Guidance for Industry

Independent Consultants for Biotechnology Clinical Trial Protocols

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research (CBER)
Center for Drug Evaluation and Research (CDER)
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Additional copies of this guidance are available from:
Office of Communication, Training, and
Manufacturers Assistance, HFM-40
Center for Biologics Evaluation and Research
Food and Drug Administration
Suite 200N
1401 Rockville Pike, Rockville, MD 20852-1448
Internet: http://www.fda.gov/cber/guidelines.htm
Phone: 800-835-4709 or 301-827-1800
or
Office of Training and Communication
Division of Communications Management
Drug Information Branch, HFD-210
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane, Rockville, MD 20857
Phone: 301-827-4573
Internet: http://www.fda.gov/cder/guidance/index.htm

Table of Contents

Contains Nonbinding Recommendations

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This guidance document represents the agency's current thinking on this topic. It does not create or confer any 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 statutes and regulations. If you want to discuss an alternative approach, contact the appropriate FDA staff. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. WHY IS FDA ISSUING THIS GUIDANCE?

On June 12, 2002, the President signed the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, which included the Prescription Drug User Fee Amendments of 2002 (PDUFA III). Secretary Thompson's letter to Congress concerning PDUFA III included an addendum containing the performance goals and programs intended to facilitate the development and review of human drugs to which the Food and Drug Administration (FDA) had committed. The letter and addendum can be found on the Internet at http://www.fda.gov/oc/pdufa/default.htm.

One commitment was the establishment of a program that allows you, a sponsor of clinical trials for certain products, to request that we, FDA, engage an independent consultant to participate in the review of your protocol for a clinical study that is intended to serve as the primary basis of a claim of efficacy. We are publishing this guidance to explain when and how you may take advantage of this program. This guidance finalizes the draft guidance of the same title dated May 2003.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe FDA's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word "should" in FDA's guidances means that something is suggested or recommended, but not required.

[1] This guidance has been prepared by the Center for Biologics Evaluation and Research (CBER) and the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration.

II. WHAT PRODUCTS ARE ELIGIBLE FOR THIS PROGRAM?

This program is available for a subset of products covered by PDUFA III. Your product qualifies for this program if:

- It is biotechnology-derived (for example, DNA plasmid products, synthetic peptides of fewer than 40 amino acids, monoclonal antibodies for in vivo use, and recombinant DNA-derived products),
- It has the potential to represent a significant advance in the treatment, diagnosis, or prevention of a disease or condition, or to address an unmet medical need, and
- The clinical study at issue is intended to serve as the primary basis of a claim of efficacy.

III. HOW DO YOU REQUEST THAT FDA ENGAGE AN INDEPENDENT CONSULTANT?

We recommend that you submit a written request to us asking that we engage a consultant as part of your request for a formal meeting, (e.g., an End of Phase 2 meeting.) You should clearly designate this as a "Request for Appointment of Expert Consultant." The request should include the information needed for the meeting as explained in FDA's "Guidance for Industry: Formal Meetings With Sponsors and Applicants for PDUFA Products,"[2] dated February 2000, and the reasons that you believe an expert consultant should be engaged. These reasons might include preliminary discussions with FDA that resulted in disagreement over the protocol or a novel or unorthodox approach to the clinical trial or its analysis.

IV. DOES YOUR REQUEST AFFECT THE PDUFA MEETING MANAGEMENT GOALS?

Yes. We will need time to select and screen the consultant for potential conflicts of interest and the consultant will need sufficient time to review the scientific issues involved. Therefore, we will extend certain of the performance goals for scheduling and holding a meeting by 60 days. We will notify you within 14 days of our intent to schedule your meeting and engage an independent consultant. We will not be able to tell you when the meeting will be scheduled until we have engaged the consultant. Similarly, if you wish the independent consultant to participate in other protocol assessment activities, such as a special protocol assessment and agreement, we will extend PDUFA performance goals related to those activities by sixty (60) days, to take into account the time necessary to select and screen the consultant. The goal for any given meeting management activity will be extended by not more than 60 days. It is our intention to schedule these activities as efficiently as possible.

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[2] See www.fda.gov/cber/guidelines.htm.

V. HOW MANY TIMES CAN YOU USE THIS PROGRAM DURING THE DEVELOPMENT OF YOUR PRODUCT?

We will engage an independent consultant under this program only once during the development of your product. This restriction does not limit your ability to request that we take to an Advisory Committee an issue pertaining to the product's marketing application review. Nor does it limit our ability to take an issue to an Advisory Committee or otherwise to seek advice on an issue.

VI. CAN YOU RECOMMEND CONSULTANTS FOR THE FDA TO ENGAGE?

You can submit a list of recommended consultants, their qualifications, and contact information for us to consider. Prospective consultants will be screened for conflicts of interest. We suggest that you do not recommend consultants:

- Whom you know to have financial conflicts,
- Who have been involved in the design or planning of the clinical trial, or
- Whom you intend to ask to be an investigator.

We may or may not select the consultant from your list of recommendations. We will notify you of our selection prior to the formal meeting.

VII. WHAT IS THE STATUS AND ROLE OF THE CONSULTANT?

Prospective consultants will be screened for potential conflicts of interest according to the criteria described in Policies and Procedures for Handling Conflicts of Interest with FDA Advisory Committee Members, Consultants, and Experts[3] (FDA Waiver Criteria 2000) and be subject to confidentiality requirements. The consultant we select may or may not already be a special government employee. The consultant may:

- Review the clinical protocol and appropriate background material,
- Participate in our meeting with you, and
- Provide us with advice on your clinical protocol and product development plan.

We will remain responsible for making scientific and regulatory decisions regarding the clinical protocol, taking into account the consultant's advice.

[3] See http://www.fda.gov/oc/advisory/conflictofinterest/intro.html

Following the completion of their service with respect to this program, consultants that we retain under contract are not restricted from other interactions with FDA. These consultants will continue to be subject to the restrictions applicable to that position. (see footnote 3).

VIII. WILL WE ALWAYS GRANT YOUR REQUEST?

We will grant your request unless we determine that engaging an expert consultant would not serve a useful purpose (e.g., it is clearly premature).

- If we grant your request: We will engage an independent consultant, of our choosing.
- If we deny your request: We will provide you with a written rationale for the denial within 14 days of receipt of your request for an expert consultant.
- If you disagree with our rationale for refusing the request: You may submit a request for formal dispute resolution.