Medical Device Product Development for Startups

- The Bitter Pill

AZBIO WEEK / CEI

8/19/2016

ERIC MILLER

PADT, INC.

Agenda

- Introduction
- Medical Device Development Fundamentals
- The Design Process
- Manufacturing and Other Stuff
- Lessons Learned & Next Steps

About

PADT

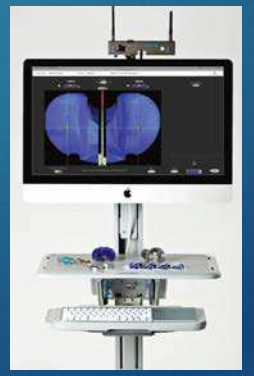
- Products and Services for Physical Product Development
- Simulation, Product Development, 3D Printing
- Dedicated Medical Device Group
- Based in Tempe
  - Albuquerque, Denver, Salt Lake City, LA

Eric Miller

- Co-Founder/Owner of PADT
- Mechanical Engineer
- UC Berkeley, '86
- FEA, Software, Design
- Marketing, HR, Operations

PADTMedical

- Team Dedicated to Medical Device Development
- Individual tasks to full product development
- ISO 13485 Certified
- In-house 3D Printing & Simulation
- An experienced team that knows engineering, design, and manufacturing.
- Up to half of our Medical work is with startups.



PADT StartUp Labs

- PADT Co-Located at CEI
  - Run CEI's 3D Printing tools
  - Provide mentoring and assistance to clients
- Design Days
  - CEI event for free face-to-face with engineers
- Access to 3D Printing at a discount to other Incubators
- Office Hours by appointment with CEI Clients

Developing a Medical Device is Different

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- Prove that it works
- Show that it doesn't harm people
- Aerospace comes close, but still not as much testing and documentation
- Requires a Quality System
- Has significant regulation
- So:
  - Takes longer
  - Costs more
  - More things to worry about
  - More things that need fixing

Why the "Bitter Pill?"

- Time for some tough Love
  - Costs you less in the long run if you plan for it
- People want to be positive and supportive and not discourage
  - Sets people up for failure
  - Under funding
  - Impossible milestones
- When you interact with professionals, it is important to be realistic
  - If you think people are charging too much or proposing too long… you are wrong.
  - The people that say "sure" are wrong or are going to drain you slowly

Medical Device Development Fundamentals

LET'S GET ON THE SAME PAGE

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Device Classes

Class 1

- Do not help support or sustain life
- Do not prevent impairment to human health
- Do not present a risk of illness of injury

- Subject to General Controls only
  - Mostly labeling, quality controls, and good manufacturing practices

Class 2

- Help support or sustain life
- May Prevent impairment to human health
- Can present a risk of illness of injury but existing methods can assure safety

- Subject to General Controls
- Subject to Special Controls
  - Labeling, standards, and post-market surveillance

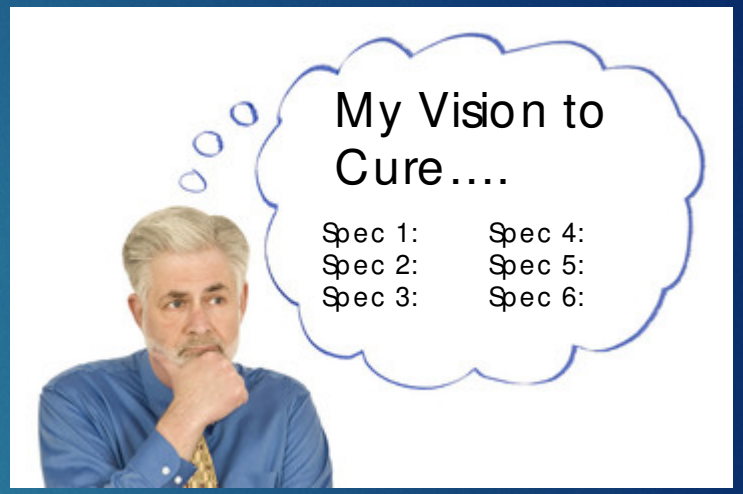
Class 3

- Help support or sustain life
- Prevents impairment to human health
- Presents a risk of illness of injury but safety can not be assured

