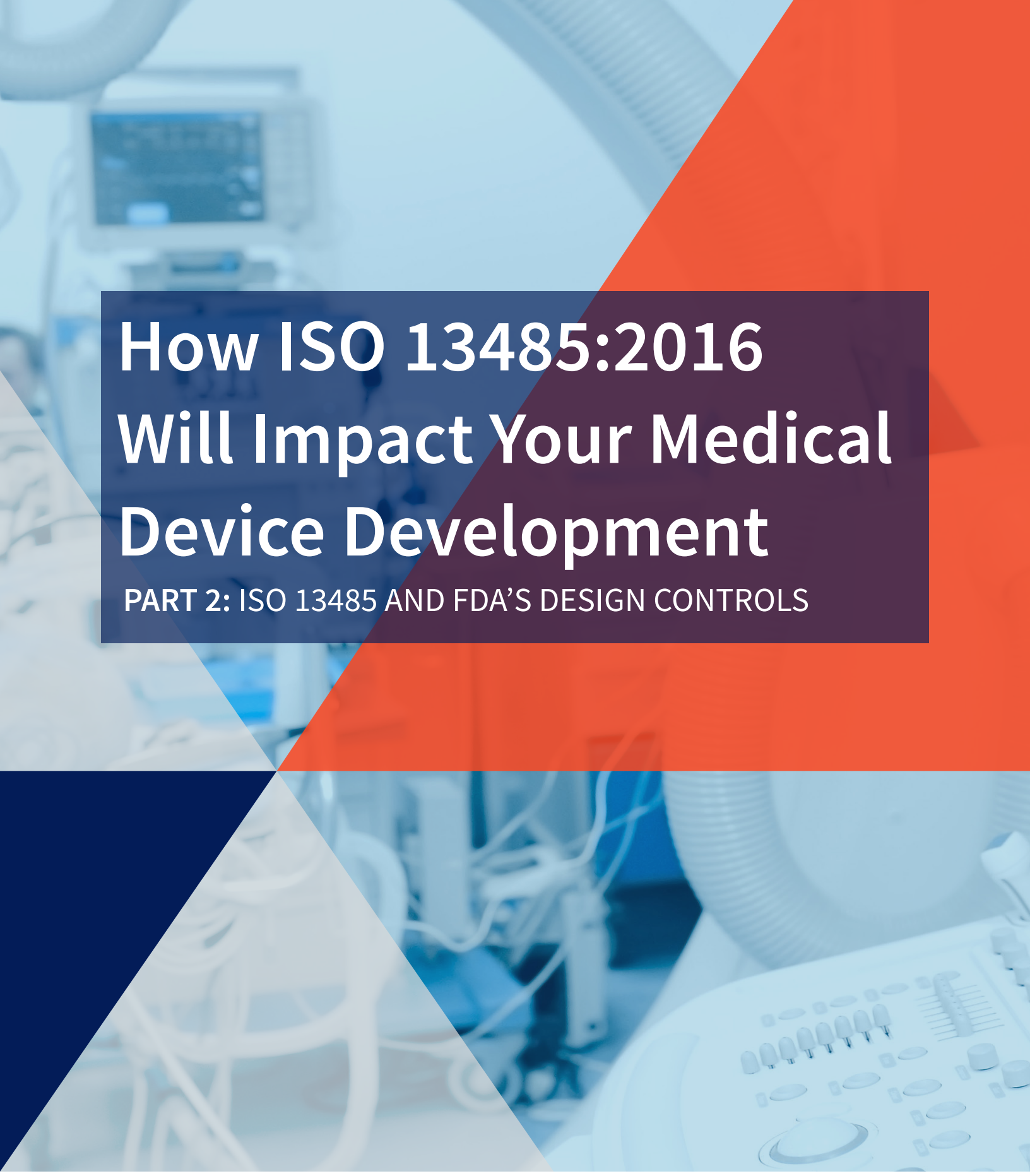

How ISO 13485:2016 Will Impact Your Medical Device Development

PART 2: ISO 13485 AND FDA'S DESIGN CONTROLS

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NAVIGATING PRODUCT DEVELOPMENT

Effective from now on, ISO recognizes medical device manufacturers that comply with ISO 13485:2016, the updated medical device quality management standard. From there, FDA plans to continue its journey to harmonize 21 CFR 820 with the international standard. These undertakings reflect actions to empower domestic manufacturers in the global marketplace, with possible consensus coming in the near future. And while the new ISO standard does not replace current FDA quality system regulations today, it will impact medical device manufacturers' compliance efforts in important ways going forward.

