

FDA Expectations for

Traceability

in Device & Diagnostic Design

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Acknowledgements

Tim Ulatowski
Dan O'Leary
Anita Fauchier
Mike Weber
Nancy Singer
Karen Steinberg
Kerry McCarter
Akos Bartha
Carl Anderson
Jackie Cassada
John Lincoln
Jim Shore
Tom Colonna
Terry Winchell
Chris Szustkiewicz
Kim Trautman
Larry Nicholson
Jan Welch
David Elder
Annamarie Kempic
Doug Throckmorton
Jonathan Lee

Agenda

fda requirements

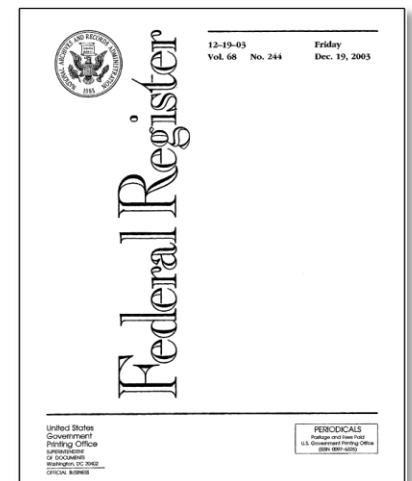
practical challenges

lean compliance solutions framework

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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)*
- *Radiation Safety Considerations for X-Ray Equipment Designed for Hand-Held Use (2008)*
- *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)
- SG3 N:15 *Implementation of Risk Management Principles and Activities Within a Quality Management System* (2005)
- 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

