ENGELBERG CENTER for Health Care Reform at BROOKINGS

Brookings Roundtable on Active Medical Product Surveillance

Overview of the Innovation in Medical Evidence Development and Surveillance (IMEDS) Program

Gregory Daniel, Managing Director and Fellow, Engelberg Center for Health Care Reform, Brookings Institution and Senior Advisor, Reagan-Udall Foundation for the FDA

Richard Moscicki, Deputy Director for Science Operations, Center for Drug Evaluation and Research, U.S. Food and Drug Administration

Troy McCall, Chief Implementation Officer, Reagan-Udall Foundation for the FDA

Wednesday, October 16, 2013

Housekeeping

- To minimize feedback, please confirm that the microphone on your telephone is muted.
- To mute your phone, press the mute button or '*6'. (To un-mute, press '*7')
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Innovation in Medical Evidence Development and Surveillance (IMEDS)

Reagan-Udall Foundation

October 16, 2013

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IMEDS Program

Background

- Mini-Sentinel has made significant progress in both development of tools and safety surveillance, and is a useful tool for FDA

- Observational Medical Outcomes Partnership (OMOP) has made considerable progress in understanding the performance of different methods for secondary use of electronic health data and in developing analytical tools to support this research

- **IMEDS** is a public private partnership within the Reagan-Udall Foundation for the FDA that aims to address several critical needs which have emerged that will influence the long-term impact of these initiatives. These needs include:
    1. Continued development of methods for using electronic health data for safety assessments and broader purposes (especially given evolving nature of data)
    2. Establishing a long-term, research agenda and corresponding governance structure to address methodological needs of Sentinel and other stakeholders
    3. Leveraging the Sentinel tools to help answer other important questions about the safety and effectiveness of interventions
    4. Training new scientists and equipping them with the knowledge and expertise to conduct safety assessments

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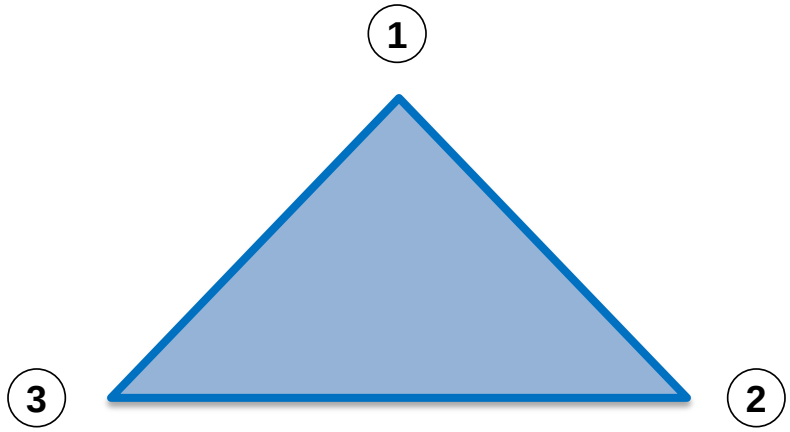
IMEDS Program

Key Areas

IMEDS will help the FDA, regulated industry and clinicians improve patient care and the safety of medical products by focusing on three areas.

IMEDS-Methods

Facilitate methods research aimed at monitoring safety of marketed medical products.



IMEDS-Evaluation

Use research findings to help understand the risks and benefits of marketed medical products.

IMEDS-Education

Train scientists in how to conduct methods research using electronic healthcare data.

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IMEDS Program

Reagan-Udall Foundation Overview

The Reagan-Udall Foundation for the FDA, which manages IMEDS, is an independent 501(c)(3) not-for-profit organization created by Congress to advance the mission of the FDA

History:

- Created in 2007 in response to the *FDA Science and Mission at Risk* report of the Subcommittee on Science and Technology
- Congress identified the need for an independent entity that could tackle the challenges identified in this report by fostering public-private partnerships

Mission:

- Support and promote better science and technical capabilities to advance regulatory science for and the mission of the FDA
- Foster public-private partnerships to drive innovative thinking and approaches to emerging science related to safety and effectiveness of FDA-regulated products

Reagan-Udall spearheads complex research collaborations involving public and private partners aimed at meeting three objectives

1. **Promoting Safety and Better Evidence** — **Includes IMEDS**
2. **Improving Regulatory Science Processes**
3. **Building Scientific Capacity**

