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Agenda

fda requirements
practical challenges
lean compliance solutions framework
FDA Requirements

traceability regulations
recent enforcement examples
example inspector questions
other requirements
21 CFR 820.30

(a) “General. (1) Each manufacturer...shall establish and maintain procedures to control the design of the device in order to ensure that specified design requirements are met.”

Translation for FDA inspectors

“The purpose of the design control subsystem is to control the design process to assure that devices meet user needs, intended uses, and specified requirements:

• Inputs must be documented
• Outputs must be documented
• Confirm that device outputs are traceable to design inputs”
21 CFR 803.18

(b) (1) (i) “…including all documentation of your deliberations and decisionmaking processes used to determine if a device-related death, serious injury, or malfunction was or was not reportable….”

Translation for FDA investigators

“A firm must demonstrate that it exercised “good faith” in any attempts to obtain required data…. In addition, the Center believes that the parameters of good faith must, at a minimum, comport with the level of risk/nature of the device….”
21 CFR 806.20

(b) (4) “Justification for not reporting the correction or removal action to the FDA, which shall contain conclusions and any followups…."

Translation for FDA investigators

“Verify that non-reported device corrections or removals meet the following criteria based on design controls:

• Risk is not increased
• Repairs are not unexpected
• Part replacement is not earlier than expected”
Warning Letter Excerpts

“You have failed to establish and maintain a design history file (DHF) to contain and reference the records necessary to demonstrate that the design was developed in accordance with the approved design plan and the requirements of 21 CFR 820.”

- warning letter to ASI Medical, 20 April 2011
Warning Letter Excerpts

“Failure to maintain adequate device history records…. For example, a review of (b)(4) Meniscal Insert DHRs found one DHR contained an inaccurate date.”

- warning letter to Advanced Surgical Design & Manufacture, 1 December 2010
Warning Letter Excerpts

“When requested, design output requirements for the upgrade from Version (b)(4) to Version (b)(4) done by (b)(4)*…could not be provided.”

- warning letter to 3CPM Company, 25 March 2010

*This change was done 7 years prior in 2003!
Example Inspector Questions

- were design characteristic acceptance criteria established and documented *prior* to design approval?
- were design outputs verified and documented against design input requirements?
- was risk analysis conducted (and documented) on the design prior to its final design approval?
- do design outputs draw a distinction between those characteristics essential for functioning of the device versus those non-essential *(e.g., aesthetic)* characteristics? How are these verified?
- review design outputs linkages wherein design outputs for one stage become design inputs for the next – how are these made clear in the documentation?
- verify that changes to device design were documented and approved – are there date discrepancies between the actual change and its approval?
- how were design changes tested to assess impact to risk or to adjacent design inputs or outputs? How was this documented?
- is there a documented traceability analysis or matrix linking product design requirements, design specifications, risks and controls, and tests?
Other Requirements

FDA Guidance Documents

• Human Factors Points to Consider for IDE Devices (1996)
• Human Factors Implications of the New GMP Rule: Overall Requirements of the New Quality System Regulations (1997)
• Design Control Guidance for Medical Device Manufacturers (1997)
• Medical Device Use-Safety: Incorporating Human Factors Engineering into Risk Management (2000)
• General Principles of Software Validation (2002)
• Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices (2005)
• Technical Considerations for Pen, Jet, and Related Injectors Intended for Use with Drugs and Biological Products (2009)
• Clinical Investigations of Devices Indicated for the Treatment of Urinary Incontinence (2011)
Other Requirements

GHTF Guidelines

• SG1 N:068 *Essential Principles of Safety and Performance of Medical Devices* (2010 draft)

• SG1 N:11 *Summary Technical Documentation for Demonstrating Conformity to the Essential Principles of Safety and Performance of Medical Devices (STED)* (2008)


• SG5 N:2 *Clinical Evaluation* (2007)

• SG5 N:3 *Clinical Investigations* (2010)

• AHWG N:2 *Unique Device Identification (UDI) System for Medical Devices* (2010 draft)
Practical Constraints

industry confusion

costs

ownership

development lifecycle
Industry Confusion

Source:
Costs

Cost of Change (incl. documentation, tracking, verifying earlier tests, add'l tests, etc.)

Time (development cycle)

Source:
Adapted from Scott Ambler, Agile Modeling (2002)
Ownership
Development Lifecycle

start traceability …?

Source:
Get to Market Now! Turn FDA Compliance into a Competitive Edge (2010, Logos Press)
Practically Speaking

• address records sought by inspectors

• capture logic through traceability

• need a systematic approach to traceability
  • cost-effective
  • generates records
  • allows easy reporting
  • maintain clear linkages
Rationale (Traceability)

• relationship to safety

• relationship to effectiveness

• relationship to risk mitigation

• relationship to testing
  • corrective actions
  • design changes/fixes
Lean Compliance Strategy

do’s v. don’ts

eight-step process

lifecycle placement
Traceability Do’s

• Form a **cross-functional traceability team**
• Clearly define accountabilities v. responsibilities in your SOPs
• **Start traceability** efforts when you make the “go/no-go” decision on a project
• Ensure that each specific feature → risk/request → tests → production characteristics (suppliers, processes, etc.)
• Plan for at least one significant **change** during product development
• Verify progress (and identify gaps) with a **mock FDA audit**
Traceability Don’ts

