

September 2008

FDA ADVISORY COMMITTEES

Process for Recruiting Members and Evaluating Potential Conflicts of Interest





Highlights of [GAO-08-640](#), a report to congressional requesters

Why GAO Did This Study

The Department of Health and Human Services' (HHS) Food and Drug Administration (FDA) has been criticized about how it recruits individuals to become members of its advisory committees and how it grants some determinations that allow members with conflicts of interest to participate in committee meetings. Advisory committee meetings can include both standing and temporary members. Temporary members only serve for a particular meeting. GAO was asked to examine FDA's advisory committee processes. GAO reported on (1) how FDA recruited individuals for membership and evaluated candidates for potential conflicts of interest, (2) barriers that were reported to recruiting qualified individuals to serve on committees, and (3) the proportion of standing and temporary members, and the frequency with which members with conflict of interest determinations participated in meetings.

GAO reviewed FDA advisory committee policies and analyzed meeting records for FDA's Center for Biologics Evaluation and Research (CBER), Center for Drug Evaluation and Research (CDER), and Center for Devices and Radiological Health (CDRH). GAO also interviewed individuals familiar with FDA's committee member recruiting process. GAO did not examine the effects of changes in FDA's advisory committee processes resulting from the FDA Amendments Act of 2007 and 2007 FDA policy revisions as it was too soon to assess them.

To view the full product, including the scope and methodology, click on [GAO-08-640](#). For more information, contact Marcia Crosse at (202) 512-7114 or crossem@gao.gov.

FDA ADVISORY COMMITTEES

Process for Recruiting Members and Evaluating Potential Conflicts of Interest

What GAO Found

Prior to the FDA Amendments Act of 2007, FDA employed several methods to recruit candidates for advisory committees and to evaluate candidates by prescreening them for potential conflicts of interest. FDA recruited candidates by announcing vacancies in the *Federal Register*, distributing recruitment brochures at advisory committee meetings and national meetings, word-of-mouth or asking current advisory committee members, and posting recruitment and conflict of interest information on FDA's Web site. To evaluate advisory committee candidates for conflicts of interest, FDA reviewed the candidates' curricula vitae and usually conducted a prescreening interview. FDA employed many of the same recruitment and evaluation practices used by organizations previously identified by GAO as employing methods that could ensure an independent and balanced advisory committee.

FDA faced barriers to recruiting qualified advisory committee candidates, particularly those without potential conflicts of interest, according to FDA officials and former FDA advisory committee members. However, GAO found that the agency may have been able to mitigate these barriers by expanding its outreach efforts. FDA staff and former FDA advisory committee members GAO interviewed generally agreed that individuals with the expertise FDA sought for its advisory committees were the same leading experts that industry sought to conduct research. In addition, word-of-mouth—the advisory committee member recruitment method FDA officials generally agreed was most effective—was limited in the number of candidate nominations it could generate. The FDA Amendments Act of 2007 modifies FDA's process for prescreening candidates for committee membership.

Standing and temporary members were 58 and 42 percent, respectively, of the 1,218 participants in the 83 advisory committee meetings held by CBER, CDER, and CDRH in 2004 and 2006 that GAO reviewed. FDA may permit an advisory committee member who has a conflict of interest, or an appearance of a conflict, and whose expertise is needed to participate in an advisory committee meeting under certain circumstances by granting a conflict of interest determination. More than half of the meetings had at least one standing or temporary member with at least one conflict of interest determination. The 200 members found to have at least one conflict of interest determination represented about 16 percent of all 83 meetings' participants. The FDA Amendments Act of 2007 limits the number of certain conflict of interest determinations that FDA can grant and FDA's conflict of interest policy revisions limit the amount of the disqualifying financial interests.

In its comments on a draft of this report, HHS noted that on August 4, 2008, after GAO provided the draft report for its review, FDA issued four final guidance documents concerning management of its advisory committees. HHS also provided additional clarifications about aspects of FDA's advisory committees. GAO revised the report to cite the final guidances and to incorporate HHS's clarifications where appropriate.

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Abbreviations

AAMC	Association of American Medical Colleges
ACOMS	Advisory Committee Oversight and Management Staff
ACS	Advisors and Consultants Staff
CBER	Center for Biologics Evaluation and Research
CDC	Centers for Disease Control and Prevention
CDER	Center for Drug Evaluation and Research
CDRH	Center for Devices and Radiological Health
EIS	Ethics and Integrity Staff
EPA	U.S. Environmental Protection Agency
FACA	Federal Advisory Committee Act
FDA	Food and Drug Administration
HHS	Department of Health and Human Services
MDAC	Medical Devices Advisory Committee
NIH	National Institutes of Health
OGE	Office of Government Ethics
PhRMA	Pharmaceutical Research and Manufacturers of America
SGE	special government employee

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United States Government Accountability Office
Washington, DC 20548

September 30, 2008

The Honorable Edward Kennedy
Chairman
The Honorable Michael B. Enzi
Ranking Member
Committee on Health, Education, Labor, and Pensions
United States Senate

The Honorable Richard J. Durbin
United States Senate

The Food and Drug Administration (FDA) is responsible for ensuring the safety and efficacy of drugs, biological products, and medical devices the American public uses every day. FDA convenes scientific advisory committees to provide independent expertise and technical assistance to help the agency make decisions about the development and evaluation of products regulated by FDA. Advisory committees include standing members, who are appointed by FDA to serve a specified term on an advisory committee, and may include temporary members, who are selected by FDA to serve at only one specific meeting.¹ Other individuals that may contribute to the advisory committee meeting discussion include guest speakers, such as researchers who are invited to present scientific papers and individuals who speak on behalf of the companies whose products are at issue. Members of the public are also allowed to speak during an open public hearing portion of the advisory committee meeting. The advisory committees' recommendations are not binding on the agency, but the agency usually follows the advisory committees' advice.

Some advisory committee members might have financial conflicts of interest for all or part of a committee meeting depending on the issues or products to be discussed. Conflicts of interest, for example, might include a member having financial investments in a drug manufacturer whose product is under review. While some conflicts of interest could require

¹Standing members are individuals appointed to serve on an FDA advisory committee and are part of the official advisory committee roster of authorized membership. Temporary members are individuals that FDA selects to serve for a specific advisory committee meeting to provide additional expertise or to ensure that a quorum of members is present to conduct a meeting.

that a member be prohibited from participating in a meeting, FDA may permit a member to participate in advisory committee meeting discussions under certain circumstances by granting waivers of the statutory prohibition on participation. FDA can also authorize a member to participate when the statutory conflict of interest prohibition would not have been violated, but there is the appearance of a conflict of interest, such that the member's impartiality involving the committee meeting's discussions could be questioned. For purposes of this report, both types of decisions are called conflict of interest determinations.² FDA has been criticized about how it recruits qualified individuals for its advisory committees and how it grants some conflict of interest determinations allowing members with conflicts of interest to participate in committee meetings. FDA maintains that its advisory committee members are preeminent scientists in their field, and that it is inevitable that some of these experts will have grants from, and contracts with, the regulated industries, which could constitute a potential conflict of interest or present the appearance of partiality. FDA asserts that its ability to make conflict of interest determinations is essential to its effort to access the most expert medical and scientific advice available. Others contend, however, that the objectivity of the advice and recommendations given by FDA advisory committees can be affected by the involvement of conflicted members.

You have expressed interest in information about how FDA identified, recruited, and prescreened qualified candidates and about FDA's use of standing and temporary members and the extent these members received conflict of interest determinations. In this report we describe (1) how FDA recruited individuals for advisory committee membership and evaluated candidates by prescreening them for potential conflicts of interest,³ (2) barriers that were reported to recruiting qualified individuals to serve

²In this report, we use the term conflict of interest waivers to refer to FDA's decision to allow an individual with a financial conflict of interest to participate in an advisory committee meeting as provided by statute. We use the term appearance authorization to refer to FDA's decision to authorize an individual to participate in an advisory committee meeting, as provided for in regulations issued by the Office of Government Ethics (OGE), when the individual's impartiality could be questioned.

³FDA uses the term prescreen to define the initial process of evaluating an individual's financial interests to determine whether that person has potential conflicts of interest prior to nominating him or her for advisory committee membership. FDA uses the term screen to define the process of evaluating advisory committee members' financial interests prior to a committee meeting to determine whether they have conflicts of interest based on the advisory committee meeting topic.

on FDA advisory committees, particularly candidates without potential conflicts of interest, and (3) the proportion of standing and temporary members in advisory committee meetings, and the frequency with which members with one or more conflict of interest determinations participated in advisory committee meetings.

To report on these issues, we reviewed the Department of Health and Human Services' (HHS)⁴ and FDA's advisory committee regulations, policies, and guidances. We also reviewed the federal conflict of interest statutes and the Office of Government Ethics (OGE) regulations. We interviewed FDA's Advisory Committee Oversight and Management Staff (ACOMS) and Ethics and Integrity Staff (EIS). We also interviewed staff such as executive secretaries, who manage advisory committees; review division directors; and advisory committee management staff from the three FDA centers that we analyzed: the Center for Biologics Evaluation and Research (CBER), which regulates biological products such as blood and vaccines; the Center for Drug Evaluation and Research (CDER), which regulates drugs; and the Center for Devices and Radiological Health (CDRH), which regulates medical devices and radiological products. We chose to analyze these three centers because most of FDA's advisory committees were affiliated with them—and these centers' advisory committee meetings represented more than 80 percent of the total FDA advisory committee meetings held in 2004 and 2006.

To examine how FDA recruited individuals for advisory committee membership and prescreened candidates for potential conflicts of interest, in addition to interviews with FDA officials, we interviewed representatives from selected advocacy organizations that participate in nominating candidates for advisory committee membership, such as the Pharmaceutical Research and Manufacturers of America (PhRMA) and Public Citizen's Health Research Group. We compared FDA's recruitment and prescreening methods to the methods used by the U.S. Environmental Protection Agency (EPA) and the National Academies,⁵ organizations we identified in 2004 as employing specific recruitment and prescreening

⁴FDA is an agency within HHS and is subject to HHS's advisory committee regulations, policies, and guidances.

⁵The National Academies consist of four private, nonprofit organizations that advise the federal government on scientific and technical matters: the National Academy of Sciences, the National Academy of Engineering, the Institute of Medicine, and the National Research Council.

methods that could ensure independent and balanced advisory committees.⁶ We updated our information on EPA's and the National Academies' recruitment and prescreening methods through interviews with agency officials.

To examine barriers that were reported to recruiting qualified individuals to serve on FDA advisory committees, particularly candidates without potential conflicts of interest, we interviewed individuals and groups familiar with FDA's advisory committee recruitment processes and officials from organizations we identified in 2004 as employing specific recruitment methods that could ensure independent and balanced advisory committees. Individuals interviewed included current and former FDA staff; former CBER, CDER, and CDRH advisory committee members; staff involved with the advisory committee process at EPA, the National Institutes of Health (NIH), and the National Academies; and staff from the Association of American Medical Colleges (AAMC), PhRMA, and consumer advocacy groups that have taken a position on FDA's nomination and selection processes for advisory committee members.

To determine the proportion of participants in advisory committee meetings who were standing members or temporary members and the proportion of those members who received conflict of interest determinations, we analyzed advisory committee meetings held by CBER, CDER, and CDRH—the three FDA centers with both the most advisory committees and the most committee meetings. We did not examine FDA's other centers' advisory committee meetings. Beginning in November 2005, FDA was required to post information on its Web site about the conflict of interest waivers it granted that allowed certain members to participate in

⁶In 2004, we reviewed the role of federal advisory committees in the development of national policies. We identified EPA and the National Academies as employing three specific recruitment and prescreening methods that could achieve independent and balanced advisory committees. The methods included (1) obtaining nominations for committee members from the public, (2) using clearly defined processes to screen for conflicts of interest, such as requesting public comment on proposed committee membership, and (3) prescreening prospective members using structured interviews. See GAO, *Federal Advisory Committees: Additional Guidance Could Help Agencies Better Ensure Independence and Balance*, [GAO-04-328](#) (Washington, D.C.: Apr. 16, 2004).

meetings.⁷ We chose to review the committee meetings held in 2004 and 2006—2 years with the most recent data when we began our work—because (1) 2004 was the last full year before FDA began to post waiver information in 2005, and (2) 2006 was the first full year in which the waiver information had to be posted. We excluded 2005 from the analysis because it was the year the Web site posting requirement began. We reviewed FDA’s advisory committee meeting records and conflict of interest determination records and assessed the reliability of these data by (1) reviewing existing information about the data and (2) interviewing agency officials knowledgeable about the data. We found that the data were sufficiently reliable for our analysis.

During the course of our work, two major actions occurred that changed FDA’s recruitment and conflict of interest policies. In March 2007, FDA issued a draft advisory committee guidance that revises FDA’s policy on how it screens individuals to determine if they have conflicts of interest for a specific advisory committee meeting.⁸ In addition, Congress amended the Federal Food, Drug, and Cosmetic Act to include, among other provisions, a section addressing recruitment, prescreening, and conflicts of interest, which took effect on October 1, 2007.⁹ At the time of our review, it was too soon to assess the effect of the changes on FDA’s processes. Consequently, this report focuses on FDA’s organization,

⁷The Web site posting was required by the Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriations Act for fiscal year 2006 and continued through fiscal year 2007. In August 2008, FDA issued a final *Guidance for the Public, FDA Advisory Committee Members, and FDA Staff: Public Availability of Advisory Committees Members’ Financial Interest Information and Waivers* (Rockville, Md.: August 2008).
<http://www.fda.gov/oc/advisory/GuidancePolicyRegs/ACDisclosureFINALGuidance080408.pdf> (accessed Aug. 5, 2008).

⁸FDA, *Draft Guidance for the Public, FDA Advisory Committee Members, and FDA Staff on Procedures for Determining Conflict of Interest and Eligibility for Participation in FDA Advisory Committees* (Rockville, Md.: March 2007)
<http://www.fda.gov/oc/advisory/waiver/COIguidedft.html> (accessed Mar. 18, 2007). This guidance states that it represents FDA’s current thinking on the topic and does not bind FDA or the public. FDA finalized the draft guidance August 2008,
<http://www.fda.gov/oc/advisory/GuidancePolicyRegs/ACWaiverCriteriaFINALGuidance080408.pdf> (accessed Aug. 5, 2008). Even after a guidance is finalized, FDA staff may use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations.

⁹See the Food and Drug Administration Amendments Act of 2007 (FDA Amendments Act of 2007), Pub. L. No. 110-85, § 701, 121 Stat. 823, 900-04 (adding § 712 to the Federal, Food, Drug, and Cosmetic Act) (codified at 21 U.S.C. § 379d-1).

processes, and conflict of interest determinations as documented prior to the 2007 actions. Appendix I describes these policy actions in greater detail and we note FDA procedures that have been affected by them throughout the report. Appendix II provides a more detailed explanation of the scope and methodology for this report. We conducted our work from October 2006 through September 2008 in accordance with generally accepted government auditing standards.

