Current Data Resources Used to Investigate Drug Products with Properties Intended to Deter Abuse

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Issues Paper Correction

• Treatment Episode Dataset (page 5, section 3.2)
  – The Treatment Episode Data Set (TEDS) is an admission-based system that includes data from facilities that receive public funds, are licensed or certified by a State Substance Abuse Agency to provide treatment, or are tracked at the state level for other reasons.
Overview

• Summary of Current Data Resources for ADF studies
• General Methodological Considerations
• Outcomes in ADF Opioid Investigations
• Questions for Discussion
SUMMARY OF CURRENT DATA
RESOURCES FOR ADF OPIOID STUDIES
Base Populations

• Categories of current data resources generally used to assess misuse and abuse of ADF opioid products
  – Poison Control Center data (convenience sample)
  – Surveys of those being assessed or entering treatment (convenience samples)
  – Population-based surveys (nationally representative and convenience samples)
  – Medical and prescription claims (Medicare/Medicaid and convenience samples)
Poison Control Centers

• Poison Control Centers collect data from calls relating to exposure to substances
  + Widespread catchment area (57 regional centers)
  + Often product-specific information
  + May include individuals that otherwise would not interact with the health-care system
- Percentage of events that result in a call is unknown
- Ability to distinguish specific formulations and generic products is unclear
- Severe overdoses and immediate deaths are unlikely to generate a call – may be underrepresented
Surveys of High-Risk Individuals

- Includes those entering or being assessed for substance use disorder treatment
  - Captures a hard-to-reach population of high-risk individuals
  - Can provide product-specific patterns of abuse
  - Can provide route-specific abuse information
- Difficult to define underlying population
- Generalizability of results is unclear
- Difficult to validate key pieces of information
General Population-Based Surveys

- Population-based surveys
  - Federal surveys are nationally representative
  - Captures wide range of abuse behaviors
  - Can focus on specific populations (i.e. students)
  - Eligibility criteria (e.g., stable residence, school attendance) may exclude individuals with more severe use disorders
  - Inability to capture same level of product and administration detail (e.g. formulation, route of abuse)
  - Most are cross-sectional in nature (although MTF does have a longitudinal component)
Claims-Based Data

• Claims-based data resources
  - Catchment can range from very large convenience samples to national census
  - Can be linked to other data sources (i.e., NDI)
  - Can be longitudinal (e.g., CMS)
    - Claims data by themselves are not sufficient to study prescription drug abuse; validation can be challenging
    - Misuse, abuse, and addiction difficult to define using medical coding or claims
    - Often not possible to determine specific drug product; not useful in determining route of abuse
**Additional Data Resources**

- Collected from alternate streams
  - Spontaneous adverse event reports
  - Drug diversion data
  - Web-based data collection, including street price
  - Regional cohort studies
- Can provide valuable insights not available through more commonly used “big data” streams
- Can be a challenge to define the relationship between metrics available in these resources and those of interest to the Agency
- Validation and verification can be an issue, particularly for web-based data collection
GENERAL METHODOLOGICAL CONSIDERATIONS
Exposure Definition and Assessment

• Dependent on level of analyses
• Group-based study design (e.g., ecologic)
  – Unit of time (e.g. month, quarter)
  – Other demographic variable
• Individual-based study design
  – Possession of (or prescription for) an ADF opioid (e.g. longitudinal studies)
  – Participation in an activity (e.g., entering substance abuse treatment, completing survey)
Misclassification and Ascertainment

• Can be an important factor in identifying abuse related to ADF products
  – pre- vs. post-transition product identification
  – “Kleenex effect” and/or counterfeiting
  – Data collection methodology (e.g., product order)

• Assessing the extent and nondifferential nature of misclassification important to interpreting analysis results
Pathways to Abuse/Misuse of Prescription Drugs and Related Adverse Outcomes

- Drug manufactured
- Drug distributed
- Drug prescribed/dispensed
- Drug diversion
  - Inappropriate use by patients
    - Patient supply
    - Patient use as prescribed
    - Health Care Utilization data
      - Abuse
      - Misuse
      - Addiction
      - Overdose
      - Death
    - Population Surveys (self-report)
    - Outcome captured in...
      - Nationally-representative household and school surveys
      - Treatment center surveys
      - Internet surveys
      - Poison Center data
      - Emergency Department Visit and Hospitalization data (claims, EMR)
      - Addiction treatment admissions
      - National Vital Statistics, linked death registry data
      - Medical Examiner data (limited availability)
      - National death certificate literal text (in development)
      - Mortality Records
OUTCOME CONSIDERATIONS
Outcome Measurement

• Multiple data sources are able to assess a variety of outcomes
• Outcomes of interest to Agency: misuse, abuse, addiction, overdose, and death
• Since many technologies focus on non-oral abuse, route-specific outcomes are also of interest
  – Not always available in current data resources
Outcome Measurement

- FDA has definitions of both misuse and abuse, but operationalizing them can be a challenge
  - Data resources have differing definitions
  - Some combine the concepts of misuse and abuse
  - Difficult to measure in claims-based resources
  - Ascertaining specific products abused can be difficult
    - Multiple product abuse adds to complexity
    - Misclassification is a significant issue
Outcome Measurement

• Addiction is a complex and nuanced concept
  – Similar to misuse and abuse, data resources do not often capture components used to assess addiction

• Overdose and mortality are easier to define
  – Few data resources can connect abuse and outcome data
  – Difficult to attribute to a specific product
Additional Outcomes

• Doctor and/or Pharmacy Shopping
  – Not straightforward to define
  – Three ER/LA PMR Studies to define, and assess in relation to misuse and abuse

• Proxy clinical outcomes (e.g. hepatitis, HIV)
  – Challenge to relate to specific ADF products

• Drug seizure levels, changes in street price
  – How to relate to outcomes of interest to FDA?
QUESTIONS FOR DISCUSSION
Questions for Discussion

• Discuss the ability of currently available abuse-related data resources to adequately characterize the underlying population of those who misuse and abuse drugs
  – How well do they capture
    • Occasional/recreational use?
    • Severe/advanced opioid use disorder?
    • Individuals in between these two extremes?
Questions for Discussion

• Discuss the ability of current data sources to distinguish ADF opioid molecules and formulations

• Discuss the ability of currently available data sources for collecting information on routes of abuse
Questions for Discussion

• Discuss the important exposures and outcomes to consider when conducting ADF opioid investigations. How well are these factors measured in currently existing data sources?
Questions for Discussion

• Discuss the best practices for measuring misuse, abuse, addiction, overdose, and mortality
  – What are the best practices for validating misuse, abuse, and addiction?

• Are there additional outcome and/or exposure measures that could be used in these studies?
BACKUP SLIDES
Abuse

• “The intentional, non-therapeutic use of a drug product or substance, even once, to achieve a desirable psychological or physiological effect”
Misuse

• “The intentional therapeutic use of a drug product in an inappropriate way, specifically excluding abuse”
  – From “Abuse-Deterrent Opioids —Evaluation and Labeling Guidance for Industry”