Day 2 Roadmap

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Overall Roadmap

• **Day 1**: Focused on improving the use of existing data sources used in ADF evaluation

• **Day 2**: Focused on use and development of new sources and capabilities for ADF evaluation
Objectives

• To determine whether the marketing of a product with abuse-deterrent properties results in meaningful reductions in abuse, misuse, and related adverse clinical outcomes, including addiction, overdose, and death in the post-approval setting (2015 Guidance).

• To determine whether products discourage riskier forms of abuse and misuse
Populations

• At least one study should include a high-risk population, such as a population of known drug abusers, but formal studies should not be limited to only high-risk populations (2015 Guidance)
  – Known drug abusers
  – Patients with new prescriptions
  – Patients on the verge of abuse
Requirements

• Identification of product-specific information, including brand and formulation
• Information on routes of abuse
• Ability to be rapidly modified, in response to changes in the prescription drug market
• Rigorous and valid outcome ascertainment
• Comparability over products
• Stability over time
Requirements (cont.)

• Well-defined populations, through probability sampling or otherwise
• Ability to measure in different populations (regions, at risk populations, demographic subgroups)
• Ability to handle drugs with small market share

• To accomplish all this, we may need multiple data sources and studies.
Data Sources: Examples

• **Probability sample**: NSDUH

• **Cohort**: FDA PMR 3033-2

• **Combination**: Hispanic Community Health Study
National Survey on Drug Use and Health

- Multistage area probability design

  State and Regions *stratification*

  Census Tracks *random*

  Census Block Group *random*

  Census Block Clusters *random*

  Households *random*
National Survey on Drug Use and Health

- Multistage area probability design
- Youths aged 12 to 17 and young adults aged 18 to 25 are oversampled
- Prescription drug use focus on 12 month period
- Questions on misuse
- Electronic images of pills used for identification
FDA Post-Market Requirement 3033-2

- An observational study using patient health records, insurance claims, and death records
- Two companion studies to develop and validate algorithms using coded medical terminologies for opioid-related overdose, death, abuse, and misuse
Probability Sample Designs

• Subjects randomly selected from some well-defined population
• Longitudinal information may or may not be obtained
• Rigorous inference to population is possible

Eg. Incidence =
\[
\frac{\text{pop. est. of subjects w/exposure and w/event}}{\text{pop. est. subjects w/exposure}}
\]
Cohort Designs

- Subjects satisfying well-defined inclusion/exclusion criteria
- Subjects have longitudinal information on exposure, risk factors, and at risk for outcomes
- Incidences and relative risks based on aggregating subject level information

Eg. Incidence = \[
\frac{\text{subjects in cohort with exposure and event}}{\text{subjects in cohort with exposure}}
\]
## Cohort and Probability Sample Designs

<table>
<thead>
<tr>
<th></th>
<th>Cohort Study</th>
<th>Probability Sample</th>
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</thead>
<tbody>
<tr>
<td>Provides a direct denominator</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Inferred population/representativeness</td>
<td>Cohort</td>
<td>Population</td>
</tr>
<tr>
<td>Allows valid estimates of incidence</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Allows exploration of relationships (eg, exposure/outcome)</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Challenges</td>
<td>Identifying appropriate cohort and obtaining information</td>
<td>Sampling or enriching for certain populations</td>
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</tbody>
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Simulated Comparison of Population and Cohort Estimates

Average number of work days missed per year due to illness or injury

Hispanic Community Health Study

• Objectives:
  – Estimate prevalences of baseline risk factors
  – Evaluate relationships between risk factors and health outcomes

• Design:
  – Probability sample embedded in multisite cohort study
  – Subjects 16,000 Hispanic/Latinos 18-74 y
  – Data collection: baseline and annual examinations

Hispanic Community Health Study: Subject Select

Communities **Non-Random**
Chosen to be enriched in Hispanics and provide breadth

Census Tracks **Non-Random**
Chosen for proximity to clinics and breadth

Census Blocks **Random**
Stratified random sampling

Households **Random**
Stratified random sampling
Day 2 Sessions

• **Session 5** National surveys: Opportunities for Evaluation of ADFs

• **Session 6** Designs That Assess Exposure and Outcome in the Same Individuals Over Time

• **Session 7** Leveraging other data: Linkages and Benchmarking

• **Session 8** Next steps
Discussion and Feedback

• Utility, strengths, and limitations of the existing national surveys
• Approaches and feasibility to modifying existing national surveys
• Development of new surveys, including internet panel surveys and other designs
• Novel study designs, including longitudinal cohort studies, and leveraging/linking multiple data sources
• Smaller local or regional studies and other types of information