FY 2020 Generic Drug Regulatory Science Initiatives Public Workshop

Drug-Device Combination Products Breakout Session – May 4, 2020

Molly Story, PhD

Sanofi – Medical Device Development Unit

Comparative Human Factors Studies

Molly Story – 4 May 2020

Disclaimer

This presentation was prepared by Molly Story in her personal capacity. The opinions expressed herein are the author's own and do not reflect the views of her employer, Sanofi.

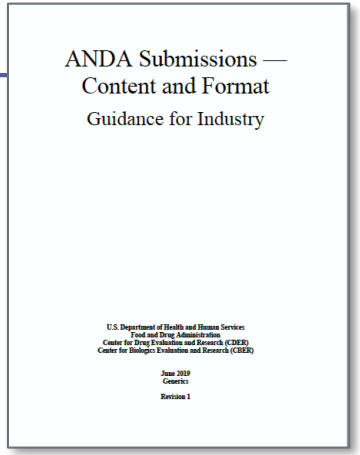
Human factors engineering for medical devices

- **Goal:** ensure that the medical device is **safe and effective enough** for use by the **intended users** to allow onto the market
  - **In the US**: Show that you followed recognized international standards and FDA guidance (such as the following) and that the test results were adequate:
    - ISO 14971:2019, *Application of risk management to medical devices*
    - IEC 62366-1:2015, *Application of usability engineering to medical devices*
    - FDA/CDRH Guidance (2016): *Applying Human Factors and Usability Engineering to Medical Devices*
    - FDA/CDER/CBER draft guidance (2016): *Human Factors Studies and Related Clinical Study Considerations in Combination Product Design and Development*
    - FDA/CDER draft guidance (2017): *Comparative Analyses & Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA*

Human factors engineering for medical devices

- Methods: qualitative, not quantitative
  - **Simulated-use testing** – sufficient for most HF questions
  - **Observe** intended users performing tasks of use.
    - **Essential tasks** = tasks required for use of the device for its intended purpose;
    - **Critical tasks** = tasks on which use error could result in harm.
  - **Interview** users afterward about any use errors & difficulties that occurred.
    - Get users' perspectives on why any use errors and/or difficulties occurred.
  - **Analyze** the data to determine root causes and priority for change.
    - Decide what caused the use errors and difficulties (**root causes**);
    - Determine what might have happened as a result (**consequences** & **severity**);
    - Determine what **user interface changes** are necessary to reduce the **use-related risks** to acceptable levels.

FDA/CDER Draft Guidance / Generics


ANDA Submissions —
Content and Format

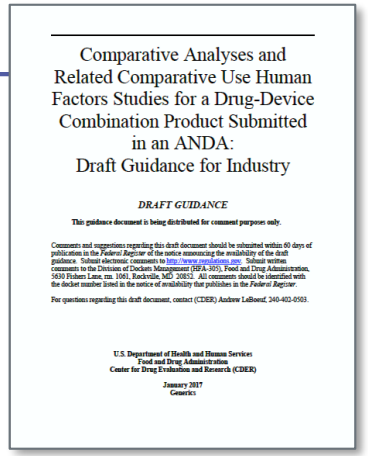
Guidance for Industry

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

June 2019
Generics
Revision 1

- **Background:** FDA/CDER/CBER (2019), *ANDA Submissions — Content and Format,* Section II
  - "Under section 505(j) [of the FD&C Act], an ANDA applicant can rely on FDA's previous finding that the RLD is safe and effective so long as the ANDA applicant demonstrates that the **proposed drug product** and the **RLD** are **the same** with respect to active ingredient(s), dosage form, route of administration, strength, and, with certain exceptions, labeling."
    - ANDA = Abbreviated New Drug Application; RLD = reference listed drug
  - Note that the regulation pertains specifically to the **drug product**, not the **drug delivery device**; the device (if any) is not mentioned

FDA/CDER Draft Guidance / Generics



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*.