Results in Brief

Prior to the FDA Amendments Act of 2007, FDA employed several methods to recruit candidates for advisory committees and to evaluate candidates by prescreening them for potential conflicts of interest. FDA recruited candidates by announcing vacancies in the *Federal Register*; distributing recruitment brochures at advisory committee meetings and national meetings; word-of-mouth or asking current advisory committee members for nominations; and posting information about the recruitment process on FDA's Web site. To prescreen advisory committee candidates, FDA officials reviewed the candidates' curricula vitae and usually conducted an interview to determine whether there was any financial interest or activity that might present a potential conflict of interest. FDA employed many, but not all, of the recruitment and prescreening methods used by EPA and the National Academies, organizations previously identified by GAO as employing methods that could ensure an independent and balanced advisory committee.

FDA faced barriers to recruiting qualified advisory committee candidates, particularly those without potential conflicts of interest, according to FDA officials and former FDA advisory committee members. However, we found that the agency may have been able to mitigate these barriers by expanding its outreach efforts. FDA staff and former FDA advisory committee members generally agreed that individuals with the expertise FDA sought for its advisory committees were the same leading experts industry sought to conduct research. In addition, the advisory committee member recruitment method generally agreed to be most effective was limited in the number of candidate nominations it could generate. Some former advisory committee members told us that other barriers to membership related to aspects of FDA advisory committee service, including the time commitment involved in preparing for and attending advisory committee meetings, the financial disclosure information reporting requirements, and the negative publicity surrounding some advisory committee meetings. FDA employed several recruitment methods to identify qualified FDA advisory committee candidates. However, we found that the agency may have been able to mitigate barriers by

expanding outreach efforts to retired experts, experts from colleges and universities, and individuals with epidemiological and statistical expertise. The FDA Amendments Act of 2007 modifies FDA's process for prescreening candidates for advisory committee membership.

Most FDA advisory committee meeting participants from the 2 recent years we analyzed were standing members who served a specified term on an advisory committee, but a large minority of participants were temporary members who served at one specific meeting. In the 83 advisory committee meetings held by CBER, CDER, and CDRH in 2004 and 2006, 58 percent of the 1,218 meeting participants were standing members and 42 percent were temporary members. FDA may permit an advisory committee member who has a conflict of interest and whose expertise is needed to participate in an advisory committee meeting under certain circumstances by granting a conflict of interest determination. About 16 percent of the members received conflict of interest determinations that allowed them to participate. Forty-nine of the 83 meetings had at least one standing or temporary member with a conflict of interest determination. Members can receive more than one type of determination and some received both a financial conflict of interest waiver and an appearance authorization. Two hundred participants in these 49 meetings had 234 conflict of interest determinations. The FDA Amendments Act of 2007 limits the number of certain conflict of interest determinations—the statutory waivers—that FDA can grant and FDA's conflict of interest policy revisions limit the amount of the disqualifying financial interests.

In its comments on a draft of this report, HHS noted that on August 4, 2008, after GAO provided the draft report for its review, FDA issued four final guidances concerning management of its advisory committees including how it determines the eligibility of advisory committee members with conflicts of interest to participate in meetings.¹⁰ The guidance documents were available to us in draft form during the course of our work and the portions of the draft guidances that we discussed in the report did not change in the final guidances. HHS also provided additional

¹⁰The four final guidances are *Guidance for the Public, FDA Advisory Committee Members, and FDA Staff on Procedures for Determining Conflict of Interest and Eligibility for Participation in FDA Advisory Committees*; *Guidance for FDA Advisory Committee Members and FDA Staff: Voting Procedures for Advisory Committee Meetings*; *Guidance for the Public, FDA Advisory Committee Members, and FDA Staff: Public Availability of Advisory Committee Members' Financial Interest Information and Waivers*; and *Guidance for Industry Advisory Committee Meetings—Preparation and Public Availability of Information Given to Advisory Committee Members*.

clarifications about aspects of FDA’s advisory committees. GAO revised the report to cite the final guidances and to incorporate HHS’s clarifications where appropriate.

Background

FDA uses advisory committees to provide expert advice and make recommendations to help the agency reach regulatory decisions, particularly concerning controversial issues or new products. FDA advisory committees are subject to the Federal Advisory Committee Act (FACA), which requires that committee memberships be fairly balanced in terms of views presented and the functions to be performed by the advisory committee.¹¹ FDA advisory committees have charters that explain the purpose of the committee and specify the number of standing committee members and the expertise needed by the members.¹² FDA advisory committee members can be medical professionals, scientists, researchers, industry leaders, consumers, and patients. At an advisory committee meeting, committee members generally meet publicly to discuss and evaluate information about a specific issue.¹³ Depending on the issues or products to be discussed at a committee meeting, a committee member may have a potential financial conflict of interest.¹⁴ In that event, FDA decides whether the member’s expertise is needed for discussing those issues or products, and if so, whether the member should be granted a conflict of interest determination—a waiver or an appearance authorization—to participate in the meeting. The members who do participate in the committee meeting may make recommendations to

¹¹5 U.S.C. app. § 5(b)(2). An FDA official told us that it also seeks to achieve gender, ethnic, and geographic balance.

¹²All federal advisory committees subject to FACA must have a charter, although the law does not require the charter to specify the number of committee members or their expertise. *See* 5 U.S.C. app. § 9(c). An FDA advisory committee charter also provides the committee’s legal authority and structure, committee meeting frequency and member compensation, annual cost estimate and reports, and committee termination. Under FACA, FDA advisory committees terminate every 2 years unless renewed, or the legislation authorizing an advisory committee specifies a different period of time. *See* 5 U.S.C. app. § 14. CDRH’s Medical Devices Advisory Committee (MDAC) and its 18 panels is, by statute, not subject to a renewal review. *See* 21 U.S.C. § 360c(b)(1).

¹³Advisory committees may meet in closed sessions to permit discussion of trade secrets, commercial, or financial information obtained from a person that is privileged or confidential, or information of a personal nature where disclosure would constitute a clearly unwarranted invasion of personal privacy. 5 U.S.C. § 552b(c).

¹⁴For this report, we refer to a “potential conflict of interest” when discussing FDA’s review of a member’s financial interests for possible conflicts of interest prior to granting a waiver or an appearance authorization.

FDA—by voting or by consensus through discussions—that are nonbinding on the agency.¹⁵ (See app. III.)

FDA Advisory Committees

FDA has 31 advisory committees that are administratively attached to FDA centers or to the Office of the Commissioner. Most of the advisory committees—25—are attached to three FDA centers:¹⁶ CDER has 16 committees, CBER has 5, and CDRH has 4.¹⁷ (See app. IV.) Advisory committees usually meet as individual committees but may meet jointly to consider issues involving shared interests. Joint committee meetings may involve two advisory committees from the same center or from two different centers depending on the issue to be discussed. Advisory committees may also have subcommittees that meet to review specific information that may be presented later to the full advisory committee.¹⁸

Advisory Committee Management

FDA's overall management and coordination of its advisory committees is the responsibility of ACOMS. Each of the three centers we analyzed also has its own advisory committee management entity—CBER's Division of Scientific Advisors and Consultants, CDER's Advisors and Consultants Staff (ACS), and CDRH's Integrity, Committee and Conference Management Branch—responsible for administrative support, such as the

¹⁵In November 2007, FDA published a draft guidance that recommends uniform voting procedures that can be used during advisory committee meetings. See FDA, *Draft Guidance for FDA Advisory Committee Members and FDA Staff: Voting Procedures for Advisory Committee Meetings* (Rockville, Md.: November 2007), <http://www.fda.gov/oc/advisory/VotingGuidance.html> (accessed Jan. 29, 2008). FDA finalized the draft guidance August 2008, <http://www.fda.gov/oc/advisory/GuidancePolicyRegs/ACVotingFINALGuidance080408.pdf> (accessed Aug. 5, 2008).

¹⁶Six other FDA advisory committees are located in the Center for Food Safety and Applied Nutrition (1), the Center for Veterinary Medicine (1), the National Center for Toxicological Research (1), and the Office of the Commissioner (3). The Risk Communication Advisory Committee, established in May 2007, is one of the three advisory committees located in the FDA Office of the Commissioner.

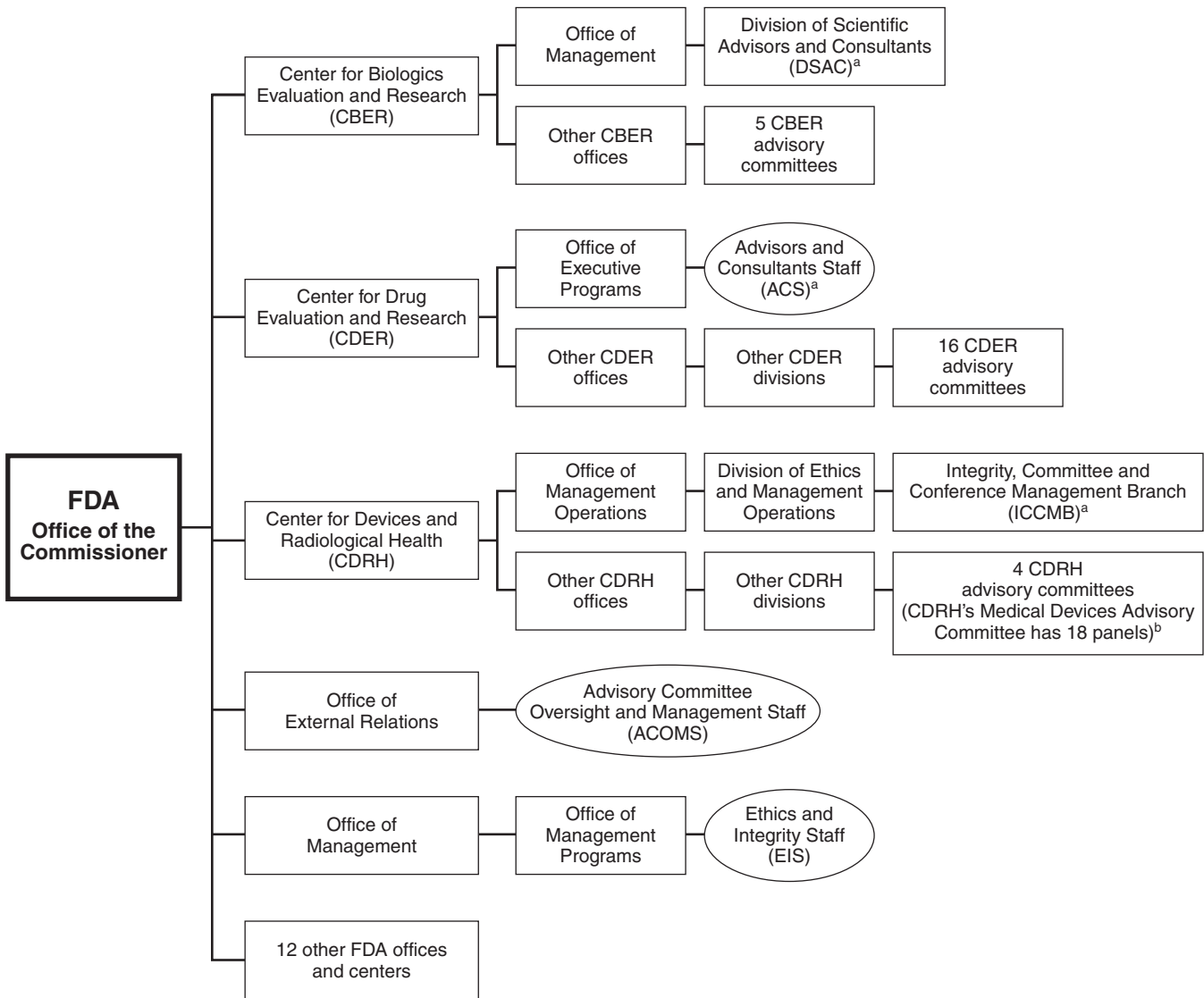
¹⁷Although CDRH has four advisory committees, its MDAC is the umbrella title for 18 statutorily-created advisory panels whose members are subject to the same legal and regulatory requirements as other FDA advisory committees. FDA counts MDAC and its 18 panels as one advisory committee. For our analysis, we treated MDAC's 18 panels' meetings as individual advisory committee meetings.

¹⁸According to an FDA official, FDA does not consider subcommittee meetings to be advisory committee meetings subject to FACA because a subcommittee provides advice to the committee rather than to FDA. This interpretation is in accordance with the FACA regulations issued by the General Services Administration. See 41 C.F.R. § 102-3.35 (2006).

preparation of nomination packages for potential committee members and the review of members' conflicts of interest. (See fig. 1.) Each FDA advisory committee has an executive secretary who manages the committee activities, including recruiting for advisory committee membership and prescreening candidates for potential conflicts of interest.¹⁹

¹⁹FACA requires agencies to designate a federal officer or employee—the designated federal official—to chair or attend every meeting of each advisory committee the agencies convene. Committee meetings may not be held without the advance approval of the designated official. *See* 5 U.S.C. app., § 10(e), (f).

Figure 1: FDA Organizational Structure for CBER, CDER, and CDRH Advisory Committee Administration Prior to August 30, 2007



Sources: Based on FDA organizational charts and GAO interviews with FDA officials.

Notes: The chart reflects the FDA organizational structure for CBER, CDER, and CDRH advisory committee administration prior to August 30, 2007. FDA amended its organizational structure on August 30, 2007. FDA advisory committees can be attached to offices or divisions. A center's advisory committees are attached to the center division or office with subject matter responsibility for the committee's issue areas. CDER and CDRH advisory committees are usually attached to a division—also referred to as a review division—and CBER's committees are more closely linked to its center's offices. For example, CDER's Anti-Infective Drugs Advisory Committee is attached to CDER's Division of Anti-Infective and Ophthalmologic Products and CBER's Blood Products Advisory Committee is attached to its Office of Blood Research and Review. ACS, ACOMS, and EIS are a part of the office they are connected to rather than a separate group under it.

^aCenter's advisory committee management staff.

^bFor purposes of this report, the 18 panels' meetings were considered to be individual advisory committee meetings.

Advisory Committee Members

There are two general types of FDA advisory committee members—standing and temporary. Standing members are appointed by FDA to a specific advisory committee, serve a specific term, and are expected to attend all committee meetings. Temporary members are appointed by FDA to serve for one specific advisory committee meeting.

Standing Members

Individuals appointed to serve on an FDA advisory committee as standing committee members generally are appointed as special government employees (SGE),²⁰ and they are subject to federal conflict of interest statutes and regulations. Standing members are chosen for their expertise and skills and are expected to provide advice on the basis of their own best judgment. Federal government employees who are not employed by FDA, such as federal employees with NIH, may also be appointed as standing members and are also subject to these conflict of interest statutes and regulations.²¹ FDA advisory committee standing members serve staggered membership terms of no more than 4 years and are expected to attend all committee meetings.²² CBER and CDER advisory committees'

²⁰An SGE is statutorily defined as an officer or employee who is retained, designated, appointed, or employed by the government to perform temporary duties, with or without compensation, for not more than 130 days during any period of 365 consecutive days. *See* 18 U.S.C. § 202(a). In general, FDA compensates advisory committee members who are SGEs for their service, reimburses them for travel, and pays them an amount for per diem expenses.

²¹FDA advisory committee members who are federal employees employed by other agencies do not receive additional compensation for their service on an FDA advisory committee.