- Subject to General Controls
- Subject to Special Controls
- Requires Pre-Market Approval
  - Scientific review: Testing or Similarity

Specifications

- Medical devices require specifications
- Not just part of good practice, it is how it is done
- Every aspect of the products behavior must be specified and designed to
  - And documented
- Many startups don't get this
  - This is my vision, now make it
  - No vision in medical. Only specifications



Quality

ISO13485

- International standard
- The FDA says: Follow this, and life is easy
- Not onerous or unrealistic
- A lot of work to set up and must be constantly maintained
- Binary: You either follow it 100% or your don't
- When done right, benefits your product development process
- Going through an update over the next 2-3 years – more expense

Quality Management System (QMS)

- The key part of ISO13485
- Documents how you are supposed to do every aspect of product development
- Once set up you need to maintain and follow
- If you don't have a QMS you need to work with a company that does
  - The "Design Authority"

Pre Market Approval

Clinical Trials

- Those Class 3 devices that need to prove that they are safe and they work
- Must submit scientific evidence
- Design a test and get approval
- Clinical trials are:
  - Long
  - Expensive
  - And may be inconclusive or fail
- High risk and expense
  - Should be reflected in plans

510k

- If a device is similar to an existing approved Class 3, you can skip the scientific proof
  - 510k is the paragraph in the FDA regulation
- You have to prove it is similar, a difficult and specialized process
- You may not pass – make sure you really are similar
- On an initial product, worth going 510k to get started
  - After success, add features that require clinical trials

Why do we do medical different?

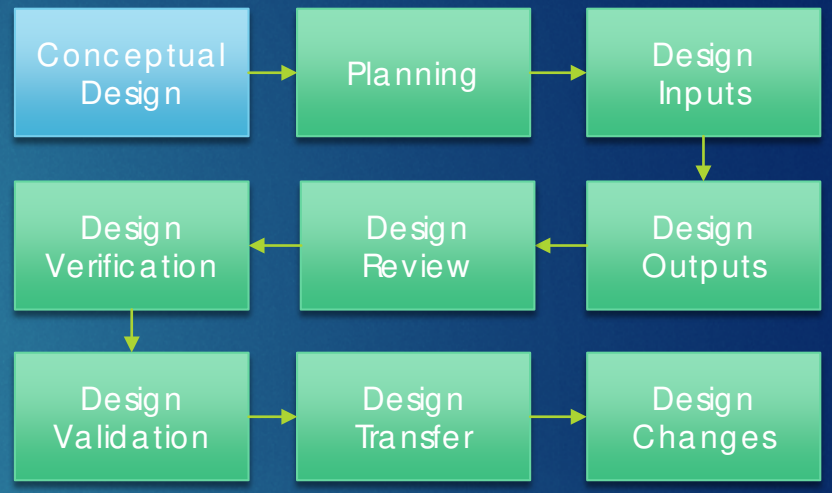
- People can get sick or die
- You can be sued
- Your reputation can be muck
- Everyone using the same process and system makes the regulation easier on everyone
- It helps make a better end product
  - This was not pushed down by no-nothing government officials.
  - It is industry developed and modified
- Better outcome is better for people and the bottom line

