Human Factors Engineering (HFE): Patient-Centric Product Design

Summary of the Podium Talks and Panel Discussion in the HFE Session of the IPAC-RS Symposium at RDD 2016 "Meeting the Quality Challenge for Orally Inhaled Drug Products" (April 21-22, 2016, Scottsdale, AZ)

Background on IPAC-RS: http://ipacrs.org/; Background on RDD: http://www.rddonline.com/

Slides and overall program from the Symposium are available at http://ipacrs.org/news-events/events/ipac-rs-symposium-at-rdd-2016-meeting-the-quality-challenge-for-orally-inha

Human Factors Engineering: Deployment in the Device Lifecycle

Julian Dixon (Team Consulting)

Human factors engineering (HFE) is an important component of any product development, but especially so for drug-device combination products (such as inhalers) because HF aspects may impact safe and effective use of the product. Increased attention to human factors has led to more formalized HF approaches being implemented by companies, as well as to more formalized regulatory expectations – such as those described in the 2016 final FDA guidance[1] and a new draft guidance[2].

In practice, HFE starts on "Day 1" of product development – through a clear identification of intended users, intended uses, and intended use environments. Such identification will require conversations with clinicians and other experts on the product development team. Next, potential use-related issues could be outlined from general considerations as well as from accumulated information on similar products (e.g., contained in public databases, user complaints, literature, or company's own files).

As the future product takes shape, the unique features of that particular drug and device will need to be analyzed from the perspective of HFE, which in turn would inform improvements or new directions in the design. Throughout product development, use-related risks will need to be re-identified and re-evaluated in an iterative fashion as the product design evolves. For this reason, a large number of smaller *formative* HF studies may be more valuable to the product developer than just a few large HF studies. Finally, an HF *validation* study would confirm appropriate design from the human factors perspective.

Over the product's lifecycle, HFE considerations have to be integrated with all aspects of product development, yet they are distinctly different from the other development functions, such as clinical trials or marketing research. Each area has its particular goals and tools, and although they can inform and support each other, they are not interchangeable or substitutable.

Human Factor Studies: Case Study – Instructions for Use for Respimat®

Sabine Kattenbeck (Boehringer Ingelheim)

This case study described how user feedback impacted the device leaflet's design. Respimat® is a soft-mist inhaler, which was a new type of inhaler when it was first introduced to the market in the early 2000s. Since its mode of operation and handling are much different from those of a pressurized metered dose inhaler (pMDI) or a dry powder inhaler (DPI), practical information about use-related errors with a soft-mist inhaler was non-existent at the time. The company, therefore, undertook a substantial effort to study human-device interactions in this case. Prior to the market launch, over 15 usability studies (formative HF studies) had been completed, and one clinical study with tens of thousands of patients was conducted where handling was the primary endpoint. Furthermore, patients' feedback was collected via questionnaires from regular clinical trials, and returned clinical trial samples of the device were analyzed.

After a decade of the product's presence on the market, the company made a decision to update Respimat's Instructions for Use (IfU) leaflet – because by then the company had additional information from user complaints, and because patients were being faced with an increased variety of device types, which increased chances of confusion and use error.

The IfU re-design started with a comprehensive risk analysis done by a multi-functional team of representatives from Production, Marketing, Call Center, and Development departments. Two versions of IfU were developed for testing. One ("focused version") was concise, focused on what should be done and why; while the '*do not*…' - type precautions were moved to a Q&A section of the package insert. The text in bullets was abbreviated, IfU's layout simplified and streamlined, images made larger, details on the inhaler display made clearer, and larger font was used throughout. The other ("comprehensive") version of the IfU had more details and explanatory information. There was no consensus among members of the multidisciplinary team, however, as to which version should be preferred.

An HF study was conducted to compare the currently used IfU, the revised comprehensive version, and the revised focused version. The study was international in nature and followed FDA guidelines. Eighty individuals participated as subjects, including patients (both naïve and experienced users), nurses, and doctors. As endpoints, the study used:

- Performance as assessed by an expert;
- Rating on the ease of use by participants; and
- Anecdotal comments and suggestions for improvements, collected via 2-hour one-on-one interviews of subjects, without prior handling training.

The study found that the focused version of the IfU was associated with fewest errors, was overall the easiest and most preferred in use. Interestingly, there were national differences with respect to preference of an IfU, but no national differences in actual use.

By contrast, the most detailed version of the IfU was associated with the most errors, was ranked by participants as the most difficult to use, and was least preferred. When it comes to instructions for use, therefore, the abundance of information matters much less than a simplified layout, short text, larger images, and clear differentiation between instructions to prepare the device vs. daily use.

The key lessons of this case study could be summarized as follows:

- Keep it simple, don't try to put everything in an IfU but only what's important.
- Focus on critical or less intuitive steps.
- Pictures and images are very important – they are viewed before the text is read.
- Selecting an optimal version is difficult, must test.

Case study: Human Factors Strategies to Address Common Use Errors for Dry Powder Inhalers (DPI) and Pressurized Metered Dose Inhalers (pMDI)

Jiaying Shen (Merck)

Such common use errors as lack of breath-actuation coordination (with pMDIs) or insufficient inspiratory force (with DPIs) may lead to patient's underdosing. If sustained overtime, underdosing may reduce clinical effectiveness. These steps in patient-device interaction, therefore, are considered critical tasks.

