This guidance was written prior to the February 27, 1997 implementation of FDA's Good Guidance Practices, GGP's. It does not create or confer rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both. This guidance will be updated in the next revision to include the standard elements of GGP's.

GUIDANCE DOCUMENT FOR TESTING NON-ARTICULATING, "MECHANICALLY LOCKED", MODULAR IMPLANT COMPONENTS

DRAFT

May 1, 1995

PLEASE FORWARD YOUR COMMENTS TO:

Orthopedic Devices Branch

Division of General and Restorative Devices
Center for Devices and Radiological Health
U.S. Food and Drug Administration

9200 Corporate Blvd.
Rockville, MD 20850

301-594-2036

GRZAN

PREFACE

Many orthopedic devices are designed with modular or multiple components which are locked together. The purpose of this document is to recommend to the device manufacturer or sponsor of a premarket notification (510k), Investigational Device Exemption (IDE), Premarket Approval (PMA) application, reclassification petition, and master file; important information that should be provided to the FDA so that the FDA will be able to determine the substantial equivalence and safety and effectiveness of devices that are made of separate parts, have nonarticulating interfaces between implant components and are assembled by the manufacturer or surgeon, e.g.:

morse taper in a femoral ball on stem;

threaded nut-bolt interface in a spinal implant;

crimping in a bone anchor;

lock and key between porous metal pads and hip stem; and

interference fit between a bone screw and intramedullary rod.

This information includes important issues and concerns, properties that should be evaluated, summaries of possible test methods, rationale/purpose of each test, pass/fail criteria or typical results for each test, literature citations, and a format for organizing data for submission to FDA.

The development of this guidance document is based on an evaluation of the literature and on the experience of the Orthopedic and Rehabilitation Devices Branch (ORDB) and is primarily intended to be a scientific position paper. Therefore, it suggests some important evaluation criteria, test procedures, and end points that FDA feels are necessary to provide reasonable assurance of substantial equivalence and/or safety and effectiveness of modular orthopedic devices. Although this guidance document contains certain administrative requirements, it does not replace the requirements of the 21 CFR 801 or 807 or the statue.

FDA may require information in addition to what is contained in this document if circumstances require it. In other instances, the sponsor may be able to sufficiently justify the omission of some tests. Suggestions and recommendations presented in this document are not mandatory requirements, but reflect data and methodologies which ORDB has determined to be acceptable. Therefore, the words "should", "must" and "shall" are not used in a regulatory sense and should not be construed as such. They express FDA's current feeling as to what constitutes good scientific decision making.

The guidance document should be viewed as a living document. As scientific knowledge changes and scientific techniques are improved, FDA will revise the document. Nonetheless, the basic objectives will remain the same.

MATERIALS AND DESIGN DESCRIPTION

Each part of each component of the implant system should be listed along with the following information:

1 the name of the component and each its parts;

2 a description of the function of each major design feature

3 the names of all other components and tissues that are expected to contact the component and the type of interface (i.e., articulating, fixed mating part, coating, tissue fixation);

4 the material composition of each component to include:

a the document number of any previous submission to FDA or other reference which fully characterized the material (e.g., a master file, 510k, literature article);

b a brief description of the material or the name and number of the voluntary standards that applies to the material (any difference in the final product and the requirements in the referenced standard must be itemized and justified);

c any trade names for the materials; and

d the names of establishments which process the material.

5 the major processing methods which determine the material microstructure and hence, its properties; and

6 details about the design (e.g., engineering drawings, model numbers, sizes, photographs) which should include the ball and liner design tolerances and manufacturing variability for interfaces.

STRENGTH, ASSEMBLY AND DISASSEMBLY

Static strength may determine the load to fracture, deformation or the relationship between assembly load and disassembly load. A measure of the loads applied to the device to assemble and disassemble components may provide information about the:

1 ease of assembly by the surgeon,
2 ease of disassembly by the surgeon,
3 ease of inadvertent disassembly in the patient,
4 possibility of high induced stresses in the assembled device, and
5 possible relationship between loosening and assembly loads.

