GDUFA Amendments of 2012 Regulatory Science Initiatives:

Request for Public Input for FY 2018 Generic Drug Research; Public Workshop

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Proteins Peptides Opioids and Abuse Deterrent (AD):

1. FDA encouraging AD Opioids

2. Typical abuse: crushing, snorting and injecting, where the drug is available to systemic circulation rapidly for an intense high

3. From generic drug development perspective, the opioid guidance *neither* address the development *nor* testing of generic AD opioid products.

4. Research needed for establishing conditions / tests required for demonstrating *the sameness* of AD potential between Reference & Test Product.

Proteins Peptides Opioids and Abuse Deterrent (AD):

Research on Following:

- Extraction Procedures mimicking real world techniques
- End points depicting whether the extraction was complete or not

Partial AUC for Establishing Bio-Equivalence

1. Product specific guidance on AUCp need to be available on a timely basis.

2. Any AUCp requirement should be based on sound scientific principles

3. PK profile / AUCp should reliably correlate with the therapeutic outcome in the patients.

4. Otherwise, additional BE metrics, such AUCp may cause significant generic barrier.

BCS III Waiver:

BCS I compounds typically enjoy the bio-waiver.

The major obstacle for seeking bio-waiver for BCS Class 3 compounds is the requirement of test product being qualitatively (Q1) and quantitatively (Q2) same as RLD (Include the guidance page)

BCS III Waiver:

In reality, the excipients used in the IR and MR products have no impact on the permeability of the API with the exception of permeation enhancers.

On that basis, a blanket requirement of Q1/Q2 on all excipients poses significant Regulatory barrier.

Therefore, research is needed on the impact of excipients on the permeability of BCS Class 3 drugs.

Specifically, figuring out mechanistic understanding of permeation enhancers and structural activity relationship

NTI Drugs

The BE and CMC requirements (such as assay criteria, BU and CU criteria) are stringent for NTI drugs relative to the regular drugs

Therefore, the definition and attributes of which drug constitute as NTI should be made clear.

Product specific BE requirements such as reference-scaled average BE and the two-treatment, four-period, fully replicated crossover design should be made available early on

This will enable the sponsor's risk assessment and appropriate formulation development at the very initial stage for NTI drugs.

Thank You