Design Control Quality for R&D Medical Devices

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Abstract

How could we associate two words like Design and Control, when, traditionally, who says "Design" already envisions a complete wide world? But positioning the safety of patients as the highest priority of any activity concerning the development of a medical device, makes it obvious that the only way to protect the public health is to establish a standard applicable for any type of device. Since a medical device could be a simple hand-tool, a complex computerized system, diagnostic system or implant, it is difficult to establish a single standard or guidance that will encompass such wide range of products. In addition to product range, issues such as company size, company structure, methods of development and methods of management have considerable influence on "How to apply the Design Control" according to 21 cfr 820.30 or ISO 13485.

A significant guidance document was provided in this area grouping different issues. The Global Harmonization Task Force (GHTF) (Study group 3) actively participated in the issuance of this guidance, named: “Design Control Guidance for Medical Device”, further published by the FDA in 1997. We can finally find significant synchronicity between the FDA requirements of 21 cfr 820.30 and ISO 13485 requirements regarding design control.

The document represents substantial assistance in the significant phases of the design as they are presented in 21 cfr 820.30 referencing ISO 13485:2003 section 7. Sections A to J retrace the following steps of the Design described in 21 cfr 820.30:

- Design and Development Planning
- Design Input
- Design Output
- Design Review
- Design Verification
- Design Validation
- Design Transfer
- Design Changes
- Design History files

The different phases provide effective support to the "Good Development Practice" and ensure an evident increase of the quality of the issued products. By establishing the logical steps of the development of a successful product, the standards also provide a very good driving support in addition to the very high added value to the quality of the product. For several years, quality and regulatory professionals are the team leaders of this side of the development phase. Today the engineers and researchers themselves are sharing in the responsibility, and are asking questions about the Design Control Process, understanding the importance in regulatory and effectiveness point of view. The Design Control methods/standards have proven themselves to be time and cost saving when they are used correctly. Our target as quality personnel should be to emphasize the quality support and to provide the adequate tools of application of the design control to our companies in order to continue to improve the safety of patients worldwide.

Full Text

According to data compiled by the FDA, a report was generated demonstrating that between 1985 and 1989, 45% to 50% of all device recalls stemmed from poor design. This dry fact, provides the answer to the question: "How could we associate two words like Design and Control? But positioning the safety of patients as the highest priority of any activity concerning the development of a medical device, makes it obvious that the only way to protect the public health is to establish a standard applicable for any type of
device. Since a medical device could be a simple hand-tool, a complex computerized system, diagnostic system or implant, it is extremely difficult to establish a single standard or guidance that will encompass such wide range of products. In addition to product range, issues such as company size, company structure, methods of development and methods of management have considerable influence on "How to apply the Design Control" of 21 cfr 820.30 or ISO 13485.

The Global Harmonization Task Force (GHTF) (Study group 3 including the European Union, United States, Canada, Australia and Japan) actively participated in the issuance of this guidance, named: “Design Control Guidance for Medical Device”, further published by the FDA in 1997. The document represents substantial assistance in the significant phases of the design as they are presented in 21 cfr 820.30 referencing ISO 13485:2003 section 7. Sections A to J retrace the following steps of the Design described in 21 cfr 820.30:

**Design and Development Planning**

The design and development planning comes to help the engineering team to organize and schedule its work. It should include for good practice not only the development activities but also the quality activities. Together, the development and quality activities will provide a very good structure for the correct development of the product.

- Verifying at any step that all the adequate decisions were taken, the patients and users needs were fulfilled, all the verifications and evaluations provided. The GHTF even advise to follow this procedure for products not falling into the design control requirements. The Europeans do not even differentiate between the different types of products for the Design controls.
- Assigning responsibilities
- Defining global time configuration
Sometimes, it is difficult to convince smaller companies of the efficacy of this organized method.

**Design Input**

Design input activities together with the design planning will organize the project (if done well!). It is an assembly of all available data on the product and its application. Which company or even investigator would like to investigate a company or a project without knowing the basis of the demand for such a product? It is during the Design Input phase that the guidelines come and ask questions. It can be said that it is more a method to ensure that the entire team is heading in the same direction, and according to the same product requirements.

In addition, the cfr 820.30 and ISO 13485 will guide the development process in the same direction. The GHTF document provides good support for understanding not only the regulatory requirements, but also for adapting these requirements to the specific company “style and product”.

![Diagram](image-url)
**Design Output**

In fact, most of the work is not mentioned in the regulatory descriptions. But from the Design Input activities to the Design Output, the road is sometimes long and complicated.

