crosslinking agent which participates in the crosslinking reaction that does not become directly incorporated into the crosslinked network. Peroxide levels range from less than a percent to as high as a couple of weight percent in the total formulation. These peroxides decompose, at a rate which is dependent upon the temperature, to form radicals which then abstract hydrogen atoms from some of the alkyl groups attached to the silicone backbone. Recombination of these radicals results in the formation of a crosslinked silicone network. One commonly used peroxide is 2,4,-dichlorobenzoyl peroxide. Decomposition of this peroxide results in the formation of small amounts of polychlorinated biphenyls and other catalyst decomposition by-products which must be, and are, removed from the cured elastomer during post-curing.

5.1.4 *Filler*—a high purity amorphous silica commercially known as fumed or precipitated silica. This silica can be treated with a silane of the formula Me_3SiX or Me_2SiX_2 where X is a hydrolyzable group or treated with one or more polysiloxane oligomers of the formula $HOMe_2SiO(SiMe_2O)_x(SiMeRO)_ySiMe_2OH$ where R is a methyl or an unsaturated alkyl group. Filler will be added at an appropriate level to provide the desired physical property profile. This level will be dependent upon the type of treatment, level of treatment, and surface area of the fumed silica. Alternatively the filler may be a crystalline quartz compound such as sand which has been ground to a fine powder. Diatomaceous earths which contain approximately 88% silica are also sometimes used.

5.1.4.1 *plasticizers/filler treating agents*—materials added during compounding of an elastomer formulation to pacify the surface of fumed silica. These materials stabilize elastomer properties and allow higher silica loadings, and therefore better reinforcement, to be attained. Filler treating agents are typically silanol ended polydiorganosiloxanes or siloxanes which

can be hydrolyzed to form silanols as described in 5.1.4. These materials are used to treat, or pacify, the highly reactive surface of fumed silica particles. Treating occurs by either hydrogen bonding or chemical reaction with the reactive silanol groups on the surface of the silica to form covalent bonds. By preferentially reacting filler treating agents with the silica surface, similar interactions with the higher molecular weight base polymer are avoided, thereby minimizing creping of the uncured elastomer and changes in hardness of the cured elastomer that would otherwise occur.

5.1.5 *Additives*—any of a class of materials usually comprised of salts or oxides of metals such as barium, titanium, or calcium.

5.1.6 *Inhibitor*—a substance or mixture of substances capable of reducing the rate of crosslinking. It typically contains an unsaturated alkyl group, capable of reacting with the crosslinker via a hydrosilylation (addition) reaction. It is composed of any suitable combination of elements such as carbon, hydrogen, oxygen and silicon.

5.1.7 *Solvent*—a liquid used to form a dispersion by mixing with an uncured elastomer. It typically is toluene or xylene but may be composed of any suitable combination of the following elements: carbon, hydrogen, oxygen and possibly silicon.

6. Packaging, Labeling, and Storage

6.1 Uncured silicone elastomer components for use in medical applications shall be supplied in proper packaging to prevent their contamination during typical conditions of shipment and storage, as well as their adulteration from the package itself.

6.2 All packages shall be labeled so as to identify the manufacturer, specific product name, and lot or batch number.

6.3 The material supplier shall provide information regarding recommended material storage conditions and product warranties.

7. Health and Safety

7.1 Because this standard applies only to uncured silicone elastomers, and most silicone elastomers are cured at the time of end use, most health and safety concerns related to the use of these materials are those encountered during handling; namely eye, skin, and respiratory exposure.

7.2 Each type of filler has its own associated hazards. Potential respiratory effects are typically of no concern, since fillers cannot easily become airborne from compounded materials.

7.3 Catalysts may have some toxicological effects, depending on concentration, form and type. Inhibitors are usually volatilized or incorporated into the elastomeric network during cure, or are at levels generally considered to have negligible toxicological effects.