²²There are circumstances when a standing member may be allowed to serve beyond their 4-year membership term including, for example, if a member in the fourth year of his or her term is selected to serve as the committee's chair and a special request is granted by HHS. A member may also serve less than 4 years; for example, if a member resigned in the second year of the term, the new member could serve the remaining 2 years.

maximum standing committee membership ranges from 9 to 26 members per committee, but most committees have 11 or 13 member maximums. CDRH's 18 Medical Devices Advisory Committee (MDAC) panels can have a combined maximum of 159 standing members.

Advisory committee charters may allow a committee to have members who serve as representatives of specific interests—consumer, industry, or patient representatives. Consumer representatives are appointed by FDA as SGEs, are subject to federal conflict of interest statutes and regulations, and are standing members on an advisory committee. These individuals present the perspective of interested individual consumers and consumer organizations, and may, for example, be consumer advocates or consumer lawyers.²³ Industry representatives are standing members; however, they are not SGEs and, therefore, not subject to the same conflict of interest laws and regulations applicable to federal employees.²⁴ Industry representatives may participate in committee discussions to ensure that the industries affected by the committee's issue jurisdiction are heard, but they are not permitted to vote on committee recommendations. Patient representatives are appointed as SGEs and are usually selected on a meeting-by-meeting basis for advisory committee meetings that focus on topics specific to a disease.²⁵ For example, an advisory committee meeting involving approval of a lung cancer drug might have as its patient representative a caregiver or an individual with the disease who can discuss patient concerns.

Temporary Members

FDA may also select temporary advisory committee members to serve for a specific advisory committee meeting given the issues or products to be discussed to provide additional expertise or to ensure that a quorum of members is present to conduct a meeting.²⁶ Advisory committee charters

²³Consumer representative members on CDRH MDAC panels are by statute to serve as nonvoting members. *See* 21 U.S.C. § 360c(b)(2).

²⁴In this report, when we discuss conflict of interest for committee members we are not including industry representatives.

²⁵CBER, CDER, and CDRH are required to have a patient representative serve on all their cancer-related advisory committees. These representatives are voting members for CBER and CDER committees, and nonvoting for CDRH committees.

²⁶Although the general rule is that a meeting quorum consists of the majority of current advisory committee members, FDA advisory committee charters may allow a committee to meet with less than a majority of its members for a specific meeting. *See* 21 C.F.R. § 14.22(d) (2007).

for the three centers indicate a maximum number of temporary members who can serve for a specific meeting, usually no more than 10 members. Temporary members are usually appointed as SGEs and are subject to conflict of interest statutes and regulations.²⁷ They may be members of the center’s consultant pool²⁸ or members of other FDA advisory committees from the same or a different FDA center. Federal employees from the Centers for Disease Control and Prevention (CDC) or NIH, for example, who provide specialized expertise for a meeting, may also serve as temporary members and are subject to conflict of interest statutes and regulations.

Federal Conflict of Interest Provisions May Permit Member Participation

FDA may permit an advisory committee member—standing or temporary—who has a conflict of interest and whose expertise is needed, to participate in a meeting under certain circumstances. There are four conflict of interest determinations—three statutory waivers and an appearance authorization as provided for in OGE regulations—that FDA can use to permit members with a conflict of interest or the appearance of a conflict of interest to participate.

Federal law prohibits federal employees, including SGEs, from personally and substantially participating in an advisory committee meeting involving a particular matter²⁹ that would have a direct and predictable effect on the employee’s financial interest or the interests of others specified by law.³⁰ In determining whether an FDA advisory committee meeting involves a

²⁷Industry representatives, whether they are temporary or standing members, are not SGEs.

²⁸FDA officials told us that centers’ consultant pools are lists of individuals who FDA has determined have expertise that may be needed in the future for a specific advisory committee meeting and usually have current SGE appointments. FDA officials also told us that consultants may be former FDA advisory committee members.

²⁹A “particular matter” is a matter involving “deliberation, decision, or action that is focused upon the interest of specific persons, or a discrete and identifiable class of persons.” 5 C.F.R. § 2640.103(a)(1).

³⁰See 18 U.S.C. § 208. According to FDA, its advisory committee meetings generally involve either (1) *particular matters involving specific parties*—typically the consideration of a specific company’s drug or medical device—which we refer to as a “specific-parties” topic; or (2) *particular matters of general applicability*—consideration of issues that affect a class of person, not specific parties, such as clinical trials for a class of drugs—which we refer to as a “non-specific party” topic. See 5 C.F.R. § 2410.102(l),(m). In addition, FDA advisory committee meetings may have topics that are non-particular matters—not subject to 18 U.S.C. § 208—typically involving consideration of recommendations on broad policy options that are directed to the interest of a large and diverse group of persons.

particular matter, FDA officials told us that they first consider each topic to be discussed at the meeting and determine whether it involves specific parties, a class of persons, or the interests of a large and diverse group of people.³¹ If one of the meeting topics involves specific parties or a class of persons, FDA officials then determine whether the advisory committee members who will attend the meeting have any conflicts of interest or the appearance of conflicts of interest involving that meeting topic. Officials told us if they are uncertain whether a meeting topic is a particular matter, the issue is referred to FDA's ACOMS and EIS. EIS may refer the issue to HHS's general counsel which may also seek advice from the OGE. The law has two waiver provisions that allow standing and temporary members to participate in an advisory committee meeting if certain criteria are met. One waiver—known as a § 208(b)(3) waiver—applies only to SGEs serving on an advisory committee subject to FACA. When granting this waiver, FDA certifies in writing in advance that the need for the SGE's services outweighs the potential for a conflict of interest at a specific upcoming meeting.³² Another type of waiver—known as a § 208(b)(1) waiver—applies to federal employees generally, including SGEs and those not employed by FDA but who are members of FDA committees. When granting these waivers, FDA must determine that the interest involved is not so substantial as to be deemed likely to affect the integrity of the services which the government may expect from that individual.³³ FDA may grant a member a full or a limited waiver—a written certification—to allow participation in the meeting. A full waiver may allow a member to participate in the discussions and to vote on recommendations. FDA may also grant a limited waiver to allow a member to discuss but not to vote on the recommendations.³⁴ In addition, there are certain situations in which the member's financial interest qualifies for an exemption from the application of the conflict of interest statutes and regulations applicable to

³¹Because FDA officials determine whether an advisory committee meeting may create a conflict of interest by first reviewing the topic or topics to be discussed, throughout this report we use the term topic instead of the term particular matter as used in the statute.

³²See 18 U.S.C. § 208(b)(3).

³³See 18 U.S.C. § 208(b)(1).

³⁴If an advisory committee meeting has more than one topic—such as both specific-parties and non-specific party topics—FDA may issue a conflict of interest waiver to limit the member from voting or participating in the discussion of one, while allowing the member to discuss and vote on the other.

federal employees, as provided by OGE regulations, and participation will be permitted despite the outside interest.³⁵

In addition to 18 U.S.C. § 208, there was a provision in the Food and Drug Administration Modernization Act, in effect prior to October 2007, which effectively prohibited CBER and CDER advisory committee members from voting on committee meeting topics involving clinical investigations or approvals of drugs or biologics in which the member or his or her immediate family could gain financially from the committee's advice.³⁶ However, FDA could grant a waiver of this voting restriction—known as the § 355(n)(4) waiver—to a member if FDA determined that his or her participation was necessary to provide the committee with essential expertise. No waiver could be granted if the meeting involved the member's own scientific work, such as work done by the member to develop a new drug being considered for approval by CDER.³⁷

Finally, federal regulations require the consideration of the appearance of a conflict of interest for advisory committee members who will be participating in a specific-parties meeting when there are circumstances in

³⁵See 18 U.S.C. § 208(b)(2). These regulatory exemptions are based on a determination by OGE that the interests involved are too remote or inconsequential to affect the integrity of the government employee's services. See 5 C.F.R. pt. 2640. For example, under the *de minimus* exception to the application of the law, an advisory committee member can participate in a committee meeting despite owning stock in a company involved in the matter before the committee, if the stock has a market value of less than \$15,000. See 5 C.F.R. § 2640.202(a).

³⁶See Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105-115, § 120, 111 Stat. 2296, 2318-20 (amending § 505 of the Federal Food, Drug, and Cosmetic Act and codified at 21 U.S.C. § 355(n)). The member must publicly disclose these conflicts—the financial interests upon which the waiver is based. FDA refers to these waivers as § 355(n)(4) or § 505 waivers; in this report we use § 355(n)(4). Although the § 355(n)(4) waivers generally were applied to CBER or CDER advisory committee meetings, an FDA official told us that it is possible there were historically some issued for other centers' meetings, for example, if CDRH had a joint meeting that involved the consideration of drugs or biologics. The FDA Amendments Act of 2007 repealed the § 355(n)(4) waiver provision, and added a new provision—referred to as a § 712(c)(2)(B) waiver—which applied the prohibition to all FDA advisory committee meetings. See Pub. L. No. 110-85, § 701, 121 Stat. 823, 900-04 (pertinent provision codified at 21 U.S.C. § 379d-1(c)(2)(B)).

³⁷In March 2007, FDA issued a draft guidance to generally not grant committee members with financial conflicts of interest exceeding \$50,000 waivers to participate in an advisory committee meeting. The FDA Amendments Act of 2007 also requires FDA to reduce the percentage of waivers—§ 208 and § 712—granted by 25 percent over 5 years, starting in fiscal year 2008.

which the member's impartiality could be questioned.³⁸ The appearance of a conflict may be created when someone in the advisory committee member's household has a financial interest that will likely be affected by the committee's actions or when one of the parties involved in the meeting has a close personal or professional relationship to the committee member.³⁹ To grant an appearance authorization, FDA determines that the interest of the agency in the member's participation in an advisory committee meeting's topic outweighs the concern that a reasonable person with knowledge of the relevant facts would question the member's impartiality in the matter before the advisory committee,⁴⁰ which may call into question the integrity of FDA's programs and operations.⁴¹ (See table 1 for a summary of the four conflict of interest determinations.)

³⁸See 5 C.F.R. § 2635.502.

³⁹These relationships would include a person who is a member of the committee member's household and any person for whom the committee member has served within the past year as a consultant, contractor, or employee. See 5 C.F.R. § 2635.502(b)(1).

⁴⁰See 5 C.F.R. § 2635.502(a).

⁴¹See 5 C.F.R. § 2635.502(d).

Table 1: Four Possible Member Conflict of Interest Determinations for FDA Advisory Committee Meetings Prior to October 1, 2007, Changes

Type of conflict of interest determination	Criteria for granting conflict of interest determinations to allow attendance at a meeting or part of a meeting	Standing and temporary member types that can receive conflict of interest determinations	
		SGEs	Other federal employees
Statutory waivers			
18 U.S.C. § 208(b)(3) waiver of the criminal financial conflict of interest specific to SGEs serving on an advisory committee subject to the Federal Advisory Committee Act	A committee member's service is needed and outweighs the potential conflict of interest created by his or her personal or imputed financial interest.	X	
18 U.S.C. § 208(b)(1) waiver of the criminal financial conflict of interest ^a	A committee member's personal or imputed financial interest is not so substantial as to be deemed likely to affect the integrity of the services which the government may expect from that member.		X ^b
21 U.S.C. § 355(n)(4) waiver of financial conflict of interest involving drugs and biologics matters ^c	A committee member—or his or her immediate family—could gain financially from the advice given but the member's voting participation is necessary to provide the committee with essential expertise.	X	X
Regulatory authorization			
5 C.F.R. § 2635.502 appearance authorization to allow a committee member to participate when his or her impartiality could be questioned	A committee member's impartiality involving specific parties meeting could be questioned by a reasonable person with knowledge of the relevant facts, but the interests of the government in the member's participation outweigh the concern that a reasonable person may question the integrity of the agency's programs and operations.	X	X

Sources: GAO analysis of applicable conflict of interest statutes and regulations and FDA information.

Notes: 18 U.S.C. § 208(b)(2) provides for the OGE to exempt certain financial interests from application of the criminal financial conflict of interest law. When a committee member's financial interest that gives rise to the conflict is covered by one of the Office of Government Ethics' regulatory exemptions, the member can participate without FDA needing to grant an individual waiver.

^aAlthough 18 U.S.C. § 208(b)(1) applies to federal employees generally, including SGEs and those not employed by FDA who are members of FDA advisory committees because 18 U.S.C. § 208(b)(3) specifically authorizes waivers for SGEs serving on FACA committees, FDA applied 18 U.S.C. § 208(b)(3) to SGEs in this context.

^bThe FDA's 18 U.S.C. § 208(b)(1) waivers we analyzed were granted only to federal employees not employed by FDA.

^cPrior to October 1, 2007, the 21 U.S.C. § 355(n)(4) waiver applied only to allowing a committee member to vote on matters related to clinical investigations and approvals of drugs and biologics, which generally involved only CBER and CDER advisory committee meetings. On October 1, 2007, the FDA Amendments Act of 2007 repealed 21 U.S.C § 355(n)(4), but at the same time also created a new provision applying a similar waiver to all FDA advisory committee members. See Pub. L. No. 110-85, § 701, 121 Stat. 823, 900-04 (pertinent provision codified at 21 U.S.C. § 379d-1(c)(2)(B)).

FDA Conflict of Interest Determination Process

The appropriate FDA center review division and committee management staff for the advisory committee meeting decide whether a member meets the requirements for an applicable conflict of interest determination to allow him or her to participate. To assist in making conflict of interest determinations, FDA uses its Waiver Criteria 2000 guidance, which provides policies and procedures for handling conflicts of interest.⁴² On the basis of the advisory committee meeting's topic and its designation, the center review division involved in the advisory committee meeting typically compiles a list of companies and products affected by the meeting's topic. The advisory committee management staff then sends a memorandum with the final list of companies and products and the FDA Form 3410—the FDA financial disclosure form—to the advisory committee members. Members review the memorandum, complete the Form 3410, and report back to FDA on whether they believe they have any personal or imputed financial interests and past involvements with the affected companies and products listed for the upcoming advisory committee meeting's topic.⁴³

The FDA center advisory committee management staff for the particular advisory committee review members' FDA financial disclosure forms and determine whether a member has a potential conflict of interest for the meeting or a part of the meeting.⁴⁴ If a member has a conflict, FDA can

⁴²The FDA Waiver Criteria 2000 guidance is titled *FDA Guidance on Conflict of Interest for Advisory Committee Members, Consultants, and Experts* (February 2000). The 2000 guidance is replaced by FDA's August 2008 *Guidance for the Public, FDA Advisory Committee Members, and FDA Staff on Procedures for Determining Conflict of Interest and Eligibility for Participation in FDA Advisory Committees*.

⁴³We were told by an FDA official that in some cases, FDA centers use OGE Form 450—generally used for annual confidential reporting of financial interests by certain federal employees—in lieu of FDA Form 3410.

⁴⁴An analysis memorandum—an internal FDA document—is prepared by FDA staff for a specific advisory committee meeting. Among other things, the analysis memorandum may indicate which members attending have conflict of interest waivers, which qualify for an exemption from the conflict of interest law, as provided for in regulations issued by OGE, which reported interests or involvement not requiring a conflict of interest determination, and which have been excluded from participating in part or all of the meeting because of a conflict of interest that FDA decides does not qualify for a conflict of interest determination.

