MEETING THE INCREASING REQUIREMENTS FOR HUMAN FACTORS CONSIDERATIONS

Human factors engineering (HFE) is now an essential requirement for all new drug delivery combination product approvals to ensure devices are safe and effective for users. This can represent a significant challenge for pharmaceutical companies, which need to make sure that any changes required happen as early as possible in the development process to avoid costly mistakes later on. Karen Guerrero, PhD, Medical Affairs Safety Platform Manager at BD Medical – Pharmaceutical Systems, outlines how they can help to streamline HFE for pharmaceutical manufacturers.

In the past, drug delivery devices were considered primary or secondary packaging, with little effort given to understanding how people interacted with the technology, or the resulting impact of user interface design. Today, it is recognised that drug delivery device presentation can have a significant impact on convenience, ease of use and acceptance by patients who self-inject. Devices represent a critical part of the user experience, and must be proven safe and effective to use prior to receiving regulatory approval.

Assessing the safety and efficacy of device use is the focus of human factors engineering (HFE), and is a required component of the regulatory approval process. HFE is defined as "the application of knowledge about human behaviour, abilities, limitations, and other characteristics of medical device users to the design of medical devices, including mechanical and software-driven user interfaces, systems, tasks, user documentation, and user training to enhance and demonstrate safe and effective use."[1]

Today's regulators demand more stringent requirements to ensure medical devices are safe and effective for the intended users, uses and use environments (Figure 1). HFE is now a prerequisite for all new medical device and drug device combination product approvals.

With the combination product market expected to reach US$177.7 billion (£128.8 billion) by 2024,[2] and more combination products targeted for home use by patients and lay caregivers, pharmaceutical manufacturers will need to make significant investments in HFE to secure approval for their new drug-device combinations. Moreover, with the inevitable increase in market penetration by biosimilars,[3] the usability, acceptability and favourability of a manufacturer's delivery device could either increasingly serve as a differentiator in crowded therapeutic spaces or comparative human factors studies could also be required to give evidence of the similarity between the Reference Listed Drug (RLD) and the drug delivery device.

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Dr Karen Guerrero
Medical Affairs Safety
Platform Manager
T: +33 4 76 04 58 15
E: Karen.Guerrero@bd.com

BD Medical
– Pharmaceutical Systems
11 rue Aristide Bergès
ZI des Iles
BP4
F-38801
Le Pont de Claix
France

www.bd.com

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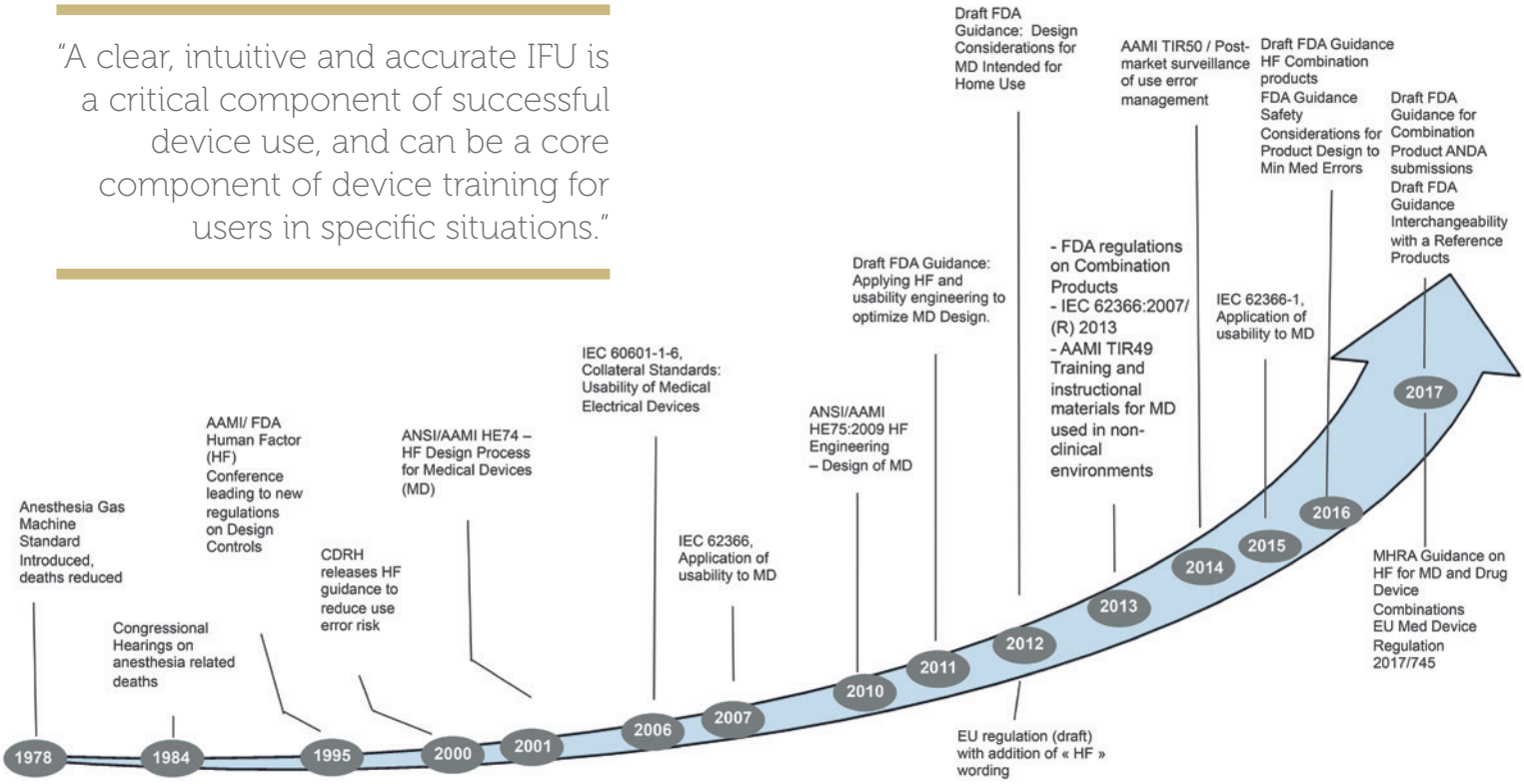

