Medical Device Communiqué

Q2 2016

QUALITY SYSTEM METRICS SHARED AT MEDCON

During the MedCon event at Xavier University, several quality system metrics were introduced to attendees by Kristin McNamara, Senior Advisor to DACRA Office of Regulatory Affairs, FDA and Marla Phillips, Director, Xavier University.

The metrics represent the output of the Medical Device Industry Consortium (MDIC) and the effort to develop standard quality system metrics that span pre-production, production, and post-production topics.

In addition, the metrics were developed to support the CDRH "Case for Quality" program.

(continued...)

QUALITY SYSTEM METRICS SHARED AT MEDCON *(CONTINUED)*

Marla explained that to arrive at the proper metrics, the team asked: "what is a risk to product quality?"

MDIC leveraged a team of more than 40 experts from industry and FDA officials, to focus on best practices and competencies. The team agreed that the right quality system metrics should help inform decisions and trigger action throughout the product lifecycle process.

What would be measured would be indicators that impact patient safety, design robustness, process reliability, quality system robustness, and failure costs, Marla said.

Another goal, she noted, was to shift the "Right First Time" mentality closer to the initial product development effort.

The group had identified eleven critical systems, which included CAPA, Change Control, Complaint Handing, Design Controls, and others.

Marla then presented three metrics: design robustness, right first time, and post-production index. We will drill down into the first two metrics here.

Design Robustness Metric

Marla explained that the "Design Robustness" metric is ideal for measuring the changes required during transfer:

$$\frac{\text{total \# of product changes}}{\text{total \# of products with initial sales in the period}}$$

This metric only includes changes required due to inadequate product or process development. The metric provides an indication of time, resources and cost for products to reach a mature state. For example, a goal should be that quality design require minimal changes, so the design team should identify issues during testing and remediate before design transfer.

In addition, the design team should track root causes of changes as early as the transfer stage. These steps would increase success in the production stage.

Right First Time Metric

Marla explained the Right First Time metric, which looks at non-conformances, would help establish the rework rate, with the expectation that the company would triage root causes.

$$\frac{\text{\# of units mfg. w/o non-conformances}}{\text{\# of units started}}$$

As Marla explained, this metric should include planned rework and set-up scrap to minimize the waste.

For this metric, Marla explained, companies must ensure that terms are defined consistently across products and sites to demonstrate that the metrics are sensitive enough to differentiate between varying levels of product quality within a single company.

Marla then asked "how sensitive is the data in your own company?" Arriving at this answer is critical to the success of rolling out metrics and sharing them with senior management.

Currently, a PWC-managed pilot has been initiated via MDIC, and eight medical device companies have already enrolled.

Next Steps

MDIC's next steps will be to review the pilot results and test the data collection feasibility of the recommended metrics.

MDIC will also understand the value of the proposed metrics to ensure they provide meaning. Marla said she expects to refine the metrics based on the feedback provided in the pilot.

For more information about the program, or to participate in an upcoming forum being held on June 28th in Washington, DC, visit this site to register (http://mdic.org/cfq/register/).

UDI COMPLIANCE:
TRAINING YOUR TEAMS

UL is updating our "Medical Device Packaging, Labeling, and Distribution" eLearning course to reflect FDA Unique Device Identifier requirements. We have asked Nancy Watts, Quality Specialist at Compliance Insight (www.compliance-insight.com), which serves as the course expert, to share key facts about UDI requirements, including key compliance dates.

A UDI Primer

FDA regulations and guidance are becoming increasingly specific for identification of marketed medical devices. These requirements are intended to facilitate the accurate reporting of any adverse events, and coordinate device recall and/or required replacement for patients, physicians, distributors and manufacturers. These regulatory updates from the FDA include clarifications on Unique Device Identifiers (UDI) requiring precise, traceable and accurate identifiers on medical devices and associated packaging components.

21 CFR Part 801 Subpart B

21 CFR 801 Subpart B describes UDI labeling requirements:

The label of every medical device and device package shall contain a unique device identifier. A UDI on a device label or package is composed of two parts, the Device Identifier (ID) and the Production Identification (PI).

Device Identifier (ID): a mandatory, fixed portion of a UDI that identifies the labeler and the specific version or model of a device.

Production Identification(s) (PI): a conditional, variable portion of a UDI containing all available identifiers including the lot or batch number, the serial number, the expiration date, and the date of manufacture. For Human Cell and Tissue Products (HCT/P) regulated as a device, the PI should also include the distinct identification code required by 21 CFR Part 1271.290(c).[1, 3]

For markings on devices, the UDI is required to be permanent, legible through processing and must not compromise the safety or efficacy of the device.[2]

These markings should be maintained through the expiry period of the device. There have been many advancements in laser labeling of devices and device labels.

