

maneuvers) during this followup period, with comparisons to baseline measurements;

(3) Regular postsurgical assessments of incontinence grade (possibly obtained from patient voiding diaries or the number of pads required per day to keep dry), as compared to baseline values; and

(4) Patient assessments of the mechanical function of the implant (such as ease of activation) during this followup period (which may be influenced by the manual dexterity or motivation of the patient).

Documentation of the effect of the device upon the patient's quality of life shall include:

(1) Prospective research designs, including pre- and postsurgical repeated measures for at least 5 years postimplantation, or until physical maturity of the subject (whichever occurs later);

(2) Standardized test questions rather than informal, yet-validated questionnaires; and

(3) Comparisons of the postsurgical scores to those measured prior to device implantation.

Any PMA for the implanted mechanical/hydraulic urinary continence device should separately analyze the degree of device safety and effectiveness by the following variables:

(1) Etiology; (2) duration and degree of urinary incontinence; (3) the device type or model implanted; (4) gender; and (5) age. Furthermore, for each explantation procedure performed on the study subjects, the following information must be provided: (1) The mode of failure of the removed device; (2) whether or not the explanted device was replaced with a new device; and (3) either the manufacturer, type and model of the new device implanted (if another implanted mechanical/hydraulic urinary continence device was implanted), or the type of treatment (if any) that the patient received for his/her incontinence (if revision surgery was not performed). Additionally, the effect of the presence of these implants upon future medical diagnoses/treatments involving the lower pelvic region in recipients of implanted mechanical/hydraulic urinary continence devices must be analyzed. Furthermore, any accessories sold with the implanted mechanical/hydraulic urinary continence device must be shown to have been effectively used in implant procedures without adverse effects.

Finally, each clinical investigation should validate the physician and patient instructions for use (labeling) that were used, particularly the instructions regarding the selection of

the appropriate device size (if applicable).

For polyurethane foam covered implants, the following additional information needs to be presented:

(1) The kinetics of end products generated from the degradation of the polyurethane material (in vivo);

(2) The frequency and incidence of infection and complication of retrieval of the implant by surgeons; and

(3) The neoplasticity of these materials and products, as well as their general toxicity, including neurological, physiological, biochemical, and hematological effects, as well as pathology following prolonged and repeated exposure to polyurethane foam covered implanted mechanical/hydraulic urinary continence devices.

Any epidemiological studies submitted should contain sufficient subjects to permit detection of a small, but clinically significant, increase in one or more connective tissue diseases (especially scleroderma) that may be associated with the use of the device.

The agency believes that insufficient time has elapsed to permit a direct evaluation of the risks of cancer and immune related connective tissue disorders posed by the presence of silicone in the human body, and that insufficient epidemiological and experimental animal data are available to make a reasonable and fair judgment of these risks. Furthermore, the potential long-term risk of hydronephrosis and/or decreases in renal function in patients implanted with the implanted mechanical/hydraulic urinary continence device, due to the chronic elevation of urethral resistance experienced postimplantation, has yet to be quantified and is a concern of the agency. Therefore, the agency will require long-term postapproval followup for any implanted mechanical/hydraulic urinary continence device permitted in commercial distribution. Well-designed clinical prospective studies with long-term followup together with experimental animal studies will be considered essential to the determination of the safety and effectiveness of the device. Further, these clinical studies must collect long-term data on the reproductive/teratogenic effects of the device as well as on the later effects on the offspring.

The risk/benefit assessment (as with the entire PMA) must rely on valid scientific evidence as defined in § 860.7(c)(2) from well-controlled studies as described in § 860.7(f) in order to provide reasonable assurance of the safety and effectiveness of the implanted mechanical/hydraulic

continence device in the treatment of urinary incontinence.

D. Labeling

Copies of all proposed labeling for the device including any information, literature, or advertising that constitutes labeling under section 201(m) of the act (21 U.S.C. 321(m)), should be provided. The general labeling requirements for medical devices are contained in 21 CFR part 801. These regulations specify the minimum requirements for all devices. Additional guidance regarding device labeling can be obtained from FDA's publication "Labeling: Regulatory Requirements for Medical Devices," and from the Office of Device Evaluation's "Device Labeling Guidance"; both documents are available upon request from the Division of Small Manufacturers Assistance (address above). Highlighted below is additional guidance for some of the specific labeling requirements for implanted mechanical/hydraulic urinary continence devices.

The intended use statement should include the specific indications for use and identification of the target populations. Specific indications and target populations must be completely supported by the clinical data described above. For example, it may be necessary to restrict the intended use to patients who have failed prior less invasive therapies and/or to patients with specific etiologies of incontinence in whom safety and effectiveness have been demonstrated.

The directions for use should contain comprehensive instructions regarding the preoperative, perioperative, and postoperative procedures to be followed. This information includes, but is not necessarily limited to: (1) A description of any preimplant training necessary for the surgical team; (2) a description of how to prepare the patient (e.g., prophylactic antibiotics), operating room (e.g., what supplies must be on hand), and implanted mechanical/hydraulic urinary continence device (e.g., handling instructions, resterilization instructions) for device implantation; (3) instructions for implantation, including possible surgical approaches, sizing, fluid adjustment (including what filling solutions may be used and how they must be prepared), device handling, and intraoperative test procedures to ensure implant functionality and proper placement; and (4) instructions for followup, including whether antibiotic prophylaxis is recommended during the postimplant period and/or during any subsequent dental or other surgical procedures, how to determine when