Figure 1: Requirements to ensure medical devices are safe and effective.

MITIGATING THE BURDEN ON PHARMACEUTICAL COMPANIES

For pharmaceutical companies, the complexity of bringing various components from different manufacturers together to create a combination product can result in disconnects and inefficiencies in generating the required usability data. Pharmaceutical development focuses on formulation first, resulting in device considerations often happening later in the development process.

From an HFE standpoint, the later in the development process that correctable use errors are identified, the costlier it is to fix them and the greater the potential impact on market launch.

As a trusted leader in the medical device industry, BD is rightfully focusing on the end user and placing emphasis on building and sharing HFE capabilities. BD has taken the initiative to build HFE capabilities and conduct comprehensive HFE testing on its devices and components, and then may provide the HFE data (when available) and regulatory guidance to their pharmaceutical customers.

The ability to obtain trustworthy data much earlier in the development process provides pharmaceutical companies with leverage that enables them to focus on other critical areas that require their resources and attention, and move towards launch sooner. This benefit is especially valuable to small pharmaceutical companies that lack resources or expertise, but can also benefit larger companies by freeing resources for other activities.

OPTIMISING DESIGN FROM CONCEPTION TO VALIDATION

BD's knowledge and experience of its products place it in a unique position to optimise combination product development at every stage. For recent products and those under development, this is accomplished through an applied, iterative, patient-centred design approach, where early studies with patients inform requirement definition and device design, which are later verified by patients through experimental investigation (Figure 2, next page). Moreover, BD's existing rigorous product testing, instructions for use (IFU) development, and design validation can streamline HFE for pharmaceutical manufacturers and improve time to market.

Design Conception

In the design conception stage, BD conducts formative studies with users to ensure the device design is robust enough to move to validation. This requires a deep understanding of the intended user populations, including the physical, cognitive and disease-related limitations of those particular patients, and potential sources of error. It also involves ensuring the study participants are representative of end users and the product can be used safely and effectively by the targeted end users. This means that during the recruitment phase for the usability studies, BD ensures that a broad population of both experienced and naive users are surveyed across multiple countries to ensure proper representation.

In addition to the formative usability testing, BD also utilises a combination of human factors and market research to improve insights into barriers to adherence, which informs the delivery device design. The collaboration of commercial, medical and design teams early in the device development process is key to developing a product well-accepted by the intended end-user populations.

Throughout this process, BD engages industrial designers to refine device design so that it reflects patient feedback and improves usability. BD has evolved its approach to device design not only to work for the target patient populations, but to provide an aesthetic appeal that may increase confidence and reduce anxiety in patients who self-inject.

