

Ombudsman's 2010 Annual Report

FDA, Center for Drug Evaluation and Research (CDER)

The CDER Ombudsman's Office includes both the CDER Ombudsman, Virginia L. Behr, and CDER's Product Jurisdiction Officer, LCDR Ayoub Suliman. CAPT Mary Kremzner was the Acting CDER Ombudsman from September through November of this year, as Ms. Behr was on extended leave. This report briefly explains the role of the CDER Ombudsman and details the number and variety of interactions between the Ombudsman's Office and its constituents for calendar year 2010.

I. The Ombudsman's Role

The United States Ombudsman's Association (USOA) defines a governmental Ombudsman as "an independent, impartial public official with authority and responsibility to receive, investigate or informally address complaints about governmental actions, and, when appropriate, make findings and recommendations, and publish reports."

The CDER Ombudsman receives inquiries and investigates complaints (in an informal, unbiased manner) from the regulated pharmaceutical industry (or the law firms representing them), health care providers, and consumers and also provides general information on product development and regulation. If requested, the Ombudsman can informally resolve disputes or disseminate information about established appeals processes and other formal mechanisms for dispute resolution. The Ombudsman also receives comments from inside and outside the Center about problems that impede CDER's performance of its mission. The Ombudsman makes recommendations for Center improvement to the Center Director but cannot require action or mandate change because ombudsmen do not have disciplinary or enforcement powers. The CDER Ombudsman works with other FDA ombudsmen to attend to cross-Center issues and to resolve inter-center disputes.

The CDER Ombudsman's mission is to quickly and impartially investigate complaints and resolve disputes between CDER and CDER-regulated industry, health care providers, and consumers by offering an informal, confidential, and neutral environment. Its vision is to improve the functionality and transparency of CDER by providing efficient resolution of disputes and by fostering communications with stakeholders.

The CDER Ombudsman follows a code of ethics and operating principles drawn from those established by the Coalition of Federal Ombudsmen (COFO), the United States Ombudsman Association (USOA), and the International Ombudsman Association (IOA). These include standards for ensuring confidentiality, neutrality, and informality. The Office reports to the Director of the Office of Executive Programs within the Office of the Center Director. The Ombudsman is a member of the Coalition of Federal Ombudsmen.

II. Contact Methods, Demographics, and Most Common Topics

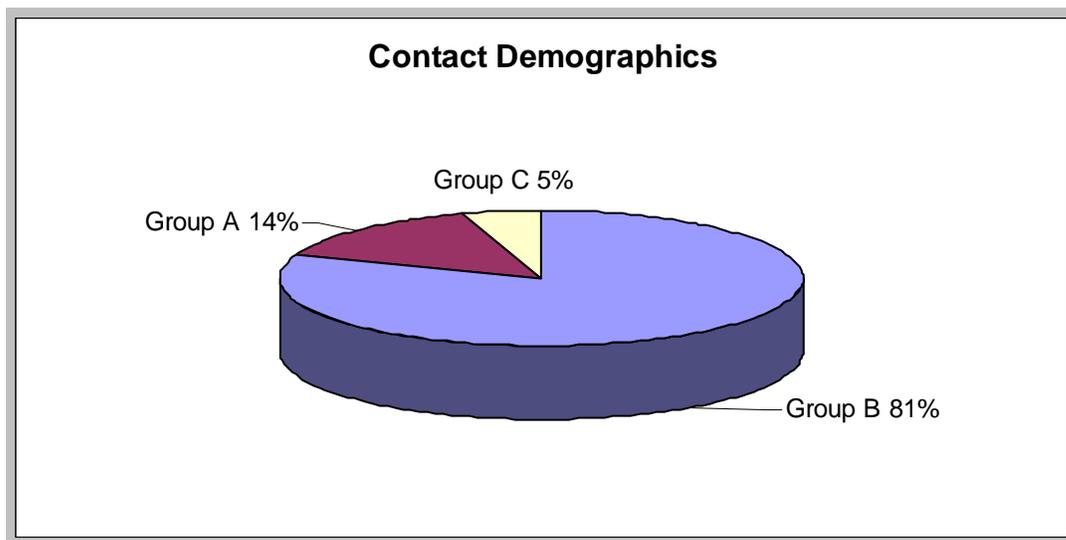
Consumers, law firms, researchers, FDA employees, and the pharmaceutical industry contact the Ombudsman by fax, phone, postal mail, electronic mail, and in person. In 2010, the Ombudsman received 1015 communications, the vast majority (98%) of which came via electronic mail and phone. In many instances, several emails or phone calls were exchanged per case; those follow-up correspondences were not counted for this report (i.e. the numbers refer to initial contacts only). Below is a list and graphic depictions of the number of contacts and their demographics. A list of the most common complaint topics follows the demographic data.