In this two-part white paper series, we explore the differences between the old and new versions of ISO 13485, as well as the anticipated FDA updates later in 2019. Taking a high-level look at these changes, we then assess their impact for medical device organizations. In addition, we try to understand the opportunities and challenges presented in adopting the standard for your organization's quality management system (QMS).

FDA Harmonization with ISO 13485 is Coming

March 2019 marked the end of the transition period from ISO 13485:2003—the QMS standard for medical devices—to its third revision, ISO 13485:2016. Manufacturers looking to align their QMS with the standard must now be in compliance with its new and updated requirements, if they have not done so already. This shift marks a new chapter for medical device QMS management, and its impact is already being felt.

One of these impacts is FDA's intent to harmonize its current QMS regulation with the standard. First announced in the spring of 2018, this harmonization work is still ongoing; a full scope for this harmonization has not yet been defined. This uncertainty can be difficult for manufacturers to manage; taking steps now to comply with what may or may not be outdated within a few years is not a worthwhile investment of time and resources. At the same time, neglecting to be

proactive in their compliance efforts could lead to remediation and other later-stage development issues that ultimately impact project timelines and result in rework.

Of particular concern for manufacturers is how FDA plans to approach updating and harmonizing 21 CFR 820.30, the agency's current requirements for Design Controls. The new ISO standard is definitely influenced by FDA's Design Controls, but there are areas of differentiation that could impact the future of US regulation around this vital aspect of medical device development and quality management. Apart from differences in scope, language, and approach, the newest edition of ISO 13485 also has broader QMS implications for Design Controls that could influence FDA's harmonization initiatives. Looking at these differences more deeply can help manufacturers project and anticipate how changes to current FDA regulations will impact their quality management activities throughout the product life cycle.

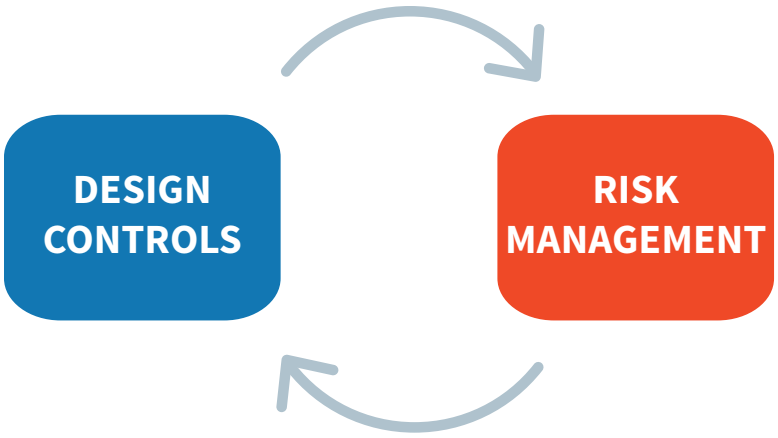
Key Differences: ISO 13485 & FDA's Design Controls

When looking at the differences between ISO 13485 and 21 CFR 820.30, it's critical to note that FDA does not necessarily anticipate wholesale adoption of the standard. Rather, they will more likely pick and choose elements to harmonize with, dependent upon factors such as feasibility, applicability, and need. With this in mind, there are a handful of areas where differentiation between the updated standard and FDA regulation for design controls could be of concern for manufacturers.

Greater Focus on Risk Management

The latest updates to ISO 13485 expand many QMS requirements for medical device manufacturers, and do so with a risk-based approach in mind. This integration of risk into broader QMS development and administration will likely continue to be a focus of the standard in years to come. Under this focus, the standard's design control requirements have been adjusted to account for risk too.

