The Product Development Process for Medical Devices – A Practical Example

by

Amy Trocke

Nov. 15, 2022

Agenda

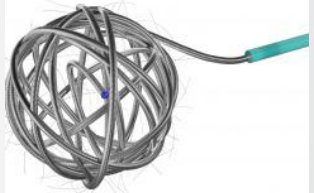
- Brief Introduction
- What is Product Development?
- Design Controls
- Product Development Process
  - Phase 1
  - Phase 2
  - Phase 3
    - Design Verification
    - Design Validation
  - Phase 4
  - Result
- Q &A

Who I Am

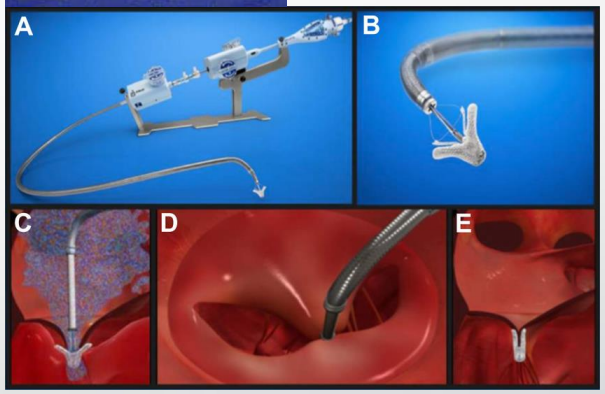
- 25-year industry veteran
- BS in Biomedical Engineering from Northwestern University
- MS in Management of Technology from the University of MN
- Current position: Sr. Engineering Manager of Structural Integrity within Structural Heart (heart valves) at Medtronic
- Previous Positions:
  - Director of Product Development at Surmodics
  - Principal R&D Engineer at St. Jude Medical, AGA, & Acist
  - Other R&D Engineering roles at Stereotaxis, Evalve, Micrus, and Angioguard

Patented Inventor: 18 granted patents, 27 patent applications

Johnson & Johnson
micrus endovascular



evalve

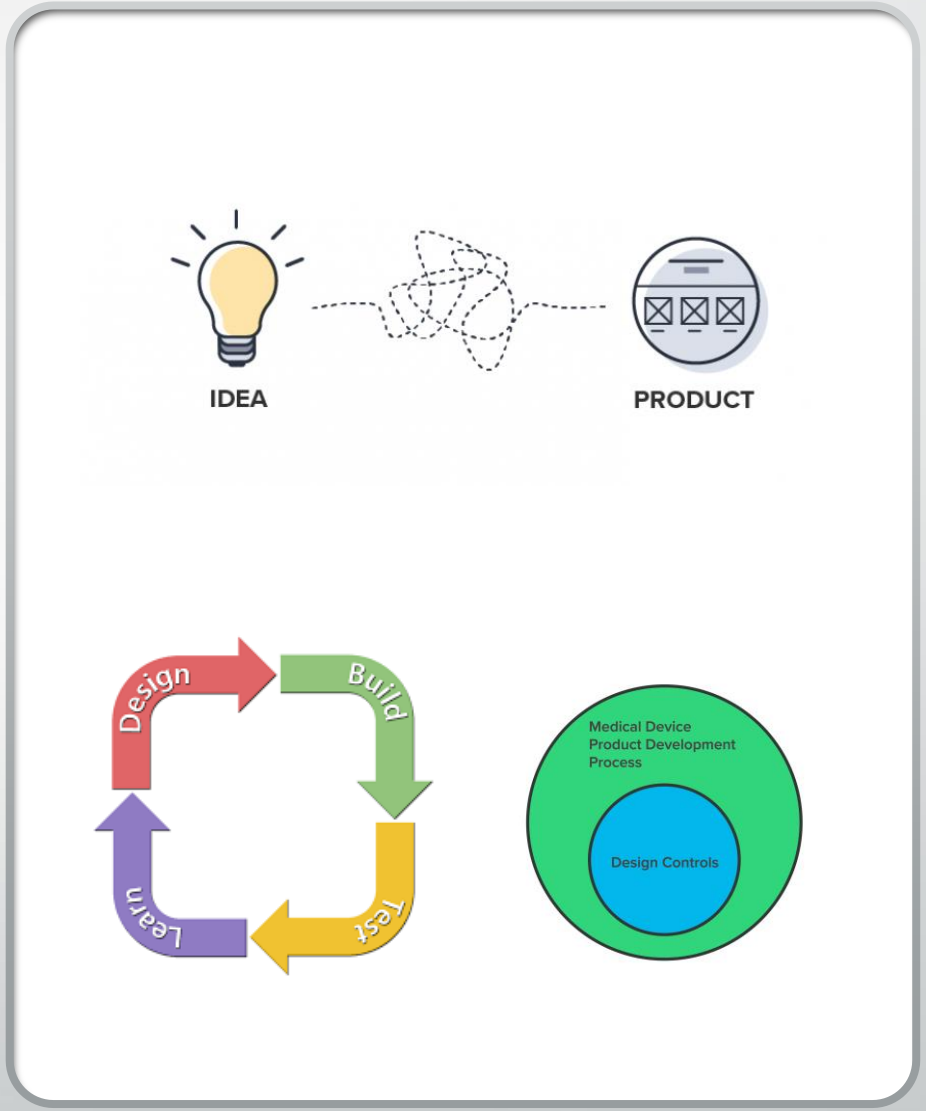


AGA MEDICAL CORPORATION
HOME OF AMPLATZER® PRODUCTS

Medtronic

What is Product Development?

- Product development is the process bringing a product from concept or idea to market release and commercialization.
- For engineers, this means design, build, test, learn, repeat.
- For engineers in medical devices, this also means design controls per FDA 820.30 and ISO 13485:2016. Design controls involve design planning to establish, maintain, and document design and development activities. They identify, describe, and define interfaces, responsibilities, and activities impacting device design. They also involve review, documentation, approval, and updates as development and changes occur.



Design Controls: FDA 820.30 & ISO 13485

Both FDA Design Controls and ISO 13485 Design and Development requirements expect you to keep documentation and records through the product development process.