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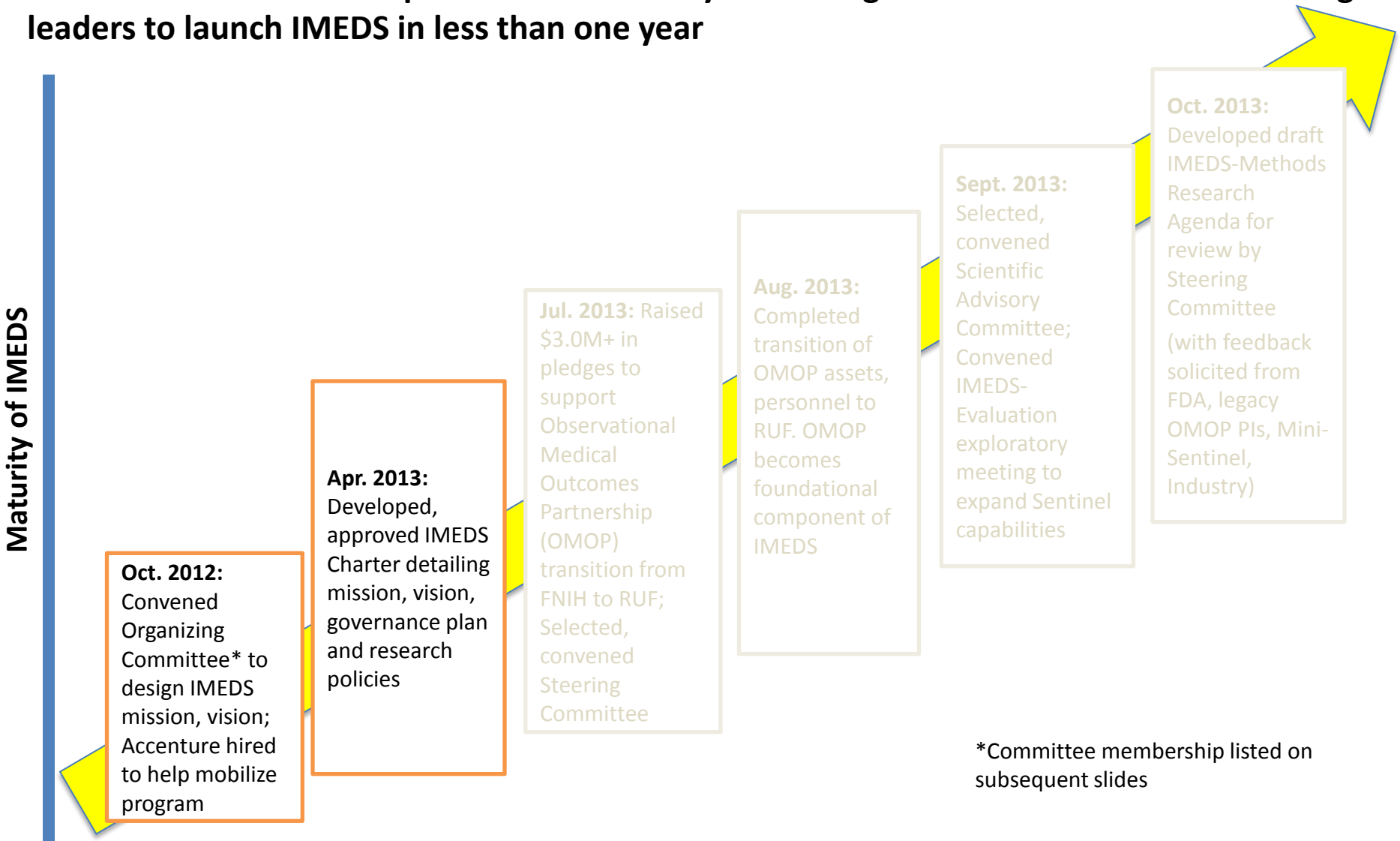
IMEDS Program

Accomplishments to Date

RUF has exceeded even optimistic forecasts by mobilizing scientific and health care thought leaders to launch IMEDS in less than one year



*Committee membership listed on subsequent slides

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IMEDS Program

Organizing Committee (Dec. 2012-Apr. 2013)