The Design Process

YOU NEED TO KNOW THIS, IT'S NOT WHAT YOU THINK

Med. Device Design Is a Set Process

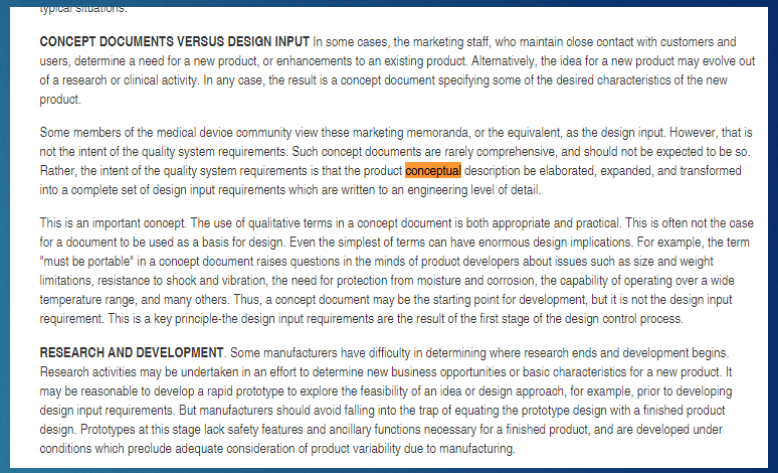
- A simple and consistent way for everyone making device:
  - Defines how you will do the design
  - Establishes what needs to be done
  - Documents that you did what you needed to do
- You can't deviate or take shortcuts
  - Do it right or FDA won't approve
  - Doing it wrong almost always ends up costing the same or more
- Documented by Design History File
- Done under ISO 13485



ISO 13485:2016

Step 0: Conceptual Design

- But wait, it is not that bad
- You can play around when you are in the conceptual design phase
  - No controls
- Does not avoid proper process
- Allows you to iterate quickly and try stuff out early
- It is important to:
  - Set a clear line between Conceptual design and controlled design
  - Not do too much in conceptual, you will have to repeat it
  - Keep in mind your design process



typical situations.

CONCEPT DOCUMENTS VERSUS DESIGN INPUT In some cases, the marketing staff, who maintain close contact with customers and users, determine a need for a new product, or enhancements to an existing product. Alternatively, the idea for a new product may evolve out of a research or clinical activity. In any case, the result is a concept document specifying some of the desired characteristics of the new product.

Some members of the medical device community view these marketing memoranda, or the equivalent, as the design input. However, that is not the intent of the quality system requirements. Such concept documents are rarely comprehensive, and should not be expected to be so. Rather, the intent of the quality system requirements is that the product conceptual description be elaborated, expanded, and transformed into a complete set of design input requirements which are written to an engineering level of detail.

This is an important concept. The use of qualitative terms in a concept document is both appropriate and practical. This is often not the case for a document to be used as a basis for design. Even the simplest of terms can have enormous design implications. For example, the term "must be portable" in a concept document raises questions in the minds of product developers about issues such as size and weight limitations, resistance to shock and vibration, the need for protection from moisture and corrosion, the capability of operating over a wide temperature range, and many others. Thus, a concept document may be the starting point for development, but it is not the design input requirement. This is a key principle-the design input requirements are the result of the first stage of the design control process.

RESEARCH AND DEVELOPMENT. Some manufacturers have difficulty in determining where research ends and development begins. Research activities may be undertaken in an effort to determine new business opportunities or basic characteristics for a new product. It may be reasonable to develop a rapid prototype to explore the feasibility of an idea or design approach, for example, prior to developing design input requirements. But manufacturers should avoid falling into the trap of equating the prototype design with a finished product design. Prototypes at this stage lack safety features and ancillary functions necessary for a finished product, and are developed under conditions which preclude adequate consideration of product variability due to manufacturing.

Step 1: Planning

- Planning is key to product development
  - Build in to the process
- This is where you:
  - Document how you will design the product
  - Identify the interfaces between different groups
  - Set down all activities that impact the process
  - Schedule
- Many startups want to skip planning because:
  - Enthusiasm
  - They think they know what to do
  - Costs money and nothing happens
- Must be updated as things evolve

SECTION B. DESIGN AND DEVELOPMENT PLANNING

I. REQUIREMENTS

§ 820.30(b) Design and development planning.

- Each manufacturer shall establish and maintain plans that describe or reference the design and development activities and define responsibility for implementation.
- The plans shall identify and describe the interfaces with different groups or activities that provide, or result in, input to the design and development process.
- The plans shall be reviewed, updated, and approved as design and development evolves.

Cross-reference to ISO 9001:1994 and ISO/DIS 13485 sections 4.4.2 Design and development planning and 4.4.3 Organizational and technical interfaces.

