Guidance for Industry

Advisory Committees: Implementing Section 120 of the Food and Drug Administration Modernization Act of 1997

U.S. Department of Health and Human Services
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Center for Biologics Evaluation and Research (CBER)
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After the comment period closes, comments should be provided in writing to the Center for Drug Evaluation and Research (CDER), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857; or Center for Biologics Evaluation and Research (CBER), 1401 Rockville Pike, Rockville, MD 20852-1448.

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I. INTRODUCTION

This document provides guidance for industry on changes to the policies and procedures being used by the Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER) with regard to advisory committees as a result of section 120 of the Food and Drug Administration Modernization Act of 1997 (the Modernization Act). This guidance document supplements the policies and procedures described in the *Policy and Guidance Handbook for FDA Advisory Committees*. In general, the guidance explains modifications, prompted by the Modernization Act, in CDER's and CBER's practices with regard to advisory committees.

II. BACKGROUND

Advisory committees provide independent advice and recommendations to the Food and Drug Administration (FDA) on scientific and technical matters related to the development and evaluation of products regulated by the Agency. Through the advisory committee system, FDA is able to secure independent professional expertise in accomplishing its mission and maintaining the public trust. CDER and CBER request advice from advisory committees on a variety of matters, including various aspects of clinical investigations and applications for marketing approval of drug products. Although the committees provide recommendations to the Agency, final decisions are made by FDA.

On November 21, 1997, President Clinton signed the Modernization Act. Section 120 of the Modernization Act amends section 505 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 355) by adding section 505(n). Section 505(n)(1) of the Act directs FDA to establish panels of experts, or to use already-established panels of experts, to provide scientific advice and recommendations to the Agency regarding the clinical investigation of drugs or the approval for marketing of drugs. FDA understands the term *panels of experts* to mean advisory committees.

Section 505(n) of the Act includes provisions for (1) additional members to be included in *new* advisory committees, (2) new conflict of interest considerations, (3) education and training for new committee members, (4) timely committee consideration of matters, and (5) timely Agency notification to affected persons of decisions on matters considered by advisory committees.

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[1]This guidance has been prepared by the Center for Drug Evaluation and Research (CDER), the Center for Biologics Evaluation and Research (CBER), and the Office of the Commissioner. This guidance document represents the Agency's current thinking on the advisory committee provisions of the Food and Drug Administration Modernization Act of 1997. 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 statute, regulations, or both.

FDA regulations in 21 CFR Part 14 establish the general procedures for Agency use of advisory committees. FDA has determined that these regulations, described in pertinent part in this guidance document, do not need to be amended for CDER and CBER to implement the modifications in advisory committee policies and procedures that have resulted from the enactment of section 505(n) of the Act.

Because CDER and CBER advisory committees are organized according to general subject (e.g., blood products, cardiovascular and renal drugs) and not according to the topic for consideration by the committee (e.g., a clinical investigation of a drug product, the content of a guidance document), CDER and CBER generally use the same policies and procedures for all advisory committees, regardless of the topic that will be considered by the committee. Consequently, unless otherwise stated, the following guidance applies to CDER and CBER advisory committees regardless of the topic for consideration.

III. MEMBERSHIP

Advisory committees generally consist of individuals possessing recognized expertise and judgment in a specific field. Members have the training and experience necessary to evaluate information objectively and to interpret its significance under various, often controversial, circumstances.

Section 505(n)(3) of the Act describes the membership requirements for *new* advisory committees that may be established under section 505(n)(1) of the Act. Advisory committees that are already chartered need not amend their membership to comply with these new provisions. However, in the interest of furthering the goals of the statutory amendments, CDER and CBER intend generally to modify current advisory committee membership on a meeting-by-meeting basis and to recharter committees, as needed, to reflect the representation described in section 505(n)(3) of the Act.

Advisory committee membership under the new statute is comprised of *core members* of the panel and other individuals who may be called upon to participate in a given meeting on an ad hoc basis. The *core members* of the advisory committee are appointed by the Commissioner or his/her designee based on their scientific or technical expertise and serve for the duration of the committee or until their terms of appointment expire, they resign, or they are removed by the Commissioner or his/her designee (21 CFR 14.80). In accordance with section 505(n)(3) of the Act, the Commissioner or his/her designee may call upon individuals to supplement the core membership on an ad hoc basis so that the group considering an issue presented to an advisory committee may also include (1) representation of consumer/patient interests, (2) representation from the interests of the drug manufacturing industry, and (3) at least two members who are specialists with expertise in the particular disease or condition for which the drug under consideration is proposed to be indicated.

