Duke | Robert J. Margolis, MD Center for Health Policy

Assessing the Public Health Impact of Prescription Drug Postmarketing Safety Labeling Changes

The Duke-Margolis Center for Health Policy • Washington, DC
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To achieve its public health mission while also limiting unintended consequences, FDA needs objective and actionable information about the impacts of prescription drug postmarketing safety labeling changes, particularly on drug utilization and treatment outcomes. However, the existing evidence base on this topic has several limitations, including a small number of studied drugs, inconsistency in the data sources and methods used for measuring impacts, and variable results between drugs and studies. The objectives for today's workshop are to: 1) describe the current body of knowledge for the impacts of postmarketing safety labeling changes on drug utilization and treatment outcomes; 2) highlight what gaps or limitations may exist in the previous research for providing actionable information to FDA decision makers; and 3) identify approaches for spurring additional studies on postmarketing safety labeling changes to address these gaps or limitations.

9:00 a.m. **Welcome and Introduction**
Mark McClellan, Duke-Margolis Center for Health Policy

9:15 a.m. **Context for the Day's Discussion**
Gerald Dal Pan, Director, Office of Surveillance and Epidemiology, US Food and Drug Administration
Objective: Provide policy context for the day's discussion, describe how it fits in with broader efforts underway.

9:30 a.m. **Communicating Drug Safety Information: An Overview of Current Regulatory Practices**
Objective: Provide an overview of how FDA assesses and communicates drug safety information that emerges in the postmarketing setting, including whether and how the agency decides to update a drug's label.

Structure:

- **Presentation:**
  - *Ann Marie Trentacosti, US Food and Drug Administration (10 min)*
  - *Mwango Kashoki, US Food and Drug Administration (10 min)*
- **Q&A** (5-10 min)

10:00 a.m. **Session I: Outlining the Need for Better Evidence on the Impact of Postmarketing Safety Labeling Changes**
Moderator: *Mark McClellan, Duke-Margolis Center for Health Policy*

Objective: Provide a brief summary of findings from the Duke-Margolis literature review, highlight the key gaps and limitations of the existing evidence base, and define key research questions that could address these gaps.

Structure:

- **Opening presentation:** *Elizabeth Richardson, Duke-Margolis Center for Health Policy (15 min)*
- **Panel remarks:**

- *Matthew Rosenberg, US Food and Drug Administration (5 min)*
- *Stacie Dusetzina, Vanderbilt University Medical Center (5 min)*
- *C. Bernie Good, University of Pittsburgh School of Medicine (5 min)*

- **Moderated discussion**

Questions to address:

- What can the general findings in the literature tell us about the impacts of FDA postmarketing safety labeling changes?
- What are the key gaps and limitations in the existing evidence base?
- What research questions would be most important to consider from a public health and/or regulatory standpoint?
- What types of drugs and labeling changes should be studied in the future – either in terms of feasibility or public health impact?

11:15 a.m. **Break**

11:30 a.m. **Session II: Selecting Data Sources and Outcome Measures for Research on Drug Safety Labeling Changes**
Moderator: *Greg Daniel, Duke-Margolis Center for Health Policy*

Objective: Identify the key data sources and outcome measures that should be used for conducting research on postmarketing safety labeling changes, and discuss their respective advantages and limitations.

Structure:

- **Panel**
  - *Patrick Ryan, OHDSI (5 min)*
  - *Joseph Ross, Yale University School of Medicine (5 min)*
  - *Stephen Woloshin and Lisa Schwartz, Dartmouth Geisel School of Medicine (5 min)*
- **Moderated Discussion**

Questions to address:

- What data sources should be considered for conducting research on safety labeling changes?
  - What are the limitations of these data sources, and how can these limitations be addressed?
  - What are the key barriers to accessing these data sources? How can these barriers be addressed?
- What are the primary outcome measures that should be assessed? What are the secondary measures that should be considered?
- In what circumstances should a prospective approach to data collection be pursued?
- What other variables should be considered?

12:30 p.m. **Lunch**

1:30 p.m. **Session III: Methodological Best Practices for Postmarketing Drug Safety Research**
Moderator: *Greg Daniel, Duke-Margolis Center for Health Policy*

Objective: Explore the methods that should be applied to answer the research questions identified in Session I, and discuss their advantages and limitations.

Structure:

- **Introductory remarks: Methodological Best Practices**
  - *Becky Briesacher, Northeastern University School of Pharmacy (10 min)*
- **Panel**
  - *David Bradford, University of Georgia (5 min)*
  - *Matthew Rosenberg, US Food and Drug Administration (5 min)*
- **Moderated Discussion**

Questions to address:

- What kind of evidence is generally needed to claim a causal effect when studying the impact of safety labeling changes?
- What methods should be used to answer the research questions identified in Session I?
- What are the advantages of these methods? What are their limitations?
- What are the key assumptions of these models for estimating a causal effect?
- What modeling challenges might be introduced by unobserved or unanticipated impacts of regulatory actions? How can these be resolved?

2:30 p.m. **Break**

2:45 p.m. **Session IV: Encouraging Research on Postmarketing Safety Labeling**
Moderator: *Mark McClellan, Duke-Margolis Center for Health Policy*

Objective: Identify the primary barriers to funding and conducting postmarketing drug safety research, the existing funding streams that might support this work, and the role that FDA and other stakeholders can play in supporting the implementation of the research agenda identified in today's discussion.

Structure:

- Panel
  - *Bruce Donzanti, Genentech/Roche (5 min)*
  - *Mary Olson, Tulane University (5 min)*
  - *Julie Lawrence, The Gordon and Betty Moore Foundation (5 min)*
  - *Carol Linden, US Food and Drug Administration (5 min)*
- **Moderated Discussion**

Questions to address:

- What additional barriers (funding, communication, or otherwise) limit researchers' ability to conduct this type of research?
- What programs or funding mechanisms already exist that could be leveraged for this research?
  - Which ones could be established in the future?
- What steps can FDA take to facilitate this research?

3:45 p.m. **Session V: Major Takeaways and Next Steps**

Moderator: *Mark McClellan, Duke-Margolis Center for Health Policy*

4:15 p.m. **Closing Remarks**
Mark McClellan, Duke-Margolis Center for Health Policy

4:30 p.m. **Adjournment**

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