Sharing the Experience of Soliqua (iGlarLixi) Advisory Committee Meeting

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Outline

- **Advisory Committee Meeting Overview**
- **Soliqua (iGlarLixi) EMDAC Meeting – 2016**
- **Lesson & learn**

What is an Advisory Committee

- **Advisory committees provide FDA with independent advice from outside experts on issues related to human and veterinary drugs, vaccines and other biological products, medical devices, and food. These issues commonly include whether a product should be approved and, if so, under what labelling conditions or constraints.**

Advisory Committee Characteristic

- **It is NOT a typical scientific meeting**
  - NOT an advisory board meeting that we ask advices to experts
- **It is part science & part play (a scene and setting)**
  - Different roles
  - Audience
    - Public setting (with a live web broadcast)
  - Rehearsals
    - A lot of rehearsals !!!

Advisory Committee Agenda

08:00 a.m.	Call to Order and Introduction of Committee
08:05 a.m.	Conflict of Interest Statement
08:10 a.m.	FDA Introductory Remarks
08:20 a.m.	Applicant presentations
09:50 a.m.	Clarifying Questions
10:05 a.m.	Break
10:20 a.m.	FDA presentations
11:50 a.m.	Clarifying Questions
12:05 p.m.	Lunch
13:05 p.m.	Open Public Hearing
14:05 p.m.	Questions to the Committee/Committee Discussion
15:30 p.m.	Break
15:45 p.m.	Questions to the Committee/Committee Discussion
17:00 p.m.	Adjourn

