DEVICETALKS | BOSTON

Medical and Drug Delivery Device Design for Biocompatibility

WHITE PAPER

PSN LABS

Overview

To be in alignment with ISO 10993 and other relevant standards, manufacturers of medical devices and drug delivery systems must incorporate biocompatibility testing into their design process. Design for biocompatibility involves considerations around material selection, manufacturing techniques, and device build that ideally must be made in the early development stages to avoid biocompatibility issues in the final product.

By integrating such considerations upfront into the design of their products, manufacturers can ensure patient safety, streamline regulatory compliance, and minimize risks of delays and recalls.

Biocompatibility is a hot topic due to growing awareness of its impact on patient safety.

The purpose of evaluating a medical or drug delivery device's biological risk—or its biocompatibility –is to ensure **patient safety**.

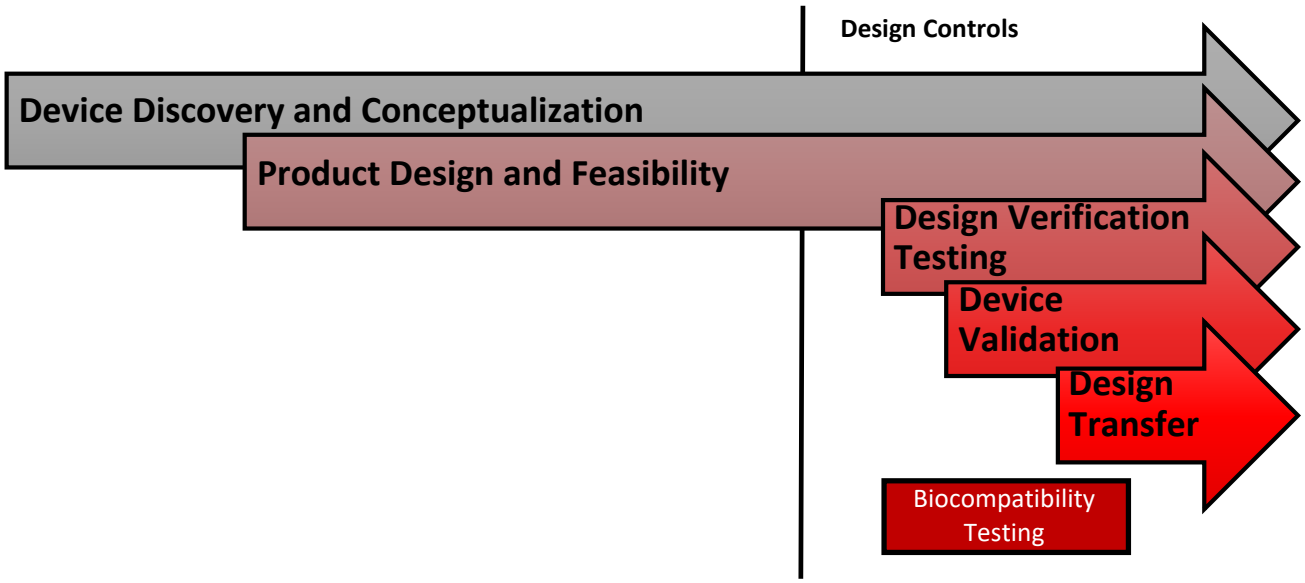
The FDA recently released industry guidance that reflects the agency's more holistic and stringent approach to biological risk evaluation. As a result, costs for biocompatibility compliance and regulatory submissions to include 510(k) review timelines have increased, while 510(k) clearance rates have decreased.

To manage this heightened scrutiny, device manufacturers can use the concept of **design for biocompatibility (DFB)**. The concept rests on the idea that testing equipment, such as that used by PSN Labs, has evolved so much that it can detect and measure infinitesimal traces of potentially hazardous chemicals in materials used to manufacture medical products. By partnering with testing labs with such equipment and capabilities, companies can leverage these resources early in the product development process and avoid issues later.

> "The concept of design for biocompatibility is more important today than at any time because the available equipment can detect these things. And when you detect and characterize that hazard, you need to understand what the risk is to the patient."
>
> –Matthew Heidecker, PSN Labs

Yet, the way biocompatibility testing is typically done today—at the very end of the product development cycle—contrasts with this new awareness and prioritization of biocompatibility (Figure 1).

Figure 1. Biocompatibility testing today



> "You may discover things at that stage that cause you to have nine-to twelve-month delays in your product launch cycle, because you potentially could fail biocompatibility."
>
> –Mark Burchnall, PSN Labs

PSN Labs' approach is radically different, as it applies a biocompatibility lens from the earliest upfront portion of the product development process (Figure 2). Thus, in addition to testing at the end, it reviews relevant use cases, makes material selection, and conducts scoping studies in prior stages.

