Your Generics & Biosimilars Industry

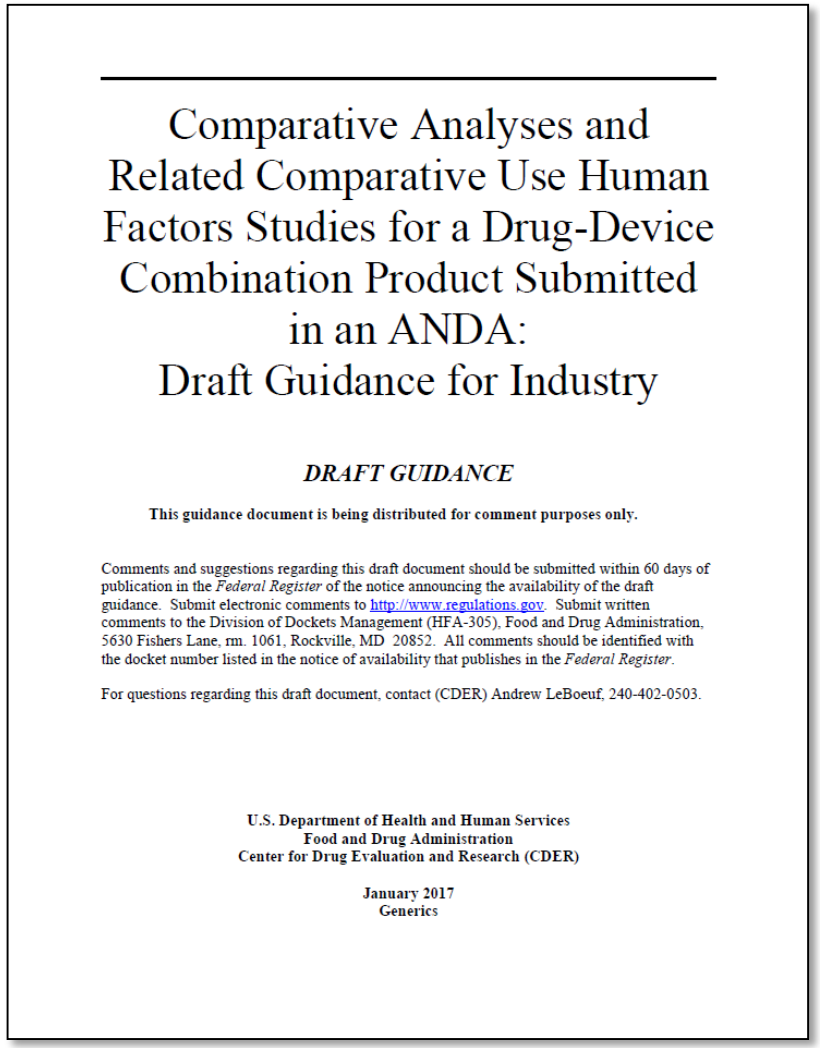
Challenges Faced in the Development of the User Interface for Generic and Biosimilar Combination Products

May 1, 2019

Guidance Released Jan 2017

Providing useful and practical support on the development of generics:

- Generic combination product to be substituted without additional HCP intervention/training.
- 3 types of Threshold Analyses
- Comparative Use HF study – intended to confirm that differences in labeling and device can be substituted with the same clinical effect and safety profile



Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA: Draft Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Andrew LeBoeuf, 240-402-0503.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

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Generics

What We Do Today

- Plan HFE activities
- Identify Users, Use, Use Environment and Operating Principles
- Identify and Capture User Needs
- Describe how the product is used
- Review Known Use Issues
- Complete a Comparative Analysis
  - Labeling, Task, Physical
- Use-Related Risk Assessments
- Eventual Comparative Use Human Factors Study
- Complete documentation, including validation of user needs

Review Known Use Issues

Known Use Issues are reviewed to understand the RLD device and as input into the Risk Management Process

Challenge:

If the Known Use Issues Review shows existing risks with the originator design, or similar products, how can those be risk controlled?

Would this motivate minor design differences driven by risk controls?

Comparative Analysis

Examine external critical design attributes of the proposed delivery device constituent part in comparison to the external critical design attributes of the RLD.

- Complete a Comparative Analysis
  - Labeling, Task, Physical
- No difference
- Minor difference
- Other difference

Challenge: When does a difference (minor or other) need to be confirmed in a comparative use human factors study, and when is other risk assessments acceptable?

Use-Related Risk Assessments

To follow Design Control, we need to show risk control and validation of user needs

Challenge: To incorporate the outcomes of the Comparative Analysis into the risk management process.

Comparative Use HF study

HF efforts are planned and revised during the project. A Comparative Use HF study's cost is hard to estimate, and could make or break the project.

HF is traditionally a qualitative science, but the Comparative Use HF study is a quantitative non-inferiority study.

Challenge: To calculate the sample size for the Comparative Use HF study.
(*d)* is the acceptable deviance above the error rate associated with the RLD.

Assumed error rates are needed to calculated the study sample size.

Which study power is required?

