Managing Scientific and Regulatory Disagreement

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Food and Drug Administration

Disclosures

- No conflicts to disclose
- We’re from the government; we’re here to help you

Really !!

CDRH Ombudsman

- Appointed to receive and investigate complaints about CDRH and to mediate or otherwise resolve disputes between that agency and entities doing business with the government
- Neutral, impartial, objective, confidential
- Resolve disagreements at an early stage before they escalate
- Conciliation, mediation, arbitration and negotiation – "shuttle diplomacy"

CDRH Ombudsman

- **Import/Export:**
  - First contact should be with District office
  - FDA Ombudsman acts as ORA Ombudsman; contact Andrew Moss in FDA Ombudsman office
  - Contact CDRH Ombudsman if CDRH has the current lead on the issue, or if difficulty in getting a response elsewhere

What Decisions Are Eligible for Appeal?

Appeals by External Stakeholders

Decisions

- NSE; NOAP; denial of de Novo petition; IDE Disapproval; PMA Nonapprovable; deficiency letters

Appeal Processes

- Most common route: 21 CFR 10.75 appeal for supervisor review of decision
- Less common; 21 CFR 10.33 request for administrative reconsideration

Appeals under 21 CFR 10.75

- Key points:
  - "Appeal" refers to a request for supervisory review as provided by 21 CFR 10.75
  - The supervisory review process was significantly changed in 2012 by FDASIA Section 603, which relates to FD&C Act Section 517A
  - FDASIA Section 603 introduced the concept of "significant decision"
  - Appeal process for review of a significant decision involves specific timeframes and other requirements

517A Decision Appeals

- Section 510(k) significant decisions
  - Substantially Equivalent (SE)
  - Not Substantially Equivalent (NSE)
- Section 515 significant decisions
  - PMA/HDE: Not Approvable, Approvable with Conditions, Approval
- Section 520(g)
  - IDE approval, disapproval
  - Failure to reach an agreement on protocol: 520(g)(7)

- All other regulatory actions not specifically called out in the guidance are not significant decisions: non-517A

517A Decision Appeals

- Appeals of 517A decisions MUST arrive at the DCC by the 30th calendar day after the date of the decision in dispute: no exceptions, placeholders, partial submissions, extensions or waivers
- Appeals received after Day 30 will be declined as untimely
- Meeting or telecon, if requested, will take place within 30 days of receipt of appeal
  - Appeal decision will be issued within 30 days of meeting or telecon
  - If no meeting is requested, decision will issue within 45 days of appeal receipt
- 517A appeal that is referred to external expertise has no timeframes

Appeals under 21 CFR 10.75

- **10.75 Appeals: Process**
  - Receipt of appeal package will be acknowledged
  - If requested, a meeting or telecon will be scheduled 30 days after receipt.
    - Reg Affairs specialist or Ombudsman rep will contact you to schedule the meeting
    - Opportunity to present your case directly to the appeal authority
    - Review team may be present at the meeting but meeting is run by the appeal authority; team is there to answer questions if needed
    - There may be an opportunity for discussion of a mediated agreement at the meeting
  - There may be follow-up questions from FDA after meeting

CASE STUDY

- Review division upholds review team's determination that a new clinical study is required because the control group was unblinded too soon.
- Company appeals to the Office Director stating control group had to be unblinded for ethical reasons
- Appeal authority, at the appeal meeting, asked both parties if a historical control could be used in lieu of beginning a new study. Allows parties to investigate and interact.
- Parties subsequently agree to historical control and marketing application is re-opened by the appeal authority.

Non-517A Decision Appeals

- CDRH expects that appeals of non-517A decisions will be received within 60 days of date of decision in dispute
- Non-517A appeal may not involve a meeting or telecon – Center's discretion
- Non-517A appeals will be handled as resources are available; there are no statutory timeframes
- That said … the Center intends to conform to the 517A timeframes for non-517A appeals, given resource constraints and competing statutory requirements

Is There a Time to Accept an Improper FDA Decision and Its Consequences?

Perspectives

Economic

- We'll leave that up to you
- Timeliness
  - Bear in mind statutory timeframe for submission of 517A appeal
  - Appeals under 10.75 can be carried through the Center to the Commissioner's Office

Regulatory

- NO TIME but it can be pre-mature
- Wait until a formal decision is made
- Look for alternative solutions
  - Strongly recommend good-faith effort to resolve disagreements through discussion

CASE STUDY

- Company receives an AI letter, which asks for a new animal study. The company disagrees.
  - OPTIONS:
    - File an appeal of the non-517A decision with the division director. **Remember you can not introduce new information in an appeal.**
    - Respond in full to the AI letter and list the scientific rationales of why a new animal study is not needed.

- Company receives NSE decision and appeals to the Office Director.

When Is It Appropriate to Request Supervisory Review and What Elements of a Request are Essential to Achieve a Fair Outcome?

CDRH Ombudsman

- **Get involved at any stage in the Center's decision-making processes**
  - Telecon, mediated meeting, resubmission to address deficiencies cited by Agency
  - No retaliation for contacting Ombudsman
- **Available to stakeholders to provide advice on various appeal processes**
  - Strategize options to challenge or appeal decisions
  - No retaliation for filing an appeal

Appeal Packet Elements

- **Cover Letter**
  - **Boldly** state that this is an appeal under 21 CFR 10.75.
  - Indicate whether you wish to have a meeting/telecon with the appeal authority to "state your case."
  - Point out the decision that you are appealing and the reason(s) for your appeal.
  - State the type of relief, which you are seeking.
    - "Draw multiple lines in the sand."
- **Appendices**
  - Data to support the reasons for your appeal

CASE STUDY

- Company receives a NSE decision. Within 30 days of receipt of the decision letter, the company files an appeal. The request the following relief from the decision:
  - Overturn of NSE decision and a finding of SE.
  - If their 510(k) is not found SE, a re-opening of the file with the company and the review division working interactively to resolve the remaining deficiencies.
- Appeal authority upholds NSE decision but removes several deficiencies cited in the decision letter, which are determined to be not relevant to SE.

Remember appeal decision trends since 2010.

Ombudsman Web Page

Website:

http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHOmbudsman/default.htm

- Resolution of Differences of Opinion
  - Center for Devices and Radiological Health Appeals Processes - Guidance for Industry and Food and Drug Administration Staff
  - Center for Devices and Radiological Health Appeals Processes: Questions and Answers About 517A - Draft Guidance for Industry and Food and Drug Administration Staff
  - CDRH SOP for Resolution of Internal Differences of Opinion in Regulatory Decision-Making
  - Guidance for Industry: A Suggested Approach to Resolving Least Burdensome
- Contact Guidelines and Confidentiality

Questions/Comments

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