II. DISCUSSION AND POINTS TO CONSIDER

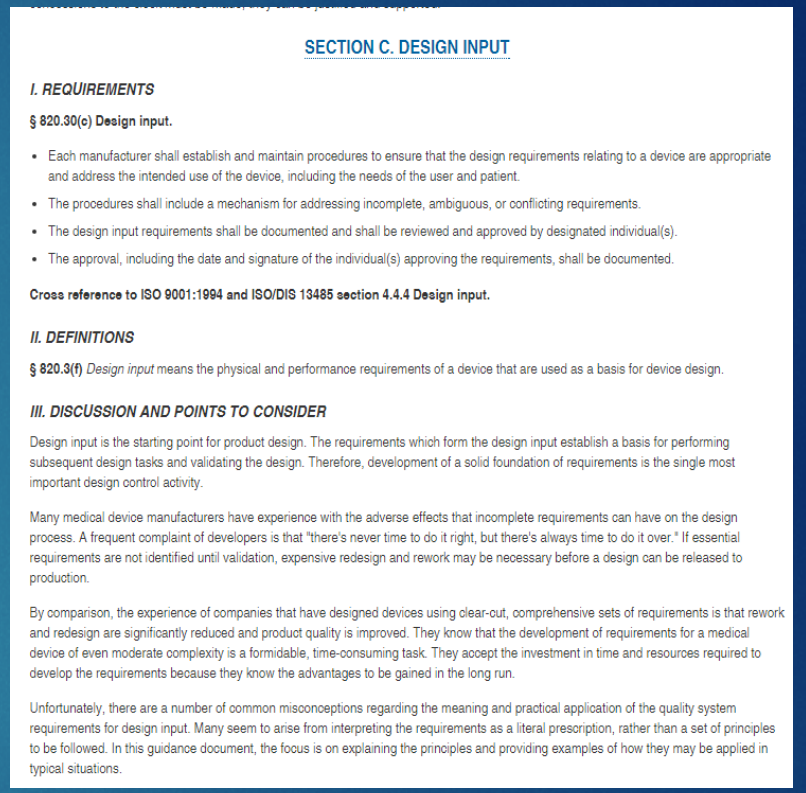
Design and development planning is needed to ensure that the design process is appropriately controlled and that device quality objectives are met. The plans must be consistent with the remainder of the design control requirements. The following elements would typically be addressed in the design and development plan or plans:

- Description of the goals and objectives of the design and development program; i.e., what is to be developed;
- Delineation of organizational responsibilities with respect to assuring quality during the design and development phase, to include interface with any contractors;
- Identification of the major tasks to be undertaken, deliverables for each task, and individual or organizational responsibilities (staff and resources) for completing each task;
- Scheduling of major tasks to meet overall program time constraints;
- Identification of major reviews and decision points;
- Selection of reviewers, the composition of review teams, and procedures to be followed by reviewers;
- Controls for design documentation;
- Notification activities.

Planning enables management to exercise greater control over the design and development process by clearly communicating policies, procedures, and goals to members of the design and development team, and providing a basis for measuring conformance to quality system objectives.

Step 2: Design Input

- It's all about the design requirements
- Someone experienced should help with this
  - Startups can be overly focused on the problem and mix business and engineering
- Not only must they be documented, they must be approved
- Three types of requirements:
  - Functional
  - Performance
  - Interface
- Don't forget: All requirements must be verified



SECTION C. DESIGN INPUT

I. REQUIREMENTS

§ 820.30(c) Design input.

- Each manufacturer shall establish and maintain procedures to ensure that the design requirements relating to a device are appropriate and address the intended use of the device, including the needs of the user and patient.
- The procedures shall include a mechanism for addressing incomplete, ambiguous, or conflicting requirements.
- The design input requirements shall be documented and shall be reviewed and approved by designated individual(s).
- The approval, including the date and signature of the individual(s) approving the requirements, shall be documented.

Cross reference to ISO 9001:1994 and ISO/DIS 13485 section 4.4.4 Design input.

