U.S. FOOD & DRUG ADMINISTRATION

FDA's Role in Drug Delivery Technology Innovation

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Hot Topic: Drug Delivery Technology

Pathway to FDA Approval of a Novel Drug Delivery Technology

- FDA approves drug product applications
- Your novel drug delivery technology must be in a drug product application to be evaluated by FDA

Chicken, Meet the Egg

- "But Pharma is not interested in my novel drug delivery technology because it has not been used in an approved drug product"
- Drug product developers need to make decision to take the regulatory risk of using a new technology
  - Drug product developers can have pre-submission discussion with FDA about their product

Why?

- CDER is primarily supported by user fees on drug product applications
- There are a large number of pharmaceutical scientists that think they have a wonderful novel drug delivery technology
  - FDA is not resourced to interact with all of you
  - Inclusion in a drug product application is proof of viability

Innovation in Generic Drug Applications

- Can a novel drug delivery technology first be used in a generic drug application?
- Yes!
- A generic drug application can use a different drug release mechanism than its reference listed drug (RLD) ~~product~~
  - It must be bioequivalent to the RLD ~~reference product~~
  - But your novel drug delivery technology gives precise control over the drug amount released?

Fentanyl Transdermal System (Patch)

- Fentanyl Transdermal System (Patch)
- RLD ~~Reference product~~ was approved with a reservoir design
- A generic product used a matrix design and was approved
  - Brand product citizen petition that requested FDA not to do this was denied

Fentanyl Transdermal System (Patch)

- The RLD ~~reference product~~ reformulated to a matrix design
- FDA later determined that reservoir systems were withdrawn for safety

Dry Powder Inhalers

- FDA approved a generic version with a device with a difference in orientation from the RLD ~~reference product~~

The Chicken and Egg Return

- Novel Drug Delivery Technologies in generic drug applications can only use inactive ingredients that have been used in FDA approved products for that route of administration
- Novel excipient generally have to first pass through the new drug approval process

Inactive Ingredient Database

- Here is how you find the list of inactive ingredients used in approved drug products
  - Inactive Ingredient Database
  - https://www.accessdata.fda.gov/scripts/cder/iig/index.cfm
- ~~If an inactive ingredient is used in less than three approved products it will not be in the IID~~Not all excipients used in approved NDAs and ANDAs are found in the IID for multiple reasons, including protection of proprietary information.
- Use FDA label to search labels
  - https://nctr-crs.fda.gov/fdalabel/ui/search

Low Global Warming Propellants

- Phase out of hydrofluoroalkane's used in Metered Dose Inhalers (MDI's) is coming
- An alternate propellent must be first approved in an NDA before generic drug applicants can begin to transition their products
- FDA will hold a workshop on this in Dec 2024
  - https://www.complexgenerics.org/events/

Summary

- FDA's application-based system poses challenges for novel drug delivery technologies
- Successful novel drug delivery technologies solve real problems but need to make the case to product developers


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