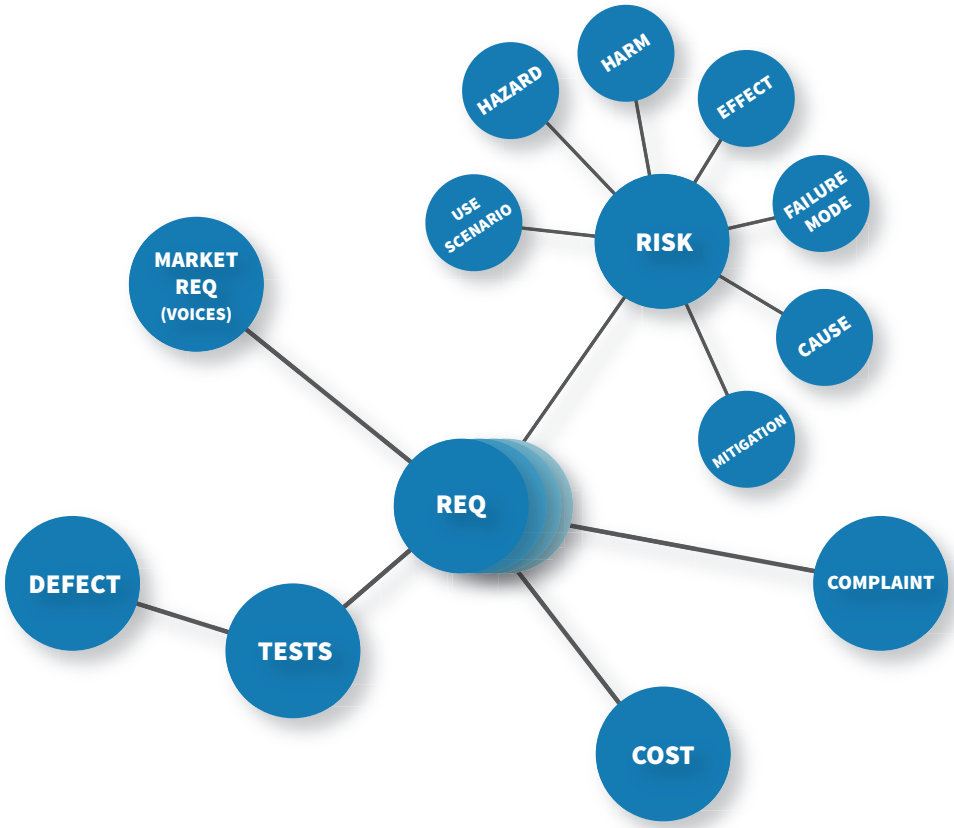
It should be noted that, while FDA's Design Controls only briefly discuss risk analysis, other QMS regulations from the agency support its inclusion in design and development stages. However, ISO 13485 differs from the regulation because it specifically calls out the need for risk management for the entire product life cycle. The standard calls for the inclusion of safety requirements, as well as identification of characteristics deemed essential for safe and proper use, into the device design. ISO 13485 also views any risk management outputs as valid inputs into the design of your device.



The updated ISO standard likewise suggests a risk-based approach not seen either in FDA regulation or prior forms of the standard: an iterative risk management process. As risk management is applied and resulting controls or mitigations are devised, the standard encourages their inclusion back into the design process. Because the ISO standard encourages integration with design controls, any risk outputs must ultimately run back through the risk management process for further analysis and evaluation.

Requirements for Traceability

In FDA's Design Controls regulation, traceability of requirements between design stages is not strictly required. Even looking at the agency's overall QMS requirements shows their definition of traceability, at present, is related more toward identifying the product during its life cycle stages. Being able to trace, for example, your design inputs to your design outputs in your premarket submission, device history file, and other product-related documents currently is not required. As industry best practice it is recommended, but not mandated.



The new ISO 13485 officially takes a stand on the issue of traceability by including it as a requirement of the design and development planning stage, along with overall QMS management. The new design controls requirements expect methods to be in place for ensuring traceability of design outputs back to design inputs and these traces documented within the design history file. Manufacturers are expected to maintain traceability throughout the product life cycle—for at least the defined lifetime of the medical device.

Accounting for Industry Shifts

FDA's QMS regulations are effective because, for the most part, they are applicable regardless of the current state of the art and related technologies, as well as other industry trends. This agnosticism can be effective at keeping the scope of QMS regulations focused. However, it additionally has the possibility of making the regulation more inflexible as the industry and technology evolve. The latest version of ISO 13485 appears to identify this as a concern and, as a result, accounts for it in its QMS requirements.

The standard achieves this accounting both directly in its design controls and elsewhere in its requirements. For example, in some of the standard's design and development requirements, there's a focus on ensuring product requirements are met when devices are interconnected. To maintain safety and proper use, the standard is concerned with making sure this growing feature of contemporary medical devices is accounted for. In addition to these sorts of technological considerations for devices themselves, the standard also includes requirements related to software used in QMS activities. FDA does have regulation related to electronic systems used during development, but ISO 13485 is far more distinct in its requirements. It requires manufacturers to validate any software used in quality management activities before its initial use and after any software changes, where appropriate.