During the lifetime of a product, the more intensive activities are performed as a result of the design Input Decisions, driving the Design Output.

The design Output per §20.30 means the results of a design effort at each design phase and at the end of the total design effort. The total finished design output consists of the device, its packaging and labeling, and the device master record. And don't forget your Risk Analysis!!!

**Design review**

The Design Review requirement just proves that the people involved in the development of standards and guidance have important industrial experience. They understood very well that an engineer, technician, professor or other professional employee can not review himself and find all the errors. Therefore, there is a requirement for an external reviewer. The design Review process provides a tool allowing an external reviewer to inspect the results of the activities, in essence doing a kind of self review.
Design Verification
At the point when the design output is finished, we have a complete product, including packaging, labeling and instructions for use. For some types of devices, the packaging aspect is not very significant. However, in many cases, packaging can make the difference between success and failure. Take for example an implant: the product could have an extraordinary design, with exceptional performance, but if the packaging is not able to keep it sterile during transportation to hospitals or if the instructions for use are not explicit enough, then this product could provoke dangerous misuses, resulting in a device which is deemed an unsafe product. Therefore, one of the important things to remember is that when we speak about a product, it will be "complete" product. Now after significant efforts, a final product is obtained. Firstly the company should be able to prove that the right product was issued by comparing it to the Design Input. A simple comparison table will be provided. In addition, the company should be able to confirm the safety of the product by in-vitro testing before the product comes in contact with humans.

Developing a Risk Analysis process from the beginning of the Design Control activities, enables the developers to provide a "list" of tests to be performed on the product. Many methods of risk Analysis are available for use and the choice of adequate method will determine the success of this critical task. For example, using again the packaging example, even if biocompatibility tests show good response of the product, should the packaging not be able to keep the product intact during air transportation, the product will not be useable. The technical preparation and performance is not simpler than the quality and reporting side of the tests. Every error can trigger a significant cost and time delay due to design change requirements and retesting. The system proves itself again as a system that can protect not only the safety of the patients but also the organization.

Design validation
Design validation shall ensure that the device conforms to defined user needs and intended uses, and shall include testing of production units under actual or simulated use conditions. Again after reviewing the Risk Analysis, and weighing the risks against the benefits, the product can proceed to animal and/or human testing. However, even though it is determined that the product fits its design criteria and conforms to specification, one cannot automatically establish that it will perform adequately under real conditions. It is easy to say “let’s check it” but it is much harder to do since the difficulties and costs of performing animal not to mention human trials are well known,

Design Transfer
For some companies, the Design Transfer process will be very simple. If the first production is simple and does not require changes in production sizes versus the units produced for the V& V (Verification and Validation) activities, it could be that the design transfer to production will be a formal activity, rather than a labor intensive one. But in case, for example of a company having facilities for research and development in another city or even country, transferring mass production can cause many problems and difficulties including possible revisions in the product, essentially in manufacturing. This is the reason it is recommended that companies cooperate with the production team from the early stages of the development. The added value is particularly welcome at the later stages of the project. But once more: the efficient method to ensure a good transfer is the Risk Analysis of production methods.

Design changes
Significant risk can be brought on by any design change. The best example of such risk is not associated with a medical device, but rather with a baby milk substitute – The Remmedia story: A certain component of the formula was changed without weighing all the consequences of the change. Several babies died and others were severely injured as a result. Again here the Risk analysis method will bring a very good support method to avoid risky design changes.

Design Master File
Although the issue of documentation was not mentioned in any of the design steps above, it is clear that without evidence one cannot support the project or prove that any activities were actually performed. Here again, the standards/laws/guidelines come to help and require the complete record system and documentation in order to be able to provide every evidence in any case. This will be a compilation of the project containing all the "secrets" of the product.
The different phases provide very efficient support to the "Good Development Practice" and ensure an evident increase in the quality of the issued products. By establishing the logical steps of the development of a successful product, the standards also provide a very good driving support in addition to the very high added value to the quality of the product. For several years, quality and regulatory professionals are the team leaders of this side of the development phase. Today the engineers and researchers themselves are sharing in the responsibility, and are asking questions about the Design Control Process, understanding the importance in regulatory and effectiveness point of view. The Design Control methods/standards have proven themselves to be time and cost saving when they are used correctly. Our target as quality personnel should be to emphasize the quality support and to provide the adequate tools of application of the design control to our companies in order to continue to improve the safety of patients worldwide.

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