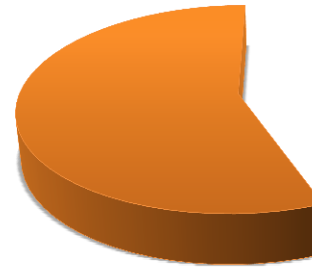


Industry Confusion

Design Requirements



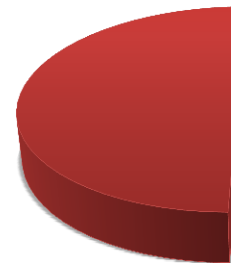
Issues/Defects/Anomalies



Tests



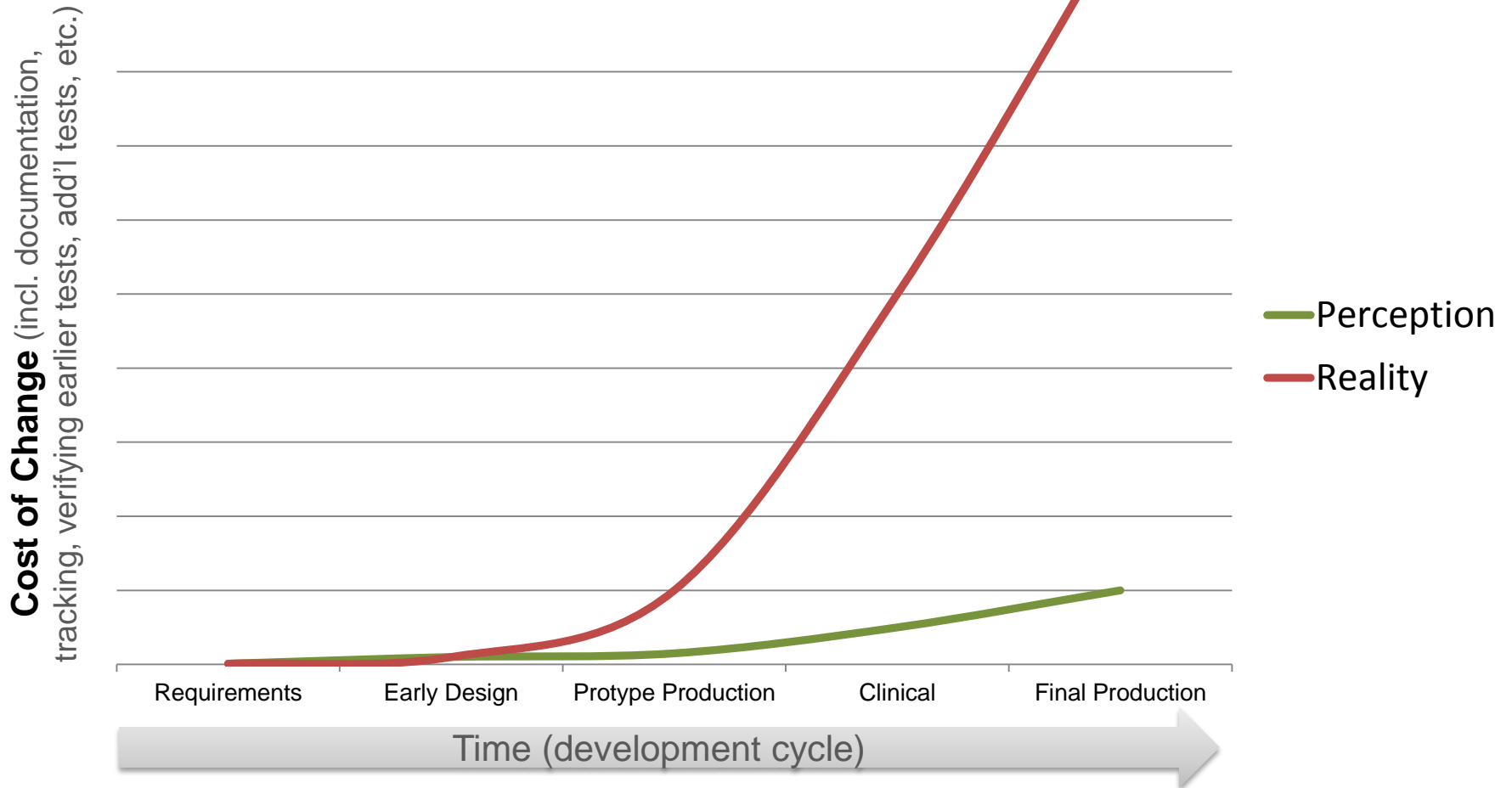
Risk Controls



Source:

Life Sciences Product Development Artifacts
Survey White Paper (Seapine Software, 2011)