Challenges in the Development of Instructions for Use for Generic and Biosimilar Products

1. Whilst the Combination Product is generic, the design of drug delivery devices is restricted by IP and therefore whilst maintaining the same key operating steps, delivery devices will inevitably look different and may have minor differences in aesthetics or functionality.
   - Acceptability of these differences is managed through Comparative Analysis (discussed above)
   - Representation of these differences in the IFU leads to challenge in understanding the acceptable boundaries without firm guidance.
2. RLD IFUs are often outdated and do not consider the current *state of art* of User Interface Design.
   - At various conferences FDA have stated that an **approved RLD IFU confirms safe and effective use** of the proposed product IFU when it is the same as that of RLD.
   - This does not allow for development of IFUs considering the latest developments in User Interface Design and poses a challenge to Generics companies when seeking to ensure that the user interface provides clear, unambiguous information to the user.

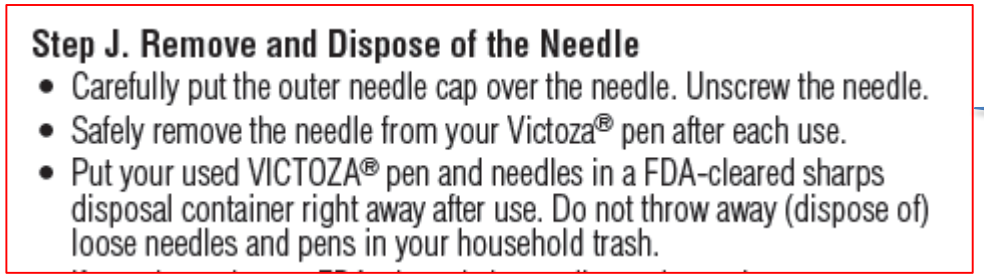
IFU Design

- Examples of areas of concern:
  - **Information Flow** – does the IFU present the necessary information in the optimal order to guide safe patient (user) use?
  - **Device presentation** – is there a device image at start to orientate the user with the product / component parts?
  - **Images** – are they clear and labelled? Do they add value or dilute the message?
  - **Warnings** – are warnings presented in appropriate location?
  - **Continuity** – do images and text maintain continuity in order to avoid patient confusion?
  - **Text** – could slightly different text could enhance users understanding or accuracy of use?
- Where IFU developer doesn't believe that RLD IFU meets these requirements there should be an allowance for enhancement of the IFU with appropriate justification and assessment of risk, in the substitutable product.
- Further discussion with and guidance from the Agency to find a balance that supports substitutability whilst allowing improvements to the user interface would be of significant benefit to both users and developers.

IFU Design

- **Information Flow** – does the IFU present the necessary information in the optimal order to guide safe patient (user) use?

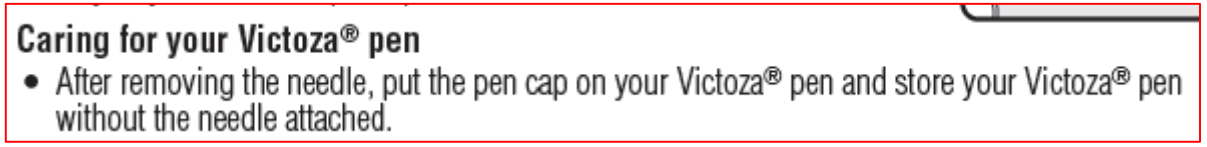
  e.g. warnings at end of IFU assume that user will read whole IFU before starting to use the device.
  E.g. Victoza® IFU:



Step J. Remove and Dispose of the Needle

- Carefully put the outer needle cap over the needle. Unscrew the needle.
- Safely remove the needle from your Victoza® pen after each use.
- Put your used VICTOZA® pen and needles in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) loose needles and pens in your household trash.

Step in IFU suggests that pen should be discarded with needle as soon as needle removed



Caring for your Victoza® pen

- After removing the needle, put the pen cap on your Victoza® pen and store your Victoza® pen without the needle attached.

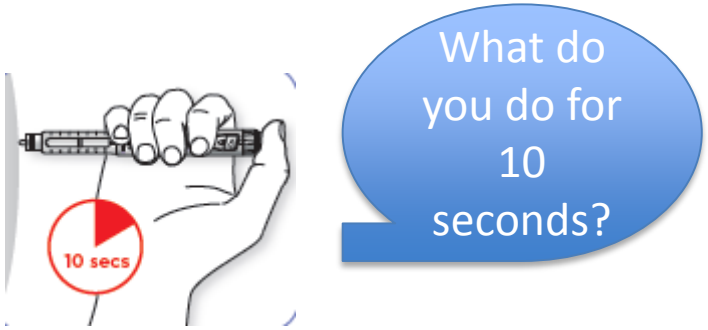
Not until a later section of general info is the instruction to keep and store pen following needle removal

- **Continuity** – do images and text maintain continuity in order to avoid patient confusion?

IFU Design

- **Device presentation** – is there a device image at start to orientate the user with the product/component parts?
  e.g. 'Remove outer needle cover' ……to some this could mean both needle covers, to others it could mean pen cap…without labelled description of components up front there will be confusion.

- **Images** – are they clear and labelled? Do they add value or dilute the message?



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Thank you

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