Demographics and (Number of Contacts)

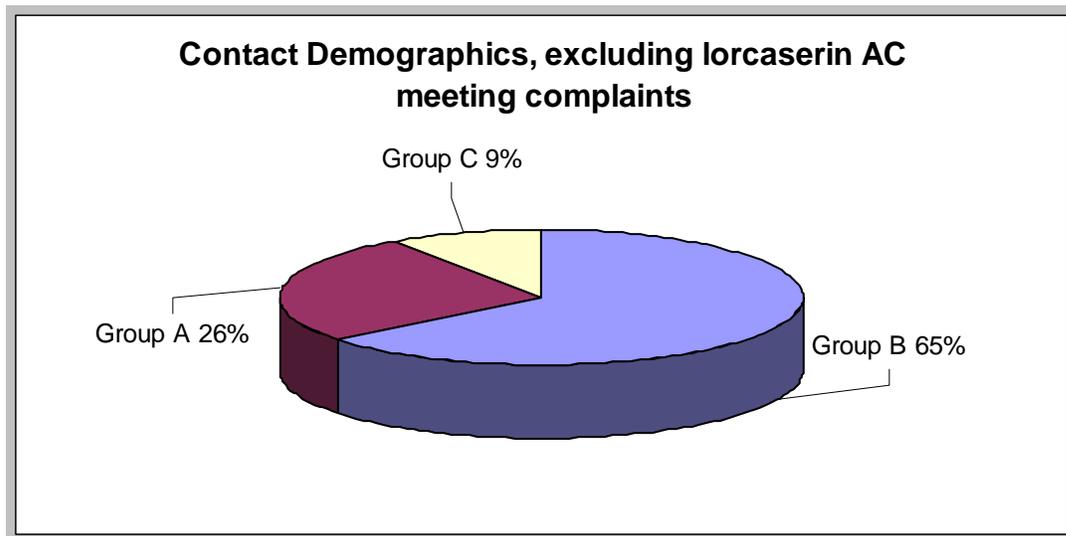
- Group A
 - Consultants (24)
 - Press (1)
 - Whistleblowers (14)
 - Law firms (19)
 - Research sponsors (10)
 - Commercial sponsors (77)

- Group B
 - Consumers (629)
 - Health care professionals (81)
 - Advocacy groups (4)
 - Other (104)

- Group C
 - CDER employees (52)



As shown by the chart above, the vast majority of contacts came from consumers. However, upon closer inspection, 467 of the 818 contacts made by this group were consumers and others (typically, investors in Arena Pharmaceuticals) concerned about the conduct of the advisory committee for lorcaserin, an anti-obesity drug under development by Arena Pharmaceuticals. If the contacts interested in that one topic are removed from the analysis, the chart looks like this:



In no particular order, below is a list of the most common complaint topics received by the CDER Ombudsman in 2010. Many of the topics above carry over as common topics from 2009. Please note that in 2011, this report will no longer include inquiries that are re-directed by the CDER Ombudsman to CDER's Division of Drug Information.

Most Common Contact Topics from the Pharmaceutical Industry, Law Firms, Consultants, and Public or Private Research Institutions

- Appeals processes, including formal dispute resolution assistance
- Whistleblower reporting of protocol violations, including falsification of data and expired drug being used in a clinical trial
- Compliance enforcement actions
 - Actions taken on marketed drugs that do not have FDA approval
 - Warning Letter receipt
 - Import/export issues, usually detained product
- Requirement for electronic drug establishment registration and listing too cumbersome
 - Beginning June 1, 2009, FDA no longer accepted paper registration and listing. Many companies, especially small businesses, complained that the 13 step electronic process was too complicated and lengthy.
- Perceived unfair handling of an issue
- Communication delays

- Office of New Drugs (OND) review delays or decisions resulting in slowed drug development
- Investigational New Drug Application (IND) and New Drug Application (NDA) requirements; review and application process questions
- Unlawful promotional activities by competitors

Most Common Contact Topics from Consumers, Advocacy Groups, and Health Care Professionals

