FDA ADVISORY COMMITTEES 101: THE BASICS
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AGENDA
♦ Understanding an FDA Advisory Committee
  ♦ What, why, when
  ♦ Logistics
  ♦ Understanding how to prepare for this high stakes interaction
    ♦ Timeline and deliverables
    ♦ Assembling the winning team

WHY IS UNDERSTANDING AND PREPARING FOR AN ADCOM IMPORTANT

ADCOM = 1 DAY PUBLIC MEETING
YEARS...years...
money
PRODUCT
man power
public relations
Approval
PATIENTS
What is an FDA Advisory Committee (ADCOM)

- > 35 FDA ADVISORY COMMITTEES
  - 18 drug
  - 18 medical devices
  - 5 biologics
  - 1 pediatric subcommittee

AN ADVISORY COMMITTEE MEETING IS NOT YOUR TYPICAL SCIENTIFIC MEETING

- It is not an advisory board meeting
- Audience is not the FDA
- Often NOT all are subject matter experts
- Provide FDA with independent, expert advise
  - Physicians, statisticians, consumer/ patient / industry representatives
- Part science – part theater
- Public service / VERY public meeting
- Allows for transparency of FDA issues and concerns
- Precise agenda
WHEN DOES FDA HOLD AN ADCOM?

“When the matter is of significant public interest, a matter is highly controversial, or there is a special type of expertise provided by the panel that could assist the Agency in its decision-making.”

Guidance for the Public and FDA Staff on Convening Advisory Committee Meetings, 2008.

SCENARIOS FDA MAY SEEK PANEL INPUT

- First-of-a-kind drugs, novel technology
- Medical product for significant new indication
- Significant uncertainty of benefit/risk
  - Fails to reach statistical significance
  - Unanticipated safety concerns
- Significant study data quality or data integrity issues
  - Substantial missing data
  - Excessive protocol deviations
  - Concerns about use of product in subpopulations
- Expert advice on scientific research, study designs, techniques

Guidance for the Public and FDA Staff on Convening Advisory Committee Meetings, 2008.

WHY IS A PANEL IMPORTANT?

- Panels **DO NOT** approve products, but their input is critical
  - Panelists make recommendations
  - ~90% of the time, FDA follows panel’s recommendations
  - Vote on effectiveness, safety, and benefit-risk
- Discussion portion of meeting is important for post-panel negotiations
  - Labeling
  - Training, education
  - Post-approval / REMS

Guidance for the Public and FDA Staff on Convening Advisory Committee Meetings, 2008.
THREE KEY SPONSOR “DELIVERABLES”
- Briefing Book
  - <100 pg summary of development program
- Presentation
  - 60-90 min oral/visual presentation
- Q&A
  - Responding with back-up slides

TYPICAL ADCOM MEETING AGENDA
SIMILAR FOR DRUGS, DEVICES, BIOLOGICS

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:00</td>
<td>Call to Order, Opening Remarks, Conflict of Interest Statement</td>
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<tr>
<td>8:15</td>
<td>FDA Introductory Remarks</td>
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<tr>
<td>8:30</td>
<td>Sponsor Presentation</td>
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<tr>
<td>10:00</td>
<td>Clarifying Questions to Sponsor</td>
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<tr>
<td>10:15</td>
<td>Break</td>
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<tr>
<td>10:30</td>
<td>FDA Presentation</td>
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<tr>
<td>11:45</td>
<td>Clarifying Questions for the FDA</td>
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<tr>
<td>12:00</td>
<td>Lunch</td>
</tr>
<tr>
<td>1:00</td>
<td>Open Public Hearing</td>
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<tr>
<td>2:00</td>
<td>Questions / Discussion</td>
</tr>
<tr>
<td>3:15</td>
<td>Break</td>
</tr>
<tr>
<td>3:30</td>
<td>Discussion / Questions / Vote</td>
</tr>
<tr>
<td>5:00</td>
<td>Adjournment</td>
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</table>

WHITE OAK: GREAT ROOM LAYOUT
Early Preparation is Key to ADCOM Success
**“TYPICAL” TIMELINE**

Advisory Committee Preparation

1. **Mock 1**
   - Kickoff Meeting
   - Draft Core & Briefing Book*

2. **Mock 2**
   - Revise Core and Briefing Book

3. **Mock 3**
   - Revise Core and Briefing Book
   - Final Briefing Book (FRN)
   - Additional Q&A Practice

Advocacy Program, Core Revisions, Speaker Training, Q&A Boot Camp, Backup Slides

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An FDA advisory committee meeting is the wrong time for an original thought!