An example of the benefits of this upfront testing is the favourable usability results

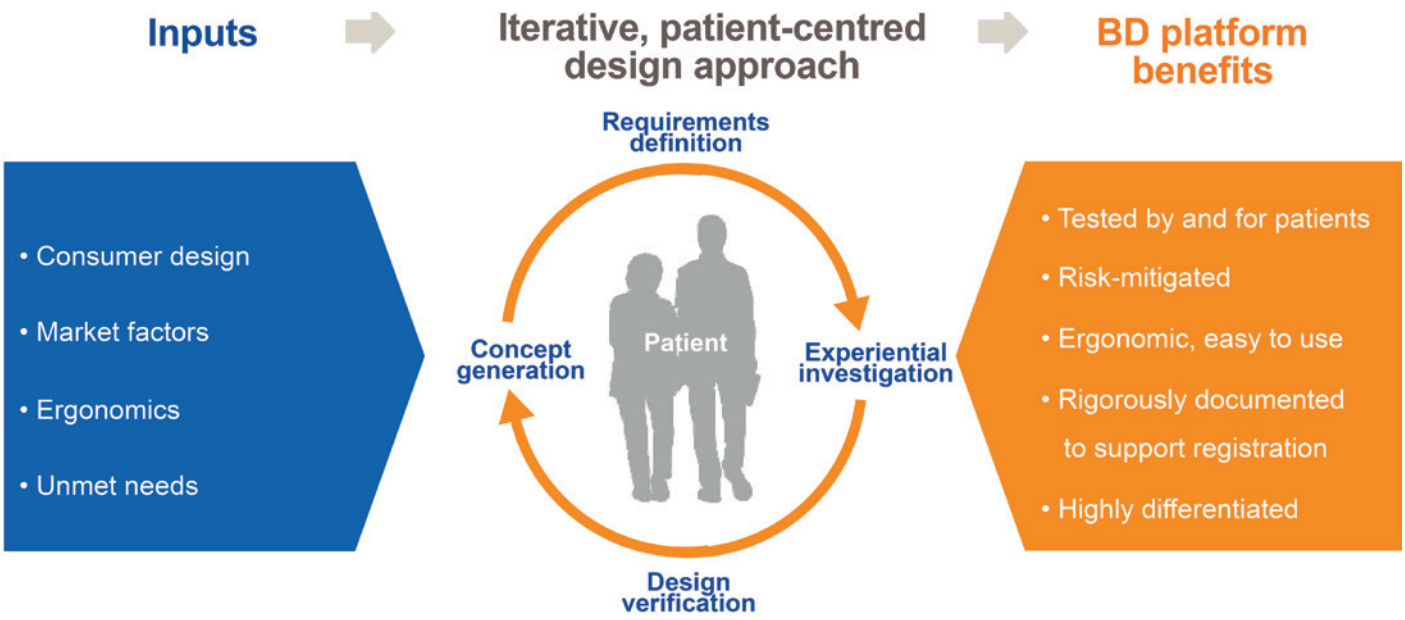

Figure 2: Using an iterative, patient-centred design approach to inform device design.

that were obtained using the BD UltraSafe Passive™ Needle Guard and secukinumab with patients who have moderate to severe psoriasis. This study found that the syringe equipped with the safety device was effective, with an acceptable safety profile and high usability.[5] BD's rigorous testing increased the confidence of a positive outcome.

BD can provide guidance to pharmaceutical manufacturers on how to design and conduct formative studies with its product and the intended users. This allows manufacturers to identify critical tasks very early on, avoiding potential design issues, and having to iterate to move to the next stage of development with the most favourable design possible.

Risk Management

The risk management aspect of BD's HFE offering includes the development of IFUs to support and enhance the safe and effective use of combination products. A clear, comprehensible and accurate IFU is a critical component of successful device use, and can be a core component of device training for users in specific situations. If the IFU is inadequate, it may result in user errors or difficulty performing tasks, and ultimately require additional testing to ensure safety risks are mitigated before approval.

As a result, entering design validation with a robust IFU is key to enabling development to proceed efficiently. BD strongly recommends that pharmaceutical customers should take into consideration the IFU developed for the device for their final combination product labelling.

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Design Validation

During design validation, BD conducts a final summative validation study to confirm that the target users can safely and effectively use the final device design. BD has vast expertise in this area with strong capabilities in performing these simulated use studies for human factors testing. The intended users are tested for their ability to complete the series of critical tasks with and without training and use of the product's IFU. The output of this study supplies usability and acceptability data to help meet the health agencies' (US FDA/MHRA[4]) HFE requirements and support pharma company combination product filings.