- Reporting of drug adverse events and medication errors
- Conduct of the September 16, 2010 advisory committee meeting to discuss lorcaserin, an anti-obesity drug under development by Arena Pharmaceuticals. More details can be found in FDA's response (Attachment A) to those who expressed concerns.
- Unavailability of drug, either because of marketing withdrawal, shortages, or IND on clinical hold
 - Example: towards the end of the year, FDA asked all manufacturers of propoxyphene-containing products (pain relievers) to voluntarily remove their drugs from the market because of concerns about serious toxicity to the heart.
- Violative conduct by pharmaceutical companies (usually off-label promotion)
- Drug costs and health insurance problems
- Complaints from consumers about their doctors or a pharmacy
- Misleading product websites and unlawful promotional advertising

Most Common Contact Topics from CDER employees

Most contacts from CDER employees were general enquiries about the Ombudsman's role or requests for help with external constituents, but some sought assistance with workplace conflict. In those cases, the Ombudsman referred the employee to the Conflict Prevention and Resolution Staff in FDA's Office of Equal Employment Opportunity and Diversity Management or to FDA's Employee Assistance Program.

III. Other Activities

The CDER Ombudsman expanded her role to include advising on internal regulatory/scientific dispute resolution cases, as supported by the publication of these CDER Manuals of Policies and Procedures (MAPPs):

- MAPP 4151.1, "Scientific/Regulatory Dispute Resolution for Individuals Within a Management Chain" (revised)
- MAPP 4151.2, "Resolution of Differing Professional Opinions: Review by *Ad Hoc* Panel and CDER Director" (revised)
- MAPP 4151.8, "Equal Voice: Discipline and Organizational Component Collaboration in Scientific and/or Regulatory Decisions"

All three MAPPs can be found in their entirety at <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ManualofPoliciesProcedures/default.htm> The Ombudsman also developed Center-wide training on the MAPPs content.

Also in 2010, the CDER Ombudsman joined the inaugural Ombudsman Resource Committee within the Coalition of Federal Ombudsmen which will serve as a resource for new ombudsman offices.

The Ombudsman remains as the CDER representative on a FDA level working group to review the Agency level appeals process for resolving internal scientific disputes. She also continues to serve as collateral duty mediator for the Agency's alternative dispute resolution program in FDA's Office of Equal Employment Opportunity and Diversity Management.

IV. Outreach Efforts

The Ombudsman's Office conducted outreach within CDER to explain the Ombudsman's functions including product jurisdiction and dispute resolution at the CDER New Reviewer's Workshops. The Office also updated its public internet site to include its mission and vision statements, an explanation of the ombudsman ethics and operating principles, and a Frequently Asked Questions section.

V. Product Jurisdiction for Combination and Single Entity Products

Many proposed products must be regulated by the FDA, but it is often not obvious which Center within FDA should take the lead for product review and regulation, particularly for combination products. LCDR Ayoub Suliman is the Center's Product Jurisdiction Officer, serving as CDER's expert on establishing the regulatory identity of products as drugs, biologics, devices, or a combination of two or more (e.g. biologic and a device combined into one product), specifically to determine which FDA Center is most appropriate for reviewing each product. The Product Jurisdiction Officer responds to all Requests for Designation (RFD) from sponsors via the FDA Office of Combination Products (OCP) under 21 CFR Part 3.7 and to other informal requests for assignment of combination and single entity (non-combination) products.

This calendar year, the CDER Ombudsman's Office responded to hundreds of informal jurisdiction questions from within and outside FDA and put forth CDER's position on 36 RFDs and 7 requests for reconsideration, most of which were drug/device combinations. More information about jurisdictional determinations can be found on the OCP website at <http://www.fda.gov/oc/combination/>.

Attachment A

Dear Sir or Madam:

Thank you for communicating your concerns to the U.S. Food and Drug Administration (FDA or the Agency) about the lorcaserin advisory committee meeting. As you know, on September 16, 2010, FDA held a meeting of the Endocrinologic and Metabolic Drugs Advisory Committee (Advisory Committee) to discuss the safety and efficacy of lorcaserin, a drug developed by Arena Pharmaceuticals, Inc. (Arena) to treat obesity. The Advisory Committee—made up of physicians, scientists, statisticians, and patient and consumer representatives—reviewed extensive background information prior to the meeting. The sponsor, FDA staff, and members of the public gave presentations during the Advisory Committee meeting. After thoroughly considering all the available information, the Advisory Committee voted 9-5 to recommend that FDA not approve lorcaserin for marketing.