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**BEST PRACTICES FOR PREPARATION**

1. Analysis of your data and audience
2. Content development
3. Test your strategy
1. ANALYZE THE DATA

♦ Credibility is paramount
♦ Show command of data
♦ Understand data limitations
♦ Address FDA questions and concerns
♦ Consider all FDA feedback during preparation
♦ Demonstrate clear benefits, safe product and need for approval

1. ANALYZE THE AUDIENCE & ENVIRONMENT

♦ Examine FDA and ADCOM precedent
♦ Know therapeutic standard-of-care and comparators
♦ Assess clinical guidelines and opinion
♦ Consider advocacy group activities
♦ Google search- what's in the news
♦ Consider timely publications (internal and external)

1. ANALYSIS: ODAC VOTING MEMBERS

<table>
<thead>
<tr>
<th>Name</th>
<th>Expertise</th>
<th>Mtgs</th>
<th>Term Exp</th>
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<tbody>
<tr>
<td>Bruce Roth, MD</td>
<td>Oncology - Genitourinary; Prostate, Bladder, RCC</td>
<td>8</td>
<td>6/30/2018</td>
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<tr>
<td>Harriet Bandman, MD, PhD</td>
<td>Oncology - Breast; Health Policy</td>
<td>2</td>
<td>6/30/2017</td>
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<tr>
<td>Bernard Cole, PhD</td>
<td>Biostatistics, Mathematics; Quality of Life</td>
<td>11</td>
<td>6/30/2017</td>
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<tr>
<td>Heidi Kupin, MD, MS</td>
<td>Geriatrics, Hematology, Oncology</td>
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<td>6/30/2020</td>
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<tr>
<td>Grzegorz Nowakowski, MD</td>
<td>Hematology: CLL, T-cell Lymphoma, B-cell Lymphoma, Non-Hodgkin Lymphoma, Follicular Lymphoma</td>
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<td>6/30/2018</td>
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<tr>
<td>Vassiliki Papadimitrakopoulou, MD</td>
<td>Oncology - Head and Neck; Lung/SCLC, Lung/NSCLC, Adenocarcinoma, Head and Neck Squamous Cell Carcinomas</td>
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<td>6/30/2019</td>
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<tr>
<td>Alberto Pappo, MD</td>
<td>Hematology – Pediatric; Cancer-Pediatric, Melanoma, Sarcoma, GI Stromal Tumors</td>
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<td>6/30/2018</td>
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<tr>
<td>Courtney Preusse, MA</td>
<td>Consumer Representative; Cancer, Breast</td>
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<td>6/30/2019</td>
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<tr>
<td>Gregory Reif, MD, PhD</td>
<td>Oncology: Lung/NSCLC, Thyroid Cancer</td>
<td>1</td>
<td>6/30/2020</td>
</tr>
<tr>
<td>Brian Rini, MD</td>
<td>Oncology – Genitourinary; Prostate, Testicular Bladder, RCC, Antiangiogenic Therapy</td>
<td>5</td>
<td>6/30/2018</td>
</tr>
<tr>
<td>Alice T Shaw, MD, PhD</td>
<td>Oncology-Thoracic, Hematology; Cancer-Lung/SCLC, Melanoma (SCLC, KK, BRAF, or EML4-ALK)</td>
<td>1</td>
<td>6/30/2020</td>
</tr>
<tr>
<td>Thomas Uldrick, MD, MS</td>
<td>Hematology, Oncology, AIDS Related Oncology; Hepatitis, Immunotherapy, Global Health</td>
<td>2</td>
<td>6/30/2020</td>
</tr>
</tbody>
</table>
1. ANALYSIS: ADCOM RADAR®: FOUR SECTIONS TO ORGANIZE THE MOST PERTINENT INFO

- Overall survival benefit
- Clinical meaningfulness
- Surrogate endpoints
- Influenced by medical need
- Comparisons to alternate therapies
- Confirmation of long-term safety results
- Potential bias (missing data, unblinding etc.)
- Justification of dose and regimen
- Desire for U.S. data

Early Preparation is Key to ADCOM Success

Best practice includes
1. Analysis of your data and audience
2. Content development
3. Test your strategy
2. CONTENT DEVELOPMENT: THREE KEY SPONSOR "DELIVERABLES"

- **Briefing Book**
  - <100 pg summary of development program

- **Q&A**
  - 60-90 min oral / visual presentation

- **Responding with back-up slides**

2. CONTENT DEVELOPMENT MESSAGE PYRAMID FOR CLARITY

- **Bottom Line**
  - Rephrase Headline

- **Example/Story**
  - Visualize it

- **Facts/Data**
  - Prove it

- **Headline**
  - One Engaging Sentence

2. CONTENT DEVELOPMENT VIGOROUS WRITING IS CONCISE

*Omit needless words... Vigorous writing is concise... This requires not that the writer make all his sentences short, or that he avoid all detail and treat his subjects only in outline, but that every word tell.*