Class Distinctions

Class I: The UDI of a class I device is not required to include a PI. A Universal Product Code (UPC) that is linked to the ID on the device label and device packaging has met the UDI labeling requirement. The UDI can be imbedded in an automated identification and data capture AIDC icon.

Class II: The UDI of a class II device requires an ID and a PI. The UDI can be imbedded in an automated identification and data capture AIDC icon.

Class III: The UDI of a class III device requires an ID and a PI. The UDI can be imbedded in an automated identification and data capture AIDC icon.

Compliance Dates

FDA has offered an implementation schedule, based on criticality and device class; after these dates manufacturers will be considered non-compliant with the regulations:

9/24/14 – Class III Labeling and Packaging and devices licensed under the Public Health Service Act (PHS Act)*

9/24/15 – Implantable, Life-supporting, and Life-sustaining devices*

9/24/15 – Class III*

9/24/18 – Class II*

9/24/20 – Class I and unclassified*

*It should be noted that the regulations require a UDI as a permanent marking on the device itself if the device is a device intended to be used more than once and intended to be reprocessed before each use.[4]

References:

1. Title 21 CFR 801 Subpart B, Labeling Requirements for Unique Device Identification
2. Draft Guidance for Industry – Unique Device Identification: Direct Marking of Devices, June 2015, 12 page guidance document
3. Guidance for Industry – Global Unique Device Identification Database (GUDID), June 27, 2014, 42-page guidance (references and glossary)
4. www.fda.gov

QSR ESSENTIALS PROGRAM

Focused on Critical 21 CFR 820 SubParts

From product design to manufacturing, employees gain more insight into a company's processes when they understand the regulatory expectations of US FDA.

That's why more than 60 companies rely on UL's QSR Essentials program, made up of 11 self-paced courses. Authored by the experts at Compliance-Insight, these courses focus on 21 CFR Part 820, SubParts A through O.

QSR Essentials contains 11 self-paced courses with built-in assessments:

- QS Regulation 1: Introduction to QSR
- QS Regulation 2: Quality System Requirements
- QS Regulation 3: Design Controls
- QS Regulation 4: Document and Purchasing Controls
- QS Regulation 5: Identification, Traceability; Production and Process Controls
- QS Regulation 6: Acceptance Activities; Nonconforming Product
- QS Regulation 7: Corrective and Preventive Action
- QS Regulation 8: Labeling and Package Control; Handling, Storage, Distribution, and Installation
- QS Regulation 9: Records
- QS Regulation 10: Servicing; Statistical Techniques
- QS Regulation 11: Application and Inspection of QS Regulation Requirements

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FDA EXPECTATIONS FOR THE DESIGN HISTORY FILE

Compliance-Insight is updating our current Design Controls course, and Nancy Watts from Compliance-Insight has prepared this article based on their work with clients.

Many device manufacturers struggle to stay current with FDA thinking on controlling the quality of both their product and the development process. Design Control is defined by the FDA as a basic requirement for medical devices in 21 CFR 820.30(a)(1):

Each manufacturer of any class III or class II device, and the class I devices listed in paragraph (a)(2) of this section, shall establish and maintain procedures to control the design of the device in order to ensure that specified design requirements are met.[1]

The necessity and practicality of design control was stated eloquently in the associated Guidance for Industry, which was published in 1997:

Design controls are an interrelated set of practices and procedures that are incorporated into the design and development process, i.e., a system of checks and balances. Design controls make systematic assessment of the design an integral part of development. As a result, deficiencies in design input requirements, and discrepancies between the proposed designs and requirements, are made evident and corrected earlier in the development process.[2]

The defined parameters for controlling the device design process include all aspects from planning and development, input and output, to any change of design prior to transfer into production which may then require additional validation or verification. Each step is documented which then becomes a critical component of the Design History File (DHF).

The role of the DHF for a pre-production device is to give a detailed audit trail of development, planning, validation, review and changes. This encourages a Quality by Design (QbD) approach to medical device development and design implementation. The QbD approach can only be achieved when the Quality System is built on well-developed procedures requiring thorough documentation and review at each step of the process.

The FDA has made this clear in a recent Warning Letter to a device manufacturer. The agency goes further to indicate that the documentation must be maintained even once the device is no longer under the control of an entity, as in the following example. In the letter dated April 6, 2016, Observation #3 indicates the inspector found deficiencies in the DHF violating basic requirements for design control by the site:

(continued...)

FDA EXPECTATIONS FOR THE DESIGN HISTORY FILE *(Continued)*

Failure of the design history file to demonstrate that the design was developed following the approved design plan and does not demonstrate that the design was developed following the requirements of 21 CFR 820 as required by 21 CFR 820.30(j).