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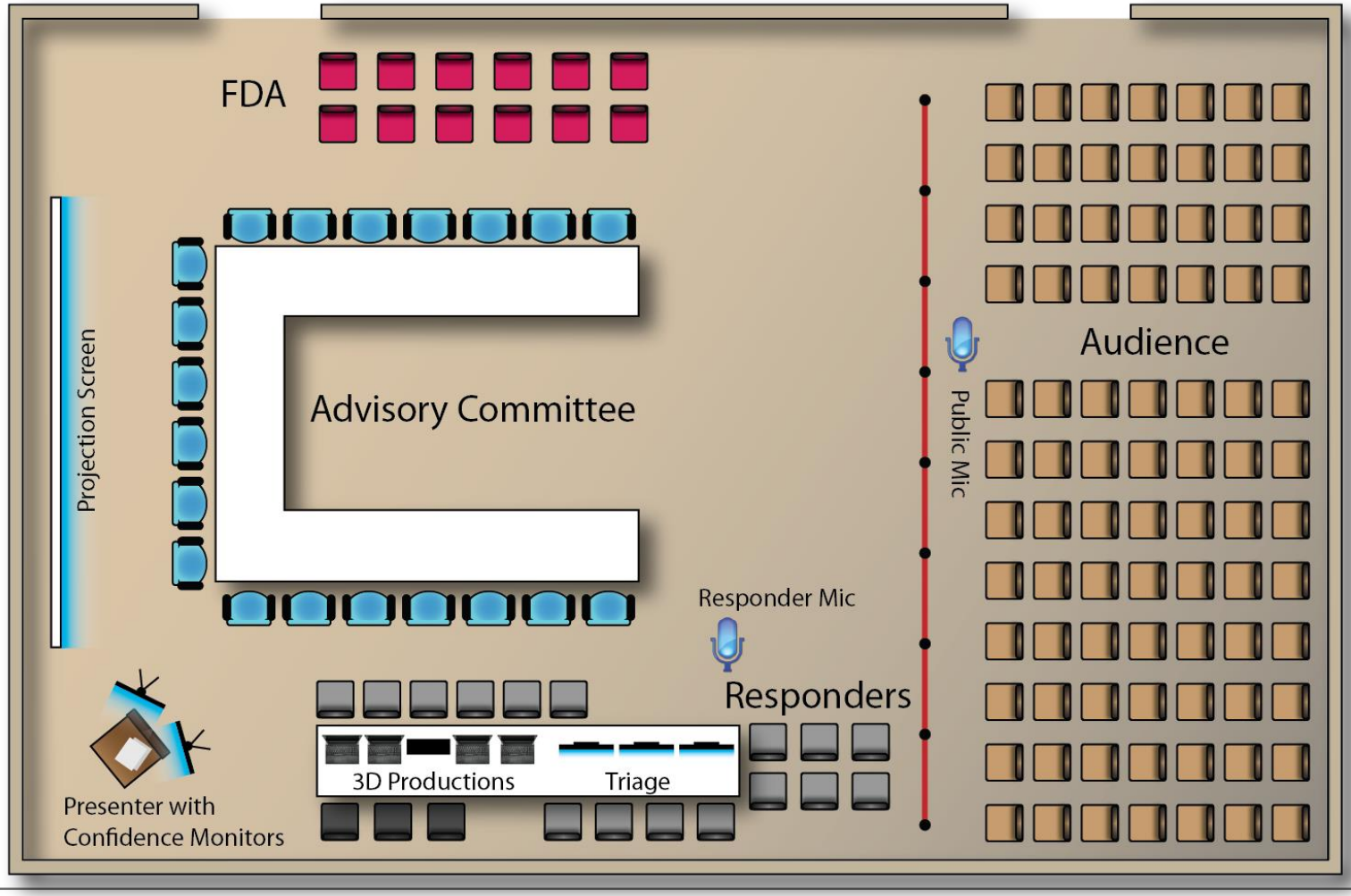
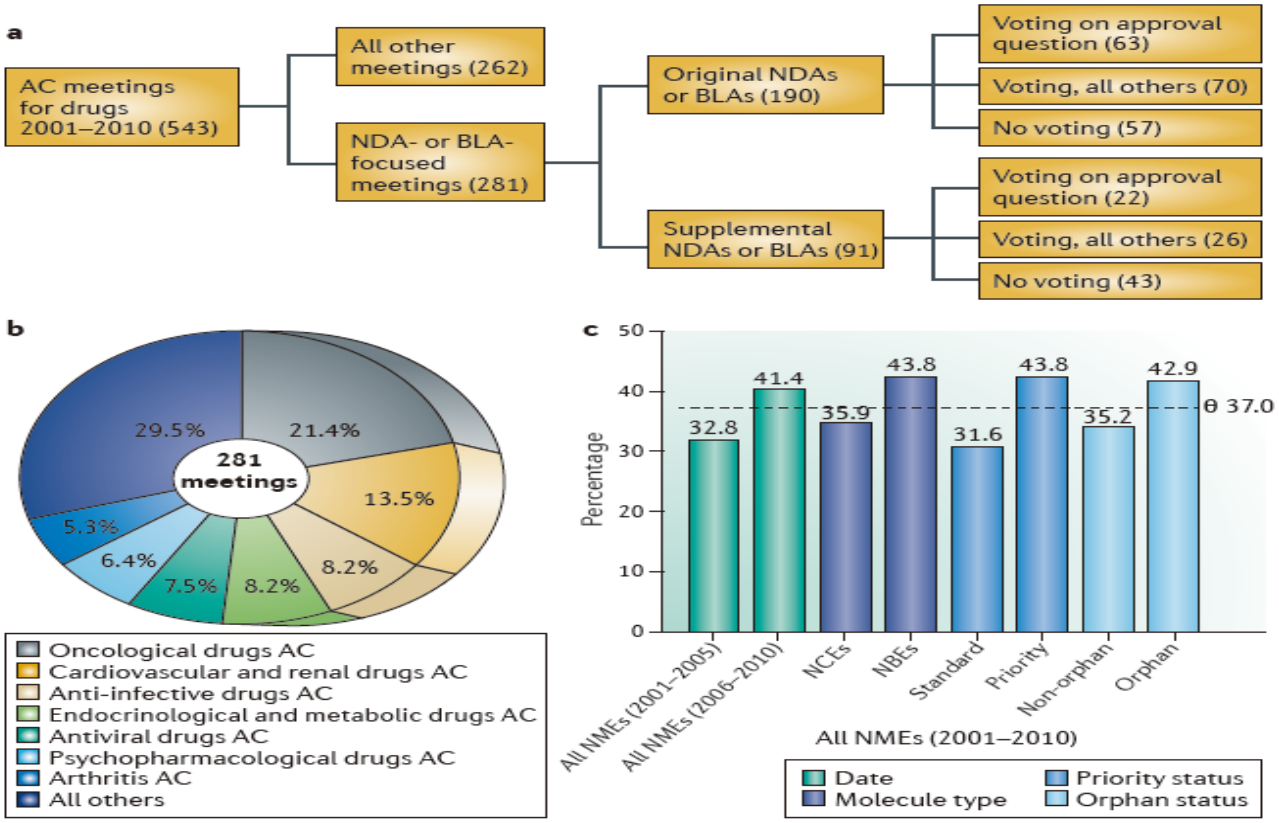
Advisory Committee Scene