Member	Organization
Lesley Curtis, PhD	• Associate Professor in Medicine, Duke University • Mini-Sentinel: Leader, Data Core
Garry Neil, MD*	• Partner, Apple Tree Partners * Non-voting member (Reagan-Udall Board Liaison)
Richard Platt, MD, MSc	• Professor and Chair of Harvard Medical School Department of Population Medicine, Harvard Pilgrim Health Care Institute • Mini-Sentinel: Principal Investigator • Legacy OMOP Executive Board member
Lee Rucker, MS	• Senior Strategic Policy Advisory, AARP • Legacy OMOP Executive Board Member
Patrick Ryan, PhD	• Head of Epidemiology Analytics, Janssen R&D • Legacy OMOP Principal Investigator
John Santa, MD	• Director, Consumer Reports Health Ratings Center
Rachel Sherman, MD and Melissa Robb, RN	• Associate Director, Office of Medical Policy, CDER, FDA • Project Director, Office of Medical Policy, CDER, FDA
Claire Spettell, PhD	• Informatics Head, Aetna
Alec Walker, MD, DrPH	• Principal, World Health Information Science Consultants

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IMEDS Program

Methods Objectives (as outlined in the IMEDS Charter)

1. Create a long-term methods research agenda that supports FDA safety activities and improves upon the methods for secondary use of data (using the OMOP 3-Year research agenda as a starting point)

2. Build an inclusive, educated community of methods researchers

3. Establish fully transparent governance to oversee implementation of research agenda

4. Establish a data environment needed for methods research
   a. Internal data / research laboratory
   b. Establish partnerships with Data Partners

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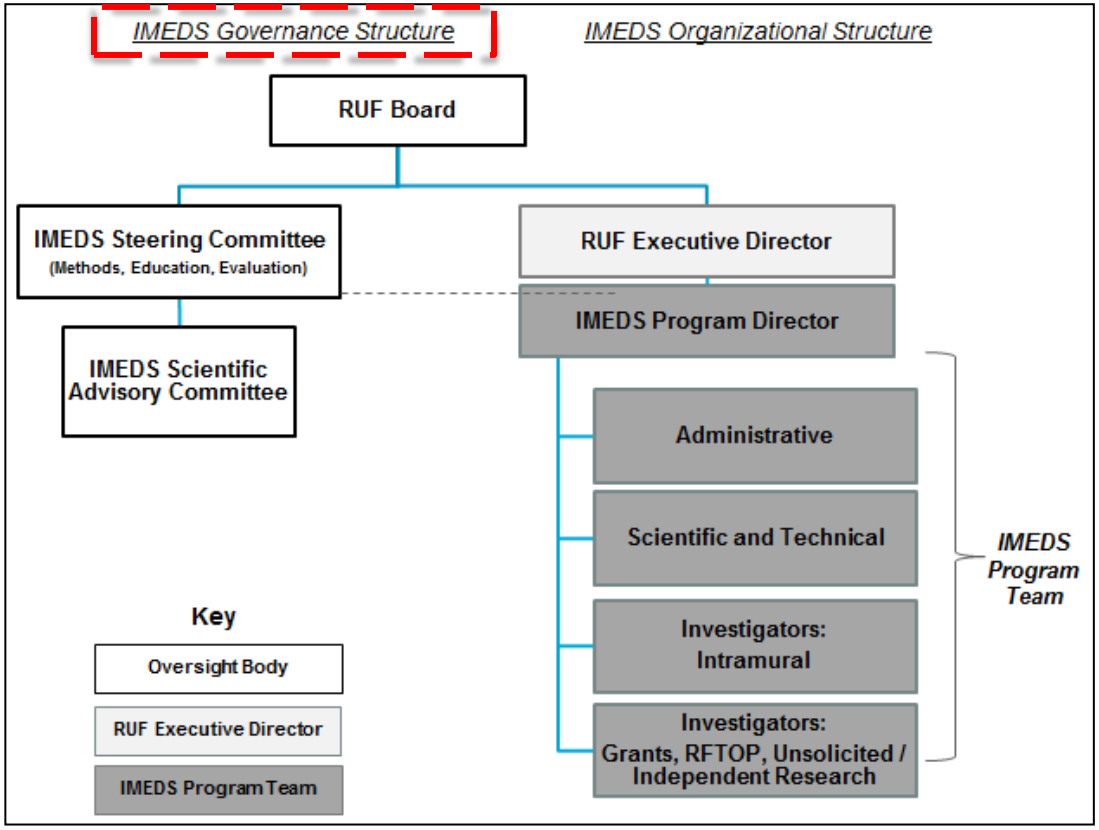
IMEDS Program