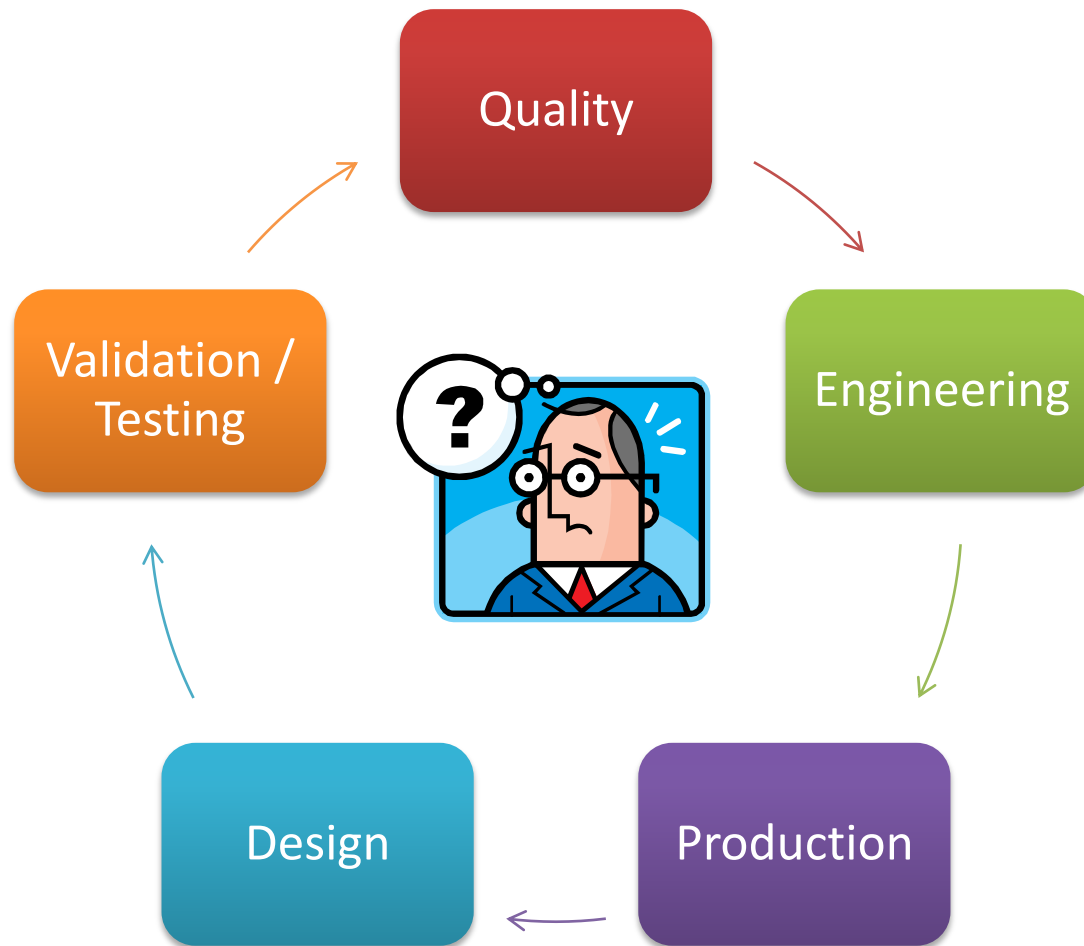
Costs



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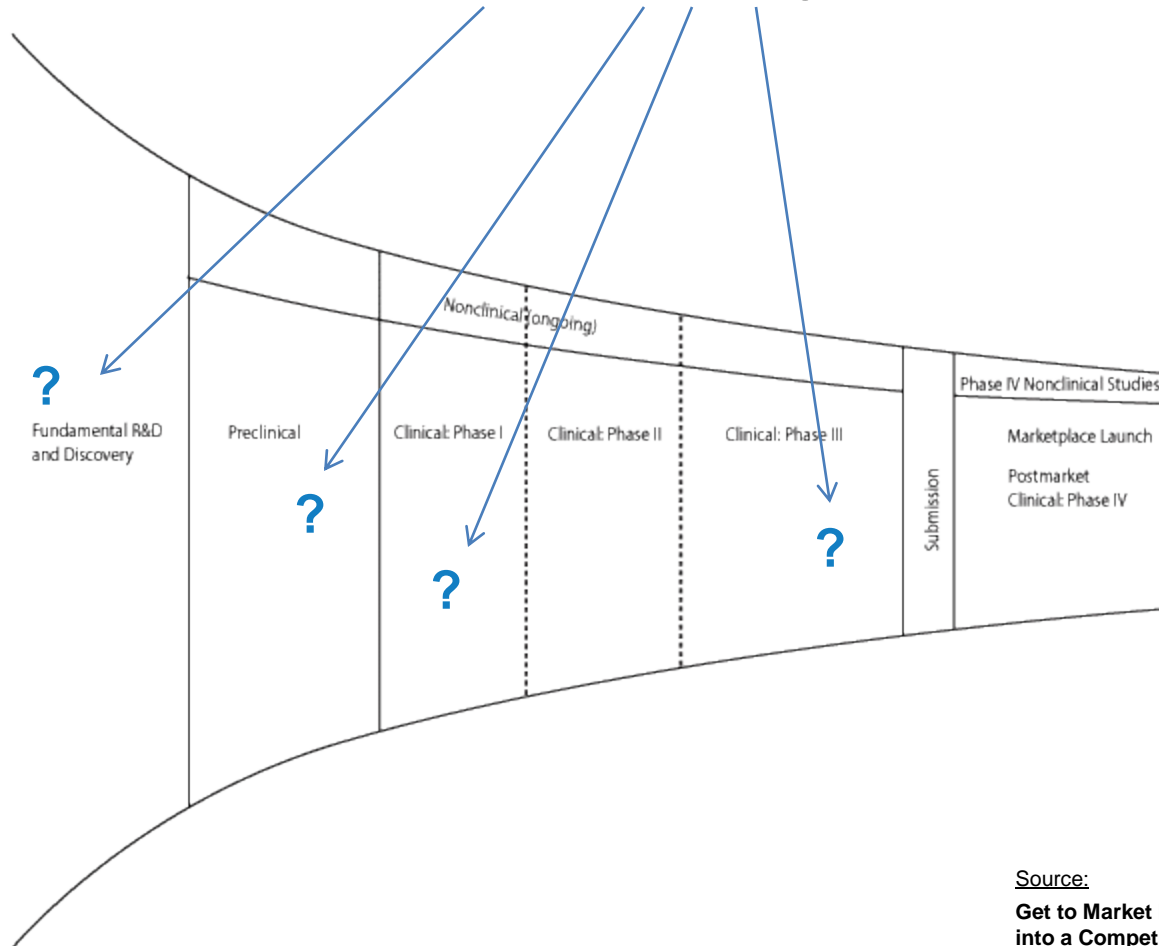
Adapted from Scott Ambler, **Agile Modeling** (2002)