Advisory Committee Impacts

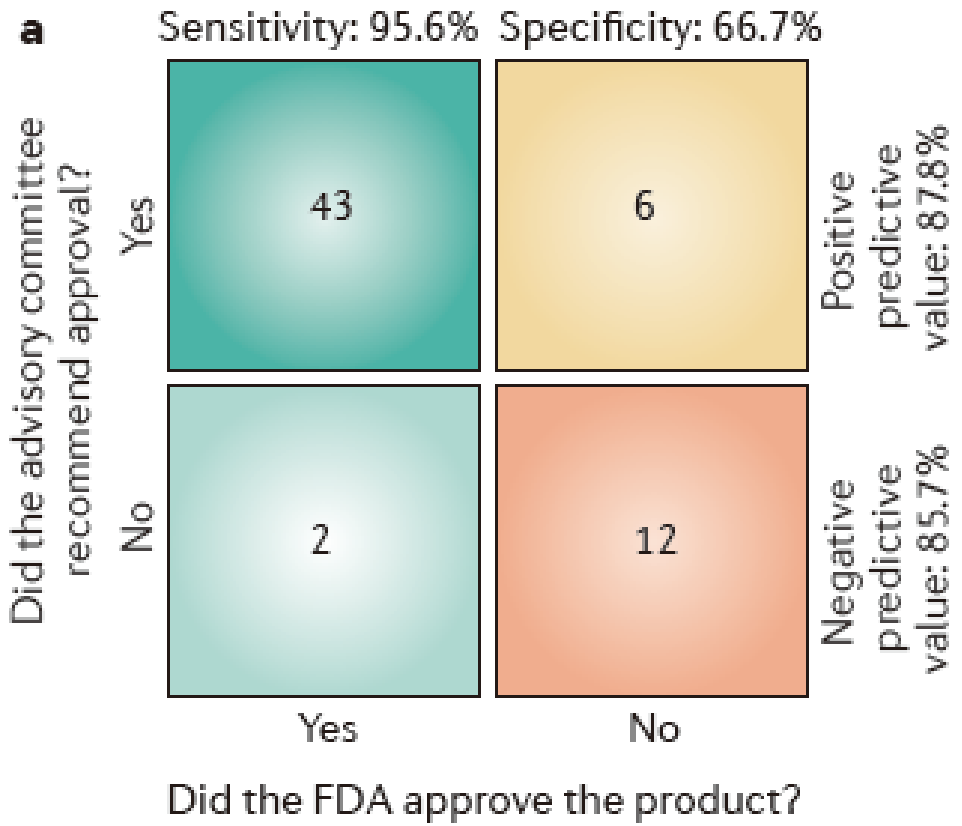
Approve *vs* **Disapprove**

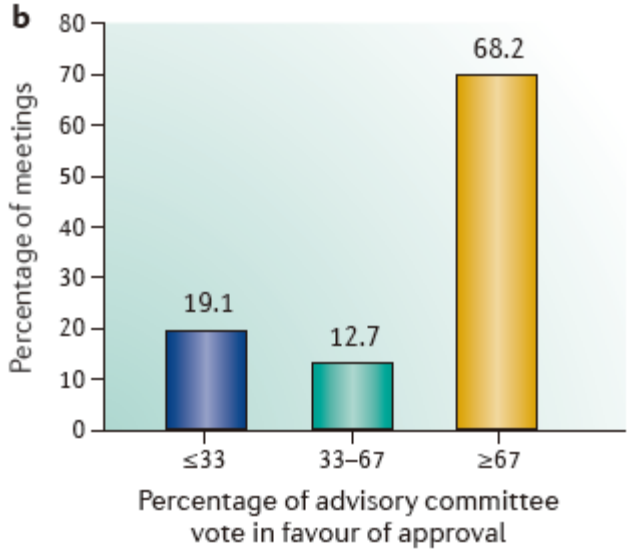
Advisory Committee Impacts

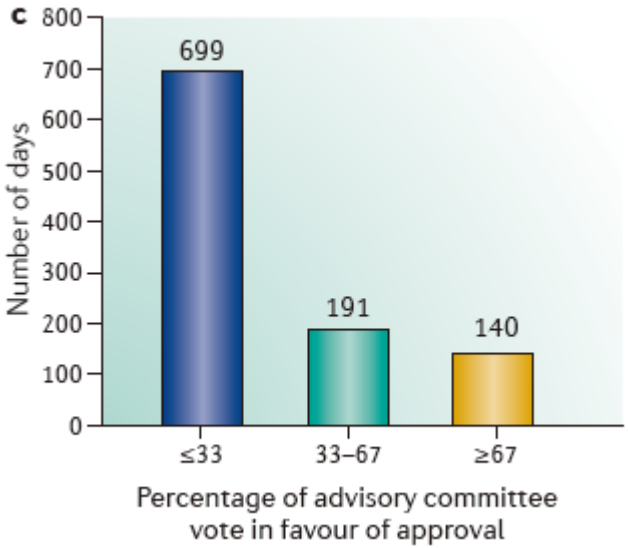


Source: Jeffrey F. Smith, Nature Reviews Drug Discovery, 2012, 11(7): 513