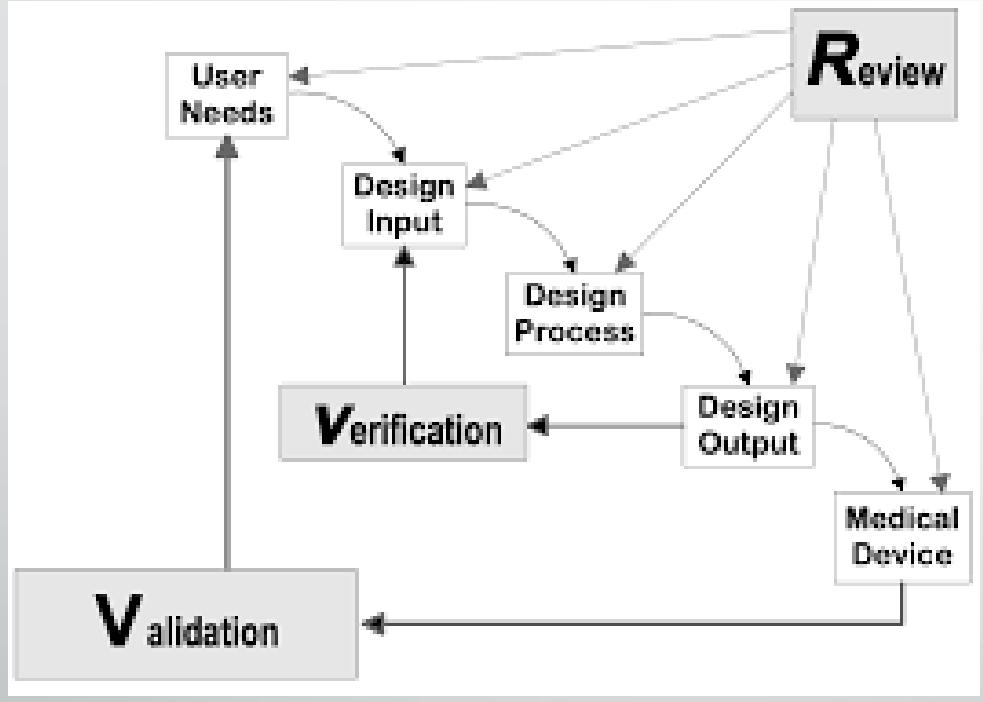
Ultimately, design outputs needs to meet design inputs and the finished device needs to meet the user needs.

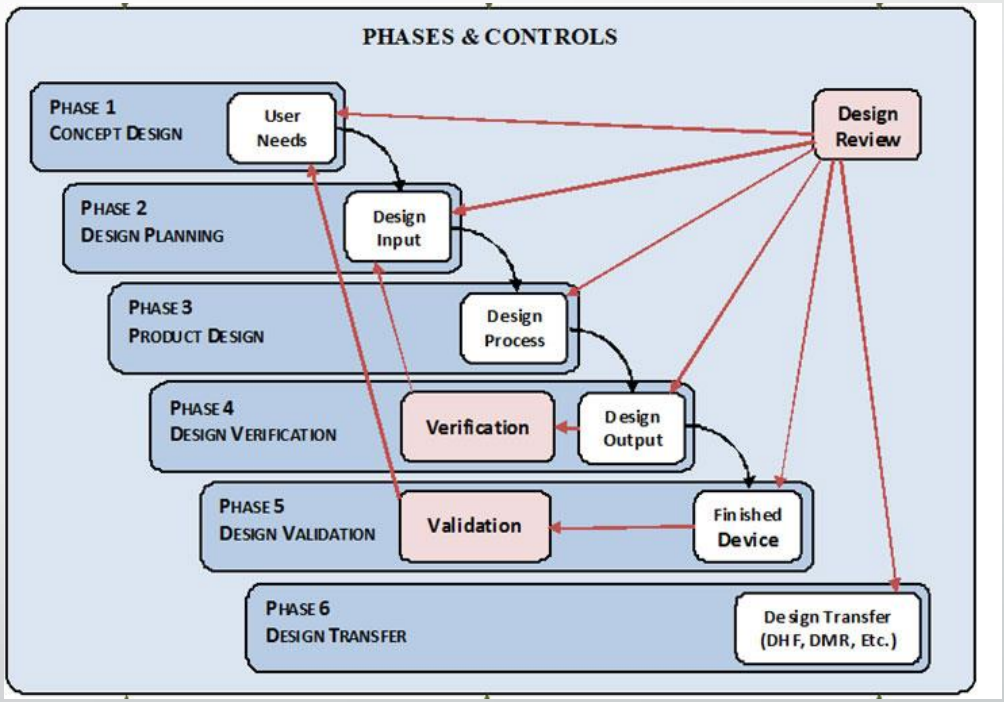
Design controls to build quality, safety, effectiveness and savings into your medical device.

Design Controls FDA 820.30	Design & Development ISO 13485:2016
(a) General	7.3.1 General
(b) Design and development planning	7.3.2 Design and development planning
(c) Design input	7.3.3 Design and development inputs
(d) Design output	7.3.4 Design and development outputs
(e) Design review	7.3.5 Design and development review
(f) Design verifications	7.3.6 Design and development verification
(g) Design validation	7.3.7 Design and development validation
(h) Design transfer	7.3.8 Design and development transfer
(i) Design changes	7.3.9 Control of design and development changes
(j) Design history file	7.3.10 Design and development files

Product Development Process

Design outputs must meet design inputs





FDA Design Control Guidance 21 CFR 820.30

Definition: Design Input

Per 21 CFR 820.30(c):

Design inputs are the physical and performance characteristics of a device that are used as a basis for device design.

It is expected that procedures are established and maintained for Design Input:

- Ensure requirements are appropriate by addressing user needs and intended use(s) in terms that are measurable.
- Address incomplete, ambiguous, or conflicting requirements.
- Document, review, and approve input requirements.