Governance Structure (as outlined in IMEDS Charter)



- **RUF Board**: selects IMEDS Steering Committee members; reviews and approves IMEDS partnerships, budget; evaluates effectiveness of IMEDS; assists with IMEDS fundraising
- **IMEDS Steering Committee**: reviews and approves IMEDS Research Agenda; provides guidance on IMEDS partnerships, external communications; selects IMEDS-Methods Scientific Advisory Committee members
- **IMEDS Scientific Advisory Committee:** provides input on IMEDS Research Agenda, research proposals and protocol

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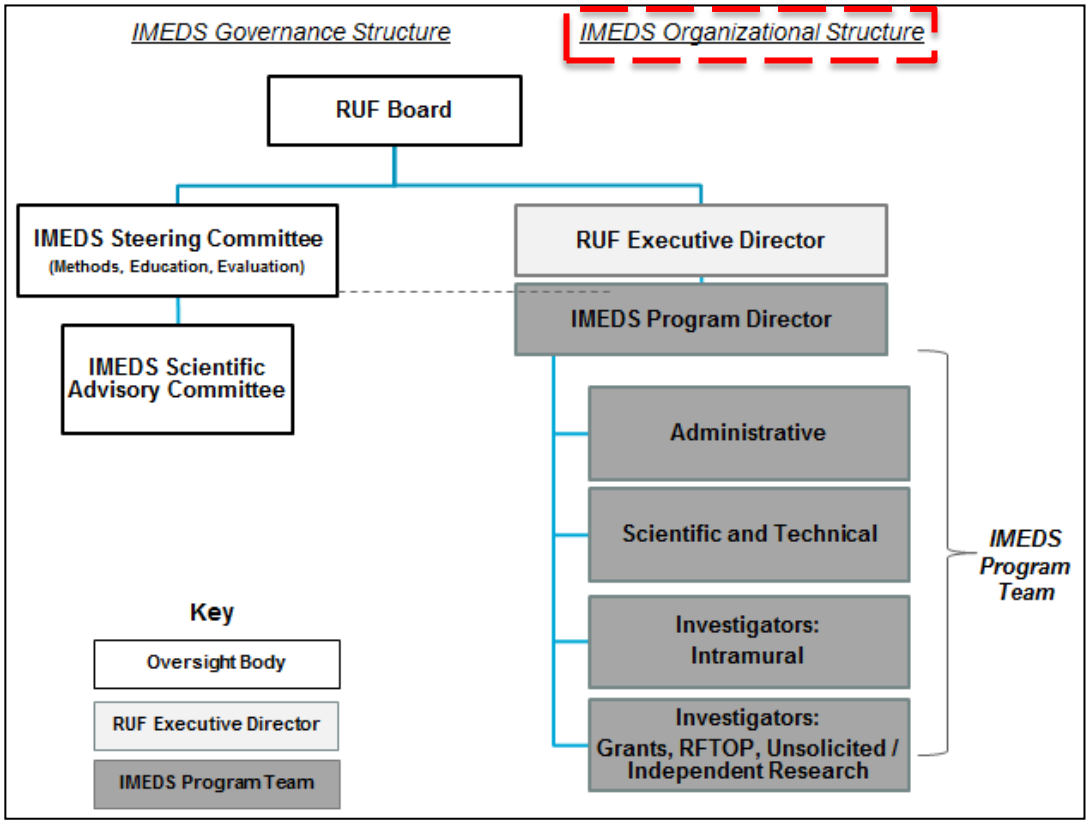
IMEDS Program

Organizational Structure (as outlined in IMEDS Charter)



- **RUF Executive Director**: hires IMEDS Program Director; ensures alignment between RUF and IMEDS missions
- **IMEDS Program Director**: day-to-day oversight of IMEDS activities; manages creation of IMEDS Research Agenda and completion of research
- **Administrative:** support the IMEDS Program Director in project and contract management for all IMEDS investigators and contractors
- **Scientific and Technical:** provide support and expertise regarding the IMEDS Data Lab and its associated features
- **Investigators:** complete IMEDS research (as assigned by IMEDS Program Director); evaluate research proposals and work products