Advisory Committee Impacts







Source: Jeffrey F. Smith, Nature Reviews Drug Discovery, 2012,11(7): 513

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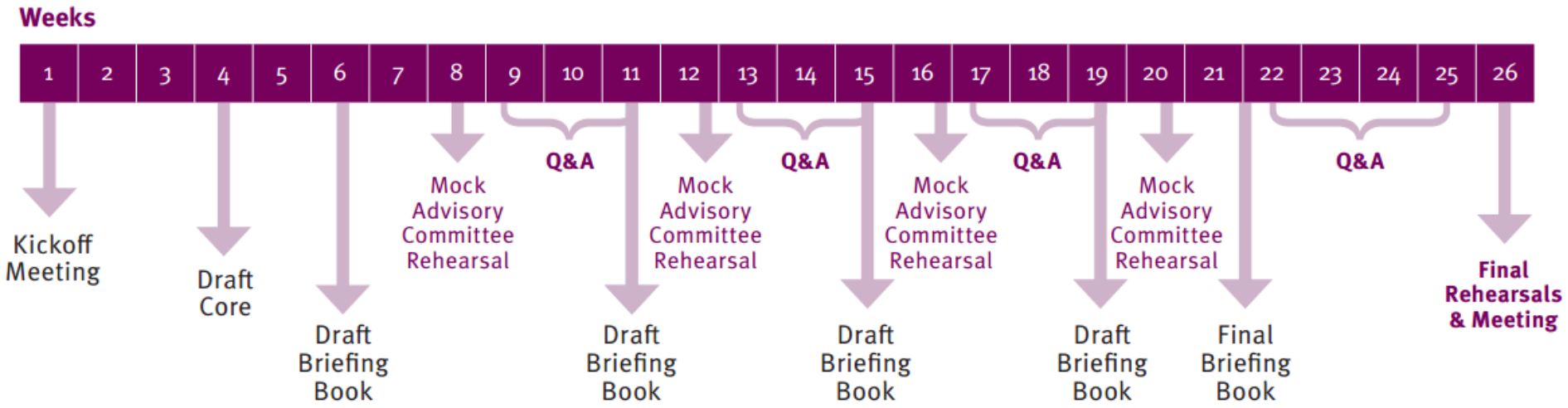
Advisory Committee Impacts