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- accept a member's decision to not participate because of the member's own decision that he or she has a conflict of interest,⁴⁵
 - exclude or disqualify a member from participating,
 - seek another individual with the appropriate expertise needed to participate who has a less significant or no conflict of interest, or
 - decide the member's expertise is needed, and that the member meets the criteria for a conflict of interest determination to allow him or her to participate in the meeting discussion and vote.⁴⁶

If there is a question about whether a member should be granted a determination, the center's advisory committee management entity may seek advice from the review division. If there are further questions about whether the determination should be granted, advice may be sought from FDA's ACOMS and EIS.⁴⁷ ACOMS and EIS review all conflict of interest determinations before their final approval. The final decision to grant or deny a determination is made by the FDA Associate Commissioner for Policy and Planning.⁴⁸ (See fig. 2.)

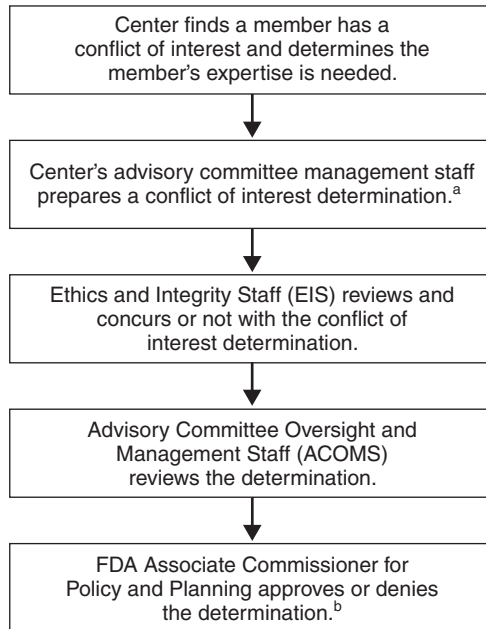
⁴⁵Advisory committee members may decide they have a conflict of interest and recuse or disqualify themselves from participating in all or part of a meeting. We were told by CDER ACS staff that ACS began tracking members' self recusals in 2006 because CDER is often asked why members do not participate in some committee meetings.

⁴⁶Conflict of interest waivers can limit a member's participation and voting in a meeting. A member may, for example, be permitted to participate in a meeting's discussions but not vote, or participate in discussions involving certain topics and only vote on those topics and vote only on certain matters.

⁴⁷EIS typically works with the director of a center's advisory committee management staff to provide advice on conflict of interest determinations and to review proposed conflict of interest waivers.

⁴⁸As of August 30, 2007, FDA changed this position title to Deputy Commissioner for Policy.

Figure 2: Conflict of Interest Determination Process for FDA Advisory Committee Members: CBER, CDER, and CDRH



Source: GAO interviews with FDA officials.

^aFor our report, FDA conflict of interest determinations are statutory § 208 and § 355(n) financial interest waivers, and appearance authorizations as provided for in OGE regulations.

^bThe FDA Associate Commissioner title was changed in August 2007 to the Deputy Commissioner for Policy.

Since November 2005, FDA has been subject to requirements related to public disclosure of its conflict of interest waivers on its Web site. From November 2005 until October 2007, FDA had been required by law to publicly post the nature and basis of conflict of interest waivers on its Web

site.⁴⁹ As of October 2007, the FDA Amendments Act of 2007 require FDA to publicly disclose on the agency's Web site, prior to every advisory committee meeting, the reasons for all waivers granted as well as the type, nature, and magnitude of the financial interests being waived.⁵⁰ In October 2007, FDA announced draft guidance⁵¹ to implement agencywide procedures for the public disclosure of (1) the type, nature, and magnitude of any financial conflict of interest for which an advisory committee member has been granted a waiver for a committee meeting on its Web site,⁵² and (2) conflict of interest waivers that would be written so that information protected from public disclosure would not appear in the waivers and thus would not need to be redacted. Public disclosure at an FDA advisory committee meeting can also, for example, include an announcement naming the attending members who have conflict of interest determinations.

⁴⁹The Web site posting was required by the Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriations Act for fiscal year 2006. Pub. L. No. 109-97, § 795, 119 Stat. 2120, 2164-65. This requirement was continued through fiscal year 2007. Continuing Appropriations Resolution, 2007, Pub. L. No. 109-289, division B, §§ 101(a) and 106(3), 120 Stat. 1257, 1311, 1313 (2006), as amended by: Pub. L. No. 109-369, 120 Stat. 2642 (2006); Pub. L. No. 109-383, § 1, 120 Stat. 2678 (2006); and Pub. L. No. 110-5, § 101, 121 Stat. 8 (2007). Waivers posted on the Web site may have had information redacted; for example, the name of a drug company in which an individual owns stock may be redacted. Appearance authorizations are not required to be publicly disclosed. The statute—18 U.S.C. § 208(d)—provides for the disclosure of waiver information for § 208(b)(1) and (b)(3) waivers upon request but allows federal agencies to redact any information that would be exempt under the Freedom of Information Act, such as an advisory committee member's confidential financial information.

⁵⁰Pub. L. No. 110-85, § 701, 121 Stat. 900-04 (pertinent provision codified at 21 U.S.C. § 379d-1(c)(3)).

⁵¹FDA, *Draft Guidance for the Public, FDA Advisory Committee Members, and FDA Staff: Public Availability of Advisory Committee Members' Financial Interest Information and Waivers* www.fda.gov/oc/advisory/waiver/ACdisclosure1007.html (accessed Mar. 18, 2007). FDA finalized the draft guidance August 2008.

⁵²Appearance authorizations and their grounds are not required to be publicly disclosed.

FDA Used Several Methods to Recruit Candidates for Advisory Committee Membership and Prescreened Candidates for Potential Conflicts of Interest

Prior to the FDA Amendments Act of 2007, FDA employed several methods to recruit candidates for advisory committees and to evaluate candidates by prescreening them for advisory committee membership.⁵³ Common recruitment methods used by FDA include announcing vacancies in the *Federal Register*, distributing recruitment brochures at advisory committee meetings and national meetings, receiving nominations by word-of-mouth or asking current advisory committee members for nominations, and posting information about recruitment on FDA's Web site. Candidates who are selected to serve on an FDA advisory committee either as a consumer representative, industry representative, or patient representative are recruited and nominated using a different process than candidates identified for standing advisory committee membership. To prescreen candidates, FDA reviewed candidates' curricula vitae and usually conducted prescreening interviews. FDA officials within the three FDA centers we studied, CBER, CDER, and CDRH, prescreened each candidate to determine whether there was any financial interest or activity that might present a potential conflict of interest if the individual were to become an advisory committee member. FDA employed many of the same recruiting and prescreening methods as those employed by EPA and the National Academies, organizations we previously identified as employing certain recruitment and prescreening methods that could ensure independent and balanced advisory committees.

FDA Employed Several Methods to Recruit Candidates for Advisory Committee Membership

FDA employed several recruitment methods to identify candidates for standing advisory committee membership, prior to the FDA Amendments Act of 2007. FDA officials in CBER, CDER, and CDRH told us that the methods commonly used to recruit candidates include announcing advisory committee vacancies in the *Federal Register*, distributing recruitment brochures at advisory committee meetings and national meetings, and receiving nominations by word-of-mouth or asking current advisory committee members for nominations. The FDA officials we interviewed stated that asking current advisory committee members for nominations was the most effective recruitment method because the members understand the advisory committee process and the commitment

⁵³The FDA Amendments Act of 2007 allows FDA to develop a new recruitment method through which an entity receiving funding from NIH, the Agency for Healthcare Research and Quality, the CDC, or the Veterans Health Administration can identify a person whom FDA can contact regarding the nomination of individuals to serve on advisory committees. Pub. L. No. 110-85, § 701, 121 Stat. 900-04 (pertinent provision codified at 21 U.S.C. § 379d-1(b)(1)(B)).

level required to serve as an FDA advisory committee member, and can communicate this information to the potential candidate. FDA staff in CBER and CDRH told us that posting vacancy announcements in the *Federal Register* was the least effective method of identifying qualified candidates because the centers received unsolicited curricula vitae from individuals seeking full-time jobs with FDA.

Other recruitment methods reported include identifying possible candidates from the center's consultant pool, which is a list of individuals whom FDA has determined have expertise that may be needed for future advisory committee meetings, and posting recruitment information on FDA's Web site. CDRH staff reported that searching the consultant pool for a potential candidate is preferred because the executive secretary and the review division are usually familiar with the individual's performance on an advisory committee and the individual is familiar with the advisory committee process. In February 2007, FDA posted on its Web site a link to information about advisory committees and available vacancies for individuals interested in advisory committee membership. From the Web site, the public can access information about current advisory committee vacancies, required qualifications to become an advisory committee member, and instructions on how to apply for advisory committee membership.⁵⁴

Candidates who are selected to serve on an FDA advisory committee either as a consumer representative, industry representative, or patient representative are recruited and nominated using a different process than candidates identified for standing advisory committee membership. FDA officials work with consumer and industry organizations to identify qualified candidates to serve as representatives. Consumer and industry groups nominate the candidates and FDA indicated that it generally accepts the organizations' recommendations for nomination.⁵⁵ For patient

⁵⁴Most of this information was available on the Web site prior to the revision. The revised Web site provides a link to the e-mail address to submit individual nominations and self nominations.

⁵⁵A group of interested consumer organizations, commonly referred to as the consumer nominating group, assists FDA with recruiting, interviewing, and assessing potential candidates to serve as voting and nonvoting consumer representatives. When there is a vacancy for an industry representative on an advisory committee, FDA publishes a notice in the *Federal Register* requesting that industry organizations send a letter stating their interest in nominating an industry representative. FDA instructs that representatives from the interested industry organizations consult with each other and select an industry representative candidate for each vacancy. See 21 C.F.R. § 14.84(d) (2007).

representatives, FDA's Office of Special Health Issues' Patient Representative Program is responsible for recruiting and nominating candidates. When an advisory committee meeting topic is of particular importance to the patient population (e.g., cancer or HIV/AIDS-related topics), the advisory committee's executive secretary will ask Patient Representative Program staff to recommend a patient representative to attend the advisory committee meeting.

FDA Prescreened Advisory Committee Member Candidates for Potential Conflicts of Interest

FDA officials in the three centers told us they prescreened advisory committee member candidates to determine whether they had any financial interests or if they were involved in any activity that might pose a potential conflict of interest, even though prior to October 1, 2007, HHS did not require its agencies to prescreen candidates at the time of their nomination to an advisory committee.⁵⁶ To prescreen candidates, FDA reviewed the candidates' curricula vitae and usually conducted a prescreening interview. The FDA officials told us that the interview is usually conducted by telephone using a prescreening form.⁵⁷ The prescreening form asks candidates to provide information about their current investments, employment and consulting relationships held in the past 12 months, and current and past contracts and grants.

FDA Used Many of the Same Recruiting and Prescreening Methods as Those Employed by Organizations Identified as Having Some Promising Recruitment and Prescreening Methods

FDA employed many of the same recruiting and prescreening methods as EPA and the National Academies, organizations found to have some promising methods that could ensure that advisory committee members are independent and advisory committees are balanced.⁵⁸ Prior to October 1, 2007, FDA generally used the same recruitment methods as EPA and the National Academies (see table 2). One exception was FDA's method for obtaining nominations for potential members from the public. FDA provides an e-mail address on its Web site for nominations, a method that relies on individuals submitting to the agency, via e-mail, a curriculum

⁵⁶The FDA Amendments Act of 2007 requires that an individual's expertise and financial disclosure report filed in accordance with the Ethics in Government Act of 1978 be reviewed when considering a term appointment to an advisory committee. Pub. L. No. 110-85, § 701, 121 Stat. 900-04 (pertinent provision codified at 21 U.S.C. § 379d-1(b)(2)).

⁵⁷FDA's prescreening form is the Prospective Special Government Employee Personal Data Sheet—Preliminary Informal Interview (FDA Form 2725a).

⁵⁸GAO, *Federal Advisory Committees: Additional Guidance Could Help Agencies Better Ensure Independence and Balance*, [GAO-04-328](#) (Washington, D.C.: Apr. 16, 2004).

vitae and contact information. In contrast, EPA’s Science Advisory Board’s Web site allows the public to self-nominate or nominate an individual to be an advisory committee member by submitting information via a form on its Web site.

Table 2: Selected Advisory Committee Recruitment Methods of FDA, EPA, and National Academies Prior to October 1, 2007

Recruitment methods	FDA	EPA	National Academies
Request nominations from professional or specialty practice societies and organizations related to the advisory committee’s general topic	X	X	X
Ask current advisory committee members for nominations	X	X	X
Ask staff within the organization for nominations	X	X	X
Publish advisory committee vacancies in the <i>Federal Register</i>	X	X	
Has brochure explaining advisory committee membership	X	X	X
Post recruitment information on organization’s Web site	X	X	X
Enable people to nominate candidates and to self-nominate directly through an electronic form on the organization’s Web site		X	

Sources: GAO analysis of FDA, EPA, and National Academies staff interviews, and [GAO-04-328](#).

Note: Represents the recruitment methods FDA employed prior to the implementation of the FDA Amendments Act of 2007. FDA still uses these recruitment methods; however, the FDA Amendments Act of 2007 provides additional recruitment methods that FDA may employ.

Prior to October 1, 2007, FDA also employed many but not all of the same prescreening methods as EPA and the National Academies (see table 3). EPA and the National Academies asked candidates to complete an official financial disclosure and background form prior to being selected as a committee member.⁵⁹ An EPA official we interviewed stated that asking candidates for detailed financial information prior to selection to an advisory committee enables EPA to identify individuals without conflicts of interest early in the advisory committee recruitment process. An FDA official told us that FDA did not ask candidates to complete a financial disclosure and background form because the form would require

⁵⁹EPA officials told us that candidates complete EPA Form 3110-48. National Academies officials told us that provisional study committee members fill out financial disclosure Form BI/COI (Background Information/Conflicts of Interest) Forms 1, 2, or 3, depending upon the type of study on which they will work.

responses about specific products or companies or both, which may not be known at the time of the prescreening interview.⁶⁰

Table 3: Selected Advisory Committee Prescreening Methods of FDA, EPA, and National Academies Prior to October 1, 2007

Prescreening methods	FDA	EPA	National Academies
Review curriculum vitae or summaries of related professional experience	X	X	X
Interview candidates about financial interests and activities	X	X	
Post a sample financial disclosure information form on the organization's Web site	X	X	X
Ask candidates to complete the organization's official financial disclosure form prior to being selected as a committee member		X	X
Post a provisional advisory committee member list on the organization's Web site for public comment on possible conflicts of interest		X ^a	X

Sources: GAO analysis of FDA, EPA, and National Academies staff interviews, and [GAO-04-328](#).

Notes: As of October 1, 2007, candidates for FDA advisory committees were required to complete an official financial disclosure form that provides information about the individual's financial interest prior to being appointed as an advisory committee member. These methods represent the prescreening methods FDA employed prior to the issuance of the implementation of the FDA Amendments Act of 2007; FDA still uses these prescreening methods.

^aEPA's Science Advisory Board publishes the names and biographical sketches of candidates on its Web site to obtain public comments on proposed candidates.