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



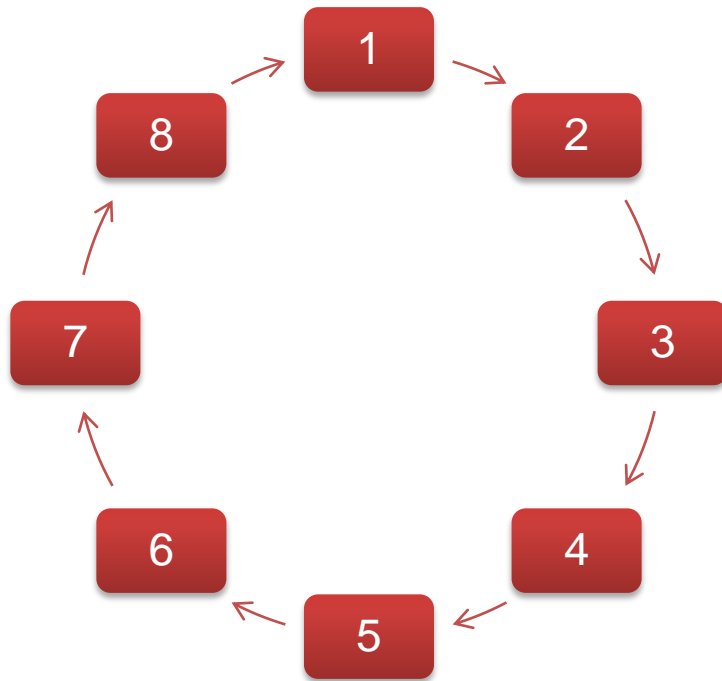
Traceability Do's

- 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

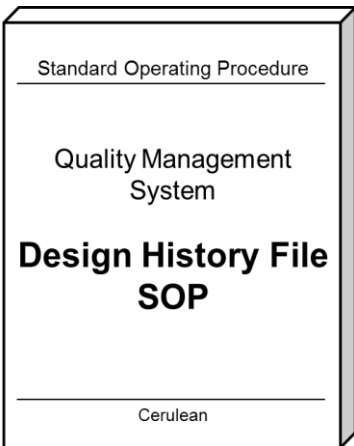
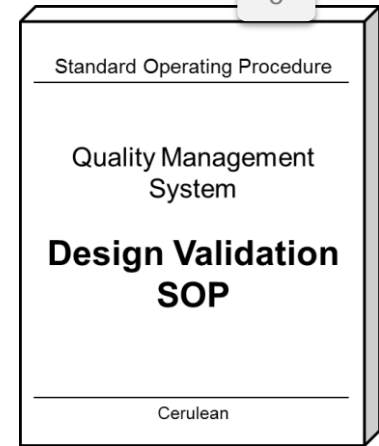
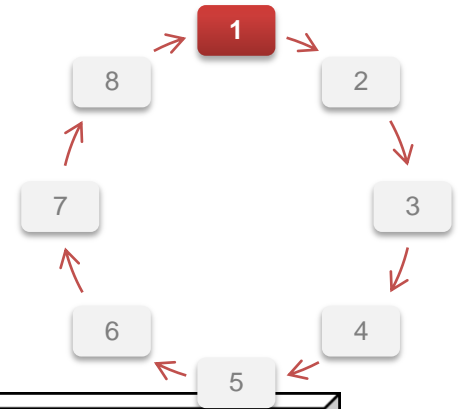
- Assume that you can remember dates, times and people involved in design decisions 4, 5, 7+ years ago
- Rely only on *internal audits* by your Quality department to catch missing traceability records
- Assume FDA inspector will only go back a few months in design history
- Forget that **traceability 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