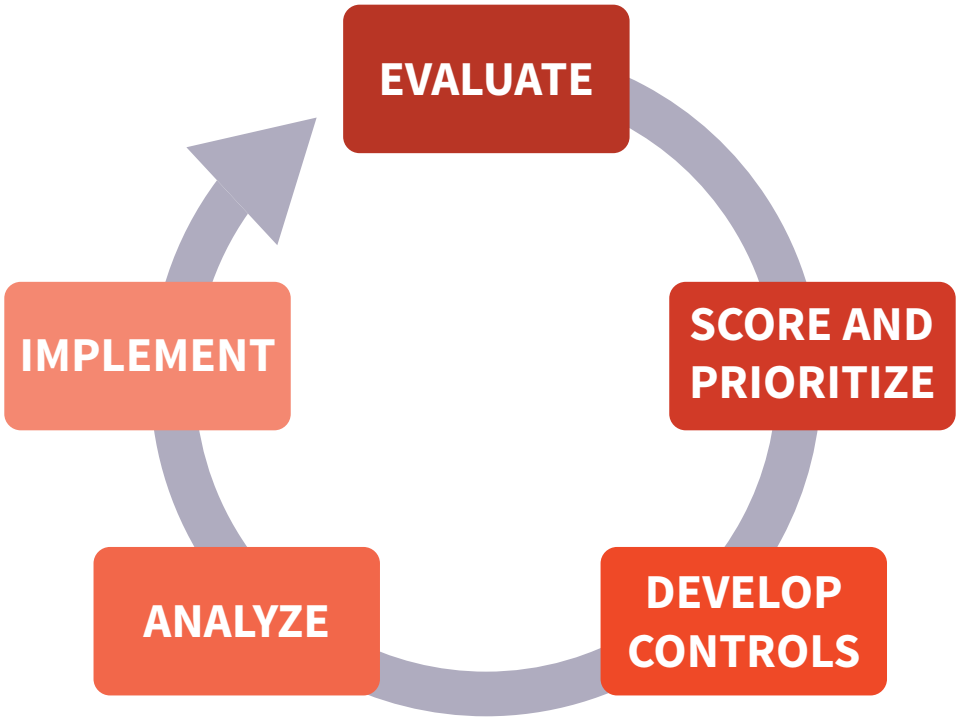
Potential Impacts

There is still no clear picture yet from FDA about what harmonization of existing QMS regulation with ISO 13485 looks like. This makes it hard for medical device manufacturers to fully account for what changes they have to make and how they impact their organization. While it's hard to say for sure what FDA will adopt and change, there are a few key impacts harmonization could have on existing regulation.

Integration of (Iterative) Risk and Design Controls

Risk management and design controls have long been linked together, but never officially codified in FDA regulations. As the agency looks toward aligning its existing Design Controls with ISO 13485, it's possible that an integrated approach might finally be required for medical device manufacturers. This shifts how risk management is conducted by many firms today, and is an important concern going forward.

Plus, adoption of the new ISO standard could result in greater encouragement of iterative risk management processes. If FDA more particularly requires risk management outputs to be incorporated as design inputs, then this will be solidified even further. For those manufacturers not already using an iterative risk program into their development activities that is integrated with design controls, planning to build that out now benefits your future compliance activities.