Examples of Design Input:

- Device functions
- Physical characteristics
- Performance
- Safety
- Reliability
- Standards
- Regulatory requirements
- Human factors
- Labeling & packaging
- Maintenance
- Sterilization
- Compatibility with other devices
- Environmental limits

Practical Example:
User Need Example: "Portable"
Define as "End user must hand carry device"
Consider dimensions and weight
Identify conflicting requirements (different units of measure) -> 5 lbs ± 1 kg
Resolve discrepancies -> 5 lbs ± 1 lbs

Definition: Design Output

Per 21 CFR 820.30(d):

Design outputs are the results of a design effort at each design phase and at the end of the total design effort.

It is expected that procedures are established and maintained for Design Output:

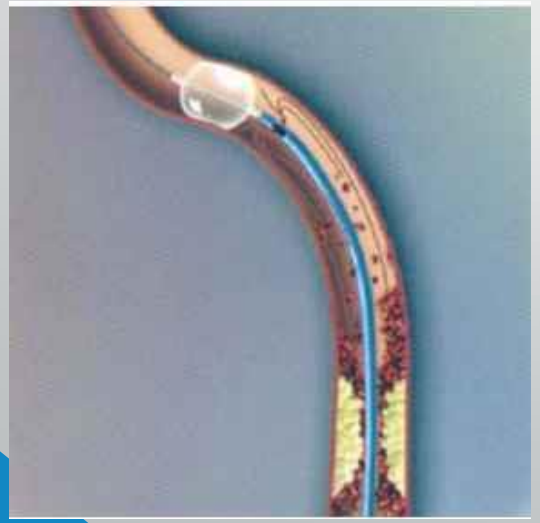
- Define and document design output in terms that allow an adequate evaluation of conformance to design input. (Appropriate testing)
- Reference definable/measurable acceptance criteria.
- Identify design outputs essential for the proper functioning of the device.
- Document, review, and approve output before release.

Typical Product Development Process (from an R&D perspective)

	Phase 1 Concept	Phase 2 Development	Phase 3 Design Verification & Validation	Phase 4 Design Transfer to Manf.	Phase 5 Production/ Commercializ'n
R&D	• User needs/VOC • Design description • Initial prototypes • Initial prints/specifications • Design & development plan • Product Requirements Document –draft	• PRD- final • Mature prototypes • Test Methods • Design Verification Plan • Final Prints • Representative processes Design Freeze	• Design Verification Testing and Reports • Design Validation Reg. Submission	Support Transfer	Support as Needed
DA	• Risk Management Plan • Hazard Analysis • DHF	• DFMEA • UFMEA • Quality Plan • DHF	• Risk Management Report • DHF	• Update/Maintain Risk Management Report	
RA	• Regulatory Strategy	• Standards List	• Regulatory Submissions	n/a	
Manf	n/a	• Draft Manufacturing Processes	• Manufacturing Transfer Plan • Device Master Record	• Manufacturing Transfer • Process Validation	

Phase 1 at AngioGuard

	Phase 1 Concept
R&D	• User needs/VOC • Design description • Initial prototypes • Initial prints • Design & development plan • Product Requirements Document –draft



1998
VOC: Jay Yadav, an interventional cardiologist, wanted to design and develop a device to filter emboli from the blood during the treatment of vascular stenosis. Initially, he wanted to treat the carotid arteries during either endarterectomy or angioplasty. In this way, the brain is protected. Initially, the company pursued a less risky regulatory path with a coronary artery indication.

Competition: PercuSurge GuideWire System, which was indicated for carotid angioplasty. It's a balloon-tipped guidewire with an aspiration device for removing plaque and debris loosened during revascularization. It's also defined as a distal occlusion balloon protection device.

VOC: Jay also wanted to maintain blood flow, and he described his concept as a filter on a wire made with a "gossamer" material.

Phase 1 at AngioGuard

	Phase 1 Concept
R&D	• User needs/VOC • Design description • Initial prototypes • Initial prints • Design & development plan • Product Requirements Document –draft

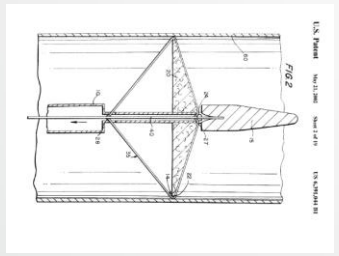
Initial Prototyping:

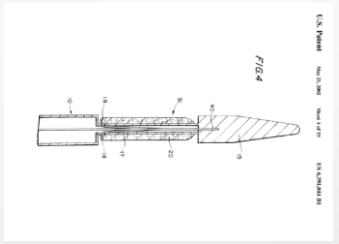
Acquired standard 0.014" guidewires.

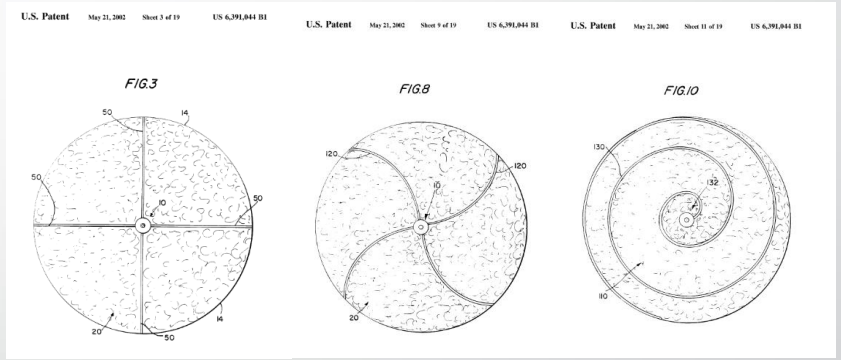
Tried various filter materials including woven materials

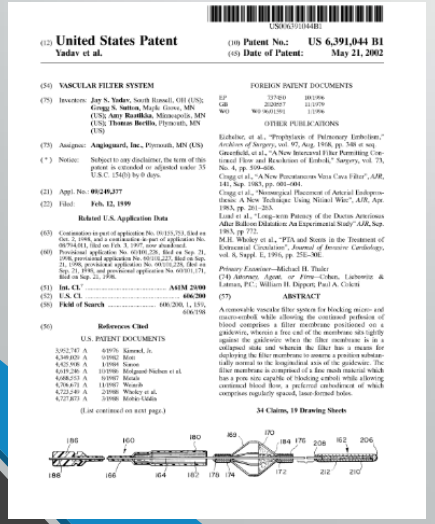
What pore size? Porosity? How would it attach to a support structure? How would it be delivered?

