CSS perspective on the Review of Preclinical Abuse Potential Data on Decision Making

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Advancements in Abuse Potential Assessments
Building on the FDA Draft Guidance for Industry
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Outline

– Abuse potential assessment of drugs under development:
  • What is abuse potential?
  • What is an abuse potential assessment?
  • Why is it important?
– Decision-making conceptual framework
– Abuse potential assessment in animals
– Conclusions and topics for further discussion
What is Abuse Potential?

- Refers to the likelihood that a drug will be used non-therapeutically, repeatedly or sporadically, for the psychoactive effects it produces.

- Examples of psychoactive effects predictive of the potential abuse of a drug include:
  - Euphoria, perceptual and other cognitive distortions, hallucinations, and mood changes
What is an Abuse Potential Assessment?

– Comprehensive evaluation of:
  • Chemical properties
  • Pharmacological and pharmacokinetic characteristics
  • Clinical data (human abuse studies, and clinical trial data relative to abuse)
– Relative to an appropriate comparator drug
Why is Abuse Potential Assessment Important?

– Characterizes the properties of a drug predictive of its abuse
– Part of the safety evaluation of drugs
– Provides the basis for:
  • Accurate risk-benefit assessment
  • Regulatory actions related to drug control
– To industry, abuse potential is a risk to be considered early on in the development plan
Abuse Potential Assessment in Animals

- Behavioral studies. Capture aspects of drug seeking and taking behaviors, and “subjective” properties
  - Traditional studies
    - Self-administration
    - Drug discrimination
  - Other behavioral models
    - Conditioned place preference
    - Intracranial self stimulation
  - Physical dependence studies
When to Assess the Abuse Potential of a Drug in Relation to the Drug Development Timeframe?

Pre-clinical Testing R&D

- Chemistry
- Receptor Binding
- Functional Assays
- Animal Pharmacology
- Animal Pharmacokinetics
- Active Metabolites
- CNS Safety Pharmacology
- Toxicology Studies

Clinical Research & Development

Phase I

- Clinical Studies-Adverse Events (AEs)

Phase II

- Clinical Studies-AEs
- Drug Discrimination in animals
- Self-Administration in animals
- Dependence & Withdrawal

Phase III

- Clinical-Studies-AEs
- Human Abuse Potential Studies
Conclusions and Topics for Further Discussion

– The abuse potential assessment of drugs is
  • Critical in the overall safety assessment
  • Based upon the comprehensive evaluation of all abuse-related data
  • Particularly challenging when evaluating NMEs with novel mechanism of action

– Traditional methodology works well when studying drugs that belong to recognized classes associated with abuse such as opioids, benzodiazepines, and amphetamine-like drugs among others
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