

DEPARTMENT OF HEALTH AND HUMAN SERVICES

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Food and Drug Administration

[Docket No. 1998D-0077 (formerly 98D-0077)]

Clinical Development Programs for Human Drugs, Biological Products, and Medical Devices for the Treatment and Prevention of Osteoarthritis; Request for Assistance

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) seeks additional information on issues related to clinical development programs for human drugs, biological products, and medical devices for the treatment and prevention of osteoarthritis (OA). We will take such information into account as we work to finalize our draft guidance issued in July 1999. Once finalized, the guidance will aid sponsors and other interested parties in developing new products to treat OA.

Before the agency can issue such guidance, a critical appraisal of certain fundamentals of the science related to OA is needed. FDA is inviting any interested party, or parties, to conduct and manage the coordination of this critical appraisal. FDA believes that the party, or parties', first step in conducting the critical appraisal would be to hold a public meeting to discuss issues related to OA assessment and trial design. FDA intends to submit to the docket all the information received in response to this notice so that interested parties may be fully informed and to facilitate participation in and coordination of these activities.

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DATES: Submit written or electronic comments on this notice by *[insert date 60 days after date of publication in the Federal Register]*.

ADDRESSES: Submit written comments on this notice to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to *http://www.fda.gov/dockets/ecomments*.

FOR FURTHER INFORMATION CONTACT: Terrie L. Crescenzi, Office of the Commissioner (HF-18), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-7864.

SUPPLEMENTARY INFORMATION: Because of the positive response to the agency's guidance on rheumatoid arthritis, the agency has recognized the need for more information on the development of human drugs, biological products, and medical devices for the treatment and prevention of OA. FDA is requesting assistance from the public in conducting scientific analyses for the purpose of finalizing the agency's current draft OA guidance.

Specifically, the agency is inviting any interested group or consortium of interested groups from academia, industry, practitioners, and patients and their representatives to conduct and manage the coordination of a critical appraisal of certain fundamentals of the science related to OA. Initially, the party or parties would organize and hold a public meeting to discuss relevant questions related to OA assessment and trial design (a number of which are suggested in this notice). FDA believes a public meeting will lead to conceptual advances not now present, and the expression of such advances in a series of concept papers. These concept papers would then be discussed at subsequent workshops, soliciting feedback from all parties including regulators from the

United States and elsewhere. Such discussion would emphasize the rationale for various approaches to key issues.

FDA welcomes other suggestions of activities that could be undertaken as part of this guidance development effort. To provide a starting point for discussion, FDA has developed a list of some key concepts that the interested parties may want to consider for discussion at the meeting.

1. Should the *scope* of the guidance apply to OA alone? Are there particular clinical subgroups of OA that need to be explicitly considered and addressed?

2. For a *claim of symptomatic relief* in OA, what are the optimal outcome measures and trial designs? Currently, withdrawal and flare designs are commonly used. These designs, while believed to be predictive, may lack generalizability. It is also difficult to understand the actual size of the treatment effect based on a flare design. If withdrawal and flare designs are not optimal, what alternative designs could be used to support a symptomatic relief claim? What should the size and duration of exposure of the safety database be for symptomatic relief?

3. Is a *claim of decreased rate of progression* useful and, if so, what would be the appropriate outcome measure(s) to establish the claim? What is the desirable duration of a trial for this claim? What comparator arms might be used?

4. For a *claim of prevention or risk reduction* for the development of OA, what are potential outcome measures? If biomarkers are used, what is their state of qualification? What is the desirable duration of a trial for such a claim? What is an appropriate safety database for a prevention of OA claim?

5. Are there *additional claims* that should be considered? If so, what outcome measures and trial designs should be used?

6. In any *long term studies*, what are the best statistical comparisons for inference testing (is, for instance, a comparison of mean changes from baseline suitable or should responses be graded according to points on established scales)? Because longer trials inevitably have substantial dropouts, what imputation methods for dropouts are most appropriate or should the trial results be based on a survival analysis or a time to event (for treatment failure) analysis?

Interested persons should submit comments and expressions of interest in conducting and managing a critical appraisal to the Division of Dockets Management (see **ADDRESSES**). Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document.

Received comments are available for public examination in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

Dated: **AUG 8 2007**

August 8, 2007.

 Jeffrey Shuren

Jeffrey Shuren,
Assistant Commissioner for Policy.

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