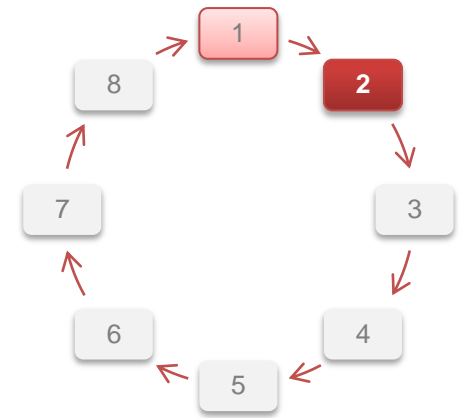


design control SOPs
product concept sheet
product specs
risk controls
traceability matrix
QC “yea/nay”
management review
audit

Design Control SOPs



Product Concept Sheet



The SmarterCompliance™ Toolkit

[INSERT YOUR COMPANY NAME]
PRODUCT CONCEPT SUMMARY

PRODUCT CONCEPT NAME: *[insert the proposed product name or your project name]*

OVERVIEW
[craft a very brief summary of your new product concept addressing what specific need / gap is being addressed, think of what you might say at a cocktail party or to friends who ask what you're working on]

INTENDED MARKET / CUSTOMER
*[what is the size of the market?]
[what are the adoption rates of similar medicines in this customer population?]
[what are the specific types of customers who would use and/or buy this product?]
[why those specific customers?]*

CUSTOMER BENEFITS
*[explain the specific customer benefits]
[what exists in the marketplace now?]*

INTENDED USE
*[what does the medicinal product do?]
[are there any known side effects - beneficial or detrimental?]
[what are the various functions and/or means of delivery?]*

DISTINGUISHING / DESIRED FEATURES
*[what are the distinguishing features of your product that set it apart from potential or current competition?]
[why should each type of customer choose your product over something else?]
[are there any specific ease-of-use, ergonomic, or reimbursement features that will set your product apart?]*

DEVELOPMENT CONSIDERATIONS
*[what are the key technologies for this product and are they available?]
[do you hold, or are you in the process of applying for, all necessary patents? if not, can they be licensed or designed around?]
[do you have sufficient resources for designing and making this product? what might you want to outsource?]
[what is its current development stage?]*

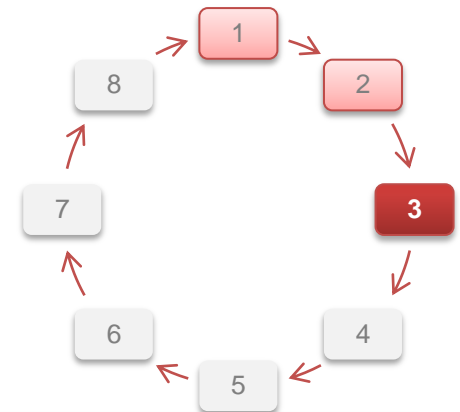
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- focus on:
 - intended use
 - desired features
 - distinguishing characteristics
- development considerations

Source:

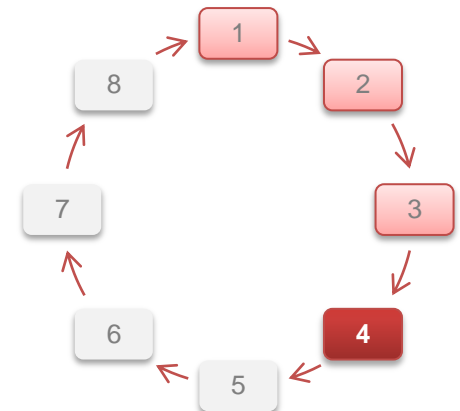
Get to Market Now! Turn FDA Compliance into a Competitive Edge (2010, Logos Press)

Product Specs



Product Component	Requirement
seal integrity	seal integrity specifications
	1. does not allow loss of product or moisture over shelf life
	2. retain sterility over shelf life
	3. does not allow alteration to finished product over shelf life
stopper	stopper specifications
	1. biocompatible
	2. not contain silicon
	3. 20mm serum stopper

