APPLYING DEVICE DESIGN CONTROL CORE PROCESSES TO THE SELECTION OF AN OFF-THE-SHELF DRUG DELIVERY DEVICE

In this article, Lilli Zakarija, President, EdgeOne Medical, examines the selection of off-the-shelf drug delivery devices by pharmaceutical and biologics companies, and shows how employing device design control processes can improve the outcome of the decision, helping to avoid costly, time-consuming mistakes and ensuring the best device is chosen.

The selection of off-the-shelf (OTS) drug delivery devices is no small task for a drug/biologic development program. In the US market, a key benefit of selecting an OTS shelf delivery device (such as a pen/autoinjector or ambulatory pump) is that it has already been 510(k) cleared by the FDA. One would assume that FDA clearance implies a robust design verification package exists (including, amongst other things, human factors formative and summative studies and data per ISO 11608 standards for pen injectors).

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Some companies that have minimal internal device expertise don't always realise that not all delivery devices are created equally and, by default, just because the device was cleared by the FDA doesn't mean the device design is adequate for their specific drug/biologic needs.

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LEVERAGE DEVICE DESIGN CONTROL CORE PROCESSES

When scanning the landscape of drug delivery devices, we see a wide range of options whose complexity is increasing as more of these devices incorporate embedded smart technology. While there are many delivery devices, what we can safely assume for each device is that it was designed with its own specific set of user needs and requirements. The output of those requirements and design efforts is the marketed design. As such, the requirements for a specific delivery device may not completely align with a drug/biologic company's needs. The best way to approach the process of selecting a delivery device is to apply some of the same design control principles for the combination product as was used in the development of the drug delivery device. Specifically:

1. Requirements: define your specific user needs and business requirements
2. Assessment: assess the array of available device options against requirements
3. Risk Analysis: for those requirements that are not met, conduct a risk analysis
4. Decision: select best delivery device for the drug/biologic.

Ms Lilli Zakarija
President
T: +1 312 300 6642
E: lilli.zakarija@edgeonemedical.com

EdgeOne Medical, Inc
455 N. Campbell Ave, #2N
Chicago
IL 60612
United States

www.edgeonemedical.com

Principle	Specific Steps	Tips
REQUIREMENTS: Define your specific user needs and requirements	1. Identify and list requirements- Potential sources for critical requirements include: patient (user); dosage; manufacturing; safety; regulatory; and business 2. Rank and prioritise requirements	• Solicit input from cross-functional team as well as stakeholders • A requirements list does not need to be exhaustive, but make sure everyone agrees on the most critical requirements
RISK MITIGATION: For those requirements not met, conduct a risk analysis	1. Source samples (whenever possible) and evaluate: a. Bench top b. Focus group / prelim human factors assessment 2. Document the output of assessment (e.g. spreadsheet)	• Make a quick note of reference that supports evidence identified or developed to support each requirement. This will come in handy later • If the drug/biologic has unique properties (viscosity and density) don't forget to inquire with the device manufacturer about the range of liquids used to evaluate their device
ASSESSMENT: Assess the candidate devices against requirements	1. Explore risk mitigation strategies to increase submission clearance and/or commercial success of certain requirements 2. Assess risk mitigation strategies that support requirements and business objectives	• Keep track of mitigating strategies that need to be implemented into the formal project once design control is initiated
DECISION: Select best device option	1. Select the device that satisfies the majority of requirements	• Keep track of all information in a spread sheet and use this as a starting point for design control documentation

Table 1: Simplified delivery device selection process.

Before diving into the details of this four-step process, consider the last time you had to make a big decision where you knew there were going to be trade-offs. Maybe it was the purchase of a new car or a new home. You write down your wish list (requirements), you look at your options and trial things out (assessment), you figure out what you may not get and how to adjust (risk analysis), and then you make your selection (decision).

The same selection principles we use for making these types of decisions apply directly to the selection process of OTS delivery devices, with the primary difference being a vernacular and a formal documentation process that is more commonly understood by device development team members than the drug/biologic development team.

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The four-step process is further explained in Table 1, with detailed examples of types of things to consider in each step along with tips.

In order to provide tangible considerations for some of the steps in the process, following are some examples (or mini-case studies) of situations that different firms encountered.