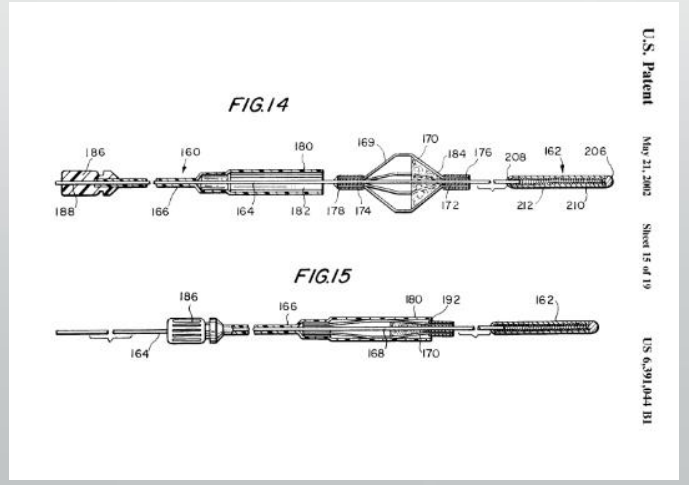
Acquired metal wire for support structure

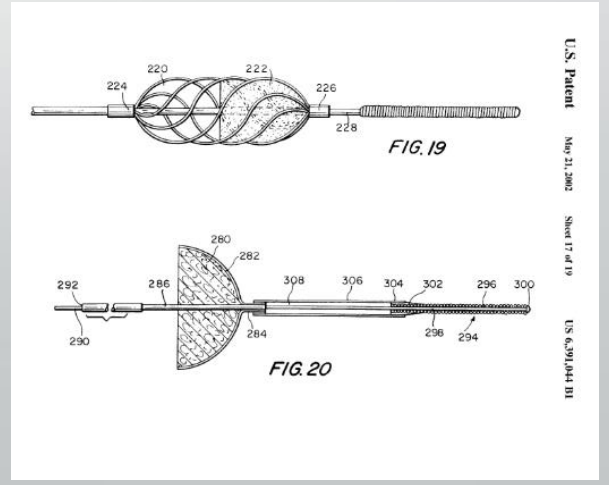










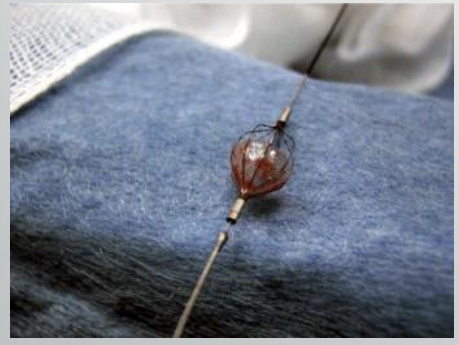


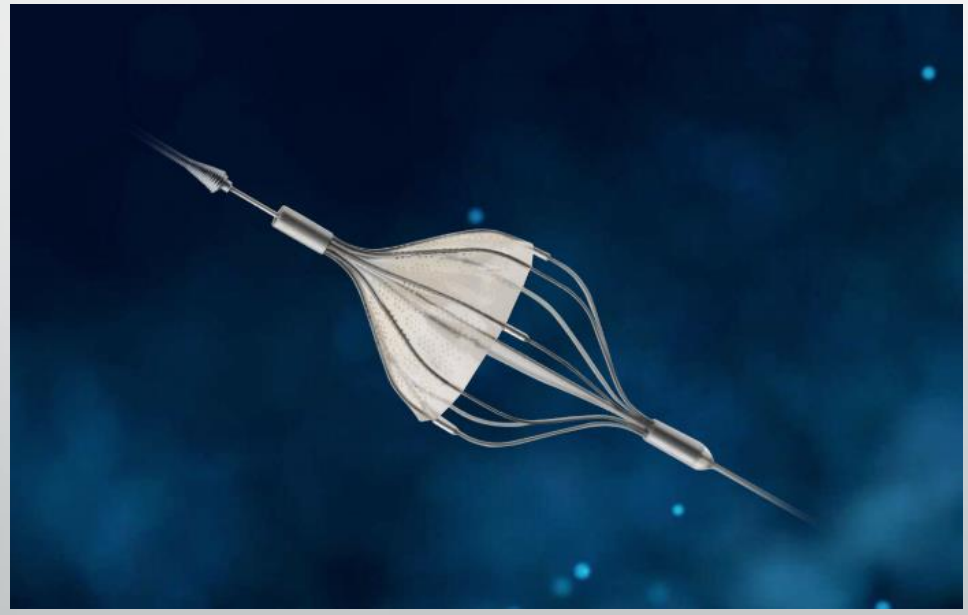
Phase 1 at AngioGuard

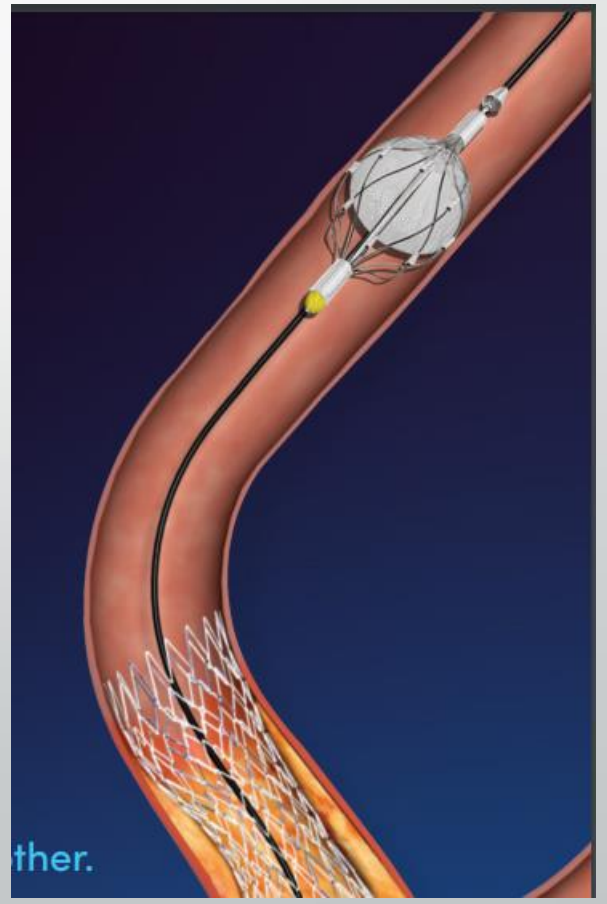
	Phase 1 Concept
R&D	• User needs/VOC • Design description • Initial prototypes • Initial prints • Design & development plan • Product Requirements Document –draft