II. DEFINITIONS

§ 820.3(f) *Design input* means the physical and performance requirements of a device that are used as a basis for device design.

III. DISCUSSION AND POINTS TO CONSIDER

Design input is the starting point for product design. The requirements which form the design input establish a basis for performing subsequent design tasks and validating the design. Therefore, development of a solid foundation of requirements is the single most important design control activity.

Many medical device manufacturers have experience with the adverse effects that incomplete requirements can have on the design process. A frequent complaint of developers is that "there's never time to do it right, but there's always time to do it over." If essential requirements are not identified until validation, expensive redesign and rework may be necessary before a design can be released to production.

By comparison, the experience of companies that have designed devices using clear-cut, comprehensive sets of requirements is that rework and redesign are significantly reduced and product quality is improved. They know that the development of requirements for a medical device of even moderate complexity is a formidable, time-consuming task. They accept the investment in time and resources required to develop the requirements because they know the advantages to be gained in the long run.

Unfortunately, there are a number of common misconceptions regarding the meaning and practical application of the quality system requirements for design input. Many seem to arise from interpreting the requirements as a literal prescription, rather than a set of principles to be followed. In this guidance document, the focus is on explaining the principles and providing examples of how they may be applied in typical situations.

Step 3: Design Output

- This is the actual design part
  - Drawings and specification documents
  - Production and process specifications
  - Compiled software
  - Work instructions
  - Quality Assurance Requirements
  - Installation procedures
  - Packaging and labeling
  - Test results that are needed
- Much more than just a “how do make it” drawing

Step 4: Design Review

- At key steps in the process, the design must be reviewed by all stakeholders
- Formal and documented step that should be done anyway
- Good Design Reviews can save huge, bad ones can cost you your product
- Done at every key stage of the design process

Step 5 & 6: Verification & Validation

- Verification
  - Make sure your design output meet your inputs
  - Mostly documenting that stuff was done
- Validation: the device meets the user's needs
  - Requires documentation and often some sort of testing
- Must be documented for review
- Can be expensive
- Passing Validation is not a given
  - Don't just assume everything will be fine
- An experienced person knows how to do this to minimize expense and risk

Step 7: Design Transfer

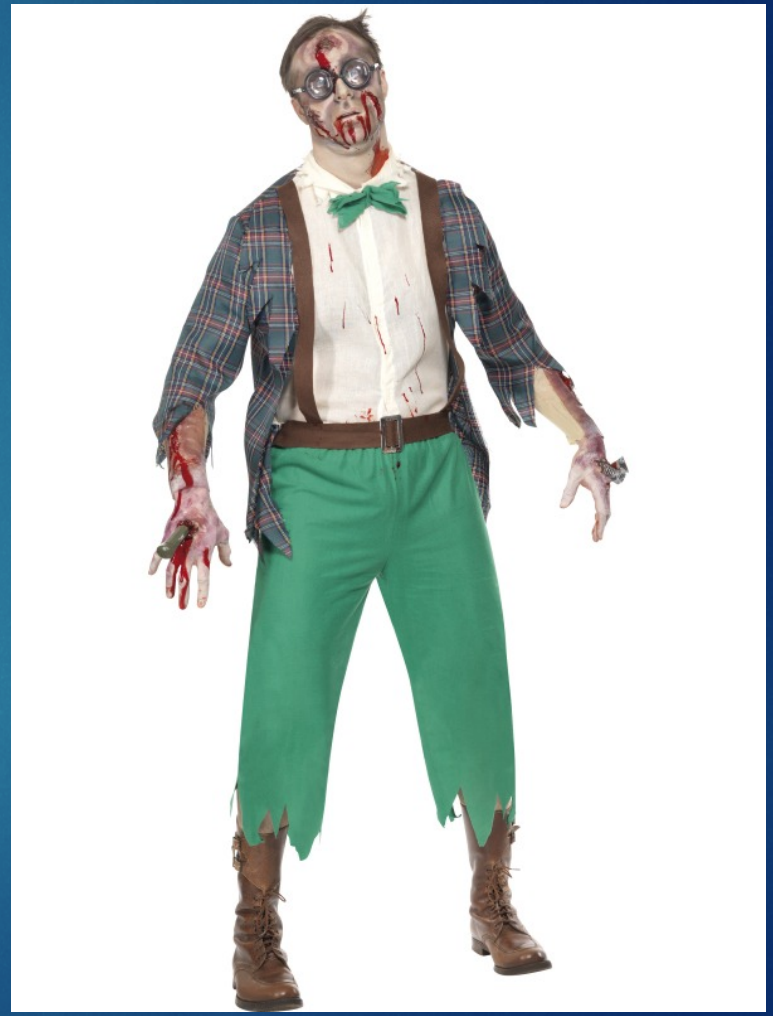
- You can't just throw a design over the wall to manufacturing
- You have to establish and maintain procedures that create a two-way communication with manufacturing
- Includes significant training documentation
- Jigs and fixtures are controlled as well
- This is a major step and expense that is often overlooked by startups
  - A failure at this point is catastrophic