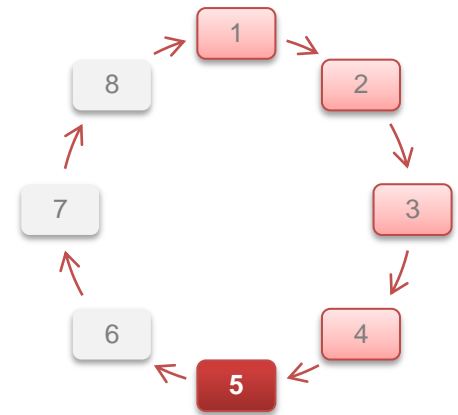
Risk Controls



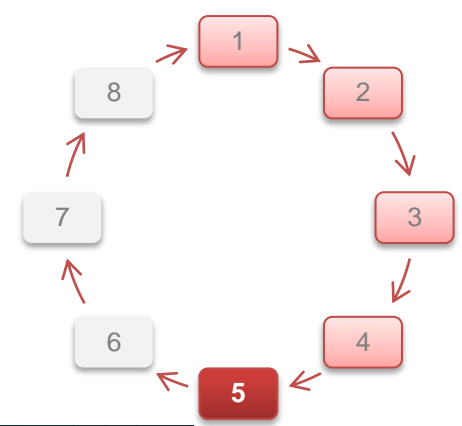
Product Specifications	Control for			
seal integrity specifications <ol style="list-style-type: none"> 1. does not allow loss of product or moisture over shelf life 2. retain sterility over shelf life 3. does not allow alteration to finished product over shelf life 	seal integrity controls <table border="1" data-bbox="900 589 1841 932"> <tr> <td data-bbox="900 589 1841 725">USP <1207></td> </tr> <tr> <td data-bbox="900 725 1841 803">stability study (ICH Q6A)</td> </tr> <tr> <td data-bbox="900 803 1841 932">USP <381> USP <87></td> </tr> </table>	USP <1207>	stability study (ICH Q6A)	USP <381> USP <87>
USP <1207>				
stability study (ICH Q6A)				
USP <381> USP <87>				
stopper <ol style="list-style-type: none"> 1. biocompatible 2. not contain silicon 3. 20mm serum stopper 	stopper controls <table border="1" data-bbox="900 1089 1841 1315"> <tr> <td data-bbox="900 1089 1841 1168">USP <88> or USP <381></td> </tr> <tr> <td data-bbox="900 1168 1841 1246">purchasing control</td> </tr> <tr> <td data-bbox="900 1246 1841 1315">see drawing</td> </tr> </table>	USP <88> or USP <381>	purchasing control	see drawing
USP <88> or USP <381>				
purchasing control				
see drawing				

Traceability Matrix

- manual (logs, spreadsheets)
- automated (database)
 - clear linkages
 - systemic reviews
 - red flag assessments

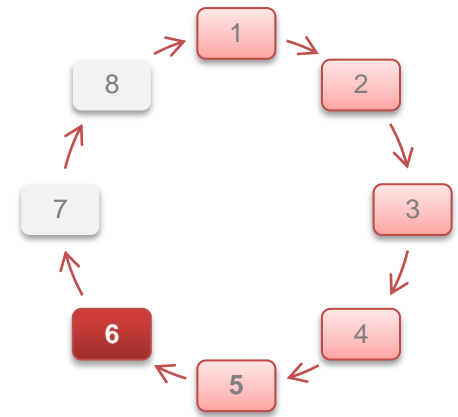


Traceability Matrix (cont'd)