As an additional service, BD can provide insights from its validation testing, along with data from previous formative studies, to help pharmaceutical manufacturers develop the appropriate protocol for their specific product filing to reflect different intended use populations, viscosities and volumes. These could include the study design and methodology, protocol, intended use, endpoints, and target user population and recruitment.

Market Launch

BD can provide commercial, medical and regulatory resources to support pharmaceutical companies' launch strategies. BD has a strong history of commercial success with combination product launches, with a recent example published in the *British Journal of Dermatology*.[5]

Within this specific publication, one of the objectives of the authors was to demonstrate efficacy, safety and usability of a prefilled syringe (PFS) with a safety device for self-administration by patients with moderate-to-severe plaque psoriasis. The study concluded that the PFS usability was high with 100% of subjects successfully self-administering treatment with high acceptability.

Overall, this positively illustrates how a combination product design can offer patients the clinical benefits of a drug, with increased convenience.

LEVERAGING INTEGRATED SYSTEMS

In addition to HFE services, the integrated nature of BD device components, including primary containers, secondary delivery systems (e.g. autoinjector or wearable injector) and add-on needlestick safety

guards, facilitate streamlined usability testing and easy-to-use product design. Because BD makes and tests these components individually and together from a technical and HFE standpoint, these data can inform pharmaceutical company test protocols and reduce the risk of unforeseen issues throughout the process.

For pharmaceutical manufacturers, this could mean reduced delays by avoiding re-testing of individual components and minimising device failures associated with a non-integrated system (e.g. injection depth variability, syringe breakage, incomplete injection). It also means increased confidence that the combination product will ultimately operate in a user-friendly manner when brought to market.

NAVIGATING REGULATORY REQUIREMENTS

Increasing regulatory requirements, both in the US and globally, when it comes to drug device combination products have created added complexity for pharmaceutical manufacturers to navigate. This is particularly disruptive for smaller manufacturers that may be resource-constrained to focus solely on the drug product itself, or for others just entering the combination product space.

BD offers HFE and regulatory affairs services to guide customers throughout the process, including providing documents and guidance to support their filing and ensuring they meet regulatory agency requirements. BD's Regulatory Affairs team has extensive experience with legislative and regulatory bodies at the local, regional and international levels, and can advise customers accordingly.

Figure 3: Elements that facilitate speedy time to market.

BD's ability to provide data on device testing, inputs to HFE protocol development, regulatory strategy or even conduct testing for the pharmaceutical company with their drug product in the BD device, can help reduce regulatory hang-ups and speed time to market (Figure 3).

In addition, BD can provide valuable insights to manufacturers seeking to "lifecycle manage" a product from one container or delivery device to another, such as from a PFS to an autoinjector. BD's ability to offer customised containers and devices enables support for evolving portfolios.

CONCLUSION

The evolving landscape of combination products and human factors engineering requirements from regulatory agencies has increased the burden on pharmaceutical companies that have historically been primarily focused on drug efficacy.

Device manufacturers should no longer be considered suppliers of components but instead as partners in the combination product development process. As a result, it is important for device manufacturers to provide support to pharmaceutical companies with their design validation requirements, especially as it relates to usability and ease of use of the delivery device.

An effective collaboration across device teams ultimately contributes to successful product development and patient acceptance. Furthermore, selecting a delivery device that has been developed by a leading medical device provider instills confidence that the device has been designed to meet end-user requirements, perform consistently within a clinical trial and also meet regulatory authority combination product regulations.

ABOUT THE COMPANY

BD is a global medical technology company advancing the world of health by improving medical discovery, diagnostics and the delivery of care. BD leads in patient and healthcare worker safety and the technologies that enable medical research and clinical laboratories. The company provides innovative solutions that help advance medical research and genomics, enhance the diagnosis of infectious disease and cancer, improve medication management, promote infection prevention, equip surgical and interventional procedures, optimise respiratory care and support the management of diabetes. The company partners with organisations around the world to address some of the most challenging global health issues. BD has more than 45,000 associates across 50 countries, who work in close collaboration with customers and partners to help enhance outcomes, lower healthcare delivery costs, increase efficiencies, improve healthcare safety and expand access to health.

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ABOUT THE AUTHOR

Karen Guerrero is Medical Affairs Safety Platform Manager for BD Medical – Pharmaceutical Systems. She contributes to product design, from concept phase (medical input) until product launch (clinical and human factors impacts assessment for BD drug delivery devices), in the context of BD-sponsored and BD customer-sponsored projects. She holds a PhD in Physiology and Pharmacology and has been working for several years in the medical devices research field.

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