For example, your design history file does not have the location of design documents or changes you made to the (b) (4) lens. Your response is inadequate as you state that you no longer maintain design records after your transfer of a PMA to (another entity).[3]

While the site may have maintained the file with every detail during their ownership, it is clear that they were unable to provide this information to the inspector during this inspection. This violates one of the clearly defined prime directives from the FDA: "if it isn't documented, it didn't happen."

Failure of a medical device manufacturer and their partners to implement proper design control procedures with the associated documentation has real world implications for the site, including a delay in the FDA's ability to review the associated applications and provide approvals.

As further evidence of their commitment to ensuring QbD, the FDA offers direct guidance on their website for those devices requiring Pre-Market Approval and notes:

PMA submissions should include a complete description of design controls that the manufacturer implements to comply with the QS regulation. If this information is lacking, FDA cannot complete the premarket review process.[4]

The agency is clearly narrowing the gap between encouraging quality through guidance and enforcing regulations.

Companies should ensure that the Design History File includes both historical and active procedures and specifications for each product, as well as schedules, meeting and minutes, and any changes that occur to the design during the development process over time.

Medical device manufacturers can meet the requirements by maintaining all design documents and changes.

References:

1. Title 21 CFR 820 Subpart C, Design Controls
2. Guidance for Industry – Design Control Guidance for Medical Device Manufacturers, March 11, 1997, 53 page guidance document references and glossary
3. Warning Letter # 26-16 dated April 6, 2016
4. www.fda.gov

THE TYPES OF MISBRANDING

This year's MedCon conference featured an official from the US Federal Trade Commission (FTC), Jon Miller Steiger, who shared details on how the FTC and US FDA work together. Steiger noted that the FTC looks at advertising substantiation, which requires that companies support their claims to consumers and health care professionals. In addition, material connections must be dislosed, such as paid endorsements.

During the session, Deborah Wolf from FDA presented from FDA offices about labeling issues. She noted that CDRH has jurisdiction over labeling for all regulated devices and over advertising for restricted devices. One of the common problems, Deborah noted, was "breaking commitments made during the premarket review process."

So while FTC focuses on false advertising and marketing statements that do not meet minimum requirements for disclosure of product information, FDA has identified many types of misbranding. For example, Deborah cited 21 CFR 801.6, which outlines that a product is misbranded if the labeling makes misleading comparisons between it and another FDA-regulated product (drug, food, cosmetic).

In our "Medical Device Packaging, Labeling, and Distribution" course (DEV41), we discuss several types of misbranded or mislabeled devices, as improper labeling could injure a patient or healthcare worker and result in regulatory action:

Misleading - A device is considered misbranded if the label is false or misleading. The device can be deemed misleading if the labeling fails to reveal material facts about consequences which may result from use of the device. Omission of material facts impairs the patient's ability to make an informed choice.

Incorrect contents - Misbranding occurs if the label does not contain: the name and address of the manufacturer, packer, or distributor, and an accurate statement of the quantity of contents.

Illegible - A device is misbranded if the required information is not prominently and legibly placed on the label in English (or in the primary language of the intended user). A device can also be misbranded if the printed lot or control numbers are not readable or if the expiry date is incorrect or not readable.

No device name - A device is considered misbranded if the established name of the device does not appear in type at least half as large as the proprietary name used.

No warnings - Misbranding occurs if a label does not bear adequate directions for use and adequate warnings against unsafe use.

Noncompliant - Misbranding occurs if a restricted device is not sold, distributed, or used in compliance with regulations.

No labeling requirement - A device is misbranded if it does not comply with an applicable performance standard labeling requirement.

Not registered - If a device was made in an establishment not registered under Section 510, or not listed under Section 510(j), or if a notice representing a device was not provided as required by Section 510(k), it is misbranded.

Our Medical Device Packaging, Labeling, and Distribution course provides you with information on current packaging and labeling requirements specified by the Quality System Regulation.

Topics in this course include: Importance of Labeling, Packaging, Label Control, and Distribution.

After completing this course, learners will be able to recognize the requirements for packaging, labeling, UDI requirements and distribution of medical devices as noted in 21 CFR 820.120-160.

To preview the Medical Device Packaging, Labeling, and Distribution course, contact Pat Thunell at pat.thunell@ul.com.

About UL EduNeering

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For more than 30 years, UL has served corporate and government customers in the Life Science, Health Care, Energy and Industrial sectors. Our global quality and compliance management approach integrates ComplianceWire, training content and advisory solutions, enabling clients to align learning strategies with their quality and compliance objectives.

Since 1999, under a unique partnership with the FDA's Office of Regulatory Affairs (ORA), UL has provided the online training, documentation tracking and 21 CFR Part 11-validated platform for ORA-U, the FDA's virtual university.