DEVICE RIGIDITY

The long term effects of the device rigidity on bone should be addressed. Too much rigidity may cause stress shielding (e.g., larger and stiffer intramedullary rod or hip stem) while too little rigidity may result in poor healing (e.g., greater movement at an interface of a modular device compared to the same device made of a solid body).

STRESS ANALYSIS

High stresses leading to deformation, fracture or increased wear of the components may be due to:

1. poor tolerances

2. inadequate instructions for attachment (e.g., excessive use of force);

3. local stress risers (e.g., corners);

4. thermal expansion of parts during sterilization; and

5. thin cross-sections.

These parameters may be evaluated in a stress analysis with mechanical testing to justify assumptions made in the analysis.

FATIGUE PROPERTIES

Cyclic fatigue testing should be considered if the device has the same design as a predicate device except for differences in features which may affect the fatigue life. Whether evaluated separately or in a single test, the wear, corrosion and fatigue properties of the device assembly should be examined in any test performed, where possible.

CYCLIC WEAR, DEGRADATION AND CORROSION

Cyclic testing should be considered for a device which has the same design as a predicate device except for differences in features which may affect loosening, cracking, deformation, corrosion, degradation and wear at interfaces. To simulate actual clinical mechanisms as much as possible, the following test method and measurement parameters should be considered:

DEVICE CHARACTERIZATION

The dimensions and tolerances that would be expected to result in the highest stresses (i.e., worst case) must be tested.

Test samples must be the final product to be shipped for clinical use.

In addition to the information listed in the MATERIALS AND DESIGN DESCRIPTION section of this documents, the exact composition and microstructure of the substrate and any modified surface present must be fully characterized quantitatively from a representative sample of the test specimens. The tolerances for the analyses must be reported. Surfaces exposed to wear must also include the following:

total number of physically and/or chemically distinct surface layers;

thickness of each layer;

drawing or photographs showing the locations of the modified surfaces on the implant and any variation in the modified surface thickness; and

roughness.

TEST METHODS

At least three identical test specimens and three identical controls must be tested. The number of samples depends on the standard deviation and the desired levels of statistical significance and difference in results between test and control specimens.

Polymer samples should be presoaked until a steady state fluid absorption (determined by weighing) is approached (about 30 days for UHMWPE). Samples must be stored and tested in isolation within a noncorrosive chamber.

Three polymer controls which are soaked as are the wear specimens but not wear tested, should be weighed to correct for ongoing fluid sorption by the wear tested components during the wear test. The soak controls should be agitated and cyclically loaded (except for tangential wear motions) as are the wear test specimens.

The volume and concentration of surrounding fluids shall be maintained during testing by avoiding evaporation or by replacing water loss.

Other test parameters should also be included in the methods if the in vitro results will more closely duplicate the in vivo results.

Specimens must be cyclically loaded in a joint simulator or other appropriate instrumentation. The device orientation and loading profile must simulate worst case fretting motions, cyclic stresses, three body wear and corrosion/degradation environment which could occur during clinical use.

Interpretation of the results may be simpler using a 37 +- 1 C, aerated saline test solution having a pH of 7.3 +- 0.5 (carbonate buffered). This is because saline leaves no deposits and the solution composition does not change with time. Ringer's or Hanks solutions may better simulate physiologic conditions and may be appropriate if corrosion is not an issue, but control of the composition, measurements of surface deposits and interpretation of the results must be more stringent than if saline is used. A 0.2% sodium azide or other suitable antibiotic may also be used. A 37 C temperature is preferred, though room temperature may be used if this has no effect on mechanisms (e.g., polymer deformation or creep). Solution temperature and pH must be monitored throughout the test. Accelerated testing (e.g., change in temperature, pH, P_{O2}, electric potential) must be validated with a real time control.