EPA's and the National Academies' prescreening methods included obtaining input from the general public whereas FDA's methods generally did not. For example, EPA's Science Advisory Board used a public notice process to obtain public comments on proposed candidates. The names and biographical sketches of candidates are posted on its Web site, and EPA requests the public to provide information, analysis, or documentation that the agency should consider in evaluating the candidates. Similarly, the National Academies publicly announces the slate of provisional study committee members by posting their biographies on its Web site, and requests public comment. FDA did not post a list of potential nominees on its Web site and did not seek public comment about potential candidates.

⁶⁰As of October 1, 2007, candidates for FDA advisory committees are required to complete the OGE Form 450 or FDA Form 3410—financial disclosure reports that provide information about the individual's financial interest—prior to being appointed as an FDA advisory committee member.

Barriers Existed to Recruiting Qualified FDA Advisory Committee Candidates, Particularly Those without Potential Conflicts of Interest, but FDA May Have Been Able to Mitigate Barriers by Expanding Outreach Efforts

According to FDA officials, former FDA advisory committee members, and a PhRMA representative, FDA faced barriers to recruiting qualified individuals to serve on its advisory committees, particularly candidates without potential conflicts of interest, although FDA may have been able to mitigate these barriers by expanding its outreach efforts. FDA officials, former FDA advisory committee members, and a PhRMA representative identified the following barriers: FDA sought the same leading experts as industry; FDA's most effective recruitment method—word-of-mouth—was limited in the number of potential candidates it could generate; and aspects of FDA advisory committee service deterred some potential advisory committee members. FDA already employed several recruitment methods to identify qualified FDA advisory committee candidates. However, FDA may have been able to mitigate barriers by focusing additional outreach efforts on recruiting retired experts, experts from colleges and universities, and individuals with epidemiological and statistical expertise. Under the FDA Amendments Act of 2007, FDA's process for prescreening candidates for advisory committee membership has been modified. (See app. I.)

Barriers Existed to Recruiting Qualified Individuals to Serve on FDA Advisory Committees

FDA officials, former FDA advisory committee members, and a PhRMA representative identified barriers that existed to recruiting qualified FDA advisory committee candidates, particularly those without potential conflicts of interest. These barriers were that FDA sought the same experts as industry, FDA's most effective advisory committee recruitment method was limited in the number of potential candidates it could generate, and aspects of FDA advisory committee service may have deterred some potential advisory committee members.

The Experts FDA Sought to Serve on Its Advisory Committees Frequently Had Industry Ties

FDA contended that it sought the same leading experts to serve on its advisory committees as industry sought to conduct its research and product trials. As a result, the experts FDA deemed most qualified to serve on its advisory committees often had industry ties, according to the agency.

FDA officials, former FDA advisory committee members, and a PhRMA representative generally agreed that many individuals who have the experience necessary to participate on an advisory committee have industry ties. FDA officials told us that private industry sponsors most medical development in the United States. As a result, people in fields relevant to FDA advisory committees gain experience from working with industry. A representative from PhRMA told us if an individual has no or

minimal potential conflicts of interest, he would question whether the person has the expertise needed to serve on an FDA advisory committee.

FDA's Most Effective Recruitment Method Had Limitations

Although FDA employed several methods to recruit advisory committee candidates, FDA staff generally agreed that word-of-mouth, such as informal discussions among FDA advisory committee members, agency staff, and interested parties, was most effective in generating nominations for qualified advisory committee candidates. FDA officials and former FDA advisory committee members told us that this recruitment method was effective because people familiar with the advisory committee process—FDA review division staff and FDA advisory committee members—can identify individuals who would be qualified to serve on advisory committees because they understand what advisory committee membership entails. Former members also noted that advisory committee members, who are experts in their field, know other qualified experts who could serve as advisory committee members. Similarly, former advisory committee members explained that asking FDA review division staff for recommendations was effective because these individuals are active in the scientific community and can also identify individuals qualified to serve on FDA's advisory committees.

Despite being effective in generating nominations, word-of-mouth recruitment is limited because only the colleagues of FDA advisory committee members or FDA staff learn about the opportunity to serve on committees rather than a broader pool of candidates. Two former FDA advisory committee members cautioned that, while they believe word-of-mouth is an effective recruitment method, it may lead to self-perpetuating committee membership, in which a limited group of peers continually comprise an advisory committee. An official from EPA echoed these concerns, stating that, although this is an effective method to recruit candidates for some EPA advisory committees, it also is problematic because he believes advisory committee members only nominate their colleagues. Similarly, former advisory committee members noted that FDA staff nominations may also be problematic. For example, one former member explained that it gives the appearance that FDA may pad its advisory committees, which could compromise the committees' perceived independence.

Some Aspects of FDA Advisory Committee Service May Have Deterred Potential Members

Some aspects of FDA advisory committee service may have also deterred qualified advisory committee candidates. More than half of the 12 former FDA advisory committee members we spoke with agreed that the time commitment involved in preparing for and attending FDA advisory committee meetings acted as a deterrent for some potential advisory

committee members. Standing members of an FDA advisory committee are expected to participate in all meetings held by that advisory committee unless they are excluded from a meeting due to a conflict of interest. For example, CDER's Anti-Infective Drugs Advisory Committee held three meetings in 2006. Unless excluded, a standing member of this committee would have been expected to attend all three advisory committee meetings.

In addition, more than half of the 12 former advisory committee members we interviewed also agreed that FDA's work-related activities and financial information disclosure reporting requirements dissuaded some people from becoming an advisory committee member, although some said that the public disclosure of an individual's conflict of interest waivers was not a deterrent.⁶¹ As mentioned earlier, advisory committee members complete financial disclosure forms before each advisory committee meeting, and since November 2005 FDA has posted information disclosing the nature and basis of advisory committee member conflict of interest waivers on its Web site.⁶²

The negative publicity surrounding certain advisory committee meetings, especially media attention to some members' ties to industry, may have also deterred some people from serving on FDA advisory committees. An FDA advisory committee management official in CDER, the center with the most advisory committee meetings held in years 2004 and 2006 combined, explained that public scrutiny concerning advisory committee members' conflicts of interest is the most difficult challenge FDA staff face in generating member nominations. The FDA official said people serving on FDA advisory committees "feel like they are in fishbowls" and are concerned that they are considered tainted if they receive a conflict of interest waiver. A representative from PhRMA echoed these concerns, stating that many FDA advisory committees receive public scrutiny, which

⁶¹National Academies, EPA, and NIH officials we interviewed did not believe that their organizations' financial disclosure reporting requirements acted as a significant barrier to recruiting qualified candidates to serve on advisory committees. However, neither EPA nor NIH is required to disclose publicly their advisory committee members' conflict of interest waivers like FDA is. An EPA official added that she does not believe the agency has granted a conflict of interest waiver to an advisory committee member in at least 5 years because the agency typically disqualifies individuals with conflicts of interest.

⁶²FDA released a draft guidance in October 2007 that would implement new agencywide procedures for the public availability of information about advisory committee members' financial interests and conflicts of interest waivers in response to the FDA Amendments Act of 2007. FDA finalized this draft guidance August 2008.

may act as a disincentive for individuals to serve on committees. Some former advisory committee members we spoke with also agreed that the media attention surrounding certain advisory committee meetings can deter people from serving on FDA advisory committees, although some former members either disagreed or said that qualified candidates should be prepared to withstand media pressure.

FDA May Have Been Able to Mitigate Barriers by Expanding Outreach Efforts

FDA may have mitigated barriers to recruiting qualified advisory committee candidates, particularly those without potential conflicts of interest, if it had expanded outreach efforts to retired experts, experts from universities and colleges, and individuals with statistical and epidemiological expertise. Former advisory committee members and representatives from entities knowledgeable about FDA advisory committee recruitment agreed that expanding outreach efforts to retired experts, experts from universities and colleges, and individuals with statistical and epidemiological expertise would be effective in recruiting qualified FDA advisory committee members, particularly those without conflicts of interest. In addition, although FDA stated that it employed several methods to recruit advisory committee members, representatives from consumer groups said that FDA should make a greater effort to recruit qualified advisory committee candidates, particularly those without conflicts of interest.

Most former advisory committee members we spoke with generally agreed that FDA could have expanded outreach efforts to retired experts in fields relevant to its advisory committees in order to mitigate barriers to recruiting qualified advisory committee candidates, particularly those without potential conflicts of interest. Retired experts are no longer employed and, therefore, may be less likely to have current ties to industry. For example, a National Academies official we spoke with explained that when the type of expertise needed for a committee lends itself to inherently conflicted professionals—for example, if a committee focuses on the operations of drug manufacturers—the organization could seek an individual who is retired. However, some FDA officials noted that retired experts may not be familiar with new science and technologies or interested in committing the time necessary to serve on an advisory committee, or they may have conflicts of interest because they consult privately.

One FDA official said that the center in which she is employed may recruit individuals who retired in the past 2 years to participate on an advisory committee or panel, but individuals retired longer than that are usually not

familiar with current technologies and are, therefore, not qualified for the center's advisory committee or panel participation. Although the majority of former advisory committee members we spoke with agreed that expanding outreach efforts to retired experts would improve FDA's advisory committee process, many former members noted that FDA advisory committees require members who are active in their field.

Most former FDA advisory committee members and the consumer groups we spoke with agreed that expanding outreach efforts to experts from universities and colleges would be effective in recruiting qualified advisory committee candidates.⁶³ FDA noted that most of its advisory committee members are already academicians. An AAMC official suggested that FDA ask medical colleges to solicit their own staff to serve on FDA advisory committees. He also told us that AAMC does not currently assist FDA with advisory committee recruitment, but it would if asked. For example, he said AAMC would be willing to post FDA advisory committee member vacancies on its Web site at no cost. However, two former members noted that academicians may receive industry funding for research or consulting and, therefore, may have conflicts of interest. The FDA Amendments Act of 2007 modifies FDA's process for prescreening candidates for advisory committee membership. For example, the act directs FDA to develop outreach strategies for potential members of advisory committees at universities, colleges, and other academic research centers.

Most former FDA advisory committee members and consumer groups we interviewed said that expanding outreach efforts to epidemiologists and statisticians would be effective in recruiting qualified advisory committee candidates, particularly those without potential conflicts of interest. According to some former advisory committee members, epidemiologists and statisticians add expertise in data analysis to FDA advisory committees. For example, biostatisticians could provide expertise in interpreting clinical trial data. Representatives from two consumer advocacy groups told us these individuals may be less likely than clinicians to have conflicts of interest and may bring a different focus to

⁶³The FDA Amendments Act of 2007 also requires FDA to develop and implement strategies to conduct outreach to potential advisory committee candidates at universities and colleges, among other entities. Pub. L. No. 110-85, § 701, 121 Stat. 823, 900-04 (pertinent provision codified at 21 U.S.C. § 379d-1(b)(1)(A)).

committee deliberations.⁶⁴ According to these consumer interest group representatives, the agency's advisory committees are overly weighted towards clinicians and clinical trialists.⁶⁵ One representative told us that clinicians are more likely to have potential conflicts of interest because they are more likely to have received industry funding, and another representative said that they generally have a bias towards product approval because they seek more options—that is, drugs and medical devices—to help with diagnosis and treatment of their patients.⁶⁶ The majority of the former FDA advisory committee members we interviewed agreed that focusing outreach efforts on recruiting statisticians and epidemiologists would be an effective way for FDA to recruit qualified advisory committee candidates, particularly those without potential conflicts of interest. In *The Future of Drug Safety – Promoting and Protecting the Health of the Public: FDA's Response to the Institute of Medicine's 2006 Report*, FDA stated in 2007 that it will increase the epidemiology expertise on its drug-related advisory committees.⁶⁷ The FDA Amendments Act of 2007 modifies FDA's process for prescreening candidates for advisory committee membership. (See app. I.)

⁶⁴A clinician is an individual qualified in the clinical practice of medicine, psychiatry, or psychology as distinguished from one specializing in laboratory or research techniques or in theory.

⁶⁵A clinical trialist is a medical researcher in charge of carrying out a clinical trial's protocol.

⁶⁶In its comments on the draft report, HHS stated that FDA has not found that one particular biomedical specialty yields potential advisory committee members with less frequent conflicts of interests.

⁶⁷HHS, FDA, *The Future of Drug Safety - Promoting and Protecting the Health of the Public: FDA's Response to the Institute of Medicine's 2006 Report* (Rockville, Md.: January 2007), <http://www.fda.gov/oc/reports/iom013007.html> (accessed Aug. 6, 2007). This report was in response to an Institute of Medicine recommendation that FDA include a pharmacoepidemiologist or individual with equivalent public health expertise on its drug-product advisory committees. This recommendation was included in the Institute of Medicine report, *The Future of Drug Safety - Promoting and Protecting the Health of the Public* (Washington, D.C.: 2006).

Most Advisory Committee Meeting Participants Were Standing Members, and Many Members Had Conflict of Interest Determinations

Our analysis of the composition of FDA advisory committee meeting participants from 2 recent years indicates that most participants were standing members, but a large minority of participants were temporary members. In the 83 advisory committee meetings held by CBER, CDER, and CDRH in 2004 and 2006, standing and temporary members were 58 and 42 percent, respectively, of the 1,218 total meeting participants.⁶⁸ An advisory committee member who has a conflict of interest and whose expertise is needed may be permitted by FDA to participate in an advisory committee meeting under certain circumstances by granting a conflict of interest determination. About 16 percent of the participants received a conflict of interest determination that allowed them to participate.⁶⁹ In 49 of the 83 meetings, at least one participating standing or temporary member had at least one conflict of interest determination that allowed the member to participate. The 200 participants with conflict of interest determinations in those 49 meetings had a total of 234 determinations. The FDA Amendments Act of 2007 limits the number of conflict of interest determinations—statutory waivers—that FDA can grant and FDA’s conflict of interest policy revisions change the amount of the disqualifying financial interests.

Most Advisory Committee Meeting Participants Were Standing Members

Standing members were the predominant participants in the 83 advisory committee meetings held by CBER, CDER, and CDRH in 2004 and 2006 that we analyzed. These 83 meetings were held before the 2007 FDA advisory committee process and statutory changes. Temporary members participated in 79 of the 83 meetings. Of the 1,218 participants in the 83 meetings, 58 percent were standing members and 42 percent were temporary. (See table 4.) The participants in CDER’s 17 meetings held in 2006 were nearly evenly split between standing and temporary members at 52 percent and 48 percent respectively.

⁶⁸For this report, advisory committee meeting participants are the standing and temporary members who attended a respective meeting. The participant total includes the number of standing and temporary members who attended each advisory committee meeting, so individual members may be counted more than once.

⁶⁹The conflict of interest determination totals do not include the FDA advisory committees’ industry representatives who are not subject to the conflict of interest statutes and regulations applicable to federal employees.

Table 4: Standing and Temporary Member Totals for 83 FDA Advisory Committee Meetings by Center, 2004 and 2006

FDA center	2004			2006		
	Standing members	Temporary members	Total members ^a	Standing members	Temporary members	Total members ^a
CBER There were 22 advisory committee meetings; 11 in 2004 and 11 in 2006	58% (96)	42% (70)	100% (166)	70% (122)	30% (52)	100% (174)
CDER There were 31 advisory committee meetings; 14 in 2004 and 17 in 2006	61% (137)	39% (86)	100% (223)	52% (137)	48% (125)	100% (262)
CDRH There were 30 advisory committee meetings; 17 in 2004 and 13 in 2006	55% (127)	45% (103)	100% (230)	56% (92)	44% (71)	100% (163)
Total (percentage averages) There were a total of 83 advisory committee meetings; 42 in 2004 and 41 in 2006, with 1,218 members	58%	42%	100% (619)	59%	41%	100% (599)

Source: GAO analysis of FDA's CBER, CDER, and CDRH advisory committee meeting records for 2004 and 2006.