Key technologies during development:

- Guidewire technology
- NiTi shape-memory alloy, shape set using superelastic properties
- Polymer dipping
- Laser ablation to "drill" the holes in the filter
- Thermal bonding
- Adhesives
- Polymer extrusion

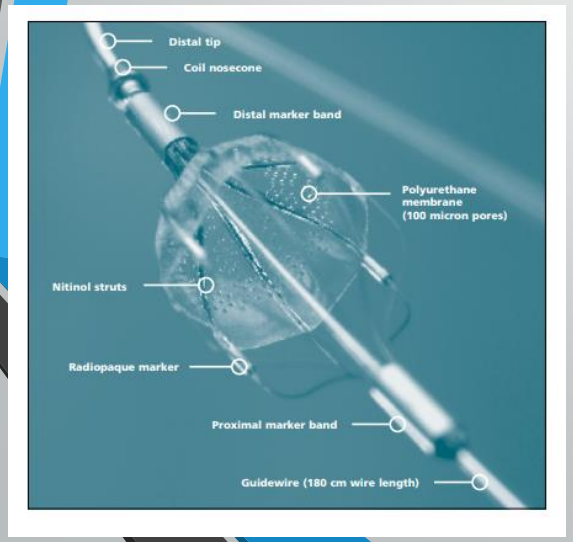


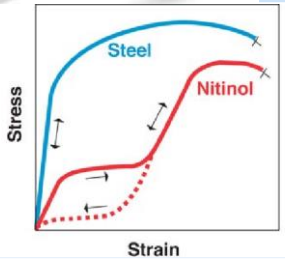
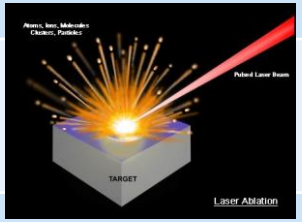




Phase 1 at AngioGuard

	Phase 1 Concept
R&D	• User needs/VOC • Design description • Initial prototypes • Initial prints • Design & development plan • Product Requirements Document –draft



Technology	Supplier/Partner	
Guidewire Technology	Lake Region Medical	
NiTi SMA	NDC?, Confluent, Ft. Wayne, Resonetics	
Polymer Dipping	Polyzen	
Laser ablation	Spectralytics	
Thermal Bonding	Beahm	
Metal Marker Bands	Johnson Matthey	

Phase 1 at AngioGuard

	Phase 1 Concept
R&D	• User needs/VOC • Design description • Initial prototypes • Initial prints • Design & development plan • Product Requirements Document –draft

Product Specification Example

Clinical / Use Req #	Clinical/User Requirement	Design Input Req #	Design Input Requirement	Specification	Source/Rationale	Test Method
Functional/Mechanical Requirements						
1	The Device shall reach the intended anatomy without excessive force	1.1	Flexibility	The deflection force of the proximal shaft tested per ASTM F206-08 shall be ≤ 1500 gf.	Specification set based on comparison testing of similarly marketed competitive devices (See TR1234)	TP-1026
2	The Device shall maintain structural integrity during anticipated clinical use.	2.1	Hub Tensile	The hub to shaft bond shall meet a 10N (2.25lbf) minimum requirement	Specification from ISO 10555-1:2013	TP-1038

AngioGuard specific design input requirements:

- Emboli capture in a bench flow loop (eventually with blood)
- Guidewire tracking-style bench tests
- Measurement and imaging equipment for inspections
- Pore size and porosity to determine the emboli size caught
- Radial force of basket structure

Remember:

Ensure requirements are appropriate by addressing user needs and intended use(s) in terms that are measurable.

Address incomplete, ambiguous, or conflicting requirements.

Phase 2 Development

- PRD- final
- Mature prototypes
- Test Methods
- Design Verification Plan
- Final Prints
- Representative processes

Phase 2 at AngioGuard

Common design input requirements for mechanical devices:

Mechanical Performance	Safety	Packaging
Trackability	Tensile strength	Seal strength
Flexibility	Torque strength	"Shake, Rattle, and Roll"
Kink resistance	Fatigue life	Environmental Conditioning
Simulated use	Biocompatibility	Aging
Flow rate	Aging	
Radiopacity	Sterilization	
Torque transmission	Particulate	
Radial force	Freedom from Leakage	

Other sources of Design Inputs: ISO Standards, FDA Guidance Documents, Competitive Review inducing 510(k)/submission documents, MAUDE database, Risk Analysis, business needs

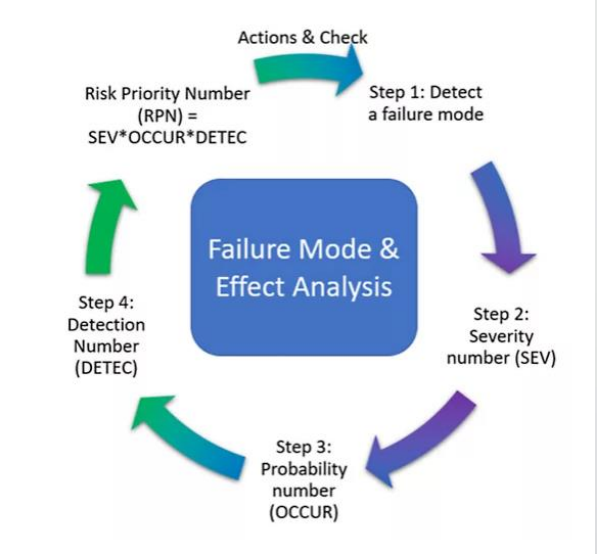
Phase 2 Development

- PRD- final
- Mature prototypes
- Test Methods
- Design Verification Plan
- Final Prints
- Representative processes