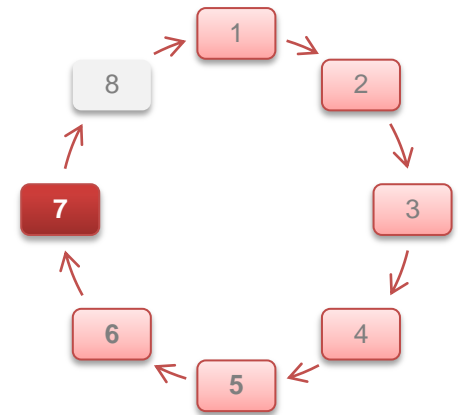
Doc. Artifacts	Documents	Related/Linked Doc. Artifacts	Test Cases	Test Runs	Issue
FRM-1 - BIOS support for VT	RD-14 - BMD Project - SRS	↑ SW-33 - Application Failure ↓ FMEA-95 - Lower Specification Limit			
FDA-2 - Electronic Signatures	RD-14 - BMD Project - SRS	↑ BIZ-21 - Not Applicable Notice ↓ FR-25 - Source Code Backup			
HW-3 - RAM		HW-47 - Hardware Durability	TC-7 - RAM - (REQ: 3)	✖ TR-17 - RAM - (REQ: 3) @ TR-18 - RAM - (REQ: 3) @ TR-272 - RAM - (REQ: 3) @ TR-273 - RAM - (REQ: 3) @ TR-274 - RAM - (REQ: 3) ✖ TR-275 - RAM - (REQ: 3) @ TR-276 - RAM - (REQ: 3)	ISSUE-14 - Open (Issue Confirmed), not assigned ISSUE-62 - Open, not assigned
	RD-14 - BMD Project - SRS	↑ BIZ-21 - Not Applicable Notice	TC-19 - RAM - (3)		
FR-4 - Login	RD-14 - BMD Project - SRS	↑ FR-297 - Functional Requirement ↓ FMEA-309 - New Document Risk Assessment	TC-58 - Compressed Sanitation Station		
BIZ-5 - General BMD Summary	RD-14 - BMD Project - SRS		TC-18 - General BMD Summary - (5)	@ TR-76 - General BMD Summary - (5) ✖ TR-95 - General BMD Summary - (5) @ TR-97 - General BMD Summary - (5)	
DES-6 - Branding	RD-14 - BMD Project - SRS	↑ BIZ-21 - Not Applicable Notice ↓ OSHA-85 - Ergonomics	TC-22 - Branding - (6)	@ TR-48 - Branding - (6) @ TR-49 - Branding - (6)	ISSUE-18 - Open, not assigned
BIZ-21 - Not Applicable Notice	RD-14 - BMD Project - SRS	↑ BIZ-5 - General BMD Summary ↓ SW-24 - Software Requirement ↓ HW-3 - RAM ↓ DES-6 - Branding ↓ FDA-2 - Electronic Signatures ↓ USER-94 - Automated Decision Process			
FDA-22 - Electronic Records					ISSUE-20 - Open, not assigned
FDA-23 - Quality Systems Regulation	RD-14 - BMD Project - SRS	↑ HAZ-310 - Wrong Alcohol Percentage			
SW-24 - Software Requirement	RD-14 - BMD Project - SRS	↑ BIZ-21 - Not Applicable Notice ↓ FR-296 - Functional Summary ↓ SW-91 - Operating System (OS) ↓ CON-28 - Security Groups	TC-10 - Software Requirement - (REQ: 24)	✖ TR-19 - Software Requirement - (REQ: 24) ✖ TR-20 - Software Requirement - (REQ: 24) ✖ TR-187 - Software Requirement - (REQ: 24)	ISSUE-6 - Open, not assigned
FR-25 - Database		@ AUD-72 - German Audio @ AUD-71 - French Audio			
	RD-14 - BMD Project - SRS	↑ SW-33 - Application Failure ↓ FR-27 - Independent Audit ↓ FMEA-95 - Upper Specification Limit			

QC “Yea/Nay”



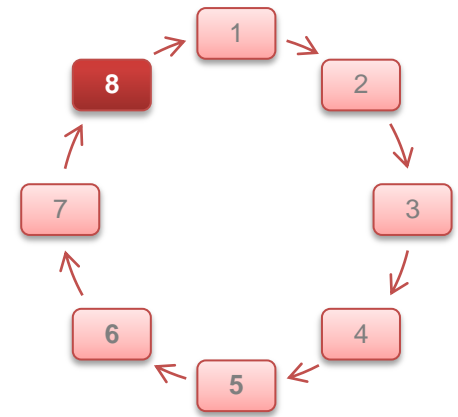
- are the test results...?
 - within specification ranges
- have a “Plan B”
 - if results indicate failure, what will you do?
 - decide potential actions ahead of time based on design and risk