Voting members of an advisory committee have expertise, as demonstrated by training, education,

and experience, in the subject matter that the committee is considering. To the extent feasible, voting members should possess skill and experience in the development, manufacture, or use of the types of drugs to be referred to the committee, and the group of voting members should reflect a balanced composition of scientific expertise through members with diverse professional education, training, and experience (21 CFR 14.80(b)(1)). *Core members* of an advisory committee will be voting members of the committee, to the extent that such participation is not prevented by conflict of interest laws and regulations. *Ad hoc committee members* who are representatives of consumer or patient interests, or who have expertise in the particular disease or condition for which the drug under consideration is proposed to be indicated, will be voting members *if* (1) the members have the requisite scientific or technical expertise and (2) this participation is not prevented by conflict of interest laws and regulations. Because of inherent conflict of interest concerns, representatives of the drug manufacturing industry will not be voting members of the committee. Furthermore, no person who is a regular full-time employee of the United States government *and* is engaged in the administration of the Act may be a voting member of an advisory committee (section 505(n)(3) of the Act).

Advisory committee members who vote at committee meetings are selected in accordance with 21 CFR 14.80 and 14.82. At the beginning of each committee meeting, those members who are voting members will be announced.

IV. CONFLICTS OF INTEREST

Members of advisory committees have long been subject to a number of conflict of interest laws and regulations, most notably 18 U.S.C. 208. Section 505(n)(4) of the Act introduces new administrative conflict of interest and associated waiver considerations. Specifically, absent a waiver, a committee member may not vote on any matter regarding the clinical investigation or approval for marketing of a drug if the member or the member's immediate family could gain financially from the committee's recommendations. In this context, consistent with conflict of interest rules, *immediate family* means an individual's spouse and minor children.

Waivers under section 505(n)(4) of the Act may be granted if the member's participation is necessary to afford the committee essential expertise. Such waivers may be granted by the Commissioner or his/her designee under the procedures described in Chapter VIII of the *Policy and Guidance Handbook for FDA Advisory Committees* that are already in place to fulfill the requirements of 18 U.S.C. 208. However, no waiver may be given if the member's own scientific work is involved. A member's own scientific work may include his/her work as a principal investigator or as a major participant in the clinical studies that are under consideration by the advisory committee.

Under section 505(n)(4) of the Act, all members of an advisory committee are to disclose publicly all conflicts of interest that they may have with regard to the issues to be considered by the committee. Currently, the executive secretary of an advisory committee generally reads a statement at the beginning of each meeting that states (1) the name of each voting member of the committee who has a conflict of interest and (2) the type of waiver, if any, that has been granted

to the member. This practice satisfies the public disclosure requirements of section 505(n)(4) of the Act.

V. ADVISORY COMMITTEE MEETINGS

A. Scheduling

Section 505(n)(7) of the Act states that FDA is to schedule advisory committee meetings so that any matter for consideration by a committee can be presented within 60 calendar days of its being ready for review. A matter is considered to be *ready for review* when the Agency and the sponsor or applicant have completed all preparatory work for its presentation at an advisory committee meeting. Division Directors in CDER and CBER, working with the Chairs and executive secretaries of advisory committees, should anticipate and schedule advisory committee meetings in a manner that complies with this statutory provision. Because advisory committee members have full schedules, advance notice is critical to ensure a quorum. Based on anticipated and pending drug applications, advisory committee meetings should be planned on a yearly basis, although it should be understood that scheduling is tentative and may be changed based on new circumstances.

To facilitate the holding of advisory committee meetings, meetings may take place through the use of electronic communications such as telephone conference calls or video conferences as authorized in section 505(n)(7) of the Act and 21 CFR 14.22(g). Nevertheless, if any member of an advisory committee is unable to participate in a meeting, the executive secretary may decide to go forward with the meeting as planned, as long as a quorum exists.

B. Quorum

A quorum, or the number of members that need to be present, to hold an advisory committee meeting is generally a majority of voting members. However, as authorized by 21 CFR 14.22(d), FDA may specify in a particular advisory committee charter that a quorum is less than a majority of total current voting members. For example, if one advisory committee is responsible for considering disparate issues, FDA may stipulate in the committee charter that a quorum is reached when a majority of voting members who are experts in the particular subject matter under consideration by the committee is present.