- **DFMEA**
- **UFMEA**
- **Quality Plan**
- **DHF**

- Standards List

Phase 2 at AngioGuard



What is Risk Analysis?
Intent of Risk Analysis per Preamble Comment #83:

- Identify possible hazards, including use error
- Calculate risk, under normal and fault conditions
- Determine risk acceptability
- Reduce unacceptable risks to acceptable levels
- Ensure changes made do not introduce new hazards

FMEA: Failure Mode and Effect Analysis
A systematic activity that evaluated potential system and product failures by identifying effects and outcomes of these failures and addressing them to eliminate or mitigate them. It also provides a documentation of this analysis.
In essence, DFMEA determines what might go wrong, how bad the effect may be, and how to prevent or mitigate it to improve product quality and reduce the risk of product failure.

Should be performed for design, use, and process in manufacturing.
For a design FMEA (DFMEA), consider each component, material, bond, and interface. Also consider the design requirements.
For a use FMEA (UFMEA), consider each step of the procedure where the device is used and what can go wrong.
For a process FMEA (PFMEA), consider each manufacturing process step.

Phase 2 at AngioGuard

Phase 2 Development

- PRD- final
- Mature prototypes
- Test Methods
- Design Verification Plan
- Final Prints
- Representative processes

- **DFMEA**
- **UFMEA**
- **Quality Plan**
- **DHF**

- Standards List

DFMEA Example

						Initial Risk				Residual Risk				
Design Input Requirement	Failure Mode	Cause	Risk Control **(Design Output)**	Harm/Effect (Applicable HA rows)	Severity (Max from HA Rows)	Occ	Occ Reference	Risk Index	Evidence of Effectiveness	Occ	Occ Reference	Risk Index	ALAP	RBA
1.1.1 Flexibility: The deflection force of the proximal shaft tested per ASTM F2606-08 shall be ≤ 1500 gf.	The deflection force of the proximal shaft is greater than 1500 gf	Braid Wire Diameter Too Large	Braid Wire Diameter Specification (PG-1234)	66 72 78	2	1	Occurrence based on Design Characterization testing documented in TR1234 – ppk 2.34 with an avg of 800gf	1	DVT Report #XXXX					
		Braid Wire Material Too Stiff	Braid Wire Material Specification (PG-1234)											
		Braid Pattern Too Stiff	Braid Pattern Specification (DW-5432)											
		Braid Pic Count Too High/Low	Braid Pic Count Specification (DW-5432)											
		Liner Material Too Stiff	PTFE Liner Material Specification (PG-4444)											
		Liner Wall Too Thick	PTFE Liner Wall Thickness Specification (PG-4444)											
		Proximal Shaft Extrusion Material Too Stiff	72D Pebax Extrusion Material Specification (PG-5555)											
		Proximal Shaft Extrusion Too Thick	72D Pebax Extrusion ID Specification (PG-5555)											
			72D Pebax Extrusion OD Specification (PG-5555)											
		Reflowed Shaft OD too small (polymer filling braid matrix too much)	Post-Reflow Proximal Shaft OD Specification (DW-6666)											
2.1.1 Hub Tensile: The hub to shaft bond shall meet a 10n (2.25lbs) minimum requirement	The hub to shaft bond breaks at a force lower than 2.25lbs.	Proximal Shaft/Hub Material Incompatible for Bonding	72D Pebax Extrusion Material Specification (PG-5555)	1 2 3	4	4	Occurrence based on Design Characterization testing documented in TR1234 – ppk .89 with an avg of 2.80lbf	3	DVT Report #XXXX					
			Hub Material Specification (DW-6666)											
		Reflowed Shaft OD Too Large (Insufficient Hub Wall Thickness)	Post-Reflow Proximal Shaft OD Specification (DW-6666)											
		Hub Bond Length Insufficient	Hub Bond Length Specification (DW-6666)											
		Hub Mold Bond Insufficient (improper melt flow/bond)	Pre-Sterile Hub Tensile Specification (DW-6666)											

*FMEA risk indices dictate the level of DV testing.

Phase 3 Design Verification & Validation

- Design Verification Testing and Reports
- Design Validation

Phase 3: Verification and Design Outputs

Per 21 CFR 820.30(f):
Design verification is confirmation by objective evidence that design output meets design input.
Establish and maintain procedures for Design Verification:

- Confirm through measurable means (e.g., test reports, etc.).
- Review, approve and document in Design History File (DHF).

Design outputs are the results of a design effort at each 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.

The device master record includes or refers to:

a) Device specifications (includes drawings, composition, formulation, component specifications)

b) Production process specifications (includes equipment specification, production methods and procedures, environmental specifications)

c) Quality assurance procedures and specifications (includes acceptance criteria and measuring and test equipment)

d) Packaging and labeling specifications (includes shelf-life)

e) Installation, maintenance, and servicing procedures

f) Bill of Materials (BOM): the complete "parts list" of all components that are needed to complete a saleable product

The outputs should include appropriate acceptance criteria to demonstrate the respective design input and associated standards are met and must be comprehensive enough to specify the device design to allow for design verification and design validation.