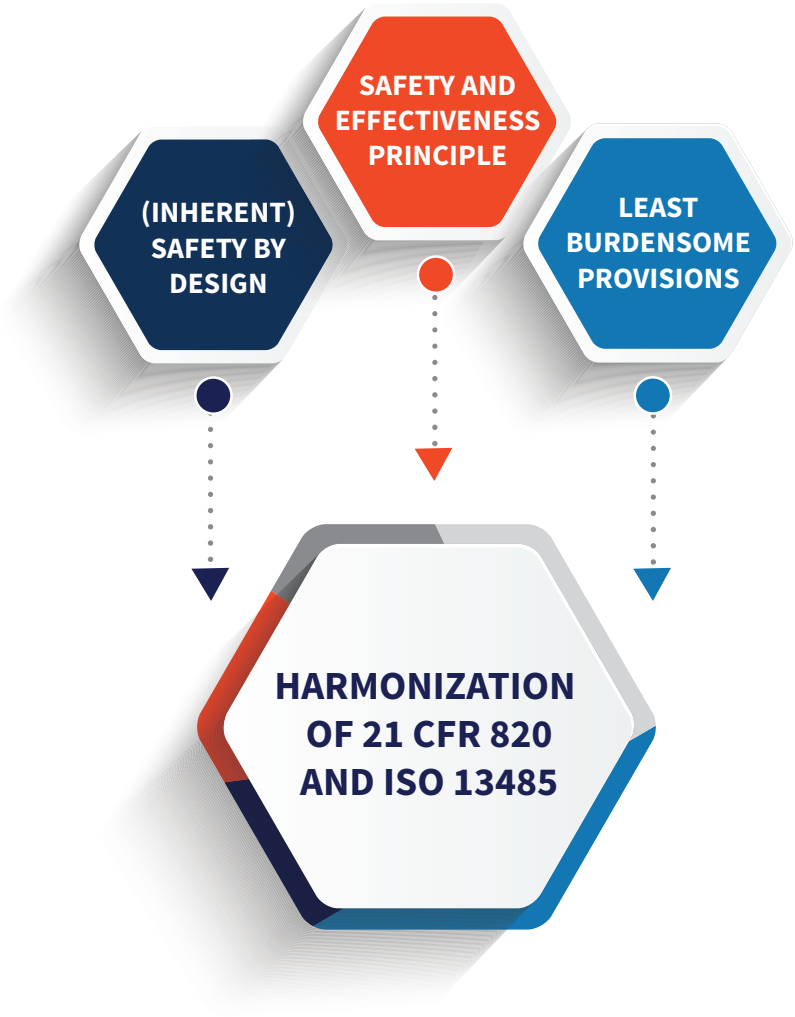


Integration of (Iterative) Risk and Design Controls

The latest edition of ISO 13485 has greater levels of specificity for its Design Controls requirements—with some exceptions. Dependent upon how these more explicit requirements align with FDA principles and regulatory imperatives, some may be adopted while others are rejected entirely.

When FDA begins evaluating how to align their Design Controls regulations with the standard, they have to do so in the context of three distinct and interrelated principles:

- (Inherent) safety by design
- Safety and effectiveness
- Least burdensome

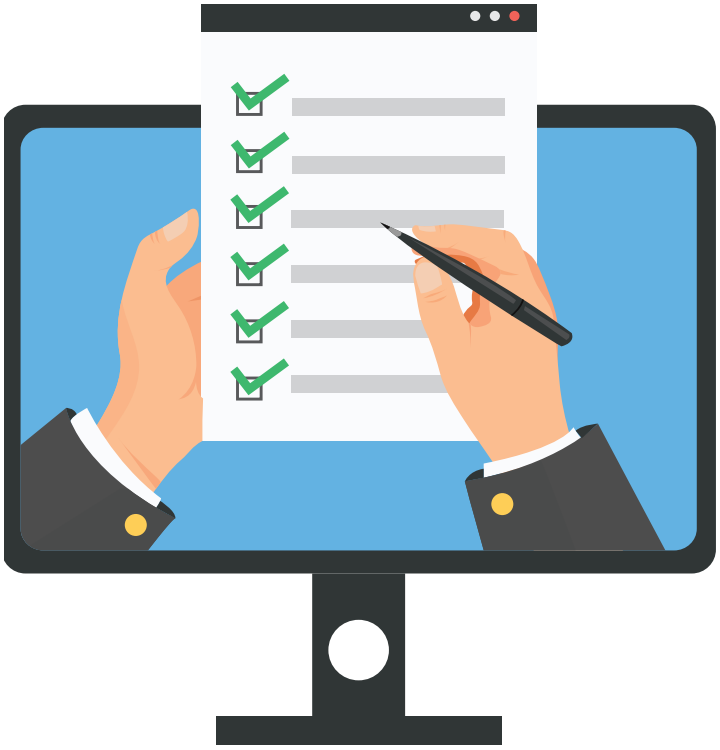


Regulators want to be sure that any changes they make to existing regulation help manufacturers maintain the safety and effectiveness of their devices and further promote the safety by design principle championed by the agency. These considerations then have to be evaluated in the context of FDA's least burdensome provisions.

FDA is more likely to enact changes that promote, maintain, or improve safety and effectiveness for users and patients that do not result in significantly more burden for both themselves and the industry. More explicit requirements for Design Controls might fall under this umbrella, and therefore need to be understood as a real concern for manufacturers to prepare for.

Expanded Requirements for Validating Design Controls Software

With the latest version of ISO 13485 requiring validation of software used in quality management processes, manufacturers already have an incentive to control and manage these systems. If FDA decides to adopt these requirements into existing QMS regulation, a major shift could commence in manufacturers' compliance work.