William Strunk, Jr. (1869–1946)
2. CONTENT DEVELOPMENT
CLEAR SLIDES TO SUPPORT THE STORY
♦ One main idea per slide
♦ Keep text on slides short & to the point
♦ Bold charts and graphs
♦ Pass the "glance" test

Primary Endpoint
(Trial 12345 and Trial 67890)

% change from baseline

Significant improvement vs. Placebo
(Trial 67890)
Significant Improvement vs. Placebo (Trial 67890)

% Change from Baseline

Treatment Week

Significant Improvement vs. Placebo (Trial 67890)

Placebo

60 mg tid

Significant Improvement vs. Placebo (Trial 67890)

Placebo

60 mg tid

120 mg tid
Significant Improvement vs. Placebo (Trial 12345)

% Change from Baseline

-10 -9 -8 -7 -6 -5 -4 -3 -2 -1 0 1 2 3 4 5 6 7 8 9 10

Treatment Week

Placebo

60 mg tid

120 mg tid

IF YOU NEED A LASER POINTER, YOUR SLIDE ISN'T FINISHED

"For God's sake, Edwards. Put the laser pointer away."

CORE PRESENTATION TYPICAL SECTIONS AND SPEAKERS

<table>
<thead>
<tr>
<th>Section</th>
<th>Typical Speaker</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>Sponsor</td>
</tr>
<tr>
<td>Unmet Need</td>
<td>External KOL</td>
</tr>
<tr>
<td>Study Design</td>
<td>Study investigator/ sponsor</td>
</tr>
<tr>
<td>Results (efficacy/ safety)</td>
<td>Study investigator/ sponsor</td>
</tr>
<tr>
<td>Training/Post Approval</td>
<td>Sponsor</td>
</tr>
<tr>
<td>Benefit Risk / Clinical perspective</td>
<td>External KOL</td>
</tr>
</tbody>
</table>
2. CONTENT DEVELOPMENT
BRIEFING BOOK DEVELOPMENT

♦ Aligns with core
♦ Demonstrates willingness to share data
♦ Provides solid overview and relevant data
♦ Structured to be easily read & reviewed
  ♦ Lengthy Executive Summary
  ♦ About 100 pages
  ♦ Summary with each major section
  ♦ Data appendices, as needed

2. CONTENT DEVELOPMENT
HOW TO BE SUCCESSFUL IN Q&A

Develop the Questions
Practice responding
Write out the answers
Decide who will respond

WRITE IT DOWN!
2. CONTENT DEVELOPMENT
THE ART OF BRIDGING

It's important to remember...
Let me put that into context...
What I can show the committee is...

2. CONTENT DEVELOPMENT
SPEAKER TRAINING PROGRAM

♦ Comprehensive Speaker Training
  ♦ One-on-one
  ♦ On-camera
  ♦ Teleprompter training
  ♦ Voice tone coaching
  ♦ Body language coaching

Early Preparation is Key to ADCOM Success

Best practice includes
1. Analysis of your data and audience
2. Content development
3. Test your strategy
Perfect Practice Makes Perfect.

3. TESTING
TEST YOUR STORY USING A MOCK PANEL

There is a big difference between an advisory board and a mock panel.

HOW TO FIND THE BEST MOCK ADVISORS

- Search for similar expertise
- Screen for prior committee experience
- Eliminate conflicts (Gov't Employees + Current Committee Members)
- Narrow using similar interests
- Narrow using experience + shared meeting attendance
MOCK MEETINGS AN ‘IN ROLE’ ACTIVITY

♦ Mock panelists stay ‘in role’ during core and Q&A
♦ Similar agenda to ADCOM
♦ Similar room layout often held in hotel rather than onsite
♦ Dress for success

ASSEMBLING THE WINNING TEAM

♦ Project lead
♦ Briefing book writers
♦ Core presenters (internal and external)
♦ Moderator – to ‘quarter back’ Q&A
♦ Q&A responders
♦ Triage leads and support – to recall slides during Q&A
♦ Back room team – to develop unanticipated responses
♦ Slide development team
♦ Stakeholder engagement team – to prepare for OPH

STEPS FOR A SUCCESSFUL ADCOM

♦ Truly understand FDA’s and ADCOM’s real concerns during product development
♦ Honestly address product’s strengths and weaknesses
♦ Clearly communicate data to support positive benefit-risk
♦ Practice perfectly – practice EARLY allowing time to analyze, develop, test and refine materials

An advisory committee can be an opportunity rather than a challenge
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