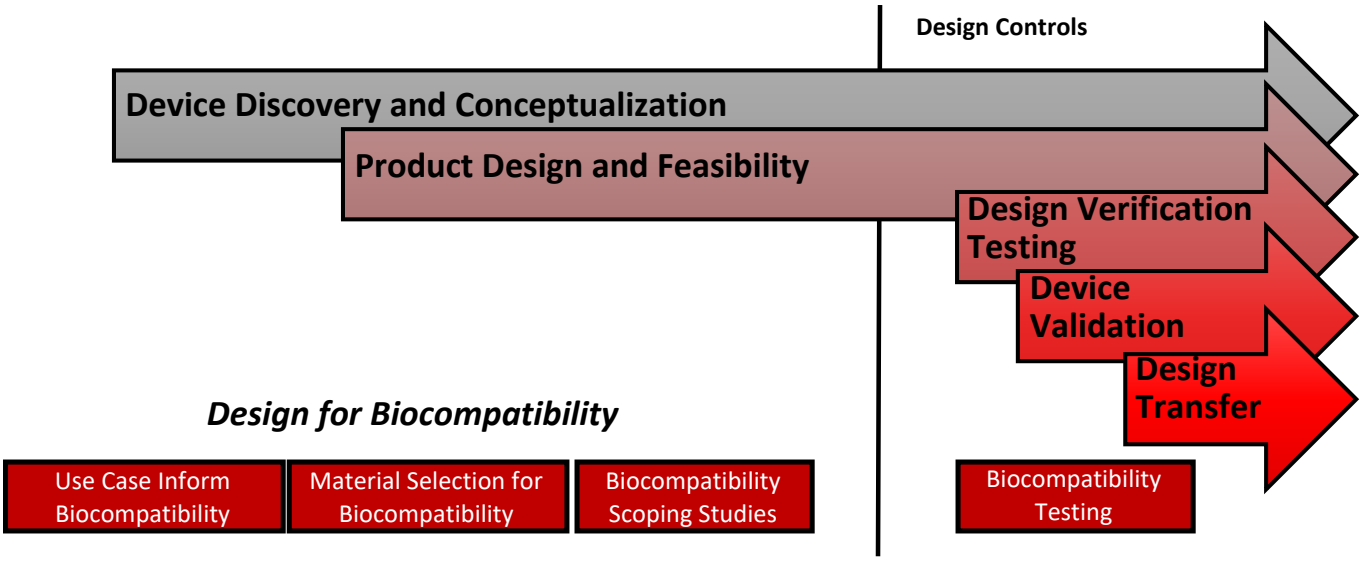
The DFB concept in more detail: What is it?

As Figure 1 highlights, device manufacturers tend to treat biocompatibility testing as a *discovery* process at the back end of the product development cycle rather than as *confirmatory* checkpoint.

Instead, what they should aim for is to ensure their products have been designed in a way that guarantees products will pass the biocompatibility test. "What we want to do is create biocompatibility [along the way] and make sure that testing on the back end is confirmatory and not discovery," Mark Burchnall, engineering director at PSN Labs, said.

The way to achieve this goal is to educate device design engineers—who are usually familiar with other DFx concepts, such as design for manufacturability, design for assembly, and design for reliability—on the importance of DFB and provide them with the tools to incorporate DFB principles at the early stages of product development.

Figure 2. PSN Labs' approach to biocompatibility evaluation



Manufacturers must incorporate five key aspects of DFB into product development to ensure compliance with DFB principles.

Those aspects concern usability, device design, material selection, manufacturing assembly, and screening and testing. Specific considerations and guidance on implementing those aspects are provided in the table below.

"The point is to understand the processes, to understand what you're doing, and to have controls in place. That's really what the FDA wants to see—they want to see that you've taken a risk-based approach to [product development]," Matthew Heidecker, vice president and principal scientist at PSN Labs, said. He emphasized that having internal conversations that help R&D and engineering teams understand the nuances and implications of product design can make a huge difference.