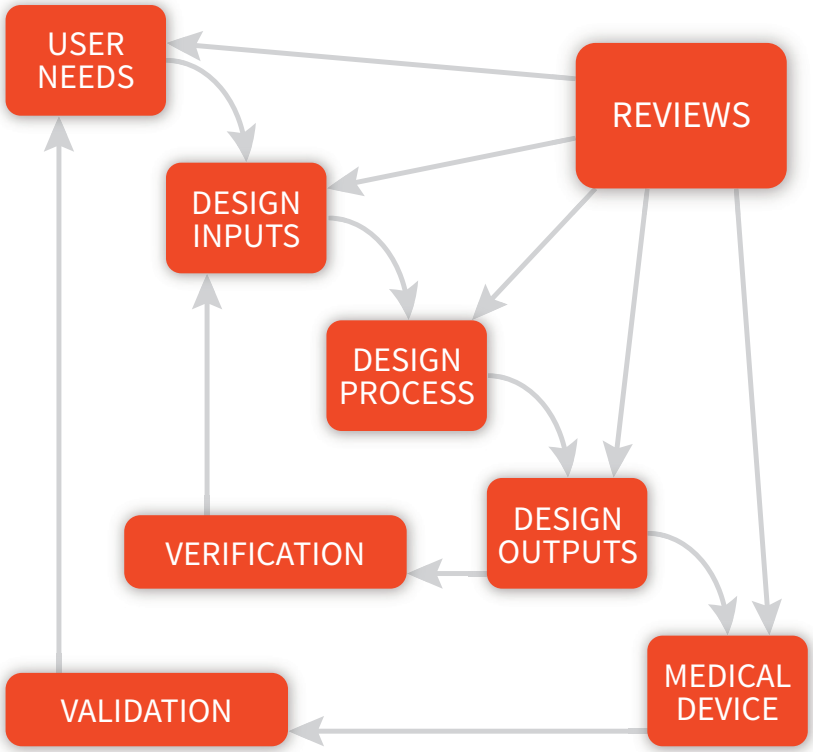


FDA does have requirements on the books for controlling computers or systems with automated processes as part of the quality system, but their scope is limited. The agency's primary concern in its QMS regulations is ensuring embedded software is controlled; the majority of requirements related to computer systems and software used in product life cycle management focus on electronic records. ISO 13485 would alter this focus at a fundamental level; any software used in the manufacturer's QMS would need to be controlled.

This realignment would involve all software leveraged in design controls and risk management activities. And, should FDA adopt the ISO standard's approach to software validation, the resulting incorporation would require a risk-based approach. Currently, 21 CFR Part 11 and 820.70(i)—FDA's QMS requirement related to automated processes—focus on validation as it relates to the software's intended use. While this is still an area of importance in ISO 13485, its primary focus is on approaching validation in a manner proportionate to associated risks.

Because of this potential shift, medical device manufacturers need to ensure that, when adopting design controls and risk management software as part of their quality systems, risk is prioritized. It's likely, too, that FDA will maintain the intended use aspect of the validation requirements, so accounting for that is key. In addition, ensuring measures are in place to make sure software validation is conducted at the appropriate times in coordination with the vendor is of high importance. All of these concerns for validation make compliance a more dynamic and involved process; medical device manufacturers should start taking them into account sooner rather than later.

Staying Ahead of FDA



As FDA works toward harmonizing its QMS regulations with the latest form of ISO 13485, many medical device manufacturers may be unsure how any resulting changes will affect their businesses. This anxiety is expected, but can and should be overcome. While it's not possible to know the full scope of what FDA has planned for ISO harmonization, evaluating where its regulation and the standard differ is a good starting point. This, in the context of the agency's continuing initiatives and principles, can provide manufacturers the ability to anticipate what FDA has in store.

Compliance can be a difficult process, especially when done retroactively. This is especially true for Design Controls; when not adequately set up as part over your overall QMS, Design Controls can be ineffective and compound your compliance and quality challenges. How your organization approaches implementation aligned with both ISO 13485 and 21 CFR 820 is already a balancing act, and will grow more complex as harmonization takes hold. Recognizing these issues and preparing for them now can offer benefits to medical device manufacturers as the transition to ISO-aligned QMS regulation comes into full effect.

About Cognition Corporation

At Cognition, our goal is to provide medical device companies with collaborative solutions to the compliance problems they face every day, allowing them to focus on their products rather than the system used to create them. We know we are successful when our customers have seamlessly combined risk management, requirements management, verification, and validation activities in Cockpit.

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