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IMEDS Program

Accomplishments to Date

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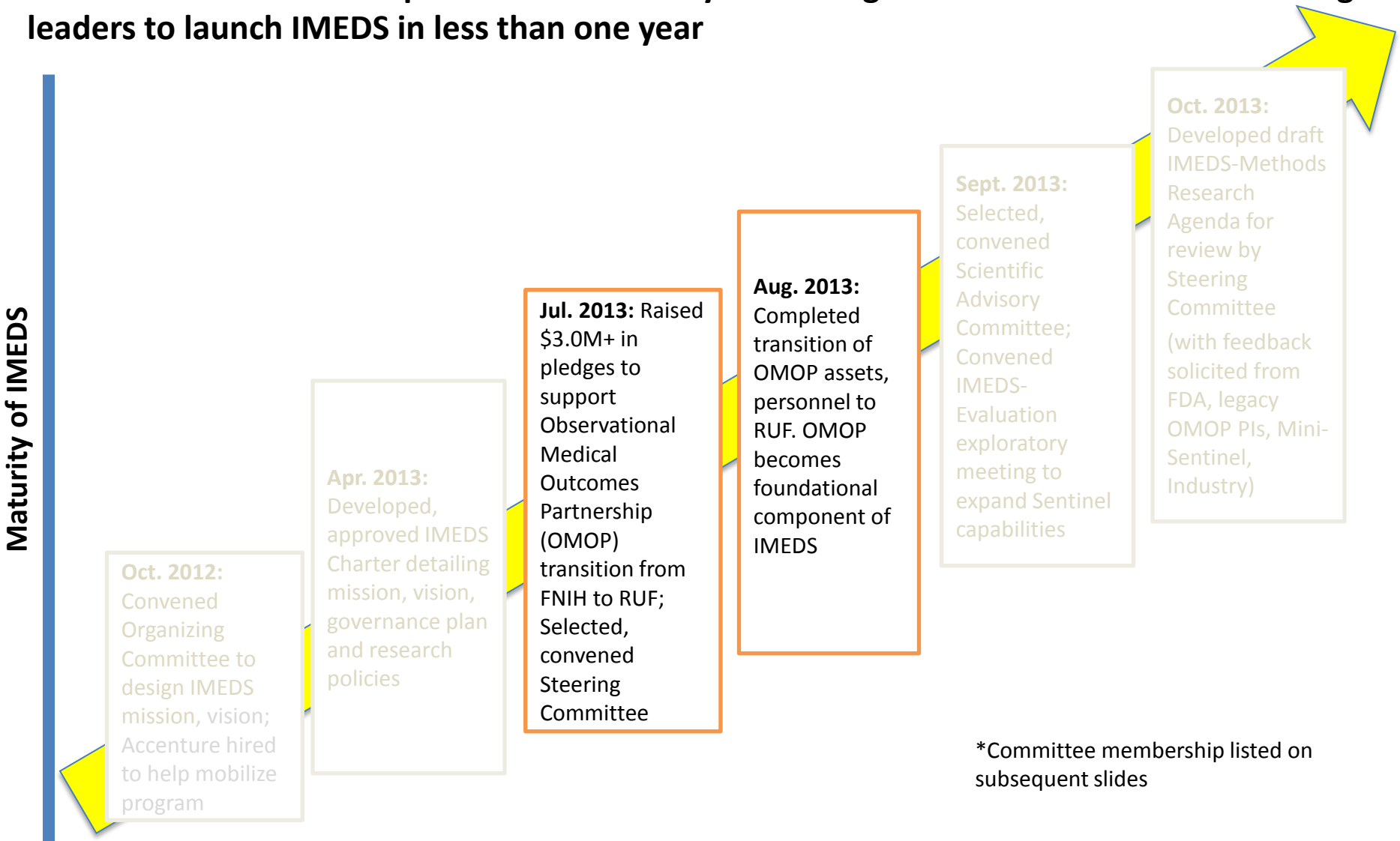

*Committee membership listed on subsequent slides

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IMEDS Program

Steering Committee (July 2013 – Present)

Member	Organization
Marcus D. Wilson, PharmD	• President, HealthCore
Elizabeth B. Andrews, PhD	• Vice President of Pharmacoepidemiology and Risk Management, RTI
Robert M. Califf, MD	• Vice Chancellor for Clinical and Translational Research, Duke University
Patrizia A. Cavazzoni, MD	• Senior Vice President for Worldwide Safety and Established Products Regulatory, Pfizer
Karen Midthun, MD	• Director, Center for Biologics Evaluation and Research, FDA
Jane Perlmutter, PhD	• Founder, Gemini Group
Michael Rosenblatt, MD	• Executive Vice President and Chief Medical Officer, Merck
John S. Santa, MD, MPH	• Director, Health Ratings Center, Consumer Reports
Janet Woodcock, MD	• Director, Center for Drug Evaluation and Research, FDA
TBD	• Reagan-Udall Board Liaison

