

# Assessing Abuse Liability in Drug Dependent Subjects

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# Overview

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- This workshop presented an overview of critical scientific and methodological issues associated with studying drug-dependent abusers.
- Topics included participant recruitment, environment of study (inpatient vs outpatient), immediate detoxifications prior to the study vs maintenance throughout the study, outcomes measures, defining study populations using DSM criteria (important revisions and the impact of DSM 5), and other methodological considerations

- When are studies in dependent subjects they most useful?
- **When they tell us something different than recreational users:**
  - Agonist/antagonist combinations
    - Evaluating withdrawal for agonist/antagonist combinations
    - Dependent subjects usually more sensitive to these effects
  - “Novel” opioids, incl. partial agonists, mixed opioids
    - May be useful as effects can vary substantially in dependent subjects depending on pharmacodynamic profile of drug
  - Physicochemical ADFs?
    - Dependent subjects may be less sensitive to ADFs (stronger motivation, other reasons for misuse, e.g., withdrawal)?
    - More sensitive (need ‘quick fix’)?
      - **No data to support either way**
  - Potential role of animal (self-administration) models
    - Understand potential impact of opioid or stimulant ADFs on reinforced behavior without ethical/logistics issues with dependent subjects

# Defining the Study Populations

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- ❑ Individuals currently dependent on opioids and thus maintained on an opioid for the duration of the study
  
- ❑ Individuals recently detoxified from opioids, or those who have a history of opioid dependence but are not currently dependent:
  - ❑ Participants are detoxified on an inpatient unit immediately prior to the onset of data collection
  - ❑ Participants referred to as „post-addicts“
  
- ❑ Recreational users who are not dependent on opioids, yet use them with measurable regularity
  
- ❑ Comparisons across these different groups are difficult, not only because of participant differences but because of design choices including route of opioid administration, doses employed, and various outcome measures employed.

- Not all opioid-dependent populations are equal
- Dependent subjects represent significant challenges
- Studies with opioid-dependent populations necessitate specialized study center and experienced staff
  - Medical management of withdrawal
  - Recruitment and subject retention

- DSM 5 changes to SUD has significant implications for Human Abuse Potential (HAP) studies
- No HAP studies using DSM 5 to date - *ClinicalTrials.gov*
- Re-evaluation and consensus between pharmaceutical industry and regulatory agencies needs to occur based on empirical findings with comparison of DSM-IV and DSM 5 criteria