The surfaces exposed to solution should be the same for all specimens and simulate corrosion as it might occur clinically. Corrosion testing of modular devices requires that corrosion is induced at appropriate interfaces and not at the outer surface. It is not enough to merely pit the outer surface of the material because this does not represent the corrosion that occurs as a result of the geometry and wear occurring at the crevice (Buckley, C.A.; et al. 1992).

Corrosion test specimens should be electrically insulated from the test apparatus to avoid galvanic corrosion effects (Higo, Y.; Tomita, Y. 1994, page 152).

MEASUREMENTS

Wear particles, wear markings, material transfer and corrosion (e.g., pitting, etched dendritic surface structure, discoloration) should be quantified after components are disassembled, and before and after cleaning if necessary. Material transfer that may occur while assembling or disassembling parts, prior to fretting, should be taken into account (Bhambri, S.K.; Gilbertson, L.N. , page 123).

Roughness and appropriate dimensions of each test specimen must be measured before and after testing to assess the effects of wear and deformation.

Weight changes of device components should be made if the test samples are small enough compared to the losses due to wear and corrosion. Samples shall be cleaned prior to weighing as outlined in McKellop, H.A.; Lu, B.; Benya, P.: 'Friction, Lubrication and Wear of Cobalt-Chromium, Alumina and Zirconia Hip Prostheses Compared on a Joint Simulator'. Trans. Orthop. Res. Soc., pp. 401, 1992. The weight loss of each wear component shall be adjusted for the change in weight of the soak controls. The room temperature and humidity during weight measurement shall be reported. The volume of wear debris shall be calculated by dividing by the density of the material.

Test methods should be validated by comparing in vitro results to in vivo results to determine if in vitro test methods are realistically simulating what occurs in patients (e.g., three body wear). This may be determined by comparing wear particles of in vitro test samples to those of explanted devices of similar design as well as in vivo and in vitro wear and corrosion rates.

After noting their location on all surfaces, wear particles should be washed off implant surfaces into the test solution. A sample of the wear particles should be characterized, then all metal particles in solution dissolved with an acid (e.g., HCl), and the total metal content in the solution, including particles, measured by AAS (atomic absorption spectroscopy) (Kovacs, P.; et al. 1992). Care should be taken to remove all particles from the test specimen surface and to completely dissolve particulate or oxidized metal (Margevicius, R.W.; et al. 1989).

Complimentary methods of monitoring fretting corrosion may be used in addition to those listed above. For example: fretting corrosion currents measured during cyclic loading or crack formation and fatigue strength before and after fretting.

BIOCOMPATIBILITY

Materials with limited or no history of successful use in orthopedic implants must be determined to exhibit an acceptable biological response equal or better than predicate or substantially equivalent devices when tested by the following methods:

ASTM F 748;
ASTM F 981; and

an animal implant model in which particles are introduced into the medullary canal (simulating stem micromotion). The study should include histological examination of the:

1. adjacent tissues, and
2. regional lymph nodes.

CLINICAL DATA

All available clinical data involving the modified surface described above should be summarized in a table. This data should include, but is not limited to information regarding loosening between parts of the device and at the bone-implant interface, frank surface coating failure or other indications of success or failure.

MANUFACTURING

The manufacturing process of the final product and test samples must be described in enough detail to give a clear understanding of the origin of significant differences between the properties of currently marketed devices.

REPORTING

To help FDA in its review and facilitate a determination of substantial equivalence and/or safety and effectiveness, a very brief summary of all information should be organized in the order shown in part VII. ORGANIZATION OF REPORTED INFORMATION. Any additional and important information not specifically mentioned in the above guidance document should be inserted into this organization where appropriate. Detailed test reports from which the summarized data originated should be organized in a similar manner (as much as possible) and included in the submission to FDA. The detailed reports should include, but are not limited to, the following:

1. Report title
2. Investigators' names
3. Facility Performing the test
   Name
   Address
   Phone Number

4. Dates
    - Test initiation
    - Test completion
    - Final report completion
5. Objectives/Hypothesis
6. Test and control samples
    - Sample selection criterion
    - Design
    - Materials
    - Processing methods
    - Differences between test samples, control samples and marketed device
7. Methods and Materials
    - Test setup schematic or photograph
    - Description of grips or potting medium interfacing with samples
    - Test equipment calibration schedule, methods and data
    - Discussion of dependent, independent and uncontrolled variables, e.g.:
        - Test and control sample parameters
        - Environment composition, pH, volume, flow, temperature, replacement
        - Electromagnetic fields, applied charge, irradiation
        - Load directions, points of application and magnitudes
        - Times (e.g. rates, frequencies, number of cycles)
        - Other
        - Rationale for choices of parameters, values, etc.
    - Methods of specimen examination (e.g., failure analysis)
    - Statistical justification for the number of samples
    - Chronological description of the test procedures
    - Deviations from referenced protocols and standards
8. Results
    - Time from manufacturing till testing commences
    - Discussion of the data and possible mechanisms
    - List of conclusions
    - Discussion of the objective/hypothesis
    - Simplifications and assumptions and their clinical implications
9. Appendices
    - Experimental data
    - Calculations
    - Bibliography of all references pertinent to the report

ORGANIZATION OF REPORTED INFORMATION

PROPERTY	CONCERNS OR ISSUES	POSSIBLE TESTING
1.STRENGTH, ASSEMBLY & DISASSEMBLY	1.EASE OF ASSEMBLY 2.EASE OF DISASSEMBLY 3.DISASSEMBLY IN THE PATIENT 4.HIGH INDUCED STRESSES (# 5) 5.LOOSENING (# 3) 6.FRACTURE & DEFORMATION	LOAD VS DEFLECTION TO FAILURE FOR VARIOUS ASSEMBLY LOADS
2.DEVICE RIGIDITY	HIGH RIGIDITY/BONE RESORPTION OR LOW RIGIDITY/BONE FRACTURE	PLOT LOAD VS DEFLECTION
3.CYCLIC FATIGUE PROPERTIES	FRACTURE, DEFORMATION, WEAR & LOOSENING	"S-N" CURVE
4.IMPROPER CONNECTIONS	EFFECT OF HIGH STRESS ON THE ENDURANCE OF THE DEVICE	INSTRUCTIONS FOR ATTACHMENT & COMPONENT MATCHING IN LABEL
5.INDUCED STRESSES AT CONNECTIONS	EFFECT OF HIGH STRESS ON THE ENDURANCE OF THE DEVICE	STRESS ANALYSIS &/OR MECHANICAL TESTING (# 1-3)
6.LOCAL STRESS RISERS	EFFECT OF HIGH STRESS ON THE ENDURANCE OF THE DEVICE	STRESS ANALYSIS &/OR MECHANICAL TESTING (# 1-3)
7.THERMAL EXPANSION OF PARTS DUE TO STERILIZATION	EFFECT OF HIGH STRESS ON THE ENDURANCE OF THE DEVICE	STRESS ANALYSIS &/OR MECHANICAL TESTING (# 1-3)
8.INSUFFICIENT MATERIAL TO SUPPORT LOADS	EFFECT OF HIGH STRESS ON THE ENDURANCE OF THE DEVICE	STRESS ANALYSIS &/OR MECHANICAL TESTING (# 1-3)
9.WEAR, CORROSION & DEGRADATION	MORE CREVICES & FRETTING DISSIMILAR METALS IN CONTACT AMOUNT, SIZES & TYPES OF IONS & PARTICULATE MATERIAL RELEASED	CREVICE CORROSION STUDY GALVANIC CORROSION STUDY FRETTING CORROSION (E.G., ASTM F 897) OR DEGRADATION
10.BIOCOMPAT-ABILITY	BIOCOMPATIBILITY OF: 1.PARTICLES 2.BREAKDOWN PRODUCTS 3.METAL IONS 4.BULK MATERIAL	
11.OTHER	NEW FAILURE MECHANISMS	LOOK FOR & EVALUATE NEW FAILURE MECHANISMS CLINICAL STUDY