Step 8: Design Changes

- The process is very flexible
  - You can change anything in the product
  - You just have to document it
- You just have to document everything
  - Takes extra time and effort
- Not too different from standard engineering change management
  - Many startups are not familiar with this process

Did this scare you?

- Good. It should
  - You need money
  - You need people
  - You need time
- Use experienced people
  - Especially when you are doing your business plan
  - Don't fit your design process to your budget.



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Manufacturing & Other Stuff

DESIGN WAS JUST THE START

Manufacturing is not a black box

- You don't just transfer to a vendor and product shows up
- FDA Requirements are the same for Manufacturing
  - Plan how you will make it
  - Establish what your steps and supply chain
  - Make it
  - Measure what you get
- Everything gets documented
- Problems and Deviations
  - Changes to the design and manufacturing process are allowed
  - Must be documented
  - Must be approved
  - Has to show it does not change design outputs

The Big Question: Where?

- In-house or Contract Manufacturing
  - The cost of setting up a quality system and capital costs drive most startups to CM's
- Be very careful if you do In-House
  - You must have experienced Medical Device MFG people on your team
  - Budget for establishing a quality system
- Picking the right CM is so important
  - Lowest bid is rarely a good idea
  - This stuff is hard and costs to do it right
  - Work with your CM from the beginning
- Note: Your clinical trial devices need to be done the same way as your final product
  - Don't switch vendors if you can help it.

More Stuff to Do

- You need to test and verify:
  - Bio-compatibility
  - Sterilization
  - Packaging
  - Labeling
- Everything must be tracked
  - Recalls & Traceability
- Input from the field is part of the Quality System
  - You have to document and make controlled design changes: Continuous Improvement

Lessons Learned & Next Steps

DON'T GIVE UP, IT'S A DOABLE THING

Some Suggestions:

- Don't Skimp, Don't use "best case" scenarios
  - Milestones that trigger more funding will kill you
- Focus
  - Do a minimum viable product for one market or application
  - Get it right, get your quality systems in place, generate revenue
  - Then add features and markets
- If possible, do a prototype manufacturing run
  - Problems will show up, figure them out early and before you are commited
- Quality should be a dedicated person
  - Not necessarily full time
- Don't treat ISO and FDA as an enemy, use it to your advantage
- Be Positive but Be Realistic

Next Steps

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- If you know all of this, you are good
- If not, get a mentor or advisor that does
- Your financial plan and schedule needs to be realistic
- Use resources out there
  - Lots of people want to help
- Resources:
  - FDA Design Guidence is online and fairly easy to read: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070627.htm

Additions from Q&A Comments

- During the product development process you need different kinds of people
  - Quality Engineers are important but are not really good at innovation and creativity
  - Design Engineers are important and provide creativity, but may not follow processes correctly
  - The key is to have both and find that balance between them
- Not a lot is really different from a business perspective from a top level for Medical Devices
  - What is different is that the costs/needs/requirements for problem solving, the team, and the customers are different.

Make it happen
Just remember to plan and document as you do it