

detailed discussion, accompanied by the results of applicable preclinical and clinical studies, of the above identified risks and the effectiveness of the device. In particular, the PMA shall include all known or otherwise available data and other information regarding: (1) Any risks known or should be reasonably known to the applicant that have not been identified in this document; and (2) the effectiveness of the specific implanted mechanical/hydraulic urinary continence device that is the subject of the application.

Valid scientific evidence, as defined in § 860.7 (21 CFR 860.7), addressing the safety and effectiveness of the device should be presented, evaluated and summarized in a section or sections of the PMA separate from known or otherwise available safety and effectiveness information that does not constitute valid scientific evidence (e.g., isolated case reports, random experiences, etc.).

A. Manufacturing Information

All manufacturing information for the device should be completely described. The information should include but, is not necessarily limited to, the chemical formulation and manufacturing procedures and processes, presented in a step-by-step manner from the starting materials to the finished product, including, but not limited to, all nonreactants (such as antioxidants, light stabilizers, plasticizers, i.e., anything added to polymer resins that is necessary for processing of the finished product) and reactants (including catalysts, curing agents, and intermediate precursors) for the pad (including polyurethane foam covering, if applicable), cuff, pump, reservoir, tubing, and all internal components, adhesives, colorants, lubricants, and filling agents (e.g., gel, saline, contrast medium, etc.). A complete master list of the common chemical names and alternate names (manufacturer's trade name or code) for all nonreactants, reactants (including intermediate precursors), additives, catalysts, adjuvants, and products should be provided.

Chemical characterization of the elastomer intermediates (i.e., network precursors) of the pad (including polyurethane foam covering, if applicable), cuff, pump, reservoir, tubing, and internal gel (if applicable) sufficient to demonstrate control of the chemical processing of the device materials should be provided. This should be based on lot-to-lot comparisons (10 consecutive lot minimum) of the following information: (1) The molecular weight distribution,

expressed as weight average molecular weight, number average molecular weight, peak molecular weight, polydispersity, and viscosity average molecular weight of these precursors; (2) analyses for volatile and nonvolatile (if applicable) compounds, such as cyclic oligomers; (3) when viscosity is used as the variable that is measured for production control, a comparison of viscosity, number average molecular weight, and volatile content; and (4) isocyanate content, acidity, isomer ratios, hydroxyl number, water content, acid number, and peroxide content (where applicable). Documentation establishing the extent of cross-linking (where applicable) in the materials of the pad, cuff, pump, reservoir, tubing, and all internal components and filling agents, or the silicone-hydride and vinyl content of cross-linked materials of the pad, cuff, pump, reservoir, tubing, and all internal components and filling agents, as well as the particle size and surface area of the silica if present in the pad, cuff, pump, reservoir, tubing, and the composition of all internal components, filling agents, or gel should be provided. A complete description of the medium used to inflate the device (saline, contrast medium, etc.) and whether and how the implant will be prefilled must also be provided.

The standard operating procedures for sterility and materials qualifications must be provided. Sterilization information should include the method of sterilization; the detailed sterilization validation protocol and results; the sterility assurance level; the type of packaging; the packaging validation protocol and results; residual levels of ethylene oxide, ethylene glycol, and ethylene chlorohydrin remaining on the device after the sterilization quarantine period, if applicable; and the radiation dose, if applicable.

A complete description of the functional testing of subassemblies and finished products performed during the manufacturing process and during quality assurance/quality control (QA/QC) testing must be provided. Functional testing performed during manufacturing and QA/QC procedures should detect any device flaws that could lead to short-term failure and should demonstrate functional integrity of the device. A QA/QC plan that demonstrates how raw materials, components, subassemblies, and any filling agents will be received, stored, and handled in a manner designed to prevent damage, mixup, contamination, and other adverse effects must be provided. This plan shall specifically include, but not necessarily be limited to, a record of raw material, component,

subassembly, and filling agent acceptance and rejection, visual examination for damage, and inspection, sampling and testing for conformance to specifications.

Written procedures for finished device inspection to assure that device specifications are met must be provided. These procedures shall include, but are not limited to, the requirement that each production run, lot or batch be evaluated and, where necessary, tested for conformance with device specifications prior to release for distribution. A representative number of samples shall be selected from a production run, lot or batch and tested under simulated use conditions and to any extremes to which the device may be exposed.

Furthermore, the QA/QC procedures must include appropriate visual testing of the packaging, packaging seal, and product. Sampling plans for checking, testing, and release of the device shall be based on an acceptable statistical rationale (21 CFR 820.80 and 820.160).

B. Preclinical Data

Complete identification and quantification of all chemicals, including residual amine containing components, volatile and nonvolatile silicone cyclics and oligomers below a molecular weight of 1,500 exhaustively extracted from each of the individual structural components (pad, cuff, pump, reservoir, tubing, and any other materials, lubricants, or filling agents) as they are found in the final sterilized device should be reported. The solvents used for extraction should have varying polarities and should include, but not be limited to, ethanol/saline (1:9) and dichloromethane. Other, more contemporary extraction techniques, such as supercritical fluid extraction, may also be useful, at least for exhaustive extraction of the silicone materials. Experimental evidence must be provided establishing that exhaustive extraction is achieved with one of the selected solvents, and the percent recovery, especially for the more volatile components, must be reported. Extracts that may contain oligomeric or polymeric species must have the molecular weight distribution provided along with the number and weight average molecular weight, and polydispersity. All experimental methodologies must be described, and raw data (including instrument reports) must be provided along with all chromatographs, spectrograms, etc. The limit of detection (two times noise level) must be provided when the analyte of interest is not detected. Laboratory test methods and animal experiments used