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IMEDS Program

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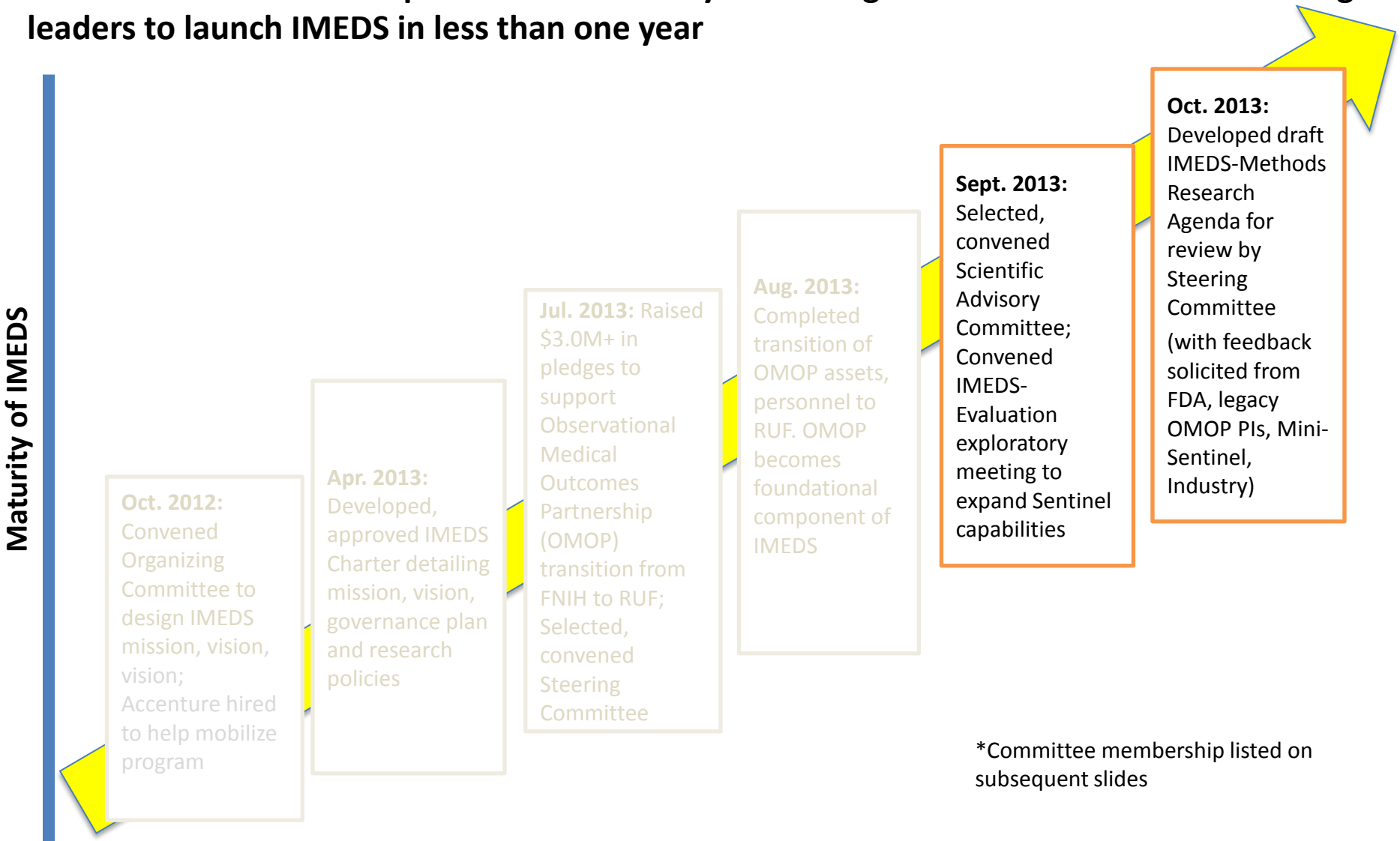

*Committee membership listed on subsequent slides

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IMEDS Program

Scientific Advisory Committee (Aug. 2013 – Present)