Note: All CBER, CDER, and CDRH advisory committee meetings held in 2004 and 2006 are included except joint advisory committee meetings and advisory committee subcommittee meetings. CDER and CDRH held 10 joint meetings in 2004 and 2006 and temporary members made up less than one-third of the combined standing and temporary member total for those meetings in both years.

^aRepresents the total number of standing and temporary members who attended each advisory committee meeting, so individual members may be counted more than once.

At Least One Standing or Temporary Member Had a Conflict of Interest Determination in over Half of the Advisory Committee Meetings

Forty-nine of the 83 advisory committee meetings we analyzed—over half of all the meetings—had at least 1 standing or temporary member with a conflict of interest determination.⁷⁰ FDA may permit an advisory committee member who has a conflict of interest and whose expertise is needed to participate in an advisory committee meeting under certain circumstances by granting a conflict of interest determination. Two hundred standing and temporary members—about 16 percent of the 83 meetings' 1,218 participants—had at least one conflict of interest determination. Forty-two of the 49 meetings—86 percent—had 2 or more members who received at least one conflict of interest determination. Ninety-five percent of CDER's 2004 and 2006 meetings had 2 or more

⁷⁰For this analysis, standing or temporary members who were industry representatives were not included because they are not SGEs and are not subject to the conflict of interest statutes and regulations.

members with determinations followed by CBER (85 percent) and CDRH (73 percent).

The 200 members had 234 conflict of interest determinations. (See table 5). Most members—167—had only 1 conflict of interest determination; 33 members each had 2 or more determinations. Standing members had 62 percent (nearly two-thirds) of the 234 determinations and temporary members had 38 percent (over one-third).

Table 5: Type and Number of Conflict of Interest Determinations for 200 Standing and Temporary Members for 49 Selected CBER, CDER, and CDRH Advisory Committee Meetings, 2004 and 2006

Type of conflict of interest determination	2004 and 2006		Total determinations
	Standing member	Temporary member	
Statutory waivers			
Financial interest waiver—special government employee (§ 208(b)(3))	104	51	155
Financial interest waiver—involving drugs and biologics topics (§ 355(n)(4)) ^a	15	12	27
Financial interest waiver—federal government employee (§ 208(b)(1)) ^b	4	5	9
Regulatory authorization			
Appearance authorization (§ 2635.502)	23	20	43
Total	146	88	234

Source: GAO analysis of FDA CBER, CDER, CDRH advisory committee meeting records for 2004 and 2006.

Notes: For all three centers, the advisory committee meetings chosen were those with (1) the advisory committee meeting designation most often used by the center’s advisory committees—for CDER and CDRH, specific-parties meetings and for CBER, non-specific party meetings, and (2) at least one standing or temporary member who received a conflict of interest determination. For all three centers, if a meeting had both a specific-parties and a non-specific party meeting topic, the meeting was included if any standing or temporary member attending the meeting received a conflict of interest determination. A participant may have been granted more than one conflict of interest determination, for example, an individual may have had both a § 208(b)(1) waiver and an appearance authorization.

^aPrior to October 1, 2007, the 21 U.S.C. § 355(n)(4) waiver applied only to voting on topics related to clinical investigations and approvals of drugs and biologics, which generally involved only CBER and CDER advisory committee meetings.

^bThe FDA 18 U.S.C. § 208(b)(1) waivers we analyzed were granted only to federal employees not employed by FDA. Although 18 U.S.C. § 208(b)(1) applies to federal employees generally including SGEs and those not employed by FDA who are members of FDA advisory committees, because 18 U.S.C. § 208(b)(3) specifically authorizes waivers for SGEs serving on FACA committees, FDA applied 18 U.S.C. § 208(b)(3) to SGEs in this context.

Among the 234 conflict of interest determinations, the most often granted determination—155—was the § 208(b)(3) financial interest waiver. Standing members had 104 and temporary members had 51 of these waivers. This waiver can be granted for either specific-parties or non-specific party advisory committee meeting topics and to standing and temporary SGE members, so it should have been the conflict of interest determination most often granted to members.⁷¹ Nearly one-half of the 155 § 208(b)(3) waivers—72—were granted to CDER meeting members, 50 to standing, and 22 to temporary members. The remaining 79 of the 234 determinations were 36 statutory waivers—§ 355(n)(4) waivers (27) and § 208(b)(1) financial interest waivers (9)⁷²—and 43 regulatory § 2635.502 appearance authorizations. The FDA Amendments Act of 2007 limits the number of certain conflict of interest determinations—the statutory waivers—that FDA can grant and FDA’s conflict of interest policy revisions change the amount of the disqualifying financial interests.

Agency Comments and Our Evaluation

HHS reviewed a draft of this report and provided comments, which are reprinted in appendix V. HHS also provided technical comments, which we incorporated as appropriate.

In its comments, HHS noted that on August 4, 2008, after we had provided the draft report for its review on July 29, 2008, FDA issued four final guidance documents concerning management of its advisory committees. The guidances include stricter limits on financial conflicts of interest for committee members, improved committee meeting voting procedures, and process improvements for disclosing information about advisory committee members’ financial interests and waivers, and for preparing and making publicly available information given to advisory committee members for specific matters considered at advisory committee meetings. These final guidance documents were available to us in draft form during

⁷¹Some CBER advisory committee meetings used previously granted § 208(b)(3) waivers—for an earlier CBER advisory committee meeting—as waivers for a current meeting. For example, the September 2006 Transmissible Spongiform Encephalopathies Advisory Committee meeting records included five previously granted § 208 (b)(3) waivers dated June 2003, September 2004, and January 2005 for members who attended the 2006 meeting. We did not analyze whether any CBER advisory committee meetings with § 208(b)(3) waivers may have been non-particular matter meetings, which are not subject to § 208.

⁷²The § 208(b)(1) waivers were granted to federal employees from other agencies, such as NIH or CDC, who participated in CDER and CBER advisory committee meetings.

the course of our work and the portions of the draft guidances that we discussed in the report did not change in the final 2008 guidances.

HHS commented on several other aspects of the draft report. First, HHS asked us to note that our findings are applicable only to CBER, CDER, and CDRH advisory committee meetings, and we revised our report to clarify that we did not include all of the FDA centers. Our work focused on those three FDA centers because most of FDA's advisory committees were affiliated with them; these centers' advisory committee meetings represented more than 80 percent of the total FDA advisory committee meetings held in 2004 and 2006.

Second, HHS commented that three groups of experts we included in the report as possible sources for expanding the agency's recruitment outreach for advisory committee members—academic experts, epidemiologists and statisticians, and retired experts—may not be more likely to be free of conflicts of interest. These expert groups were identified by individuals we interviewed as sources they believed could be less likely to have conflicts of interest, and we attributed the statements to those individuals in the report. In addition, the FDA Amendments Act of 2007 discusses FDA's advisory committee recruitment methods and directs FDA to develop and implement strategies on effective outreach to the academic community.

Third, HHS commented that the comparison of the recruitment methods used by EPA and the National Academies to FDA's recruitment methods did not consider additional restraints FDA may have in selecting qualified, minimally conflicted individuals to serve on an advisory committee. However, the report focuses on EPA's and the National Academies' methods to identify potential advisory committee members and uncover conflicts of interest that are not employed by FDA. The approaches employed by these other organizations may provide additional options that FDA could use to expand the pool of potential advisory committee members.

Finally, HHS commented on our use of the term conflict of interest determinations. Throughout our report, we used the term to include both conflict of interest waivers and appearance authorizations granted to advisory committee members to allow them to participate in advisory committee meetings. Although the standards for these determinations are different, they are all made to allow members to participate in advisory committee meetings notwithstanding ethical concerns over their participation. We revised the report to clarify that the FDA Amendments

Act of 2007 provisions involving the agency's advisory committees only apply to conflict of interest waivers.

As we agreed with your offices, unless you publicly announce the contents of this report earlier, we plan no further distribution of it until 30 days from its date. We will then send copies to others who are interested and make copies available to others who request them. In addition, the report will also be available at no charge on our Web site at <http://www.gao.gov>.

If you or your staffs have any questions about this report, please contact me at (202) 512-7114 or crossem@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this report. GAO staff who made major contributions to this report are listed in appendix VI.



Marcia Crosse
Director, Health Care

Appendix I: Major 2007 Actions Affecting FDA Recruiting and Conflict of Interest Determination Processes

In 2007, two major actions occurred that affect the Food and Drug Administration's (FDA) processes for recruiting and prescreening individuals for advisory committee membership and for granting financial conflict of interest waivers to allow members to participate in advisory committee meetings. Those two actions were the passage of the FDA Amendments Act of 2007—an amendment of the Federal Food, Drug, and Cosmetic Act¹—and FDA's draft March 2007 conflict of interest guidance.²

The FDA Amendments Act of 2007 modifies the agency process for prescreening candidates for advisory committee membership. The act requires FDA to develop and implement strategies to conduct outreach to potential advisory committee candidates at universities and colleges, other academic research centers, professional and medical societies, and patient and consumer groups. FDA may also develop a new committee member recruitment method, which would allow entities, such as universities and other academic research centers, receiving funding from the National Institutes of Health, the Agency for Healthcare Research and Quality, the Centers for Disease Control and Prevention, or the Veterans Health Administration, to identify a person whom FDA could contact about the nomination of individuals to serve on advisory committees. Under the prescreening modification, a candidate for FDA advisory committee membership, as of October 1, 2007, completes the Office of Government Ethics Form 450 or FDA Form 3410—financial disclosure reports that provide information about the individual's financial interests—prior to being appointed as an FDA advisory committee member. According to the FDA Amendments Act of 2007, this pre-appointment financial review is intended to reduce the likelihood that a candidate, if appointed as a member, would later require a statutory conflict of interest determination to participate in advisory committee meetings.

¹Pub. L. No. 110-85, § 701, 121 Stat. 823, 900-04 (codified at 21 U.S.C. § 379d-1) (adding section 712 to the Food, Drug, and Cosmetic Act).

²See FDA, *Draft Guidance for the Public, FDA Advisory Committee Members, and FDA Staff on Procedures for Determining Conflict of Interest and Eligibility for Participation in FDA Advisory Committees* (Rockville, Md.: March 2007), <http://www.fda.gov/oc/advisory/waiver/COIguidedft.html> (accessed Mar. 18, 2007). FDA finalized the draft guidance August 2008, <http://www.fda.gov/oc/advisory/GuidancePolicyRegs/ACWaiverCriteriaFINALGuidance080408.pdf> (accessed Aug. 5, 2008).

Conflict of interest determinations to allow a member with a conflict to participate in an advisory committee meeting are affected by both FDA's draft March 2007 guidance and the FDA Amendments Act of 2007. The draft guidance provides that an advisory committee member with personal financial conflicts of interest—referred to as disqualifying financial interests in the guidance—generally would not be allowed to participate in an advisory committee meeting if the combined value of those interests exceeds \$50,000. FDA would not grant a waiver in those circumstances unless the FDA Commissioner determined a waiver was appropriate. Two provisions of the FDA Amendments Act of 2007 affect conflict of interest determinations. First, the law repealed 21 U.S.C. § 355(n)(4)—the § 355 (n)(4) waiver—that applied only to members voting on FDA advisory committee meeting matters related to the clinical investigations and approvals of drugs and biologics—usually Center for Biologics Evaluation and Research (CBER) and Center for Drug Evaluation and Research (CDER) advisory committee meetings. The law also created a new waiver provision—the § 712(c)(2)(B) waiver—to all FDA advisory committee members. Under the new provision, an individual or a member of his or her immediate family who has a financial conflict of interest cannot participate unless FDA determines that a waiver is necessary to afford the advisory committee essential expertise. The law also limits the number of waivers that FDA can grant advisory committee members, reducing the number of waivers (per total meetings) granted annually by 5 percent for a total reduction of 25 percent over 5 years.³

³Pub. L. No. 110-85, § 701, 121 Stat. 901-02 (pertinent provisions codified at 21 U.S.C. § 379d-1(c)(2)(B) and (C)). The law provides that fiscal year 2007 shall be the base year from which to determine the number of waivers that cannot be exceeded to meet the yearly 5 percent reductions.

Appendix II: Scope and Methodology

In this report, we examined FDA’s advisory committee member recruitment, selection, and conflicts of interest prescreening and screening processes, as well as the agency’s use of temporary and standing advisory committee members.¹ We chose to analyze three FDA centers—CBER, CDER, and CDRH—because most of FDA’s advisory committees were affiliated with them—and these three centers’ advisory committee meetings represented more than 80 percent of the total FDA advisory committee meetings held in the two years we included. We did not examine FDA’s other centers’ advisory committee meetings. Specifically, we describe (1) how FDA recruited individuals for advisory committee membership and evaluated candidates by prescreening them for potential conflicts of interest, (2) barriers that were reported to recruiting qualified individuals to serve on FDA advisory committees, particularly candidates without potential conflicts of interest, and (3) the proportion of standing and temporary members who participated in advisory committee meetings, and the frequency with which members with one or more conflict of interest determinations participated in advisory committee meetings.

During the course of our work, two major actions occurred that changed FDA’s recruitment and conflict of interest policies. (See app. I.) In March 2007, FDA issued a draft advisory committee guidance that revises how FDA screens individuals to determine if they have conflicts of interest for a specific advisory committee meeting.² In addition, Congress amended the Federal Food, Drug, and Cosmetic Act to include, among other provisions, a section addressing recruitment, prescreening, and conflicts of interest,

¹FDA advisory committees may select temporary members to serve for a particular advisory committee meeting to provide additional expertise, to ensure a quorum of members is present to conduct a meeting, or both. Like standing members, temporary members who are not industry representatives are appointed as special government employees. They may be members of other FDA advisory committees from the same or a different center, or may be members of a center’s consultant pool. Federal employees from, for example, the Department of Health and Human Services, the Centers for Disease Control and Prevention, or the National Institutes of Health may also serve as temporary members.

²See FDA, *Draft Guidance for the Public, FDA Advisory Committee Members, and FDA Staff on Procedures for Determining Conflict of Interest and Eligibility for Participation in FDA Advisory Committees* (Rockville, MD.: March 2007) <http://www.fda.gov/oc/advisory/waiver/COIguidedft.html> (accessed Mar. 18, 2007). FDA finalized the draft guidance August 2008, <http://www.fda.gov/oc/advisory/GuidancePolicyRegs/ACWaiverCriteriaFINALGuidance080408.pdf> (accessed Aug. 5, 2008).

which took effect on October 1, 2007.³ At the time of our review, it was too soon to assess the effect of the changes on FDA's processes, consequently, this report focuses on FDA's organization, processes, and conflict of interest determinations as documented prior to the 2007 actions.