- Assume that you can remember dates, times and people involved in design decisions 4, 5, 7+ years ago
- Rely only on *internal audits* by your Quality department to catch missing traceability records
- Assume FDA inspector will only go back a few months in design history
- Forget that **traceability records** help you prove safety, efficacy, and compliance
- Lose sight of traceability costs – design changes include documentation changes, test changes, test re-work, etc.
Eight-Step Process

1. design control SOPs
2. product concept sheet
3. product specs
4. risk controls
5. traceability matrix
6. QC “yea/nay”
7. management review
8. audit
Design Control SOPs
Product Concept Sheet

- focus on:
  - intended use
  - desired features
  - distinguishing characteristics

- development considerations

Source: Get to Market Now! Turn FDA Compliance into a Competitive Edge (2010, Logos Press)
## Product Specs

<table>
<thead>
<tr>
<th>Product Component</th>
<th>Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>seal integrity</strong></td>
<td><strong>seal integrity specifications</strong></td>
</tr>
<tr>
<td></td>
<td>1. does not allow loss of product or moisture over shelf life</td>
</tr>
<tr>
<td></td>
<td>2. retain sterility over shelf life</td>
</tr>
<tr>
<td></td>
<td>3. does not allow alteration to finished product over shelf life</td>
</tr>
<tr>
<td><strong>stopper</strong></td>
<td><strong>stopper specifications</strong></td>
</tr>
<tr>
<td></td>
<td>1. biocompatible</td>
</tr>
<tr>
<td></td>
<td>2. not contain silicon</td>
</tr>
<tr>
<td></td>
<td>3. 20mm serum stopper</td>
</tr>
</tbody>
</table>
## Risk Controls

### Product Specifications

<table>
<thead>
<tr>
<th>Seals integrity specifications</th>
<th>Control for</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. does not allow loss of product or moisture over shelf life</td>
<td>USP &lt;1207&gt;</td>
</tr>
<tr>
<td>2. retain sterility over shelf life</td>
<td>stability study (ICH Q6A)</td>
</tr>
<tr>
<td>3. does not allow alteration to finished product over shelf life</td>
<td>USP &lt;381&gt;, USP &lt;87&gt;</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stopper</th>
<th>Stopper controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. biocompatible</td>
<td>USP &lt;88&gt; or USP &lt;381&gt;</td>
</tr>
<tr>
<td>2. not contain silicon</td>
<td>purchasing control</td>
</tr>
<tr>
<td>3. 20mm serum stopper</td>
<td>see drawing</td>
</tr>
</tbody>
</table>
Traceability Matrix

• manual (logs, spreadsheets)

• automated (database)
  • clear linkages
  • systemic reviews
  • red flag assessments
**Traceability Matrix (cont’d)**

![TestTrack | BMD Traceability Matrix](image-url)
QC “Yea/Nay”

• are the test results…?
  • within specification ranges

• have a “Plan B”
  • if results indicate failure, what will you do?
  • decide potential actions ahead of time based on design and risk
Management Review

• during design transfer

• relate *traceability data* to…
  • risk assessments
  • design specifications for materials / suppliers

• *do not forget*: relate to cost
  • senior management must factor in ROI
Audit

• audit **traceability records** prior to
  • IDE submission (*if any*)
  • market application submission (510(k))
  • any licensing agreements (due diligence)
  • patent applications / changes
  • long-term archival

• **every 2 years otherwise**
  • consider a mock FDA audit and gap analysis
Development Lifecycle & 8 Steps

Formal traceability

(Adapted from: Get to Market Now! Turn FDA Compliance into a Competitive Edge (2010, Logos Press))
Key Takeaway Review

- core regulatory requirements ✓
- four practical constraints ✓
- eight-step lean compliance strategy ✓
Want More?

**Traceability Resources**
http://www.seapine.com/traceability.html

**Six Exercises To Strengthen Traceability**

**How To Have A Painless FDA Audit**
http://downloads.seapine.com/pub/papers/PainlessFDAAudit.pdf

**The Seapine View Blog**
http://blogs.seapine.com/

**Seapine Life Science Solutions**
http://www.seapine.com/lifesciences.html
About Your Presenter

**John Avellanet** solves compliance problems for clients with practical solutions. Winner of the 2009 Best of Business award by the Small Business Commerce Association, Mr. Avellanet has earned international acclaim for his business-savvy, pragmatic compliance advice.

His latest book, *Get to Market Now! Turn FDA Compliance into a Competitive Edge in the Era of Personalized Medicine*, has earned multiple five-star reviews from industry publications, blogs, Amazon.com readers, and former FDA officials.

He has a breadth of experience designing, implementing, and being accountable for quality systems and compliance programs for FDA, the ICH, GHTF, and ISO. For more than 15 years, John served as an executive accountable for compliance, records management, and information technology, most recently as a C-level executive for a *Fortune 50* combination medical device and biotech subsidiary.

In 2006, Mr. Avellanet founded his private FDA compliance consulting and training firm, **Cerulean Associates LLC**.
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