After the Advisory Committee meeting, FDA began receiving correspondence from numerous parties questioning the views of FDA staff and comments made by FDA staff during the meeting, as well as accusations that scientists with appropriate expertise had not evaluated lorcaserin's safety and efficacy data. FDA takes all comments and concerns about advisory committee proceedings seriously and wants to take this opportunity to address some of the concerns about our policies and procedures.

FDA achieves its mission to protect and promote the public health through rigorous evaluation of all data submitted in support of a new drug application (NDA). Often, the data submitted raise challenging or novel scientific issues relating to the drug's safety and/or efficacy. FDA advisory committees serve an important function by providing the Agency with an independent, expert evaluation of the data during the drug review process. FDA ensures that during the meeting, the full spectrum of views of the data are presented to the committee and that all committee members have the opportunity to ask questions and present their own views on the data. FDA staff also routinely present their own reviews, conclusions, and individual perspectives of the data. This practice ensures that differing opinions are transparently presented and debated and allows the committee to make recommendations after taking into account all perspectives. This public process helps FDA obtain expert advice during the review process and increases the transparency to those with an interest in a particular matter. Although FDA highly values the opinions of the independent experts on the committee and often incorporates those opinions into its decision-making process, FDA makes the final decision about whether a drug should be approved. Advisory committee votes and recommendations are not binding on the Agency.

FDA has strict rules governing conflicts of interest for both employees and advisory committee members. With certain limited exceptions, FDA employees and their families cannot hold a financial interest in any company that is significantly regulated by FDA. FDA employees must report their financial interests on a yearly basis and their reports are reviewed by Agency ethics staff. FDA has not been made aware of any evidence to

suggest that these rules were not followed by the FDA staff at the lorcaserin Advisory Committee meeting.

Similarly, advisory committee members must report to FDA any financial interests they hold related to the subject matter of the advisory committee meeting. FDA screens advisory committee members broadly for financial or other relationships that could present even the appearance that they have conflicts of interest that could affect their impartiality. For the lorcaserin meeting, as with all advisory committee meetings, all Advisory Committee members were appropriately screened for conflicts of interest.

Although FDA strives to have broad representation of appropriate medical and scientific specialties on its advisory committees, optimal representation is often difficult to achieve given the strict conflict-of-interest regulations that apply, as well as calendar conflicts, which may limit the availability of experts for the selected meeting dates. The lorcaserin Advisory Committee included representation from the fields of Endocrinology, Cardiology, Pharmacology, Health Policy, Epidemiology, Biostatistics, Internal Medicine, and Clinical Research. In hindsight, FDA regrets that no toxicologist participated in the meeting. However, a team of FDA toxicology experts reviewed the lorcaserin NDA and interpreted the data related to the lorcaserin carcinogenicity studies. Moreover, the lorcaserin carcinogenicity studies were also thoroughly reviewed and discussed by the Center for Drug Evaluation and Research (CDER) Executive Carcinogenicity Assessment Committee, and the results of this scientific assessment were included in the background documents provided to the committee and discussed in Agency presentations at the Advisory Committee meeting.

Consistent with the FDA's policy on transparency, FDA announces the dates for advisory committee meetings in advance through publication of a notice in the Federal Register, and the Agency posts all advisory committee briefing materials on its public website 48 hours prior to the meeting. Prior to the public posting of the documents, they are kept in strict confidentiality with only the advisory committee members and the sponsor having the opportunity to review them. As soon as possible after an advisory committee meeting has concluded, a transcript of the meeting is made available on FDA's public website. In this way, the diverse views of all participants, both FDA employees and advisory committee members, are made available to the public.

After obtaining advisory committee input on an NDA, FDA completes its review of the application and communicates its findings to the sponsor. FDA considers all of the data contained in the application and conducts its own independent analysis of the data before making a decision as to whether the benefits of the drug outweigh its risks for the proposed use. FDA believes that this rigorous review process leads to the most appropriate decisions about the safety and efficacy of proposed new drugs.

FDA remains committed to ensuring that its advisory committee process is conducted according to applicable statutes and regulations and will continue to make these proceedings transparent to the American public. With regard to the specific allegations

made against FDA staff, FDA will continue to review these allegations and if misconduct is identified, will take appropriate action.

Again, we appreciate you taking the time to express your concerns.

Sincerely,

The U.S. Food and Drug Administration