The impact of use errors can be evaluated via Human Factors (HF) studies, and supplemented with information obtained from clinical trials. To address identified use errors, a sponsor can employ a range of approaches, starting with improving the product's design, if possible. Next in the order of preference, according to ISO 14791 "Medical Device Risk Management", are such approaches as adding alarms to alert the user when an error is made, and optimizing IfU (keeping in mind, however, that not all users would read their IfU prior to use). In case there are residual risks that cannot be removed in other ways, user training may play a role, although this route is less preferred due to practical obstacles in the way of consistent implementation outside of clinical trials.

A patient's prior experience with other inhalers may contribute to use errors, and at the same time interfere with appropriate training on the new inhaler due to the patient's false sense of sufficient knowledge from prior use. For example, a pMDI requires a slow, deep inhale; while a DPI requires a fast and forceful quick inhale. But a person experienced with one type of inhaler may erroneously use the same technique on a different type of inhaler yet resist re-training. Furthermore, some DPIs require a twist, others a cap-load to dose, or a simple open-close to reload the dose; and there is currently no standardized IfU, increasing the potential for users' confusion.

Even after optimizing device design and IfU, residual use errors may remain. Clinical-trials' data could be used for additional information about the extent of clinical harm, if any, caused by residual use errors. In particular, early clinical data on a given device might be useful for understanding the impact of use errors. Information about use errors with similar previous devices could also be useful during development and regulatory interactions.

Roundtable Discussion
Panelists: Session speakers (J. Dixon, S. Kattenbeck, J. Shen) and Irene Chan (FDA/CDER/DMEPA)

Q There've been numerous studies published showing that 50% or more of patients have frequent use errors. What is the root cause? Is it because of insufficient training? Or because devices are not designed as patient-centric as they should be?

A Both. We can do better designs, but there will always be a gap. Users are very creative coming up with new ways to make errors. Nevertheless, improvements are possible and should be pursued. FDA and industry are keenly interested in innovations, including through digital tools to improve adherence and correct use.

Q Would there be value in a packaging with two levels of instruction? How would they be regulated?

A There are limitations to short IfUs, therefore companies must provide more complete details separately. Among non-inhalation products, there have also been instances of packaging with quick reference guides in addition to a regular, comprehensive instructions leaflet. FDA regulators have allowed such combinations if there is data to show that patients do not ignore important details, and if the shorter guide achieves its intent without creating new hazards. From FDA's perspective, a user interface includes the packaging, drug's pouch, IfU, as well as the product itself. All elements could be equally important in guiding the user, and thus will be evaluated by regulators from the HF point of view.

Q What is the panel's perspective on using clinical data vs. simulated-use studies to assess safety and efficacy of medical devices?

A Some companies have used information from clinical trials to support claims of safe and effective use. FDA, however, does not regard clinical trials as interchangeable with HF studies. One key difference is that clinical trials are conducted in a controlled environment, in circumstances unlike those of actual use. The extent of user training and investigator involvement do not match users' experiences in the real world. Another key difference is the study design, methodology, specific endpoints, and data interpretation. Clinical evidence, therefore, is additive to an HF validation; clinical data can be useful but should not be over-interpreted for the HF purposes.

Q Can at least the severity of harm due to use errors be estimated from clinical trials?

A Clinical results can be helpful but are not sufficient because there are other unknowns related to HF that are unavailable from clinical data. At the same time, engineers need to work with clinicians to assign severity scores when conducting their risk analysis. ISO standard 14791 recommends severity assessment based on clinical data.

Q Half of use errors with pMDIs is the same regardless of which product is used. Is there any potential to improve pMDIs themselves? It is an old, established technology. What is a realistically achievable limit for correct use of pMDIs, in your opinion, e.g., 60-70%?

A pMDIs can be, and are being improved - not just the canister but the user interface, including IfU. FDA does see differences from one company to another. HF studies, however, are not set up to measure percentage of correct use, and FDA's acceptance criteria for HF aspects are not quantitative. The goals and nature of human factors are fundamentally qualitative. For example, an error that occurs less frequently but has a greater potential for harm would be of concern to the regulatory Agency.

Q A 2016 Draft FDA Guidance[2] from the Office of Combination Products mentions different types of studies. What are the linkages between simulated-use study, actual-use study, and pivotal trials?

A The focus of an actual-use study is strictly on human factors, and this type of study is not often used for inhalation products, although other product types have used them more frequently. For example, for injectables with highly concentrated formulations that may cause pain and therefore affect use, an actual-use study would be recommended. Or a specific clinical review division may request an open-label study, perhaps because they have seen some issues. In inhalations, the majority of HF studies are simulated-use. A simulated-use study is a must because it shows what a user may do when an actual product is in play, not a placebo. The environment of use also matters (e.g., home, hospital, etc.). Industry should discuss their questions and study designs with FDA as early as possible.

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This summary was prepared by the IPAC-RS Secretariat.

If you have questions or would like further information, please contact info@ipacrs.org

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