



# Postmarketing Abuse Deterrent Studies (Category 4)

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## Disclaimer

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# Outline

- Postmarketing Study Goals
- Postmarketing Study Challenges
- Formal Studies versus Supportive Data
- Formal Study Design Considerations
  - Data Source, Exposure and Outcome, Comparators, Risk Factors
- Supportive Data Design Considerations
- Broader Challenges
- Conclusion

## Postmarketing Study Goals

- To determine whether the marketing of the potentially abuse-deterrent formulation results in a significant decrease in estimates of abuse compared to estimates of abuse in non abuse-deterrent formulations
  - Population- *and* use-based estimates
  - Uncontrolled study conditions
- “The product has demonstrated reduced abuse in the community.”

## Postmarketing Study Challenges

- Data that directly measure abuse are limited
- Optimal study design features not yet established
- Exposure can be difficult to determine
- Compared to classical pharmacoepi studies, “non-traditional” confounders and risk factors are important
- Outcomes may not be straightforward
- Multiple studies may be necessary

# Formal Studies versus Supportive Data

<b>Formal Studies</b>	<b>Supportive Data</b>
<b>Outcomes provide meaningful measures of abuse and abuse deterrence</b>	<b>Provide additional context on specific aspects of abuse</b>
<b>Ideally produce nationally representative estimates</b>	<b>May measure outcomes related to abuse (e.g., diversion, street price)</b>
<b>Assess overall and route-specific abuse and abuse deterrence</b>	<b>May include sources that are not easily generalizable (e.g., internet)</b>
<b>Sufficiently powered to assess meaningful changes in abuse</b>	<b>Contribute to totality of evidence</b>

## Formal Study Design Considerations – Data Source

- Inclusion of individuals at multiple levels of risk – low, moderate, and high
- Adequate coding system to measure exposure and outcome
- Sufficient numbers of individuals to analyze exposure of interest, comparators, and outcomes
- Careful data resource description and background rates based on actual data
- May require linking of multiple data resources

## Formal Study Design Considerations – Exposure and Outcome

- Should be carefully defined, justified, and validated
- Pilot studies may be necessary
- Reported abuse outcomes should measure both prevalence and frequency
- Both average level and trends over time should be measured
  - Allow adequate time for meaningful trend analyses
- Interim analyses are preliminary results



## Formal Study Design Considerations - Comparators

- Perennially difficult and critical issue
- Postmarketing data for non-abuse and abuse deterrent formulations are not always available
- Concurrent comparisons to other opioids also useful, but should consider:
  - Relative utilization levels, time on market, relative abuse levels, and route of abuse
  - Multiple comparators may be necessary
- Both branded and generic products should be included

## Formal Study Design Considerations – Risk Factors

- Important to control for variables that may affect how product is used
- Some confounders are specific to drug abuse investigations and may require new methods to measure
  - Personal or family history of substance abuse
  - Mental health issues, recent legal troubles
  - Geographic variability and demographics

# Supportive Data Design Considerations

- Goal and rationale of data should be clearly stated
  - What do these data contribute to the characterization of abuse?
  - How do these data contribute to assessment of drug abuse as defined by the formal study protocol?
- State whether data are descriptive or analytic in nature
- Use of geographically diverse settings is encouraged

## Broader Challenges

- Characterization of quantitative links between pharmacokinetics, clinical studies, and postmarketing or community-based investigations
- Optimal assessment and validation methods for postmarketing studies of abuse
- Better understanding of optimal methods to assess the effects of ADF formulations on community prescription drug abuse

## Conclusions

- In addition to good study practices, there are unique design and analysis considerations specific to studies of abuse and abuse deterrence
- May require novel strategies (e.g. linking datasets) or more than one investigation to adequately address research question
- The broad challenges remain as the science evolves, and innovative approaches are welcome