Phase 3
Design Verification & Validation

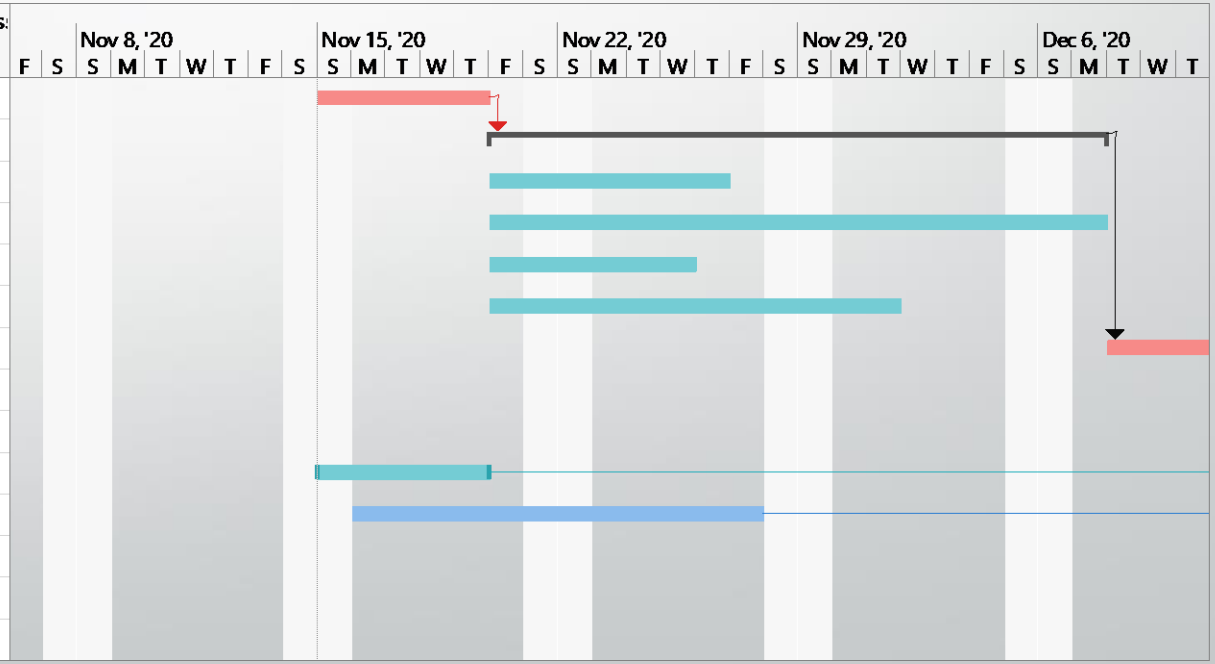
- Design Verification Testing and Reports
- Design Validation

Phase 3 at AngioGuard

Build & Test Final Design:
verifying the design outputs meet the design inputs.

Project Management: Keeping track of it all

ID	Task Mode	Task Name	Duration	Start	Finish	Predecessors
1		Develop Designs	5 days	Sun 11/15/2	Thu 11/19/2	
2		**Procure Parts**	**12 days**	**Thu 11/19/2**	**Mon 12/7/21**	
3		Wire	5 days			
4		Liners	12 days			
5		Distal Rings	4 days			
6		Molded Hubs	8 days			
7		Inspection	3 days	Tue 12/8/2(	Thu 12/10/2	2
8		Build & Package	5 days	Fri 12/11/2(	Thu 12/17/2	7
9		Sterilize	10 days	Fri 12/18/2(	Thu 12/31/2	8
10		Develop Tests	5 days	Sun 11/15/2	Thu 11/19/2	
11		Procure Test Equip	10 days	Mon 11/16/	Fri 11/27/2(	
12		Run Tests	5 days	Fri 1/1/21	Thu 1/7/21	9,10,11
13		Analyze Data	2 days	Fri 1/8/21	Mon 1/11/21	12
14		Write Report	2 days	Tue 1/12/21	Wed 1/13/21	13



Phase 3 Design Verification & Validation

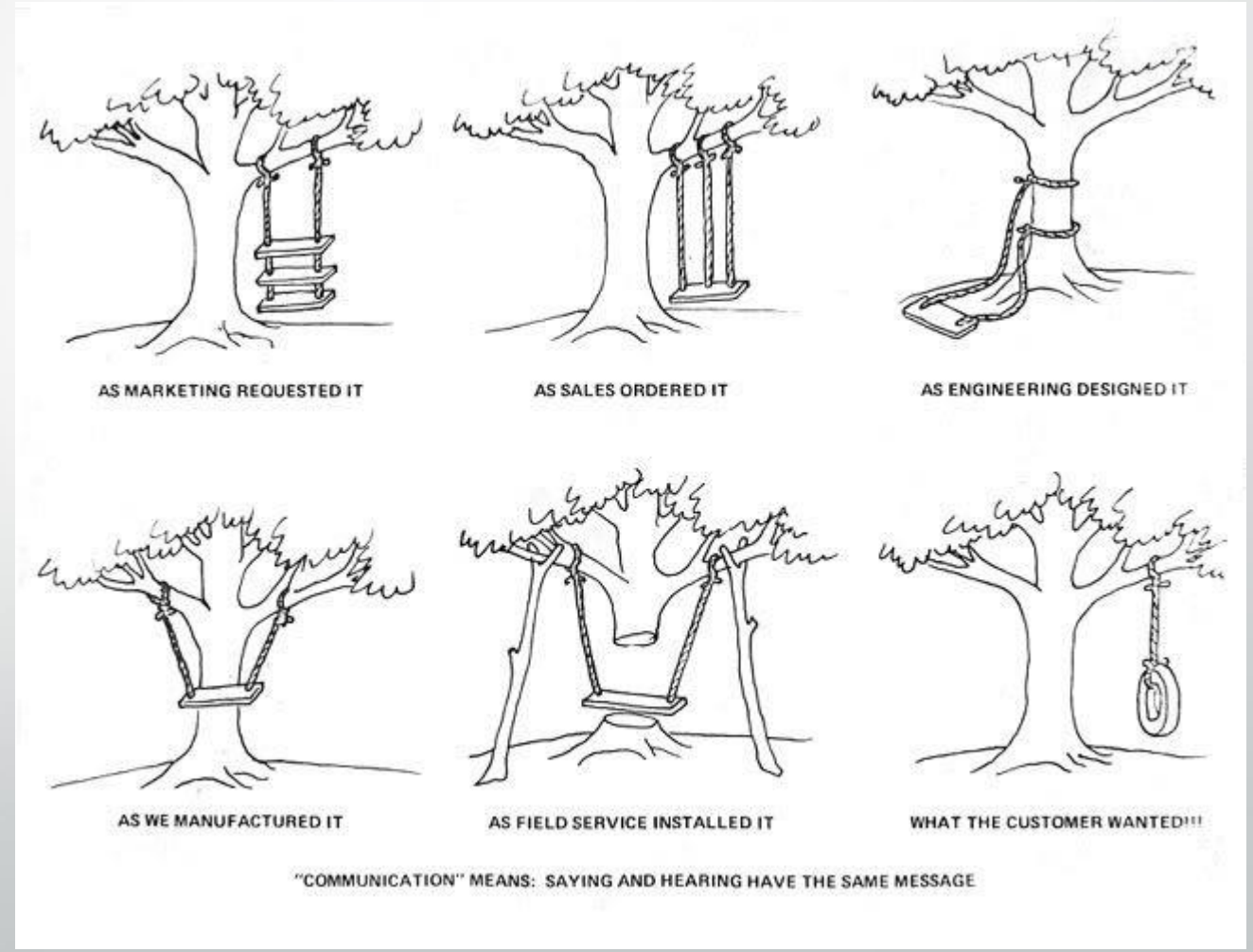
- Design Verification Testing and Reports
- Design Validation

