The A to Z on FDA Advisory Committee Meetings

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Topics

• Purpose of Advisory Committee (AC) and of Nonprescription Drug Advisory Committee (NDAC) specifically
• When convened and issues
• Who the members are and how they are selected
• Role of the Chair
• How FDA prepares
• Aligning with FDA prior to the meeting

What is the Purpose of an Advisory Committee?

• FDA uses advisory committees to obtain independent expert advice on scientific, technical and policy issues
  – NDAC serves that function for nonprescription drug issues
What is the Formally Established Purpose of NDAC?

- NDAC was established on August 27, 1991
- Its specific function was described as follows
  - The committee reviews and evaluates available data concerning the safety and effectiveness of over-the-counter (nonprescription) human drug products for use in the treatment of a broad spectrum of human symptoms and diseases.

Three Basic Considerations Go Into a Decision to Convene the NDAC

- Is the matter of such significant public interest that it would be highly beneficial to obtain the advice of an AC as part of FDA’s regulatory decision-making process?
- Is the matter so controversial that it would be highly beneficial to obtain AC committee advice as part of FDA’s regulatory decision-making process?
- Is there a special type of expertise that an AC could provide that is needed for FDA to fully consider a particular issue?
NDAC Seldom Meets Alone

- Many issues in Division of Nonprescription Clinical Evaluation (DNCE) and Division of Nonprescription Regulation Development (DNRD) are collaborative with another OND review division or another office in CDER
  - Thus, many NDAC meetings are infused with advisory committee members from the collaborative review division AC
- Generally chaired by NDAC chair

Some Topics NDAC Has Been Convened to Consider During The Past Decade

- First-in-class prescription to nonprescription switch
  - Nasacort, Oxytrol for Women, Alli, Plan B, Mevacor
  - Unintended consequences of not having a healthcare provider involved in the treatment decision and oversight
- Issues related to Consumer Study Designs and Analysis
  - How should thresholds for success be determined?
  - How should the duration of an actual use study be determined?
  - How should low literacy data be considered in the success or failure of a label comprehension study?
- Efficacy or safety related to monograph ingredients
  - Should consumer antiseptics be expected to provide clinical benefit by reducing infection?
  - Are cough/cold ingredients effective and safe in children?
  - Is there an association between phenylpropanolamine and hemorrhagic stroke and is phenylpropanolamine safe for over-the-counter?
Who Is On The NDAC?

- Core of 14 voting members
- Selected by Commissioner or designee
- Areas of expertise include
  - Internal medicine – Family practice
  - Toxicology – Clinical pharmacology
  - Pharmacy – Dentistry
  - Related specialties – Consumer interests
- Consumer Representative recommended by consortium of consumer-oriented organizations or other interested persons
- Non-voting Industry Representative identified with global industry interests

How Members Are Selected for the Committee

- Committee membership must be “fairly balanced”
  - Ethnic, gender, and geographic diversity
  - Recognized expertise and judgment in a specific field
- Method of nomination
  - Self-nominated
  - Referred for consideration
  - FDA-identified
- FDA reviews qualifications of nominees
- For NDAC, Directors of DNCE and DNRD choose members and chair
  - Then vetted by Advisors and Consultants staff
Role of the Chair

• Understand and communicate purpose of the meeting
• Keep NDAC on task / topic
• Involve all committee members in discussion
• Encourage members with topic-specific expertise to participate
• Constructively challenge unclear statements, misperceptions and misinformation to insure voting is based upon accurate information
• Provide sponsor with fair opportunity to make their case and respond to questions
• Keep to the schedule
• Run the meeting fairly, objectively

How Does FDA Prepare for an AC Meeting?
What Happens in DNCE?

• Reviewers complete reviews of NDA data
• Division(s) and Office(s) identify the issues and presenters
• Division Director (DD)(s) & Office Director(OD)(s) plan Briefing Package (BP)
• DNCE DD
  — Writes executive summary for BP & reviews BP for clarity and content
  — OD may or may not be actively engaged in this step
• DNCE DD runs FDA presentation practice sessions
  — Time is tight and there may only be time for 3 or 4 of these
  — Initial questions for the committee are drafted
• DD prepares introductory talk for NDAC meeting
• DD(s) and OD(s) fine tune questions for committee
Aligning with FDA
What’s Possible?

• Discuss certain aspects of the meeting with FDA
• Inform FDA of any concerns
• Discuss the presentations (in generalities) with the goal of making the most of the time during the meeting
  – Time allotment needed
  – Find areas of common ground to avoid repetition
    • Study design description

Aligning Before the AC Meeting (ADCOM)
“Late Cycle Meeting” (LCM)

• Focus on information sharing, planning for ADCOM, and planning for the remainder of review
• Held at least 12 days before the AC
• **Agency Provides BP to Applicant > 8 days prior to LCM**
  – Meeting agenda and attendees
  – Assessment of need for risk management actions
  – Memo outlining
    • Dates of discipline review (DR) letters issued
    • Potential questions and/or issues for discussion for AC meeting
    • Statement saying if there are no substantive issues for a discipline
    • Date Agency’s background package for AC meeting was sent
Questions

HOW SHOULD A SPONSOR PREPARE FOR AN NDAC MEETING?
An FDA advisory committee meeting is the wrong time for an original thought!