- **Competitive intelligence**
  - Documents are available on FDA Website
- **Trends in approvals and guidance**
  - Provide useful insight into the “behind the scenes”
- **The human factor**
- **Public forum**
- **Critical review**
- **Transparency**

Advisory Committee Preparation Timeline



Source: Virginia Cox, Regulatory Rapporteur, 2014, 11(11): 5

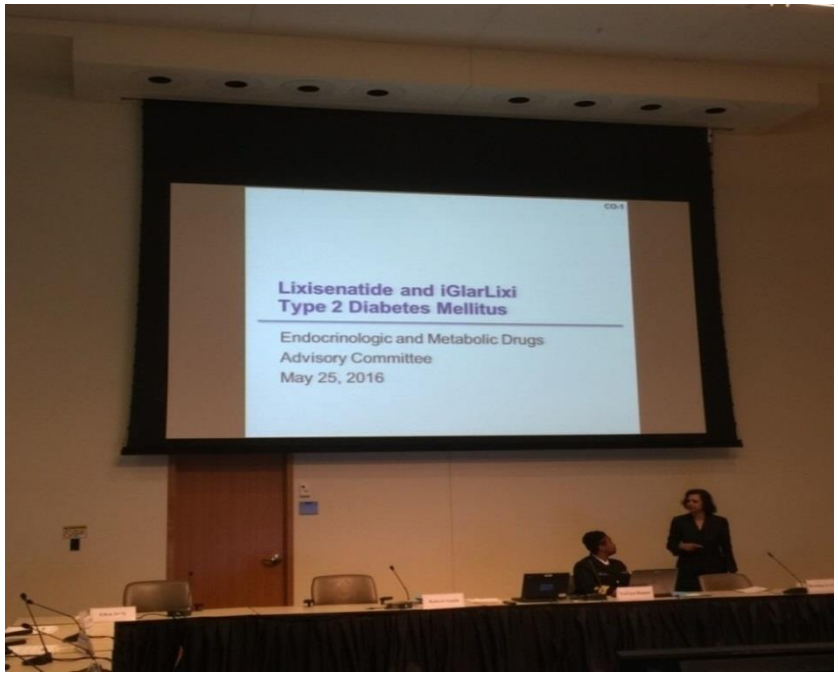
Soliqua (iGlarLixi) EMDAC Meeting on May 25th, 2016

Background

- **Seeking Approval of Lixisenatide and iGlarLixi for Treatment of Type 2 Diabetes**
- **Lixisenatide – GLP-1 agonist**
  - **Marketing authorization in Europe – 2013**
    - Subsequently approved worldwide
  - **Lixisenatide NDA submitted – 2015**
    - Long-term cardiovascular outcomes study (ELIXA)
  - **CV safety shown for both Lantus and Lixisenatide**
- **iGlarLixi – fixed ratio combination of two products**
  - **Lantus® – insulin glargine**
  - **Lixisenatide – GLP-1 agonist**

Soliqua (iGlarLixi) EMDAC Meeting

- **EMDAC (Endocrine and Metabolic Drugs Advisory Committee) Meeting on May-25-2016**
- **Meeting at FDA White Oak Campus (8am – 5pm)**



Note: On May-24-2015, AdCom of iDegLira (Novo) Liraglutide + degludec insulin combination