1. Requirements

Often a single individual is tasked with the responsibility of identifying the delivery device options for a specific drug/biologic program. In one specific example, a drug company was working on the identification of a pen injector their drug. They assumed, since the pen injector was already 510(k) cleared, that they didn't need to do any other work/documentation for their files. Before the formal decision was made to select and incorporate the pen injector into the drug development program, a cross-functional team of individuals was deployed to audit and qualify the pen manufacturer.

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The manufacturer passed the audit, but the team ultimately chose a different device because later in the drug development process, other critical device requirements were identified that ultimately disqualified the original injector pen manufacturer as a candidate. Had there been consideration of requirements beyond simply requiring 510(k) clearance, the drug manufacturer could have saved time and money to avoid the audit and qualification of a pen injector manufacturer they will never use.

2. Assessment

Another company was prepared to select a pen injector for their drug even though they had received some preliminary feedback that their patient population gave the particular injector low usability marks. The company wanted to select the device for the sole reason that the device had recently been cleared for use in the US market. The team believed that the recent FDA clearance decreased their time and risk to commercialisation. While this may be true, the firm didn't realise that they were going to need to generate their own human factors data (formative and summative) to support that this specific device met the requirements of their specific drug patient population. The drug company's preliminary feedback data already pointed to the fact that they would mostly likely have issues generating satisfactory summative studies with the targeted pen injector.

3. Risk Analysis

When issues are identified, risk mitigation discussions allow for brainstorming on how best to resolve those issues. A drug company was assessing two different designs for their own custom drug delivery device, and was seeking an external recommendation on

which device design to pursue given the unique risks inherent with each design. In order to develop the recommendation, the drug company was asked to provide their risk profile for that specific project. The response was: "We are willing to take high risk". The external recommendations were presented to the drug company keeping in mind the drug company's risk profile, but upon presentation of the recommendations, the drug company immediately said they were not willing to take on that much risk for the project.

This was not a surprise, and the next layer of recommendations was presented with a lower risk profile. Every organisation has a different (business) risk profile. As such, each company needs to determine what risk mitigating strategies may or may not be palatable for their own business.

4. Decision

There are many examples of OTS devices being selected for commercialisation, but the point to highlight in this step is not that the selection has been made. Rather, by making the selection and gaining business consensus to proceed with a particular device, this decision is the trigger for initiation of design controls to develop formal documentation that supports the device selection, along with formal qualification testing of the device for the specific drug or biologic. This is an important point, because despite all the interpretation and discussion about the recent FDA combination product regulations, one of the pain points that has surfaced in a recent survey of companies in the combination product space,[1] is that companies are still confused about how to handle development of combination products where one of the constituents is an OTS medical device.

This pain point is a broad statement. However, one of the myths consistently encountered is "OTS devices are already marketed and cleared medical devices by the FDA, therefore no further documentation is required". It's perceived as a simple "plug-and-play" scenario. Unfortunately, it isn't quite that simple. Combination product companies, per the new regulations, must follow design control processes even if the selected device is OTS.

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SMOOTHER TRANSITION INTO FORMAL DESIGN CONTROL

The obvious benefits of applying design control best practices to the selection of an OTS delivery device include:

- An integrated approach that seeks to incorporate critical cross-functional and stakeholder input from the beginning
- Early identification of potential risks
- Exploration of risk-mitigating strategies.

The additional benefit in following this process is that all the information and content generated directly feeds into the formal device design control documentation that commonly begins upon selection of the device. This simplifies the start of the device documentation and allows the team to continue to build on the information already generated, rather than starting from step one and rehashing information already sourced and reviewed.

Bridging the transition into formal device design controls is still a struggle for some companies, and this could be a simple method of aligning the team toward the desired goal of a qualified OTS device for their targeted drug or biologic.

REFERENCE

1. *"Highlighting Challenges in the New Combination Product Regulatory Landscape". EdgeOne Medical: Report, February 2016.*

ABOUT THE AUTHOR

Lilli Zakarija is co-founder and president of EdgeOne Medical, Inc, an ISO 13485-certified medical device testing firm and consultancy focused on supporting combination products through the device development (design control) process. Prior to founding EdgeOne Medical, Lilli developed and led the global device engineering function for Baxter's BioScience division (now Baxalta) in support of all their combination (biologic & device) products and single-use, disposable medical devices. Ms Zakarija has a BS in Biomedical Engineering and a Masters in Engineering Management from Northwestern University (Evanston, IL, US), and an Executive MBA from Kellogg School of Management (Evanston, IL, US).