7.4 Suitability for intended use (i.e. biocompatibility) must be determined on final devices tested in their intended applications. Information about the biocompatibility of cured silicone elastomers is most relevant to the selection of device constituents, and is specific to preparation, sterilization and testing conditions.

7.5 Where uncured silicone elastomers are applied to the body directly and cured *in situ*, consideration must be given to formulation components and cure by-products. Some of these elastomers utilize cure systems which generate organic compounds which can cause local tissue irritation.

7.6 Toxicological test data on uncured materials applies only when all formulating and manufacturing starts with specified ingredients, and is accomplished in accordance with accepted quality standards such as ISO 9001 and current Quality System Regulations/Good Manufacturing Practices (GMP) regulations promulgated by the FDA.

8. Sterilization

8.1 Manufacturers of uncured silicone elastomers may supply such materials sterile or may want to advise fabricators on sterilization methods. These methods should be validated before use.

8.2 Ethylene oxide is highly soluble in silicone. Those users sterilizing with ethylene oxide must do testing to ensure acceptable levels of residues if such sterilized material is used as is (See references). Cell culture tests, such as Practice F 813, may be used to show absence of sterilant residues.

8.3 Autoclave sterilization of uncured elastomers, gels, and foams is not typically used and is not recommended because it may result in fabrication difficulties. Specific details relating to autoclaving will not be discussed here because it is more typically performed on devices made from fabricated elastomers.

8.4 Radiation sterilization of uncured elastomers, gels and foams is not typically used and is not recommended. Additional information about radiation sterilization is available in Part II.

9. Quality Control Provisions

9.1 Silicone elastomers should be designed and manufactured utilizing quality control programs such as that discussed in ANSI/ASQC CI (Specification of General Requirements for a Quality Program), preferably in accordance with ISO 9001 and ISO 9002 standards. Batch-to-batch consistency/acceptability can also be monitored by matching product performance to lot acceptance requirements, providing these are specific and reasonably narrow.

9.2 Manufacturers of uncured silicone elastomers will inform customers of changes in formulation, test methods, specifications or packaging. Details of the changes and a means to identify when each change occurred shall be provided.

9.3 Sterilization will be performed using quality standards such as:

ANSI/AAMI ST46 Good Hospital Practice: Steam Sterilization and Sterility Assurance
ANSI/AAMI ST41 Good Hospital Practice: Ethylene Oxide Sterilization and Sterility Assurance
ANSI/AAMI ST50 Dry Heat (Heated Air) Sterilizers
ANSI/AAMI ST29 Recommended Practice for Determining Ethylene Oxide in Medical Devices
ANSI/AAMI ST30 Determining Residual Ethylene Chlorohydrin and Ethylene Glycol in Medical Devices
AAMI 13409-251 Sterilization of Health Care Products—Radiation Sterilization—Substantiation of 25kGy as a Sterilization Dose for Small or Infrequent Production Batches
AAMI TIR8-251 Microbiological Methods for Gamma Irradiation Sterilization of Medical Devices

10. Keywords

10.1 elastomer; foam; gel; HCR; high consistency rubber;

liquid silicone rubber; LSR; moisture cure; medical device material; peroxide cure; platinum cure; RTV

APPENDIX

(Nonmandatory Information)

X1. RATIONALE

X1.1 Medical devices made from silicone elastomer are widely used in the care of public health and have a history of biocompatibility in many applications. This standard educates the user as to the formulation of such elastomers, the first level at which biocompatibility of the ultimate device is affected. Also impacting the biocompatibility of the finished device is the fabrication of the silicone elastomer; fabrication is addressed in the companion standard.

X1.2 The previous version of this standard has now been split into two parts, one addressing formulation, and one, fabrication. The codes previously used in this standard were not widely accepted by manufacturers, and therefore the monograph had minimal utility. The information provided here (and some suggestions for further investigation) at least provide a starting point from which the user can seek guidance on the biological impact of silicone formulations. Manufacturers' responsibilities as defined here are now or are expected to be practiced in the industry; manufacturers can be differentiated on the basis of the information they provide on the topics introduced herein.