Management Review



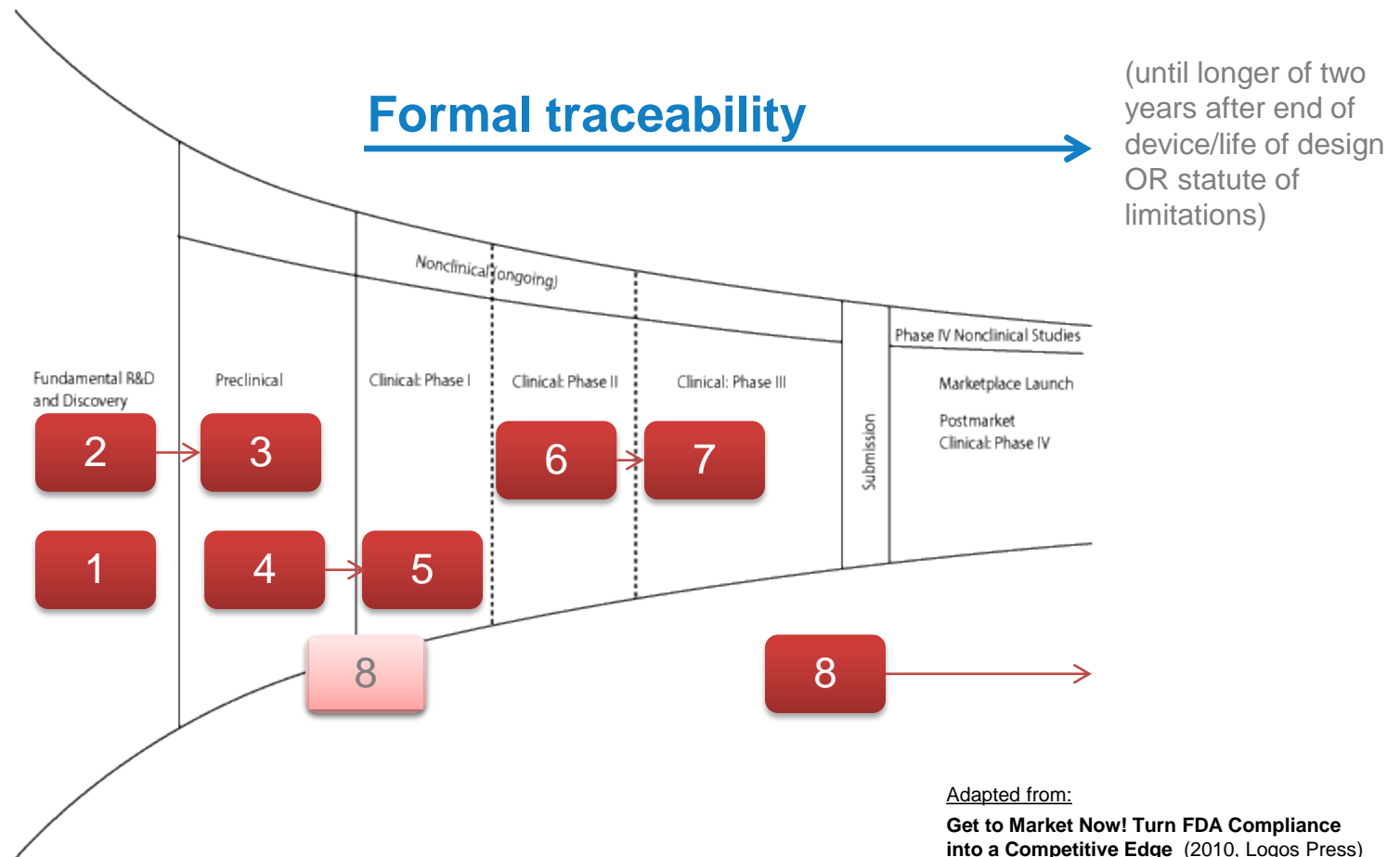
- during design transfer
- relate **traceability data** to...
 - risk assessments
 - design specifications for materials / suppliers
- *do not forget*: relate to cost
 - senior management must factor in ROI

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



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

<http://downloads.seapine.com/pub/papers/SixExercisesStrengthenTraceability.pdf>

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>

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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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