To address our objectives, we performed a literature review of studies related to FDA advisory committee member recruitment, selection, and conflict of interest prescreening and screening processes. We reviewed Office of Government Ethics and federal conflict of interest laws, and Department of Health and Human Services' (HHS) and FDA's written policies, guidance, reports, and forms related to advisory committee management. We interviewed individuals and groups familiar with FDA's advisory committee member recruitment, selection, and conflict of interest screening processes including FDA staff, selected former advisory committee members,⁴ and representatives from the Association of American Medical Colleges (AAMC), Center for Science in the Public Interest, Pharmaceutical Research and Manufacturers of America (PhRMA), and Public Citizen's Health Research Group. In addition, we reviewed FDA's advisory committee meeting records and conflict of interest determination records for advisory committee meetings held by three FDA centers—CBER, CDER, and CDRH—in 2004 and 2006. We chose to analyze these three centers because most of FDA's advisory committees were affiliated with them—and these centers' advisory committee meetings represented more than 80 percent of the total FDA advisory committee meetings held in 2004 and 2006. Details on the scope of our work and methods to address each objective follow.

To examine how FDA recruited individuals for advisory committee membership and prescreened candidates for potential conflicts of interest, we reviewed HHS and FDA written policies, guidances, reports, and forms

³Pub. L. No. 110-85, § 701, 121 Stat. 900-04 (codified at 21 U.S.C. § 379d-1).

⁴We identified former CBER, CDER, and CDRH advisory committee members to interview by determining which FDA advisory committees in each center held the most meetings in 2006, and from these advisory committees, which members' service ended during 2006 and 2007. Of these former advisory committee members, we contacted those who either did not receive a conflict of interest waiver in 2006 or who served as an advisory committee chair. Because these criteria yielded fewer former CBER advisory committee members than former CDER and CDRH advisory committee members, we also contacted former CBER advisory committee members who received conflict of interest waivers in 2006. We asked these former members whether barriers exist to recruiting qualified individuals to serve on FDA advisory committees, particularly those without conflicts of interest, and how FDA could improve its recruitment process.

related to advisory committee management. These documents include HHS's *Federal Advisory Committee Management Handbook*, FDA's *Policy and Guidance Handbook for FDA Advisory Committees*, and FDA's quarterly reports to Congress on its efforts to identify and screen qualified people for appointment to FDA advisory committees. We also reviewed advisory committee information on FDA's Web site and examined FDA forms used to prescreen candidates for advisory committee membership.

In addition, we interviewed staff from FDA's Advisory Committee Oversight and Management Staff; FDA's Ethics and Integrity Staff; staff from CBER, CDER, and CDRH; and advocacy organizations that nominate individuals to serve on FDA's advisory committees, including PhRMA and Public Citizen's Health Research Group. We also interviewed officials from organizations we previously identified as employing specific recruitment and prescreening methods that could ensure independent and balanced advisory committees. These organizations are the U.S. Environmental Protection Agency (EPA) and the National Academies.

To examine barriers that were reported to recruiting qualified individuals to serve on FDA advisory committees, particularly candidates with no potential conflicts of interest, we interviewed individuals and groups familiar with FDA's advisory committee recruitment process and officials from organizations we identified in 2004 as employing specific recruitment methods that could ensure independent and balanced advisory committees. Individuals interviewed include staff from CBER, CDER, and CDRH office, review division, and advisory committee management; 12 former CBER, CDER, and CDRH advisory committee members; staff from EPA, the National Institutes of Health, and the National Academies who were involved with the advisory committee process at their organizations; and staff from AAMC, PhRMA, and consumer advocacy groups that have taken a position on FDA's nomination and selection processes for advisory committee members.

To determine the proportion of participants in FDA's CBER, CDER, and CDRH advisory committee meetings who were standing members or temporary members, we reviewed FDA's advisory committee meeting records for 83 meetings held by the 3 centers in 2004 and 2006. The 83 meetings did not include (1) the 10 joint advisory committee meetings—meetings involving 2 advisory committees—held in 2004 and 2006, which were analyzed separately, or (2) advisory committee subcommittee meetings, which are not covered by the Federal Advisory Committee Act. Beginning in November 2005, FDA was required to post information on its

Web site about the conflict of interest waivers it granted that allowed certain members to participate in meetings.⁵ We chose to review the committee meetings held in 2004 and 2006—2 years with the most recent data when we began our work—because (1) 2004 was the last full year before FDA began to post waiver information in 2005, and (2) 2006 was the first full year in which the waiver information had to be posted. We excluded 2005 from the analysis because it was the year the Web site posting requirement began. To verify the number of standing and temporary members who attended the 83 meetings, we reviewed the 2004 and 2006 FDA advisory committee meeting records, which included meeting minutes, meeting summaries, meeting transcripts, lists of meeting attendees, and annual committee member rosters—the list of standing members—for the years 2004 and 2006. If an advisory committee meeting was conducted for more than 1 day, a standing or temporary member was included in the analysis, if the member attended at least 1 day of the meeting.

To analyze the number and type of conflict of interest determinations received by standing and temporary members, we analyzed 49 of the 83 CBER, CDER, and CDRH advisory committee meetings held in 2004 and 2006. The following criteria were used to select the 49 meetings: (1) the advisory committee meetings with the designation most often used by the centers—for CDER and CDRH, specific-parties meetings and, for CBER, non-specific party meetings, and (2) advisory committee meetings that had at least one standing or temporary member who received at least one conflict of interest determination. If an advisory committee meeting involved both a specific-parties and a non-specific party meeting topic, the

⁵The Web site posting was required by the Agriculture, Rural Development, Food and Drug Administration and Related Agencies Appropriations Act for fiscal year 2006 and continued through fiscal year 2007. In August 2008, FDA issued a final *Guidance for the Public, FDA Advisory Committee Members, and FDA Staff: Public Availability of Advisory Committee Members' Financial Interest Information and Waivers* (Rockville, Md.: August 2008). <http://www.fda.gov/oc/advisory/GuidancePolicyRegs/ACDisclosureFINALGuidance080408.pdf> (accessed Aug. 5, 2008).

meeting was included if any standing or temporary member attending the meeting received a conflict of interest determination.⁶

To determine the number and type of conflict of interest determinations among the 49 advisory committee meetings' standing and temporary members, we created a participant-level data collection instrument to retrieve information from FDA's advisory committee meeting records and conflict of interest waiver records for each advisory committee meeting included in the project analysis. We reviewed the following records to collect the needed data: conflict of interest waivers and their conflict of interest checklists,⁷ acknowledgement and consent for disclosure of potential conflicts of interest forms,⁸ and appearance authorization memorandums.⁹ Information we collected included the advisory committee meeting participant's status (for example, standing or temporary member) and the conflict of interest determination (for example, § 208(b)(3) waiver). When FDA issued its March 2007 *Draft Guidance for the Public, FDA Advisory Committee Members, and FDA Staff on Procedures for Determining Conflict of Interest and Eligibility for Participation in FDA Advisory Committees*, we narrowed the scope of our work and excluded an assessment of whether FDA adhered to its

⁶To determine the designation of an advisory committee meeting (e.g., non-specific party and specific-parties), we reviewed the meeting inventory sheets FDA provided. When the inventory sheets did not indicate a designation, we determined the designation from records available on FDA's advisory committee Web site (www.fda.gov/oc/advisory) including *Federal Register* advisory committee meeting notices, advisory committee meeting minutes and summary minutes, a meeting's conflict of interest waivers, and advisory committee meeting transcripts. If the designation could not be determined from the meeting records, we asked FDA to provide the designation.

⁷Conflict of interest waivers—documented in memorandums—describe the reasons why a conflict of interest waiver is requested for a participant, and indicate if the waiver was granted. The conflict of interest checklists are attached to waivers and provide more detail on why the participant's conflict of interest waiver was requested, e.g., the value of the stock held in a drug company affected by a new drug application being considered by the advisory committee.

⁸An acknowledgement and consent for disclosure of potential conflict of interest form is attached to a member's waiver and provides a shorter summary of conflicts of interests involved. The member signs the form to allow public disclosure of his or her conflict of interest information for a particular advisory committee meeting. An FDA official stated that these forms are used for specific-parties meetings.

⁹An appearance authorization—also referred to as an appearance determination—memorandum describes reasons why a conflict of interest appearance determination is requested for an individual and allows him or her to participate in the advisory committee meeting despite the appearance concerns.

FDA Waiver Criteria Document (2000) when it made its conflict of interest determinations for the meetings we analyzed. To assess the reliability of the conflict of interest determination information we summarized, we reviewed questions from 5 percent of the data collection instruments completed for the 49 advisory committee meetings for accuracy in transferring conflict of interest determination information from the FDA records, and determined the information collected was sufficiently reliable for our report.

We conducted our work from October 2006 through September 2008 in accordance with generally accepted government auditing standards.

Appendix III: Factors That May Affect FDA Advisory Committee Meeting Recommendations

FDA may, like other federal agencies, determine its advisory committees' meeting topics to suit its own purposes. There are many factors involved in conducting an FDA advisory committee meeting that may affect a committee's recommendations to the agency, in addition to any possible effects from a committee member's conflicts of interest. Also, like other federal agencies, FDA generally has the freedom to accept, reject, or modify its advisory committees' recommendations.¹ The following discussion of various meeting factors is limited to FDA's CBER, CDER, and CDRH advisory committees. For each advisory committee meeting, the FDA staff involved may include individuals from the review division² with subject matter expertise on the advisory committee's meeting topics and the division director; the review team—the FDA staff working on a particular product being considered by the advisory committee; the advisory committee's executive secretary; and the center's advisory committee meeting management entity.

Pre-Advisory Committee Meeting Decisions

- *Who should be selected as standing advisory committee members?* The FDA advisory committee charters—the committee's organizational document—list the expertise a committee's standing members should have. The review division is involved in the selection of nominees for a committee's standing members and the expertise they represent. It has been suggested that a member's type of expertise may affect how the member analyzes the information provided at an advisory committee meeting and what recommendation decision the member makes.
- *Who should be selected as the advisory committee chair?* Review divisions determine who is selected to serve as an advisory committee's chair rather than committee members choosing a chair from among themselves.³ In consultation with the review division, the chair's responsibilities may include helping develop the meeting's agenda and

¹The Federal Advisory Committee Act (FACA) provides that, unless otherwise specified by statute or presidential directive, advisory committees shall be utilized solely for advisory functions. 5 U.S.C. app. § 9(b).

²CBER's advisory committees are more closely aligned with their offices. For this appendix, the term review division is used to include both the CDER and CDRH review divisions and CBER's offices.

³We were told that the committee chair is usually selected based on FDA's observations of an individual's participation as a member of an advisory committee. For example, whether the individual exhibits the ability to remain focused on the meeting topic and whether the other committee members appear to respect the individual's expertise.

topic questions, deciding the meeting's voting procedure, monitoring the length of meeting presentations, and approving meeting minutes.

Advisory Committee Meeting Decisions

- *Why is an advisory committee meeting needed?* Although an advisory committee may have a regular meeting schedule, the advisory committee's review division decides when an advisory committee meeting is needed.⁴ Meetings may be held when there are controversial issues that committee advice could help the agency resolve. For example, in July 2007, two of CDER's advisory committees met jointly to consider whether Avandia, a diabetes drug, should remain on the market given concerns that its use increased heart risks for those with diabetes.⁵
- *What is the advisory committee meeting's topic and what questions are to be answered?* The review division selects the topic, develops the issues FDA seeks advice on into topic questions for the advisory committee to address at the meeting, and compiles the background information for the committee to review.⁶

Other options for developing possible meeting topics:

- *Subcommittee meetings:* The review division may select a limited number of advisory committee members—including at least two standing members—and other consultants to serve as a subcommittee to discuss and develop an issue of FDA's choosing. The subcommittee then provides this information to an advisory committee for its consideration.⁷

⁴For example, CDRH conducts an annual closed session, approved by the office director, with its standing advisory committee members. During this session, the review division updates the members about possible upcoming advisory committee meeting topics and devices in process for approval.

⁵See FDA, www.fda.gov/ohrms/dockets/ac/cder07.htm#EndocrinologicMetabolic (accessed Oct. 18, 2007) for CDER's July 30, 2007, joint advisory committee meeting of its Endocrinologic and Metabolic Drugs Advisory Committee and Drug Safety and Risk Management Advisory Committee.

⁶Additional information is provided to the advisory committee by the company at issue in the meeting. For example, a company sponsoring a new drug for approval will provide data to support the efficacy and safety claims for its product.

⁷A subcommittee meeting of this type is not subject to FACA because the subcommittee is providing information to an advisory committee rather than making recommendations to FDA. See 41 C.F.R. § 102-3.35 (2006).

- *Homework assignments:* FDA may also select advisory committee members and other experts to conduct homework assignments,⁸ again on issues of FDA's choosing. A homework assignment may involve, for example, an in-depth review of an issue that may be considered as a potential topic at an upcoming advisory committee meeting or review of a product early in its development.
- *Are temporary members needed, and if yes, who should be selected?* The review division will determine whether the standing committee members able to attend the meeting have the needed expertise to address the topics to be discussed at the advisory committee meeting. If additional expertise is determined to be necessary, temporary members can be selected to serve on the committee for the meeting.⁹ The review division decides which individuals—usually from the center's consultant pool—are selected to serve as temporary members. Each center maintains a consultant pool and selects the pool's individual experts.
- *Are guest speaker presentations needed, and if yes, who should be selected?* The review division may determine that additional information needs to be presented at an advisory committee meeting. The division can select and invite guest speakers to make presentations and answer questions before the committee.¹⁰ Guest speakers may, for example, be members of other FDA advisory committees, individuals from a center's consultant pool, federal employees from other agencies, or national or international experts from outside FDA. Guest speakers do not vote, and they do not participate in the committee's discussions.
- *Are patient representatives needed, and if yes, who should be selected?* CBER, CDER, and CDRH cancer-related advisory committees are required to have patient representatives participate in all advisory committee meetings. For other advisory committees, the review division considers the topic to be discussed at a particular meeting when determining whether it is necessary for a patient representative to serve at an advisory

⁸A homework assignment can not be given to more than three advisory committee members or the assignment would constitute an advisory committee meeting, according to an FDA official.

⁹Temporary members may also be selected to attend an advisory committee meeting to ensure there is a meeting quorum.

¹⁰A guest speaker may be paid to attend an advisory committee meeting. For example, if a CDER review division decides to invite a guest speaker who is not a federal employee, the division may pay the speaker from its division funds.

committee meeting. Patient representatives usually serve on advisory committees that focus on disease-specific topics such as reviews of products and therapies for HIV/AIDS and cancer diagnosis and treatment.¹¹ When participating in CBER and CDER advisory committees' meetings, patient representatives usually vote, but when participating in CDRH's committee meetings, they do not vote.

- *Who should be selected to make FDA's presentations at meetings?* A review division's role at an advisory committee meeting is to present the issues and data concerns the advisory committee will consider, and to pose questions to the committee throughout the meeting. For example, a review division director may introduce the committee meeting topic—for example, a new drug approval application, provide the regulatory history concerning how similar drugs were developed, describe any issues that have arisen with similar drugs, and discuss the types of clinical trials used to evaluate the previously approved drugs. The review division determines which FDA staff attend the meeting and whether they make presentations.