Research the Committee Members

- Understand members’ values and beliefs
- Research backgrounds and professional affiliations
- Analyze prior votes and rationales
- Review media quotes
- Read pertinent publications
- Predict questions or challenges
- Proactively address key perceptions
HOW TO INTERACT WITH THE CHAIR

When Committee not in session, as leader of the Sponsor’s team, I should talk with the Committee Chair:

- Prior to the meeting being called to order at 8 AM
- Only when approached by the Chair
- At the start of the lunch break
- During all breaks
- Whenever I can
Chair Controls Sponsor’s Interactions with the Committee

• Allow/solicit answers to questions not posed to Sponsor (including during Committee discussion period)
• Allow Sponsor to present additional data responsive to questions
• Allow Sponsor to correct misinterpretations

Interacting with the Chair

Above dependent on Sponsor-Chair Communication

• Before meeting starts
  • Introduce yourself
  • Ask if anything sponsor needs to know/can do to facilitate mtg
• Start/end of breaks as appropriate
• Utility of afternoon 5 minute presentation to address committee issues
• DO NOT ABUSE ANY OF THE ABOVE!
As the presenting Sponsor, would you rather have an effective or an ineffective Chair?

- Effective
- Ineffective

Preparing for an Effective Chair

- Potential pros:
  - Will work with sponsor in fair manner
  - Minimizes tangential discussion
  - More likely to correct errors in Committee discussion/statements
  - Less likely to be deferential to FDA positions

- Potential cons:
  - Will ensure discussion centers on most contentious issues – risking “negative” tone
  - Less likely that Sponsor can finesse interpretations
Preparing for an Ineffective Chair

- Potential pros:
  - Less likely that discussion will be focused on Sponsor’s weakest elements
  - More likely for discussion to be based on perceptions rather than data/facts
  - Potentially higher impact of thought leaders/consumer reps etc.
- Potential cons:
  - More likely to be deferential to FDA’s positions
  - Potential to be personal agenda driven

Strong program → effective Chair
Weaker program and FDA support → less effective

Sponsor Misconceptions and Mistakes
“Assuming too much”

- Assuming Committee Members...
  - will read your briefing book
  - understand ANYTHING about consumer/behavioral research
  - share the perspectives of target consumer
Sponsor Misconceptions and Mistakes
“What we have here is a failure to communicate”

• Failing to
  – relate data to clinical context – especially behavioral data
  – establish real-world consumer context in data-driven manner
  – define and focus on determinants of benefit/risk of proposal

The Most Common Mistakes

• Being dismissive of risk
• Overstating benefits
• Conclusions not supported by data
What Works

• Focus on key messages
• Get to the point
  – Clear and explicit
• Honestly assess risk
• Use anecdotes/consumer experiences sparingly
• Stick to pre-specified analysis plan
• Anticipate and pre-empt FDA’s concerns
• Anticipate and pre-empt Committee concerns
• Be data-driven/fact-based to the degree possible and acknowledge when you are not
• Own your weaknesses/limitations
  – Contextualize why they are not decisive

Questions
“If you can’t explain it simply, you just don’t understand it well enough.”

Albert Einstein

Organize Your Key Messages

- One Engaging Sentence
- Prove It
- Visualize It
- Rephrase Headline
Importance of Key Messages in Planning NDAC Communications

- 3 key messages = 1 scientific story
  - If Committee “gets” key messages and nothing else they would vote your way
- Entire presentation built around key messages
  - Ensure they are rigorously and clearly communicated
- Messages reinforced with briefing book, presentation and Q&A

The ART OF Q&A
Please rate each of the following for its impact on your vote. (Sponsor Presentation, Briefing Book, Q&A)

Percent responding “Quite a Bit” or “Very Much?”

- Presentation: 71%
- Briefing Book: 79%
- Q&A: 87%

The Art of Bridging

Challenging Question → Answer → Bridge → Message Pyramid
SELECTING THE PRESENTATION TEAM

How to Select Presenters
Role of Key Opinion Leaders

- Knowledge of the product
- Appropriate credentials
  - Medical, regulatory, consumer behavior
- Highly-regarded external clinicians
  - Must be able to commit to the time requirements
SELECTING THE RIGHT MOCK PANEL

Select Your Mock Panelists Carefully

• What to look for:
  – Prior advisory committee experience
  – Similar expertise as committee member
  – Special expertise on key issues
  – Independent thinkers
## Find the Match

<table>
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<tr>
<th>Current Member</th>
<th>Potential Mock Candidates</th>
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| Richard A Neill, MD, Chair  
Family Medicine, Primary Care  
*Attended 11 meetings* | Eric P Brass, MD, PhD  
Former NDAC Chair  
Clinical Pharmacology  
NDAC VC 1997-2001 (*4/10 with Neill)* |
|                  | Louis R Cantilena, MD, PhD  
Former NDAC Chair  
Toxicology, Pharmacology  
NDAC VC 2001-2004 (*3/10 with Neill)* |
|                  | Henry W Williams, Jr, MD, MPH  
Prior Voting Member  
Family Medicine, Preventive Medicine  
NDAC VM 2000-2004 (*2/10 with Neill)* |

## Summary

- Keep open lines of communication with FDA
- Put yourself in the position of ADCOM members
- Practice OFTEN
- Hold REAL mock committee rehearsals
- Have clear, well-articulated key messages
- Anticipate questions and answer directly
Questions