Abuse Liability Assessment
Regulatory Guidance

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Abuse Potential

- Characterizes the ability of a drug to produce positive psychoactive effects, which is viewed as correlated with, or predictive of its intentional use in non-medical situation, repeatedly or even once

- Positive psychoactive effects may include euphoria, hallucinations, perceptual and other cognitive distortions, and mood changes
Why is abuse potential assessment important?

- Healthcare providers, patients, and the public need to know whether the new drug is likely to be abused after approval and marketing
- For protection of the public health
- Because a scientific assessment of the properties of a drug are most predictive of its abuse
- Part of the safety evaluation of drugs
- Provides the basis for regulatory actions related to drug control
FD&CA Regulations

- Applies to human and animal drug products and biologics, and any product that contains a controlled substance
- Prevalence of prescription drug abuse
- Abuse is a safety concern (FDAAA 2007)
- Regulations
  - Product labeling
  - Risk management
  - Marketing and promotion
  - Proposal for scheduling in the Controlled Substances Act (CSA)
FDA Draft Guidance for Industry–Assessment of Abuse Potential of Drugs


**Decision Tree – Recipient of 2012 CDER Regulatory Science Excellence Award**

- Applies to Abuse Potential Assessment
  - NME: CNS-Active Opioids, Stimulants, Depressants, Hallucinogens, Cannabinoids
  - Not NME: “abuse deterrent formulations”
- Integrates all safety information related to abuse in NDA
- NDA requirements [21 CFR § 314.50 (5) (vii)]
NDA Sections on Abuse Potential Data

- Drug product labeling (Module 1)
- Chemistry (structure, synthesis) (Module 3)
- Pharmacology (binding, animal and human data, behavioral studies, overdose) (Module 2)
- Clinical Trial Data (AE analysis) (Module 4 & 5)
- Pharmacokinetics and pharmacodynamics
- CSA scheduling proposal (Module 1)
  - Comparison to a pharmacologically similar drugs
    - Toxicity and performance impairment
    - Physical dependence and tolerance
    - Subjective effects – “liking”, “euphoria”, “high”
20 QUESTIONS - Abuse Potential Assessment Decision Tree (ROADMAP)

1. Chemistry?
2. Binding?
3. Receptor Function?
4. AEs in animals?
5. PK in animals?
6. CNS-active?
7. Effects in animals?
8. Reward effects in animals?
9. Physical dependence in animals?
10. Study plans?
11. Abuse AEs in patients?
12. Abuse AEs in healthy humans?
13. Human abuse potential study?
14. Reward effects in humans?
15. Abuse AEs in larger patient population?
16. Submission complete?
17. NDA info shows abuse?
18. Reports of actual abuse outside U.S.?
19. Label appropriate?
20. INVITRO ANIMAL HUMAN ADMIN
Food Drug & Cosmetics Act (FD&CA 1938)

- Determine abuse potential of drug products
- Drug scheduling recommendation
- Labeling: Drug Abuse & Dependence Section
- Risk management recommendations

Controlled Substances Act (CSA) 1970

- Regulation of controlled substances, prevent drug diversion
- Registration of manufacturers, distributors, healthcare practitioners
- Drug scheduling

Food And Drug Administration Amendments Act (FDAAA) 2007

- Postmarketing studies and clinical trials
- Safety related labeling changes
- Develop and comply with risk evaluation & mitigation strategies (REMS)

Food And Drug Administration Safety & Innovation Act (FDASIA) 2012
2012 FDASIA (July 9, 2012)

- 5th PDUFA Reauthorization
- Provides FDA with funding and a predictable and efficient review process for human drug and biologic products.
  - Expands user fees to generic drugs and biosimilar biologics.
  - Changes the way FDA approves clinical trials, approves medical devices, expands postmarketing surveillance capabilities, shortens timelines for various actions and decisions
2012 FDASIA (July 9, 2012)

• Drug Shortages – Work with industry to identify and resolve manufacturing problems as early as possible. Most problems relate to quality issues and infrastructure in various facilities

• Ban on two so-called “Bath Salts”
2012 FDASIA (July 9, 2012)

• Ban on Small Molecule Synthetic Cannabinoids (K-2, “Spice”)
  • Chemically defined
  • Must demonstrate CB1 receptor activity
  • Must demonstrate agonist functionality

• Abuse Deterrent Guidance development
Summary

- CNS activity is demonstrated by receptor binding activity, PK/PD data, and analysis of profile of pharmacological effects and adverse events profile

- If animal and human abuse potential studies and the AEs profile do not show rewarding effects or other abuse-related behaviors or pharmacology similar to other controlled substances, a scheduling recommendation is unlikely

- Sponsors are encouraged to proactively interact with FDA in planning to conduct abuse potential studies