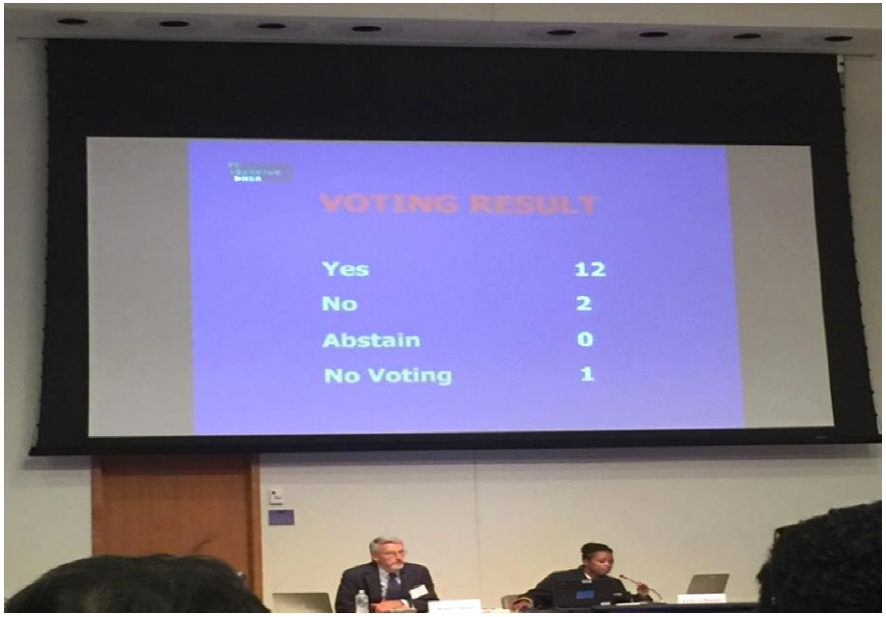
Soliqua (iGlarLixi) EMDAC Meeting

- **One Voting Question: approval of iGlarLixi**
- **4 Discussion Questions**
  - **Approval of lixisenatide**
  - **Benefits of using iGlarLixi in patients not treated w/ BI or GLP-1**
  - **Benefits of using iGlarLixi in patients failed w/ BI or GLP-1**
  - **Clinical concerns w/ fixed-dose combo: dosing flexibility, pen devices**
- **15 "voting" members including 2 Biostatisticians** (James Neaton and Martha C Nason)
  - **14 members voted at the end (J Neaton left prior to voting)**

Soliqua (iGlarLixi) EMDAC Meeting

- **Voting Question**:

  Based on data in the briefing materials and presentations at today's meeting do you recommend approval of the lixisenetide/glargine fixed-combination drug delivered using the proposed pen devices for the treatment of adult patients with type-2 diabetes mellitus?



Out of 14 votes:

12 "Yes" and 2 "No" (*mainly due to a concern on proposed pen devices*)

Soliqua (iGlarLixi) EMDAC Meeting Presentation

- **7 presenters in iGlarLixi / Lixisenatide Meeting:**
  - Paul Chew (Sanofi Sr. VP - Moderator)
  - Neil Skolnik (External expert – Need of New Treatment)
  - John Newton (Sanofi VP – MoA of lixisenatide and iGlarLixi)
  - Rachele Berria (Sanofi VP – Efficacy of lixisenatide and iGlarLixi)
  - Kristen Sharma (Sanofi VP – Safety of lixisenatide and iGlarLixi)
  - René Belder (Sanofi VP – FDA Points to Consider)
  - Luigi Meneghini (External expert – BR)
- **90-min for sponsor presentation, followed by 15-min Q&As**
- **Additional QAs/sponsor clarifications after open public hearing**

