Tufts Health Care Institute Program on Opioid Risk Management

Guidelines for the Development of Abuse-Deterrent Opioid Formulations

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Tufts Health Care Institute

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Human Abuse Liability Studies

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Human Abuse Liability Studies

- Key elements to include in the guidance
  - Step 1: Chemical Entity
    - Pre-clinical
    - Clinical Phase I: Detect signal

If evidence of abuse liability, and wish to continue develop an ADF and move to Step 2

Human Abuse Liability Studies

- Key elements to include in the guidance
  - Step 2: Untampered ADF
    - Intact Tablet vs Intact Control

Human Abuse Liability Studies

- Key elements to include in the guidance
  - Step 3: Tampered ADF
    - Based in part on benchtop testing
    - Tampered ADF vs Tampered Control

Human Abuse Liability Studies

- Example 1: SR Oxycodone+capsaicin
  - Step 1: Chemical Entity
    - Can rely on known abuse liability of oxycodone
  - Step 2: Untampered ADF
    - Intact Tablet vs OxyContin
  - Step 3: Tampered ADF
    - Chewed SR Oxycodone+capsaicin vs Chewed OxyContin

Human Abuse Liability Studies

- Example 2: “Fort Knox” Oxycodone
  - Step 1: Chemical Entity
    - Can rely on known abuse liability of oxycodone
  - Step 2: Untampered ADF
    - Intact Tablet vs Intact OxyContin
  - Step 3: Tampered ADF
    - Chewed “Fort Knox” Oxycodone vs Chewed OxyContin??

Studies required of all “abuse-deterrent” opioid formulations

- A one-size-fits-all is not possible, given the diversity of the ADF approaches
- Standard abuse liability assessments (e.g. McColl & Sellers 2006; Griffiths et al. 2003; Preston & Jasinski 1991) and self administration

Important Factors

- Factors that may affect the specific study designs used:
  - Pharmacokinetics of the drug/formulation
  - Route of administration (e.g. IV, PO, etc.)
  - Study population (e.g. dep vs non-dep)
  - Relative cost of tampering (e.g. cost of tools needed to extract drug, level of expertise required, etc.)

Potential label claims

- Claim A: “Ratings of drug liking were lower for Drug X than for Control Y”
- Claim B: “Self administration of Drug X was lower than for Drug Y”

Scientific studies needed to support each claim

- Claim A: Standard test procedures
- Claim B: Self administration procedures (e.g. drug versus money progressive ratio)

Experimental Complexities

- Discussed advantages and disadvantages of including self administration
- How to interpret magnitude of subjective effects?
  - Magnitude of ADF and non-ADF ratings of liking differ by 15 mm
- How to interpret patterns of subjective effects?
  - ADF and non-ADF have different patterns of good and bad effects