Member	Organization
Robert Ball, MD, MPH, ScM	• Deputy Director, Office of Surveillance and Epidemiology, Center for Drug Evaluation and Research, FDA [Non-Voting Member]
Jesse Berlin, ScD	• VP, Johnson & Johnson Epidemiology
Lesley Curtis, PhD	• Associate Professor, Duke University School of Medicine
Ralph Horwitz, MD, MACP	• Senior Vice President for Clinical Sciences Evaluation, GlaxoSmithKline; Harold H. Hines, Jr. Professor Emeritus of Medicine and Epidemiology, Yale University
Steve J. Jacobsen, MD, PhD	• Director of Research and Evaluation, Kaiser Permanente
David Martin, MD, MPH	• Director of the Division of Epidemiology, Office of Biostatistics and Epidemiology, CBER, FDA [Non-voting member]
Jennifer Clark Nelson, PhD	• Associate Investigator at Group Health Research Institute (GHRI) and Affiliate Associate Professor in Department of Biostatistics , Univ. of Washington
Sally Okun, RN	• Vice President of Advocacy, Policy and Patient Safety, PatientsLikeMe
Marc Overhage, MD, PhD	• Chief Medical Informatics Officer, Siemens Healthcare
Nancy Santanello, MD, MS, FISPE	• VP and Head of Epidemiology, Merck Research Laboratories
Azadeh Shoaibi, MS, MHS	• Methodology/Epidemiology Lead, Sentinel Initiative, Office of Medical Policy, CDER, FDA. [Non-voting member]
Miriam Sturkenboom, PhD, PharmD	• Professor, Analysis of Observational Data, Departments of Medical Informatics and Epidemiology, Erasmus University Medical Center

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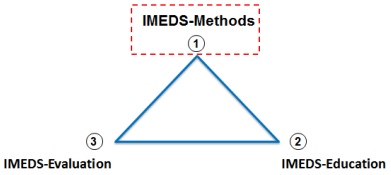
IMEDS-Methods

Research Agenda Overview



- **IMEDS-Methods Mission:**
  - To support FDA's mission by initiating and facilitating the execution of methodological research aimed at improving upon the tools for conducting post-marketing safety surveillance using automated healthcare data.

- **High level areas recommended by the Scientific Advisory Committee (SAC):**
  - Convert the results of the "OMOP Experiment" into practical advice for the conduct and interpretation of Mini-Sentinel work.
  - Assess new tools being developed in and for Mini-Sentinel.
  - Move beyond what was done in OMOP or has been done in Mini-Sentinel to develop tools and data that would assist FDA and other stakeholders in monitoring the safety of medical products.

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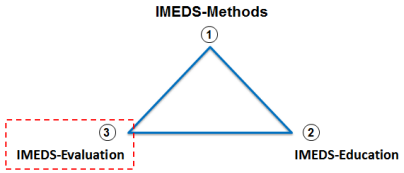
IMEDS-Evaluation

Background



- IMEDS-Evaluation's vision is to apply lessons learned from IMEDS-Methods and the tools, capabilities, and data partners used through Mini-Sentinel (MS), to enable non-FDA entities (such as Industry) to sponsor safety assessments of marketed medical products. These assessments would be completed using an IMEDS distributed database (comprised of the MS Data Partners) and facilitated by an IMEDS coordinating center.

- FDA has mentioned how critical IMEDS-Evaluation is to helping it monitor the safety of marketed medical products, and Industry leaders have also expressed a desire to conduct safety assessments using data from the same populations and sources as FDA currently does through MS (i.e., IMEDS-Evaluation).

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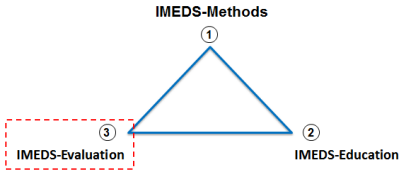
IMEDS-Evaluation

Background (continued)



- IMEDS-Evaluation could enable:
  - Proactive monitoring of marketed medical products utilizing MS tools and capabilities.
  - More efficient opportunities for pharmacovigilance plans (e.g., Phase IV studies).
  - Replication with sensitivity analyses of MS queries.

- Discussions with FDA, MS Data Partners, and Industry have indicated that while there are several legal, financial, and operational questions to be addressed, there is some alignment on the importance of and need for a mechanism such as the one that IMEDS-Evaluation will create.