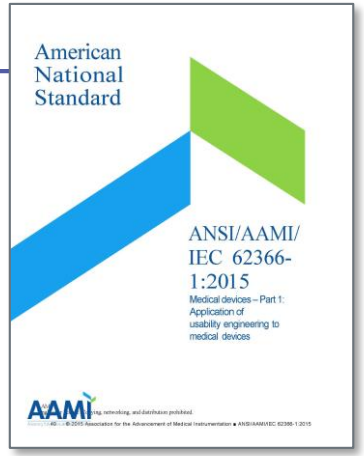
For questions regarding this draft document, contact (CDER) Andrew LeBoeuf, 240-402-0503.

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

January 2017
Generics

- **Background:** FDA/CDER (2017, draft), *Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA,* Appendix A.i
  - The goal is to "…confirm that the **use error rate**, for the critical tasks(s)… **is not worse** than the corresponding **use error rate** for the RLD when used by patients and caregivers in representative use scenarios and use environments…."
  - "FDA would generally accept a proposed generic combination product that had the same rates of error as the RLD, as demonstrated by an adequately designed comparative use human factors study or studies."
    - The terms "**severity**" and "**harm**" do not appear in the guidance document.

Int'l. Std. on HF for Medical Devices



- **Guidance from IEC 62366-1:2015**
  - Section 5.5, Select the hazard-related use scenarios
    - "The manufacturer shall select the hazard-related use scenarios to be included in the summative evaluation.
    - " The manufacturer shall select either:
      - "**all** hazard-related use scenarios; or
      - "the **subset** of the hazard-related use scenarios based on the severity of the potential harm that could be caused by use error (e.g. for which medical intervention would be needed)."
  - Annex A, section 3.21: rationale for definition of use error
    - "During the usage of a medical device, not every occurrence of a use error causes a **hazardous situation** and not every occurrence of a use error leads to **harm**. The same type of use error could lead to harm in one situation, while it is harmless in another."

Personal Analysis of Guidance Document / Generics

- **Aspects with which I agree:**
  - Compare the user interactions with **both products**, as identified in the task analyses and as described in the two sets of instructions for use.
  - Identify the possible use errors that users could make due to **user confusion** between the reference product and the proposed new product.
  - Perform an analysis to determine the potential for hazardous situations and harm resulting from **use errors associated with the differences in design**.
  - If the differences are more than "minor," perform a human factors evaluation of the **proposed new product** with the intended users:
    - People who are **naïve** to the device type, and
    - People who are **familiar** with the existing / predicate / RLD device(s);
    - Focus on the **critical tasks**, i.e. on which use error could cause **harm**.

Personal Analysis of Guidance Document / Generics

- **Aspects that concern me:**
  - Stance that use errors are equal, and number of use errors is meaningful.
    - Study participants might make **use errors on different tasks** with the 2 devices, leading to different hazardous situations with **different levels of potential harm**.
  - "**Minimize differences**" between the proposed new device and the RLD:
    - Appears in the guidance 5 times;
    - **Prevents** technological advancement or even mitigation of known risks.
  - Sponsors are encouraged to make their **instructions** the same, too.
    - A lot of old instructions are bad, especially if they were written before human factors assessments became expected and common practice.
  - No guidance is provided regarding **changes made to the RLD device** in the future.
    - What happens if the RLD manufacturer changes the delivery device? Must the generic be taken off the market because **it's no longer "the same"**?

Human factors engineering for medical devices

- **Human factors testing** assesses the **user interface**, *not the user.*
  - When use errors occur, they indicate that something went wrong in the **interactions** between user and device; and human factors engineers *blame the user interface, not the user.*
- Methods: qualitative, not quantitative;
  - ***Numbers don't tell the story because use errors are not equal.***

  - Common use errors might not matter.
    - Example: inserting a blood glucose test strip into a BG meter upside-down:
      - Up to 50% probability

  - Uncommon use errors might matter a lot.
    - Example: filling abdominal cavity, rather than pain pump, with pain medication:
      - At time of FDA action: 8 deaths and 270 serious injuries; occurrence rate : 0.01%

THANK YOU