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Design Output: A Review of 21 C.F.R. §820.30(d) and FDA Warning Letter Trends

Introduction

Does your company properly manage Design Outputs? The FDA routinely examines this area as part of an audit process. In this article we review what it means to have your design outputs in order as well as present some recent warning letter examples.

What Are Design Outputs?

Design Outputs exist within your Design Controls environment, which is a component of your Quality Management System (CFR 820).

The FDA formally outlines their Design Output expectations in 21 C.F.R. §820.30(d)):

(d)*Design Output.*
Each manufacturer shall establish and maintain procedures for defining and documenting design output in terms that allow an adequate evaluation of conformance to design input requirements. Design output procedures shall contain or make reference to acceptance criteria and shall ensure that those design outputs that are essential for the proper functioning of the device are identified. Design output shall be documented, reviewed, and approved before release. The approval, including the date and signature of the individual(s) approving the output, shall be documented.

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Design Outputs are the artifacts associated with the creation of your device (Design Stage). They include items such as:

- Drawings
- Project Development Plans
- Block Diagrams
- Flow Charts
- Requirement Specifications
- Functional Specifications
- Quality assurance specifications and procedures
- System or subsystem design specifications
- Production and Process specifications
- Packaging & Labeling Instructions

Which Design Output artifacts you ultimately select is based on what you consider "essential for the proper functioning of the device." A common approach to help distill your list is to leverage Risk Management processes (FTA/FMEA). Those areas of the device, whose failure could impact the effectiveness, safety, and reliability, are considered essential design outputs. Resultant control measures are Design Output candidates.

All of Design Output artifacts are tracked within your Device History File (DHF) which describes how you designed your device.

The finished Design Output feeds your Device Master Record (DMR) which fully specifies the device, its packaging and labeling.

While the focus is on the end result (the finished DMR), it's quite common to have Design Outputs delivered at each phase of development, each with specific acceptance criteria. So the Design Outputs need to be comprehensive enough to drive the Verification and Validation plans which support your acceptance criteria.

The finished design output feeds your Device Master Record (DMR) which fully specifies the device, its packaging and labeling.

Reviews, Updates & Approvals

It is important that your company be able demonstrate to an auditor that your Design Outputs were reviewed and approved before being released. This must include the date and signature of the approver. Missing the date and signature is red flag easily caught by auditors.

Some Recent Warning Letter Examples

A review of the warning letters issues in 2010 to date yield the following examples:

1) Company: Advanced Sterilization Products

   Summary: Missing an essential Design Output

   Failure to establish and maintain adequate procedures to ensure that those design outputs that are essential for the proper functioning of the device are identified, as required by 21 CFR § 820.30(d);

   For example, the "Instruction For Use" (IFU) for CycleSure Biological Indicators (BI) revisions 101011-01 and 101011-02 stated that the BI media color change (from purple to yellow) and/or turbidity change (from clear to turbid) should be evaluated as a positive result. However, your firm did not provide adequate "Instructions for Use" for users to be able to accurately interpret the color change. Also, there were seven complaints (b)(4) from users stating that they were unable to identify the positive or negative BI test results. Consequently, your firm failed to establish acceptance specifications for positive CycleSure BI read-out test results in order for users to clearly

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determine test outcomes for BI's used as positive controls or process challenges.

2) Company: 3CPM Company Inc

Summary: Missing essential Design Outputs and signature approval records.

Failure to establish and maintain adequate procedures for defining and documenting design output in terms that allow an adequate evaluation of conformance to design input requirements, as required by 21 CFR 820.30(d). For example:

a. When requested, design output procedures and/or requirements for the upgrade from Version (b)(4) to Version (b)(4) done by (b)(4) and for the upgrade from Version (b)(4) Research device to Versions (b)(4) Research, Research Waterload device done (b)(4) could not be provided.
b. When requested, no evidence that design outputs were established and evaluated against design inputs document (b)(4) was provided.
c. There is no record of review and approval of device labeling, including review and approval of the labeling for the Research Version (b)(4) released (b)(4)

3) Company: Sometech Incorporated

Summary: Missing SOP for defining/approving Design Outputs. Missing date and signature approval records.

Failure to establish and maintain adequate procedures for defining and documenting design output in terms that allow an adequate evaluation of conformance to design input requirements, as required by 21 CFR 820.30(d). For example:

(a) Your firm's design output procedure, SQP04 Rev 10 "Design and Development Procedure" dated July 24, 2008, Section 3.5.2

i. Does not adequately state procedures for defining and documenting design output in terms that allow an adequate evaluation of conformance to design input requirements;
ii. Does not contain or make reference to acceptance criteria and does not ensure that those design outputs that are essential for the proper functioning of the device are identified;
iii. Does not provide that design output should be documented, reviewed, and approved before release; and
iv. Does not provide that the approval, including the date and signature of the individual(s) approving the output, should be documented.

(b) The following design outputs for the LVT100 design project did not include the date of the individual(s) approving the output:

i. SQP04-5 Rev 1 "(b)(4)" dated July 21, 2008;
ii. SQP04-5 Rev 1 "(b)(4)" dated July 21, 2008;
iii. DQP04-7 Rev 1 "Approval of Parts" dated April 14, 2009;
iv. Dwg. No. M103M00434 Rev 0 "(b)(4)" dated June 10, 2008;
v. SQP04-4 Rev 0 "(b)(4)" dated January 11, 2008; and
vi. "(b)(4)" Rev 0 "(b)(4)" dated July 21, 2008.

4) Company: Impact Instrumentation, Inc.

Summary: Missing SOP for defining essential Design Outputs.

Failure to adequately establish and maintain procedures for defining and documenting design output in terms that allow an adequate evaluation of conformance to design input requirements, as required by 21 C.F.R. 820.30(d). For example, your firm did not ensure that those design outputs that are essential for the proper functioning of the Uni-Vent® 731 Series Model EMV+ device are identified.

SPK and Associates would like to hear from you. We invite you to share your Design Output questions, experiences, and advice.

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