Voting members, as discussed in the previous paragraph, generally refers to *core members* of a committee (see section II above). However, when additional voting *ad hoc members* are added to the committee to provide needed scientific and technical expertise at a particular meeting, a quorum will be based on the combined total of core members plus the added temporary voting scientific members.

VI. ACTION ON COMMITTEE RECOMMENDATIONS

Advisory committees provide recommendations to the Agency on matters brought before them for consideration, but final decisions on such matters are made by the Agency. Section 505(n)(8) of the Act directs the FDA official responsible for the matter to notify affected persons of the Agency's decisions on advisory committee recommendations within 90 calendar days of the committee recommendation. As used in this guidance with respect to the clinical investigation of a drug or the approval for marketing of a drug, the FDA official responsible for the matter (i.e., the *primary Agency decision maker*) is the individual (generally a Division Director or Office Director) who has the authority to approve the application (see CDER MAPP 4634.1, CBER SOP 8405). To maintain consistency with FDA disclosure of information regulations (e.g., 21 CFR Part 20 and §§ 312.130 and 314.430), *affected persons* with respect to advisory committee recommendations means the *sponsors* of clinical investigations and/or *applicants* for FDA approval of drug products on which an advisory committee has provided advice.

To implement this provision, the primary Agency decision maker should, within 90 calendar days of the committee recommendation, review the committee's recommendation and notify the affected persons of the status of FDA's decision on the matter. If no decision has been reached within this time frame, the primary Agency decision maker should notify the affected persons and indicate the reasons for no decision. The rationale for decisions and reasons for no decisions should be documented.

VII. EDUCATION AND TRAINING

Section 505(n)(5) of the Act directs the Agency to provide education and training to each new member of an advisory committee before the member participates in a committee meeting. Advisory committee members may be trained in a variety of ways, including the review of written materials and videotapes, attendance at advisory committee meetings prior to appointment to a committee, one-on-one discussions with FDA staff, attendance at new advisory committee member orientation, and attendance at CDER's new reviewer training sessions. New members should be given the opportunity to attend at least one advisory committee meeting prior to their appointment as members. When members are recruited to serve, executive secretaries should convey the expectation that new members attend appropriate training sessions. The executive secretary should provide a new member with appropriate orientation materials (written and/or videotaped) and should have one-on-one discussion(s) with a new member concerning his/her service on the committee prior to the member's participation in his/her first meeting.

GLOSSARY

Advisory committee: A committee, board, commission, council, conference, panel, task force, or subgroup thereof that is not composed entirely of full-time Federal officials or employees and that is established by statute or is utilized by the Department of Health and Human Services (Department) or FDA to advise or make recommendations on matters relating to the programs, responsibilities, or activities of the Department or FDA. As used in this guidance document, *advisory committees* means scientific and technical advisory committees. (See 5 U.S.C. App. 2, § 3; 21 CFR 10.3(a); 21 CFR Part 14; and the *Policy and Guidance Handbook for FDA Advisory Committees*.)

Advisory committee member: An individual appointed to serve on an advisory committee. Members may have scientific expertise and/or represent patient, consumer, or industry interests. Members may be voting or nonvoting.

Affected persons: As used in this guidance document, affected persons refers to sponsors of clinical investigations and/or applicants for FDA approval of drug products on which an advisory committee has provided advice.

Chair: An advisory committee member who is appointed to preside at committee meetings and ensure that all rules of order and conduct are maintained during each session.

Core members: Members of an advisory committee that are appointed by the Commissioner or his/her designee because of their scientific or technical expertise and serve for the duration of the committee, or until their terms of appointment expire, they resign, or they are removed by the Commissioner or his/her designee.

Executive secretary: The individual responsible for an advisory committee's overall administrative management.

Immediate family: An individual's spouse and minor children.

Panel of experts: See "advisory committee."

Primary Agency decision maker: As used in this guidance document, with respect to a matter regarding the clinical investigation of a drug or the approval for marketing of a drug, the primary Agency decision maker is the Agency official, generally a Division Director or Office Director, who has authority to approve the application.

Ready for review: For purposes of this guidance document, a matter is considered to be ready for review when the Agency and the sponsor or applicant have completed all preparatory work for its presentation at an advisory committee meeting.