Phase 3 at AngioGuard

Design Verification
– Output meets Input
– "I made the product *correctly*."
Design Validation
– Specifications meet user needs and intended use(s)
– "I made the *correct* product."

Types of Design Validation:
- Simulated Use on the Bench
- Pre-clinical study (animal study)
- Clinical study

Verification vs. Validation

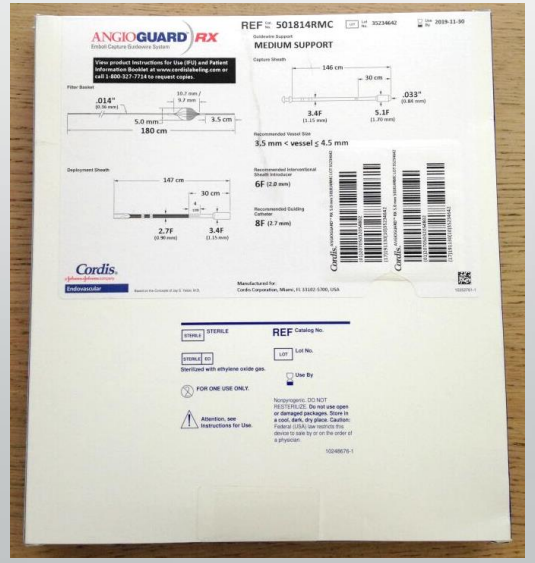


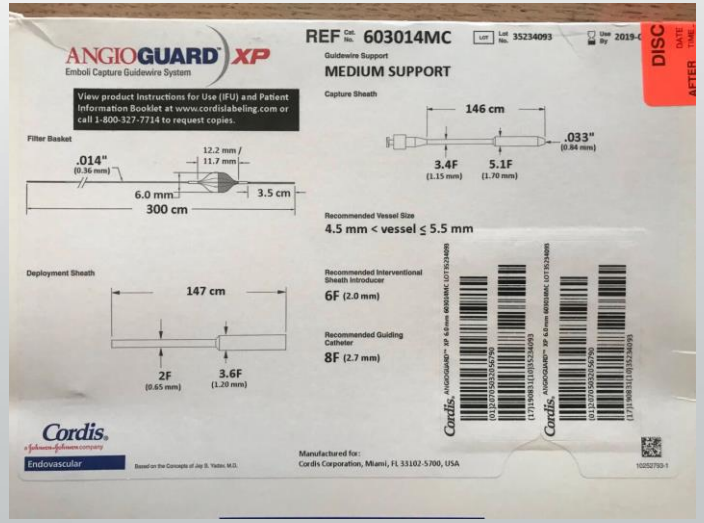
Phase 4 Design Transfer to Manf.
Support Transfer
• Update/Maintain Risk Management Report
n/a
• Manufacturing Transfer • Process Validation

Phase 4 at AngioGuard

Per Design Transfer 21 CFR 820.30(h):
Establish and maintain procedures to ensure correct Design Transfer into production specifications.

- Is the Design accurately transferred to Production?
- A final stage of development is frequently done to ensure all outputs are adequately transferred.





Results:

News | July 8, 1999

Cordis Acquires Angioguard

Cordis Corp. (Warren, NJ) has acquired AngioGuard Inc., a Minneapolis-based developer of a containment technology designed to protect the heart and brain from embolic particles potentially dislodged during interventional medical procedures. Terms of the agreement were not disclosed.

"In combination with Cordis' best-in-class carotid stent systems, currently under clinical investigatior the US and Europe, AngioGuard's embolic containment technology could enable Cordis to offer customers and patients a total solution for the interventional treatment of carotid artery disease," saic Patrick J. O'Neill, Ph.D., Cordis Worldwide Group VP, Research & Development and New Business Development.

During interventional procedures such as carotid stenting and saphenous vein graft stenting, emboli (fragments of plaque or debris) that may be dislodged can pose significant risk of stroke or acute myocardial infarction. AngioGuard has developed proprietary embolic containment technology desigr to protect the heart and the brain from these particles. AngioGuard's technology incorporates a guide with a filter that is placed distal to (beyond) the target lesion to capture and retrieve emboli throughou these procedures.

O'Neill noted: "European approval to market the AngioGuard technology for coronary applications ha just been received, and we expect approval for carotid applications later this year. We also intend to rapidly initiate US clinical trials."

FDA U.S. FOOD & DRUG ADMINISTRATION

April 6, 2022

Dunia Bram
Principal Specialist, Regulatory Affairs
14201 N.W. 60th Avenue
Miami Lakes, Florida 33014

Re: K220654
Trade/Device Name: ANGIOGUARD XP Emboli Capture Guidewire, ANGIOGUARD RX Emboli Capture Guidewire
Regulation Number: 21 CFR 870.1250
Regulation Name: Percutaneous Catheter
Regulatory Class: Class II
Product Code: NTE
Dated: March 4, 2022
Received: March 7, 2022

Dear Dunia Bram:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

Q & A