CDER Forum for International Drug Regulatory Authorities
September 25, 2006

Igor Cerny, Pharm.D.
Director, Advisors & Consultants Staff (ACS)
CDER
Cerny@CDER.FDA.GOV
(301) 827-7001

Advisory Committee Laws & Regulations

- FDA Advisory Committees operate within the Federal Advisory Committee Act, (FACA) passed 10/6/1972.
- Regulations: 21 CFR Part 14
- 1997 Food and Drug Modernization Act (FDAMA) Highlight: Representatives of consumer, patient, and *industry* interests on panels

Federal Advisory Committee

- Definition: Any committee, board, commission, council, conference, panel, task force, initial review group, special emphasis panel, working or other similar group which is not composed entirely of full-time officers or employees of the Federal Government. It is established or utilized by a department or agency to advise or make recommendations on matters relating to programs, responsibilities or activities of the department or agency.

Advisory Committee Facts/Procedures

- Under the Federal Advisory Committee Act - **most** advisory committee meetings are **open to the public** (NDAs, supplements, post-approval risk/benefit issues, etc.).
- Open Public Hearing – interested members of the public may advise the committee
- Meetings discussing trade secret or commercial confidential information are closed to the public (INDs, e.g.)
- Meetings are held at hotels in Washington, DC metropolitan area or in FDA buildings

Advisory Committee Facts/Procedures, *continued*

- FDA has each meeting recorded and a transcript is available through FDA's Freedom of Information Office; Website.
- Meetings notice in Federal Register; FDA Website and Information hotline (800-741-8138)
- Audience members include:
  - Press (Pink Sheet to CNN)
  - Private video companies
  - Stock market analysts
  - Patients, consumer advocacy groups
  - Other drug companies/ sponsors

Each Review Group within CDER is Associated with an Advisory Committee

- Oncology Office:
  Oncology Drugs Advisory Committee;
- ODE I – Cardiovascular & Renal:
  Cardio-Renal Drugs Advisory Committee;
- ODE I – Pulmonary & Allergy:
  Pulmonary and Allergic Drugs Advisory Committee;
- CDER has **16** standing Advisory Committees

Composition of an Advisory Committee

- Committees are composed of members who are noted researchers/scientists in their field of specialty
- The members are appointed as “Special Government Employees” (SGEs)
- Advisory Committees provide FDA with expert independent scientific and technical advice
- Committee recommendations are not *binding – FDA may reject or accept the advice*

Composition of an Advisory Committee, *continued*

- Members and Chair Appointed By Commissioner and serve up to Four Years
- Members include Consumer, Industry, and sometimes Patient Representatives – all represent broader interests
- Consumer and Patient Representatives appointed by FDA; however, Industry Reps are nominated by Industry
- Committees are usually supplemented with additional Consultants

Who Can Recommend a Prospective Member?

- **Referrals come from:**
  - Former/Current Advisory Committee Members
  - FDA Scientists
  - Professional Societies and Journals
  - Academic Institutions
  - Consumer and Patient Groups
  - Self Nominations
  - Industry

FDA Aims for a Diverse Advisory Forum

- FDA wants to have its Advisory Committee members mirror the population of America with regard to
  - age
  - race
  - sex
  - ethnicity
  - geographic location

Why Do We Have these Meetings?

- To provide additional expertise to assist FDA in making a timely decision
- To increase credibility of FDA's decisions
- Open FDA's "BLACK BOX"
- To provide a forum for public input into FDA's decisions (Open Public Hearing)
- Increase awareness of a public health issue

Typical Issues at these Meetings:

- Safety, Efficacy, Risk/Benefit Questions
- Dosing concerns
- Target population or labeling issues
- New Molecular entity/New Indication
- Rx to OTC Switches
- Guidelines/Study/Protocol Designs
- Appeals of FDA Decisions

Flow of a "Typical" Advisory Committee Meeting (1 of 2)

Order of Events is Quite Varied:

- Call to order/introduction of panel
- Reading of the Conflict of Interest Statement
- FDA welcome/focusing the issues
- Sponsor or FDA Presentation
- FDA or Sponsor Presentation

Flow of a "Typical" Advisory Committee Meeting (2 of 2)

Order of Events is Quite Varied:

- Open Public Hearing (announce 1 hour; times during meeting vary)
- Committee Discussion
- Committee Vote
- Adjournment

Roles of the Meeting Participants

- **FDA Staff - <u>The Review Division</u>**
  - Determines the need for the meeting;
  - substantively evaluate product application
  - identify need for extra expertise
  - develop background materials, rehearse + <u>presentations</u>, questions to the Committee
  - limited number will sit at the table

Roles of the Meeting Participants

- **<u>Drug Company/Sponsor Role:</u>**
  - **Develops Background Materials**
  - **Slides**
  - **Rehearsals Presentations,**
  - **Answer questions**

Background documents to the Committee

- Both CDER and the sponsor prepare separate documents ("backgrounder") that summarize the data as they see it.
- Prepared for the AC members, both will post onto the web 1 business day before the meeting
- AC members get the backgrounders 18 business days before the meeting (up to them to read it!)

Background document – sponsor considerations

- Draft Disclosability Guidance requires sponsor to submit backgrounder with "material exempt from disclosure" no later than 48 business days prior to AC
- Fully releasable package due 22 business days prior (FDA backgrounder at 19 days)
- Fully releasable backgrounder states that the information contained within is "available for public disclosure without redaction" or "fully releasable"

The Conflict of Interest (COI) Dilemma

- The consultants FDA uses are noted scientists; regulated industry uses them too!
- How to balance the need for outside experts while protecting against potential COI?
- FDA must look at not only the product at hand, but also the member's financial interest in the "competing products."
- If the SGE has interests in affected parties, needs a waiver to participate.

Criminal Conflict of Interest Statute Title 18 U.S.C. 208

- **Prior to Every Meeting, SGE is re-valuated for Conflict of Interest Relative to the Meeting Topic + "competing products"**
- **Competing products are anticipated to "significantly" gain or lose market share depending upon FDA decision**
- **CPs are used for same indication or in the same therapeutic category/class?**

What Are the Types of Interests Are Screened?

- Stocks and Investments
- Primary Employment
- Consultant Work
- Contracts / Grants / CRADAS
- Patent / Royalties / Trademarks
- Expert Witness Activities
- Teaching / Speaking / Writing
- Department Heads / Administrative Duties
- Exceptions for Institutional Directors

Conflict of Interest *Continued*

- Interests Are Also Imputed to the Spouse, Minor Child, and Employer.
- There are Provisions for on excludable interests – WAIVERS
- FDA May NOT Grant a Waiver for an Advisory Committee Member to Review Their Own Work
- Current FDA Criteria Used for COI Screening Are Found on the Web

FY '06 Appropriations Bill

- ***"none of the funds made available in this Act may be used to…grant a waiver of a financial conflict of interest…***
- ***[this] shall not apply to a waiver…if – (1) not later than 15 days prior to a meeting of an advisory committee , the Secretary of HHS discloses on the Internet website of the FDA…the nature and basis of such waiver…."***
- **Any SGE Who Needs a Waiver MUST Have This Waiver Posted on the Web 15 Calendar Days Before the Meeting**

Conflict of Interest Dilemma

- Congress, Consumer Watchdog Groups, the Public Want AC Members With "Minimal Conflicts" – Who Doesn't? Is That Possible?
- Ideal AC Member Has Practitioner + Clinical Trials Experience
- Where Does One Get Clinical Trials Experience?

Conflict of Interest Dilemma *Continued*

- Since Drug Development Is Primarily Funded by Private Sector, Most Clinical Trial Experience Is Gained by Working With Industry-Sponsored Trials
- FDA Doesn't Want AC Members Who Lack Clinical Trial Experience – Can't Properly Advise FDA, Can Hurt the Company, Hurt the Public (95% of Time, FDA Agrees With AC)
- FDA will continue to refine how it determines and discloses the Balance Between Experience and "Conflict"

Websites of Interest

- Where to find backgrounders & waivers on the Web: http://www.fda.gov/ohrms/dockets/ac/acmenu.htm
- Disclosability Guidance at: http://www.fda.gov/cder/guidance/3479dft.htm
- Conflict of Interest Criteria at: http://www.fda.gov/oc/advisory/conflictofinterest/intro.html