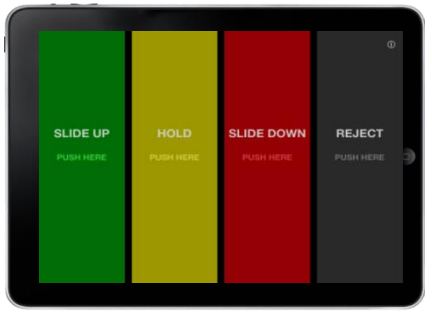
Soliqua (iGlarLixi) EMDAC Meeting Q&A

- **During Q&A sessions, answer AdCom questions**
  - The moderator determines and calls the responder
  - **Must be prepared to answer any kind of questions**
- **Include sponsor representatives and KOLs: efficacy, safety, statistics, device, …**
  - 11 Clinical (efficacy, safety)
  - 2 Biostatistics
  - 3 Pen/device/regulatory (Sanofi)
  - 1 PK (Sanofi)
  - 1 pre-clinical (Sanofi)

Soliqua (iGlarLixi) EMDAC Meeting Responder

- **The responder decides whether he/she wants to show the slide, hold it or reject it**

- **If no data slide prepared,**
  - **Responders directed not to say “After the break” but to come up with a simple answer and have the moderator decide and say if “After the break” → War room**



Soliqua (iGlarLixi) EMDAC Meeting Triage

- **Responsible for drafting and call-up Q&A slides for responders**
- **Well organized slide decks => call-up a slide within 1-2 sec**
  - Slide decks integrated in an iPad with search function
  - Calls up a slide to 3D => 3D sends it to the responder screen
    - To ensure correct verbal communication of Q&A slide number to 3D
- **6 Triage people**
  - 4 efficacy and safety
  - 1 Biostat
  - 1 for all others

Soliqua (iGlarLixi) EMDAC Meeting On-site War Room

- **Provide data/analyses/slides that the Moderator says "After the break"**
- **Roles defined**
  - War room lead, scribers (capturing questions)
  - Clinicians/PV/PK: create answers with stat lead
  - Biostat lead: coordinate biostat team and work with other function leads for answers
  - Biostat on-site team: on-site support in collaboration with the B&P remote team for needed analyses
  - Slide makers (CRO): to make presentation slides
- **Limited access: even for presenters/responders unless called by the war room coordinator**

Soliqua (iGlarLixi) EMDAC Meeting Remote War Room

- **Support the on-site team by providing data and analyses for “After the break”**
- **B&P remote war room**
  - **Lead communicators w/ the on-site B&P team**
  - **Communication by emails or phones**

Briefing Books

- **2 Briefing Books (FDA, Sponsor) provided to the AdCom members (~3 wks prior) and published (a few days prior)**
- **Sanofi Briefing Book (BB) preparation**
  - **Final BB - before Mock 3**
  - **Many posthoc analyses were incorporated in the final Sanofi BB**
- **FDA BB: Sanofi communicated typos (major & minor) to FDA on 11-May**
  - **No change in the FDA BB (as already sent to AdCom members)**
  - **Critical corrections noted at the FDA presentation slides**

Q&A Slides

- **Goal: prepare to answer to any questions => "YES" vote**
  - "An FDA AdCom meeting is the wrong time for an original thought"
- **Q&A process:**
  - Develop key questions and comprehensive listing of questions
    - Create strategic responses and identify responders
  - Organized by module/topic with associated triage & responders
  - Prepare supporting data and draft scripts
  - During QA practices/rehearsals/mocks, answers tested/refined
    - For a fine-line question between responders, process fine-tuned
- **Overall, >2,000 Q&A slides organized by topic**
- **A separate deck for BB slides of figures and tables**

Lesson and Learn

- Anticipated the workload & ensured sufficient resource assigned
  - Roles, responsibilities and assignments clearly defined
- Prioritized the analyses requested and delivered in order
- Familiar with the data and worked closely (biostat & progs)
- Teamwork, timely communication & information sharing
- Improved running time by splitting into small datasets
- Created easy-to-use template programs for frequently used analyses (eg, KM, 95%CI)
- Used a robust program for similar analyses (eg, MI, subgroup)
- Documentation with complete information of all analyses for easier tracking for future reference

Practice, Practice, Practice!

THANK YOU