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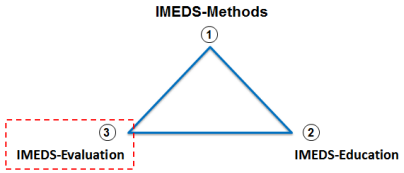
IMEDS-Evaluation

Potential Engagement Types



1. **At the time of NDA or BLA as part of a risk management (pharmacovigilance) plan**
   - Prior to approval, the manufacturer proposes using the IMEDS distributed database as part of a pharmacovigilance plan
   - FDA determines if the system could be used by the manufacturer to fulfill a postmarketing requirement (PMR) or postmarketing commitment (PMC)

2. **New signal arises from Mini-Sentinel query**
   - To *reactively* engage the IMEDS distributed database (i.e., after an FDA MS query is made public or disclosed to the manufacturer through ongoing discussions with FDA)
   - Opportunity for further refinement of signal using sensitivity analyses on the MS query (e.g., by modifying definition of exposure or adverse event measured) to evaluate the robustness of the MS query results

3. **Proactive safety surveillance queries**
   - To *proactively* engage the IMEDS distributed database with the intent of conducting safety surveillance
   - This engagement may (or may not) be restricted to safety concerns in which the rarity of the condition, drug exposure, or safety events are such that data from multiple data partners would be required
   - May be used for evaluating Risk Evaluation and Mitigation Strategies (REMS)

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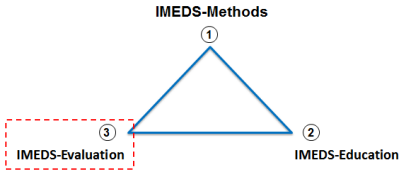
IMEDS-Evaluation

Recent Progress



- September: Reagan-Udall assembled a small group of senior leaders from FDA, Industry, and Data Partner communities to explore the feasibility of IMEDS-Evaluation. Group consensus was to continue advancing IMEDS-Evaluation and to develop the infrastructure necessary to advance a potential pilot. Attendees for this discussion included:
    - Mark McClellan (Chair, Reagan-Udall Foundation; Brookings Institution)
    - Michael Rosenblatt (CMO, Merck; IMEDS Steering Committee Member)
    - Marcus Wilson (President, HealthCore; IMEDS Steering Committee Chair)
    - Janet Woodcock (Director, CDER, FDA; IMEDS Steering Committee Member)
    - Other senior leaders from Aetna, BMS, Humana, Kaiser, Novartis, Optum, Pfizer

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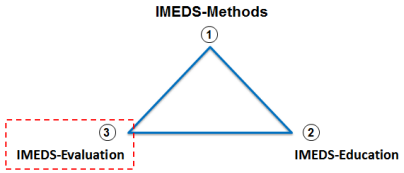
IMEDS-Evaluation

Recent Progress (continued)



- October: Currently developing a draft "Concept of Operations" which details how Reagan-Udall would implement IMEDS-Evaluation. This document will address:
  - Potential IMEDS-Evaluation pilots (i.e., research projects which could be conducted using the IMEDS distributed database)
  - Cost of operating the IMEDS-Evaluation pilots
  - How research teams conducting these safety assessments will be formed
  - How the learnings from these pilots will (or will not necessarily) be applied in FDA and Industry

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IMEDS Program

Next Steps

- ❑ **Oct.-Nov.**: Finalize remaining issues on the IMEDS Research Agenda
- ❑ **Oct.-Dec.:** Secure funding commitments of $5-7M for 2014 to enable implementation of Year 1 Research Agenda, ideally through a combination of Industry, Non-Profit and other supporters.
- ❑ **Early Nov.:** Complete draft IMEDS-Evaluation "Concept of Operations" to detail operating plan for 2+ pilot projects
- ❑ **Early Nov.:** OMOP-IMEDS Symposium (Nov. 5-6) in Bethesda, MD
- ❑ **Mid Nov.:** Present to McKinsey CMO Roundtable forum to continue to build upon earlier momentum for IMEDS, including introducing the concept of IMEDS-Evaluation.
- ❑ **Mid Nov.:** Initiate the RFP process of Year 1 Research Agenda
- ❑ **Nov.-Dec.:** Continue building financial support for IMEDS program areas from Industry, non-profit foundations and other organizations

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IMEDS Program

Conclusion

For further information:

Web: http://www.reaganudall.org/

(includes IMEDS Charter)

Email: IMEDS@ReaganUdall.org

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