Abuse Deterrent Guidance One Year Later. What have we learned?

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The opinions and information in this presentation are those of the author and do not necessarily reflect the views and policies of the FDA
Based on current experience, there may be a need to refocus our attention on relevant aspects of the guidance

- **Scope.** What type of products qualify for AD development and labeling? When should an AD formulation be developed?

- **In vitro studies.** What studies provide meaningful data? Is there a need for a decision tree approach?

- **Pharmacokinetic studies.** How should the effect of food or alcohol be weighed?

- **Human abuse potential studies.** Need to emphasize that these studies should address relevant routes of abuse.
Scope of the Guidance

• Guidance was written for opioid drug products
  – High risk of overdose leading to death associated with the misuse and abuse of opioids

• What products are eligible for AD claims?
  – A product associated with high levels of abuse and with serious consequences of abuse
  – Primarily ER and IR single entity high strength opioid products

• When is there value in developing an AD formulation?
  – Existing products are abused by a specific route of abuse, and the AD formulation is expected to have a “meaningful” impact on abuse
• In 2013, CSS was involved in the review of 30 submissions for abuse deterrent formulations
  – INDs – 22
  – NDAs – 8
Category 1. In vitro-testing

• What studies provide meaningful data?
  – Comparative studies. The ADF should offer an advantage over currently abused products, and resist abuse/misuse by the relevant routes of abuse
  – Current guidance calls for assessing simple and complex methods for bypassing the AD properties of the formulation.
Category 1. In vitro-testing

- Is there a need for a decision tree, or a performance evaluation scheme?
  - We believe that the guidance may have to include a proposal a decision tree or scheme. Though it may be challenging to develop one
  - In this “envisioned” scheme the effect of minimal interventions to bypass the AD properties of the formulation would be studied first, and the performance of the ADF would be evaluated in relation to a product that is being abused (comparator)
  - Based on performance (Pass or Fail) under simple conditions, testing of the ADF should continue in a stepwise approach with increasing complexity
Based on current experience, it is critical to explore food effects prior to human abuse potential studies. In some instances, a food effect may be present with the intact or manipulated formulation.
PK studies. Food effect

Simulated opioid Cmax values
• In our example a food effect is present when taking intact and manipulated ADF
  – Current guidance recommends to conduct human abuse potential studies under fed conditions to maximize exposure if there is a food effect
  – In our example, under fed conditions it is likely that no differences in “drug liking” between manipulated and intact product will be observed
PK studies. Food effect

- Explore food effect prior to the initiation of human abuse potential studies
- Based on the PK profile of the manipulated and intact formulation under fed and fasted conditions, human abuse potential studies may have to be conducted under fasted, or fed, or both conditions
- If the effect of food is considerable, food may be all that one needs to bypass the AD properties of the formulation
Category 3. Human abuse potential studies

• Must address relevant routes of abuse
• Still some challenges on the interpretation of data from IN studies
  – How to interpret concurrent liking and mild nasal discomfort?
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