Advisory Committee Meeting Conflict of Interest Determinations

- *What companies and products are determined to be affected by the meeting topic?* After an advisory committee meeting's topic is selected, the review division compiles a list of the companies and products it determines are affected by the topic. The list is then reviewed by the advisory committee's management entity, for example, CDER's Advisors and Consultants Staff. The more affected companies or products involved, the greater the possibility that committee members may have financial interests in an affected company or product, and the greater the possibility that members may have conflicts of interests.
- *To which advisory committee members with conflicts of interest does FDA decide to grant conflict of interest determinations?* For each advisory committee meeting, the center's advisory committee meeting management entity reviews each member's possible conflicts of interest based on the information the member self reports on his or her FDA financial disclosure form—3410—and determines whether they will affect the individual's ability to participate in the meeting. If there are members that are determined to have conflicts of interest, the review division may seek individuals with similar expertise, who do not have conflicts of

¹¹An FDA official told us that patient representatives serve as ad hoc members of the advisory committee for a particular advisory committee meeting.

interest, to participate in the meeting as temporary members.¹² Advisory committee members who have conflicts of interest, but who have expertise the review division determines is needed for the committee's meeting topic, can be given a conflict of interest determination if the standards of the applicable statutes and regulations are met.

Recommendations from the Advisory Committee Meeting

- *How does the advisory committee reach its meeting's recommendation—by voting or reaching a consensus?* The review division, which determines the meeting topic and questions, can indicate whether the committee should vote or reach a consensus on the recommendations made at the committee meeting. A committee chair may also decide that an issue should be addressed by a vote of the members. Generally, committee members vote when a meeting has a specific topic, such as a new drug approval application. There may be instances when the members reach a consensus opinion without voting.
- *What options does FDA have concerning the advisory committee meeting's recommendation?* Following an advisory committee meeting, the center's review division evaluates the advisory committee's recommendation to determine whether FDA should accept or reject it, have the committee discuss the meeting topic again, or hold workshops on the meeting topic subject. FDA, like other federal agencies, generally does not have to accept its advisory committees' recommendations.

Recent Studies on FDA Advisory Committee Meeting Recommendations

Recent studies have focused on whether FDA advisory committee members with conflict of interest determinations that allow them to participate in the committee meetings may influence the committee's recommendations.

- Public Citizen's 2006 study:¹³ The Public Citizen study on FDA conflicts of interest found a "weak relationship" between an FDA advisory committee member who had a conflict of interest and who also voted in favor of the drug at issue. The study also found that excluding advisory committee

¹²The review division usually looks to the center's consultant pool to find alternate experts, but may also go outside FDA.

¹³See P. Lurie, C. Almeida, N. Stine, A. Stine, and S. Wolfe, "Financial Conflict of Interest Disclosure and Voting Patterns at Food and Drug Administration Drug Advisory Committee Meetings," *The Journal of the American Medical Association*, vol. 295, no. 16 (2006). See also FDA's comment on the article at www.fda.gov/oc/advisory/analysis.html.

members (standing members) and voting consultants (temporary members) who had conflict of interest determinations would not have altered the overall vote result—whether favorable or unfavorable toward a drug—of any advisory committee meeting studied.

- National Research Center for Women & Families 2006 report:¹⁴ The National Research Center’s report, which included information from other studies of FDA advisory committees and their members with conflicts of interest, concluded that “it is possible to understand how a few committee members with conflicts of interest can have a disproportionate impact on approval recommendations.”¹⁵ The report stated that because FDA has its advisory committees meet to discuss controversial or innovative products, “the public might therefore expect that many of the drugs and devices reviewed by advisory committees would not be recommended for approval.”¹⁶ Using 11 randomly selected CDER and CDRH advisory committees, the report found that 79 percent of the 89 products reviewed between 1998 and 2005 were recommended for approval, and that the recommendations were usually unanimous.¹⁷
- FDA’s 2007 study:¹⁸ A research firm under contract with FDA assessed the relationship of FDA advisory committee members’ expertise and their financial conflicts of interest. The study concluded that (1) standing advisory committee members with higher expertise were more likely than other standing members to have been granted conflict of interest waivers, (2) alternative members—temporary members—could be found for a specific advisory committee meeting, but many of them would likely require conflict of interest waivers, and (3) the ability to create a conflict-of-interest-free advisory committee was speculative.

¹⁴See D. Zuckerman, *FDA Advisory Committees: Does Approval Mean Safety?* National Research Center for Women & Families (Washington, D.C.: 2006).

¹⁵Zuckerman, 3.

¹⁶Zuckerman, 1.

¹⁷The report used attributed quotations from FDA advisory committee meeting transcripts and vote tallies to analyze voting patterns of four types of advisory committee meeting participants (physician only, physician plus scientific degree, doctorate only, and consumer representative).

¹⁸See N. Ackerley, J. Eyraud, M. Mazzotta, *Measuring Conflict of Interest and Expertise on FDA Advisory Committees*, Eastern Research Group, Inc. (Lexington, Mass.: 2007).

Appendix IV: FDA Advisory Committees for the Three Centers Analyzed

Center for Biologics Evaluation and Research

- Allergenic Products Advisory Committee
- Blood Products Advisory Committee
- Cellular, Tissue and Gene Therapies Advisory Committee
- Transmissible Spongiform Encephalopathies Advisory Committee
- Vaccines and Related Biological Products Advisory Committee

Center for Drug Evaluation and Research

- Anesthetic and Life Support Drugs Advisory Committee
- Anti-Infective Drugs Advisory Committee
- Antiviral Drugs Advisory Committee
- Arthritis Advisory Committee
- Cardiovascular and Renal Drugs Advisory Committee
- Dermatologic and Ophthalmic Drugs Advisory Committee
- Drug Safety and Risk Management Advisory Committee
- Endocrinologic and Metabolic Drugs Advisory Committee
- Gastrointestinal Drugs Advisory Committee
- Nonprescription Drugs Advisory Committee
- Oncologic Drugs Advisory Committee
- Peripheral and Central Nervous System Drugs Advisory Committee
- Pharmaceutical Science and Clinical Pharmacology Advisory Committee
- Psychopharmacologic Drugs Advisory Committee
- Pulmonary-Allergy Drugs Advisory Committee
- Reproductive Health Drugs Advisory Committee

Center for Devices and Radiological Health

- Device Good Manufacturing Practice Advisory Committee
- Medical Devices Advisory Committee¹
 - Anesthesiology and Respiratory Therapy Devices Panel
 - Circulatory System Devices Panel
 - Clinical Chemistry and Clinical Toxicology Devices Panel
 - Dental Products Panel
 - Ear, Nose, and Throat Devices Panel
 - Gastroenterology-Urology Devices Panel
 - General and Plastic Surgery Devices Panel
 - General Hospital and Personal Use Devices Panel
 - Hematology and Pathology Devices Panel

¹The Center for Devices and Radiological Health's Medical Devices Advisory Committee (MDAC) is the umbrella title for 18 statutorily authorized advisory panels whose members are subject to the same legal and regulatory requirements as other FDA advisory committees. FDA counts MDAC and its 18 panels as one advisory committee. For our analysis, MDAC's 18 panels' meetings were treated as individual advisory committee meetings.

**Appendix IV: FDA Advisory Committees for
the Three Centers Analyzed**

- Immunology Devices Panel
- Medical Devices Dispute Resolution Panel
- Microbiology Devices Panel
- Molecular and Clinical Genetics Panel
- Neurological Devices Panel
- Obstetrics-Gynecology Devices Panel
- Ophthalmic Devices Panel
- Orthopaedic and Rehabilitation Devices Panel
- Radiological Devices Panel
- National Mammography Quality Assurance Advisory Committee
- Technical Electronic Product Radiation Safety Standards Committee²

²This committee, by law, has 5 members who represent governmental agencies including state and federal governments, and 10 members who represent industry and the public. *See* 21 U.S.C. § 360kk.

Appendix V: Comments from the Department of Health and Human Services



DEPARTMENT OF HEALTH & HUMAN SERVICES

OFFICE OF THE SECRETARY

Assistant Secretary for Legislation
Washington, DC 20201

AUG 28 2008

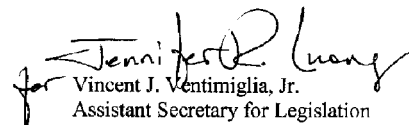
Marcia Crosse
Director, Health Care
U.S. Government Accountability Office
441 G Street NW
Washington, D.C. 20548

Dear Ms. Crosse:

Enclosed are the Department's comments on the U.S. Government Accountability Office's (GAO) draft report entitled, "FDA Advisory Committees: Process for Recruiting Members and Evaluating Potential Conflicts of Interest" (GAO-08-640).

The Department appreciates the opportunity to comment on this draft before its publication.

Sincerely,


for Vincent J. Ventimiglia, Jr.
Assistant Secretary for Legislation

Attachment

**COMMENTS OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS)
ON THE U.S. GOVERNMENT ACCOUNTABILITY OFFICE'S (GAO) DRAFT
REPORT ENTITLED, "FDA ADVISORY COMMITTEES: PROCESS FOR
RECRUITING MEMBERS AND EVALUATING POTENTIAL CONFLICTS OF
INTEREST" (GAO-08-640)**

The Food and Drug Administration (FDA) appreciates the opportunity to review and comment on the Government Accountability Office's (GAO) draft report. As the report acknowledges, during the time period covered by the report, FDA has issued new guidance to determine eligibility for participation of advisory committee members with potential conflicts of interest. The new guidance establishes a more stringent policy to limit waivers of conflict of interest beyond the requirements in the applicable law. We have made a number of additional improvements to our advisory committee process that are not described in the report -- including final guidance on public disclosure of advisory committee members' financial information and waivers, final guidance on voting procedures, final guidance on availability of briefing materials, draft guidance on criteria for when to hold an advisory committee meeting, and website improvements. These actions occurred during the period of the report. We expect these new policies to further strengthen public confidence in the integrity of FDA's advisory committees.

We have a number of general comments on the report, as described below.

Scope

The GAO report is based on data from CBER, CDER, and CDRH advisory committee meetings held in 2004 and 2006. We suggest that the findings in the report be clearly identified as limited in applicability to CBER, CDER, and CDRH committees.

Recruitment efforts

The GAO report suggests that FDA may have been able to mitigate acknowledged barriers to recruiting qualified advisory committee candidates without potential conflicts of interest.

1. An additional variable that is not discussed in the report is FDA's efforts, consistent with FACA, to achieve gender, ethnic, and geographic balance. FDA strives for members from across the United States and for individuals who are as diverse as the United States. In addition, we strive for diversity in points of view to facilitate thorough discussions of all sides of the issues. These efforts may limit the pool of experts for recruiting.
2. The GAO report suggests that FDA could have expanded its recruitment efforts to "experts from college and universities." We note that individuals from academia make up the bulk of the standing members and temporary voting members that serve on our committees. These sources are clearly not without potential conflicts of interest, as the financial interests of the academic institution employing such experts are imputed to the member under the laws that we must apply.
3. The GAO report suggests that FDA expand outreach to "individuals with epidemiological and statistical expertise". We have not found that any one particular biomedical specialty reliably yields lower conflict of interest issues. We have found that our statisticians and

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epidemiologists are as likely to have significant conflicts of interests as other special government employees (SGEs) because they are as likely to be involved in medical/pharmaceutical research as other specialists.

4. The GAO report also identifies retired experts as a possible source of conflict-free members. FDA has concerns, as noted on page 37 of the report, that many retired individuals may not have remained current with rapidly evolving technologies. In addition, it has been our experience that retired experts often have large pharmaceutical stock portfolios and, if still active in their field, may be actively involved in pharmaceutical consulting – both of which are potential conflicts of interest.
5. In the report, GAO compared methods used by EPA and the National Academies to FDA methods. We believe that extrapolating findings from experts in one industry to another should be done cautiously. Companies that develop new drugs and devices naturally seek the best scientific expertise to help develop such products and the experts experienced with such product development consequently have unique insights that can greatly benefit the FDA. As a result, many scientists with expertise and knowledge of FDA-regulated products have financial ties to the pharmaceutical industry. The FDA has an additional burden that neither the EPA nor the National Academies deal with – the timelines within the Prescription Drug User Fee Act (PDUFA) and within the Medical Device User Fee Modernization Act. For example, PDUFA sets time limits within which FDA must decide the fate of a particular New Drug Application or supplement. This means that the FDA must strive to locate not only a qualified minimally conflicted SGE within a certain period of time, but also one that is available to serve on the committee at the time it must meet.

Use of term “conflict of interest determinations”

The GAO report defines the term “conflict of interest determinations” to include both (1) waivers of the statutory conflict of interest prohibitions and (2) determinations that the agency may make under 5 CFR 2645.502 concluding that a reasonable person with knowledge of the relevant facts would not question the impartiality of the individual. We believe that combining these two very different determinations in one term is confusing and misleading. A waiver or exception is granted only after determining that a potential conflict of interest exists but that the statutory standard for a waiver can be met. If there is a potential conflict of interest, FDA may not authorize the individual's participation under the provisions of 5 CFR 2645.502 but must instead apply the statutory criteria for waivers.

In contrast, an impartiality determination may be made when the statutory prohibition on participation does not apply but the individual or FDA has asked for a review of whether his participation would create an appearance of a conflict. In those cases where FDA has issued an impartiality determination, the agency has concluded that a reasonable person with knowledge of the relevant facts would not question the impartiality of the individual or has authorized the

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employee to participate because the interest of the Government in the employee's participation outweighs the concern that a reasonable person may question the integrity of the agency's programs and operations.

We note that the report in several instances inaccurately uses the term "conflict of interest determination" when "waiver or exception" should be used. We have identified these instances in FDA's technical comments that accompany these general comments.

Appendix VI: GAO Contact and Staff Acknowledgments

GAO Contact

Marcia Crosse, (202) 512-7114 or crossem@gao.gov

Acknowledgments

In addition to the contact above, Martin Gahart, Assistant Director; George Bogart; Helen Desaulniers; Adrienne Griffin; Cathleen Hamann; Martha Kelly; Deitra Lee; Amanda Pusey; Daniel Ries; Opal Winebrenner; and Suzanne Worth made key contributions to this report.

Related GAO Products

Federal Advisory Committee Act: Issues Related to the Independence and Balance of Advisory Committees. [GAO-08-611T](#). Washington, D.C.: April 2, 2008.

Drug Safety: Further Actions Needed to Improve FDA's Postmarket Decision-making Process. [GAO-07-856T](#). Washington, D.C.: May 9, 2007.

NIH Conflict of Interest: Recusal Policies for Senior Employees Need Clarification. [GAO-07-319](#). Washington, D.C.: April 30, 2007.

Drug Safety: FDA Needs to Further Address Shortcomings in Its Postmarket Decision-making Process. [GAO-07-599T](#). Washington, D.C.: March 22, 2007.

Food and Drug Administration: Decision Process to Deny Initial Application for Over-the-Counter Marketing of the Emergency Contraceptive Drug Plan B Was Unusual. [GAO-06-109](#). Washington, D.C.: November 14, 2005.

Federal Research: NIH and EPA Need to Improve Conflict of Interest Reviews for Research Arrangements with Private Sector Entities. [GAO-05-191](#). Washington, D.C.: February 25, 2005.

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University Research: Most Federal Agencies Need to Better Protect against Financial Conflicts of Interest. [GAO-04-31](#). Washington, D.C.: November 14, 2003.

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