> "Having these conversations early in the development process is what makes design for biocompatibility sustainable, it's what makes the industry sustainable, and it's what makes the development process go less expensively and quicker."
>
> – Matthew Heidecker, PSN Labs

	Considerations	Guidance for implementation (Issues R&D teams should understand)
1. Usability	• Form, fit, and function must be addressed from a biocompatibility perspective • Risks to patient safety associated with the use of the device must be understood • Instructions for use must be done with biocompatibility in mind	• Whether the device is intended as single use or reusable • Severity of the outcome for failing biocompatibility • Contact duration with the user (limited, prolonged, permanent) • Contact region (blood, skin, tissue)
2. Device design	• Product development must follow a biocompatibility-informed risk-based approach • Design inputs must capture biocompatibility end goals and tests required at conclusion • Engineering must incorporate biocompatibility guidance	• Device shelf life • Device use environment • The balance between functional performance and safety goals • The impact of manufacturing techniques
3. Material selection	• Construction materials, including appropriate grade of plastic, must be selected on ability to meet biocompatibility requirements • Identification of correct materials at the start of the development cycle can minimize testing risk at the end	• Additives • Color • Standards such as USP Class VI • Medical/healthcare grade resins • How materials are processed vis-à-vis effects on biological safety (e.g., mold release, sterilization techniques, additive changes)
4. Manufacturing assembly	• Material processing should be paired with appropriate controls • Contract manufacturing should be compatible with clean room controls, ISO 13485 quality system, change control processes, and appropriate material handling and sourcing • Manufacturing representative prototypes should be used early in the development cycle	• The impact of assembly techniques on biocompatibility • 3D-printed components are not biocompatibility surrogates • Processing techniques may degrade polymers and affect functional and/or biocompatibility requirements
5. Screening/ Testing		• Consider USP Class VI materials • Consider assembly mechanisms that do not rely on adhesives or processes that can introduce contamination or degradation • Screening tests should be incorporated in early development stages to inform material selection

Standards adoption headwinds can serve as a signal to device manufacturers to do the right thing.

Despite growing awareness about the importance of biocompatibility assessments of medical and drug delivery devices, a major obstacle to integrating biocompatibility considerations into design is the disconnect between the new information and guidance coming out and their non-adoption in biocompatibility test standards. This disconnect produces ambiguity in manufacturers and testing laboratories, as well as jeopardizes patient safety when manufacturers fail to adopt standards aimed to be protective.

Another questionable trend for which the FDA is on high alert is so-called answer-shopping. Answer-shopping occurs when a manufacturer sends units of their product to multiple testing labs in anticipation that at least one lab will provide a favorable biocompatibility assessment; the FDA has pointed to regions in Asia where unqualified labs tend to flourish.

To avoid the temptation of answer-shopping, manufacturers should choose their lab partners carefully by looking at their accreditations, data processes, and staff they use to evaluate products. Any lab can say that they do ISO 10993-18; the real question is—are they actually accredited for each part of the process, as ISO/IEC 17025:2017 is not an umbrella standard? It applies to each and every test and many labs are not accredited for the tests that they ultimately do.

Further, these standards are not a one-size-fits-all type of test. The experimental paradigm is device and use case dependent. As a lab, PSN Labs tailors the experimental structure to the device whereas most labs require you, the device maker, to tell them what to test. This delineates PSN Labs and provides a competitive advantage.

As a cutting-edge company in the space of accelerated ageing and end-of-life biocompatibility, PSN Labs has positioned itself to be at the forefront of FDA requirements on end-of-life biocompatibility which continue to evolve in real time.

"The FDA is interested in what we're all interested in—which is patient safety, and patient safety across the life of the device. Chemical characterization is the key puzzle piece and you want to go with a lab that is highly experienced in this arena," Heidecker observed.

> "Biocompatibility testing is not a foolproof approach—it depends on your device and on a multitude of other factors. Education is key."
>
> –Mark Burchnall, PSN Labs

Contributors

Mark Burchnall
Engineering Director, PSN Labs

Mark is a product development consultant with over a decade of experience in the Medical Device and Pharmaceutical sectors. As the Director of Engineering at PSN Labs, Mark leads the engineering department, offering invaluable support to clients in new product development, test method development, functional prototyping, contract manufacturing, and on-market remediation. His team specializes in designing devices that incorporate various design principles, including manufacturing, assembly, sustainability, biocompatibility, reprocessing, and reliability.

Mark's background encompasses the development of innovative healthcare solutions in areas such as drug delivery, surgical robotics, pharmaceutical packaging, and catheters. His expertise ensures patient safety and regulatory compliance throughout the design process. Mark holds a Bachelor of Science in Mechanical Engineering from Purdue University and a Master of Science in Mechanical Engineering from the University of Cincinnati.

Matthew Heidecker, PhD
Vice President and Principal Scientist, PSN Labs

Matt Heidecker is the Vice President and Principal Scientist at PSN Labs. Matt's background includes a B.S. in Plastics Engineering Technology from Penn State-Erie, and a Ph.D. in Materials Science and Engineering from Penn State University. He has spent the last 17 years working in a variety of industries across the world, with the past 7-years at PSN Labs. PSN Labs focus on wholistic product development, testing, and manufacturing that provides a harmonized approach which leads to successful biocompatibility outcomes for medical devices as the focus is on appropriate material selection, design, and manufacturing principles.