

should exceed the loads expected during device handling and after implantation.

Other components of the implanted mechanical/hydraulic urinary continence device or accessories, such as tubing connectors, extension adapters, and specialized tools used during the insertion procedure, should be evaluated appropriately. Testing of these components or accessories should reflect the anticipated conditions of use; for example, tubing connectors should be demonstrated to be able to maintain connection to the device for the expected life of the device.

C. Clinical Data

Valid scientific evidence, as defined in § 860.7(c)(2), which includes information from well-controlled investigations, partially controlled studies, studies and objective trials without matched controls, well-documented case histories conducted by qualified experts and reports of significant human experience with a marketed device from which it can fairly and responsibly be concluded by qualified experts that there are reasonable assurances of the safety and effectiveness of the implanted mechanical/hydraulic urinary continence device. Detailed protocols for the clinical trials, with explicit patient inclusion/exclusion criteria and well-defined followup schedules, should be specified. FDA believes that 5-year followup data are necessary in order to characterize the safety and effectiveness of the device over its expected lifetime; however, appropriately justified alternate followup schedules will be considered. Any deviations from the protocol should be stated and justified. Time-course presentations of restoration of continence (dryness) or significant improvement in continence, as well as other information on the anatomical and physiological effects of the implanted mechanical/hydraulic urinary continence device (including all adverse events) should be provided. Full patient accounting should be reported, including: (1) Theoretical followup (the number of patients that would have been examined if all patients were examined according to their followup schedules); (2) patients lost to followup, excluding deaths, should include measures taken to minimize such events (with all available information obtained on patients lost to followup) and should not exceed 20 percent over the course of the study; (3) time course of revisions, including all explant and repair data; and (4) time-course of deaths (stating the cause of death, including the reports

from any postmortem examinations). As part of this patient accounting, each clinical report should clearly state the date that the data base was closed to the addition of new information. Detailed patient demographic analyses and characterizations should be presented to show that the patients enrolled in the study are representative of the population for whom the device is intended.

A statistical demonstration, based on the number of patients who complete the required study period, should show that the sample size of the clinical study is adequate to provide accurate measures of the safety and effectiveness of this device. The statistical demonstration should identify the effect criteria, clinically reasonable levels for Type I (alpha) and Type II (beta) errors, and anticipated variances of the response variables. The statistical demonstration should also provide any assumptions made and all statistical formulas used (with copies of any references). A complete description of all patient randomization techniques used, and how these techniques were employed to exclude potential sources of bias, should be provided. Statistical justifications for pooling across several demographic or surgical variables, such as the etiology and duration of incontinence, age, gender, concomitant medical conditions, various anatomical abnormalities, the type or model of the device implanted, the number and type of treatments (if any) attempted to restore continence prior to device implantation, device usage (initial implantation versus revision), investigational site, degree of patient motivation and manual dexterity, surgeon experience and technique, and pad or cuff placement site, should be provided. The data collected and reported should include all necessary variables in order to permit stratification and analysis of the study data required to evaluate the risk/benefit ratio for each clinically relevant subpopulation of patients.

Appropriate concurrent control/comparison groups should be included and justified and, if not, their absence must be justified. All hypotheses to be tested must be clearly stated. Appropriate statistical techniques must be employed to test these hypotheses as support for claims of safety and effectiveness. For each relevant subgroup, a sufficient number of patients need to be followed for a sufficient length of time to support all claims (explicit and implied) in any PMA submission.

To evaluate the risks to the patient from the implanted mechanical/

hydraulic urinary continence device, clinical studies should include time-course presentations of clinical data demonstrating the presence or absence of tissue erosion, infection, pain/discomfort, injury to the upper urinary tract due to either urinary retention or hydronephrosis, continued or worsened incontinence, leakage, wear, tubing kinking/breaking or disconnection, pump failure, cuff or pad failure, hematoma, seroma, inguinal hernia formation, fibrous capsule formation, fistula formation from urethral erosion, urethral scarring, bleeding, urethral stricture, development of bladder hyperreflexia, reoperation, wound dehiscence, pelvic abscess, and fistula to the skin, including any effects on the immune system (both local to the device and systemic) and the reproductive system, without regard to the device relatedness of the event. The diagnostic criteria for each type of immunological and allergic phenomenon should be defined at the beginning of the study, and all cases should be well-documented utilizing these criteria. Patients must be regularly monitored for the occurrence of such adverse events for a minimum of 5 years post-implantation, or until physical maturity of the subject (whichever occurs later).

The effectiveness of the device may be assessed by an objective and standardized recording/measurement of: (1) The ability of the device in vivo to either restore or significantly improve urinary continence; and (2) the enhancement of a patient's quality of life following implantation of the device; both of which should be balanced against any risk of illness or injury from use of the device. FDA understands that evaluation of the degree of benefit involves, in part, an assessment of patient quality of life, which relates to the postoperative function of the device. Such evaluation includes subjective factors and relates to patient expectations. Assessments of the in vivo performance of the device's function, on the other hand, should provide some objective measure of device effectiveness.

Documentation of the anatomical and physiologic outcomes of implantation of an implanted mechanical/hydraulic urinary continence device shall include:

(1) Regular postsurgical evaluations of the functional (i.e., inflation and deflation) characteristics of the device for at least 5 years postimplantation, or until physical maturity of the subject (whichever occurs later);

(2) Periodic postsurgical urodynamic testing (such as measurements of leak point pressure and the volume of urine leaked into a pad after a standard set of