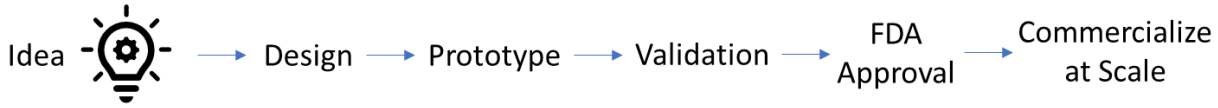
The Process to Commercialize a Medical Sensor

for Scale, Quality, Performance and Profit

David DiPaola – DiPaola Consulting, LLC

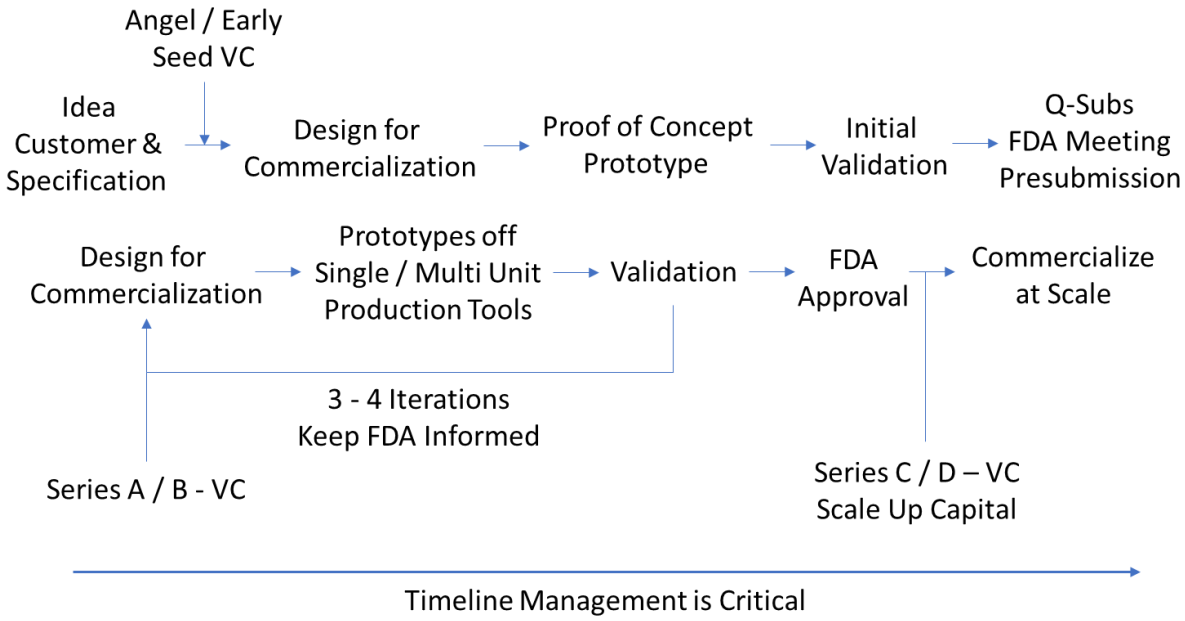
It is often mistaken that the commercialization process prior to scaling is a design, a lab prototype and experimental validation. Too often entrepreneurs and companies are ready to launch a medical product without a customer or an understanding of their needs, consideration for manufacturing and quality nor any evaluation of a supply base just to name a few. Here is visual example of this thought process:

Diagram 1: Typical Commercialization Process



This article challenges this thinking and presents an alternative process that starts with an idea accompanied by the end customer's specifications, a thorough review of the method for manufacturing, definition of a quality plan and an understanding of your validation requirements at the component and device levels. When a product is first being conceptualized in modeling, these prior topics need to be at the forefront of the designer's mind. There should also be consideration of your potential supply base and their capabilities. Furthermore, a plan should be developed for the path through the FDA approval process. Once this is complete, an iterative design is developed with a constant reassessment of performance, manufacturing, quality, validation and FDA approval. Here is an alternative proven model I have used for many years commercializing products in both automotive and medical devices.

Diagram 2: Alternative Commercialization Process



What is design for commercialization? Before you design your medical device consider the following questions:

1. How will it be manufactured and what tools / processes will be used?
2. How will it be tested (validation, in production and returns from the field)?
3. How will dimensional analysis be completed?
4. What controls are needed to ensure quality?
5. Who will be the suppliers of the components and what are their capabilities?
6. What is your path for FDA approval?
7. What are the customer's specifications?
8. What are potential failure modes and how can they be mitigated?
9. How can this core technology be used as a building block for derivative products once in production (keeping as much of the design as possible the same)?

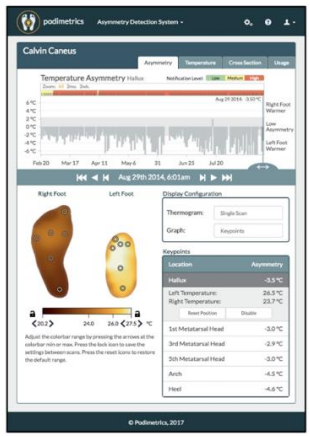
For example, let's say you are designing a flex circuit for use in a medical device and the critical envelop is the size of a dime. The first items you want to consider is the customer specifications for desired performance, environmental exposure, FDA regulations and how it will be validated as this will dictate the materials used. Next, how will the flex circuit be manufactured at scale and who will be the supplier. This will dictate specific design rules such as minimum trace width, separation between traces, copper thickness, tolerances and via requirements many of which play into tolerance stack analysis. Next, one evaluates quality requirements for testing in production and dimensional analysis. Test pads requiring pogo pin contact are larger than expected and can eat up valuable space in a small design and hence cannot be an afterthought when scaling (it could change design in production – very expensive). Furthermore, it is critical to develop a plan for on-going dimensional analysis (spaced is needed for fiducial markers) to ensure both capability and compliance to developed specifications that influence performance. Asking a supplier to hold tolerances beyond their capability adds significant cost to products. On the topic of quality, a failure modes and effects analysis can be performed to add features to the design that will minimize risk of failures or out of specification conditions. Lastly, can this flexible circuit be part of a core design building block for derivative products? If so, can specific features (plating for solder / wirebonding, test pads, passive configurations, etc) be added for universal use across multiple products? These are just some examples to consider when developing a product for design for commercialization.

An area where design for commercialization is not as strict is in the initial prototype for proof of concept. Here, not all the questions above need to be answered. However, one still wants to consider design for commercialization because if the initial prototype doesn't consider specific elements of this, one may not have truly shown conceptual proof. It is critically important that design for commercialization is adhered to once proof of concept is demonstrated and full design validation will follow.

Let's look at two examples; 1) a medical device where design for commercialization was considered much later in the development cycle and 2) a medical device using design for commercialization upfront. The first, Podimetrics Remote Temperature Monitoring (RTM) System is a device that monitors temperature

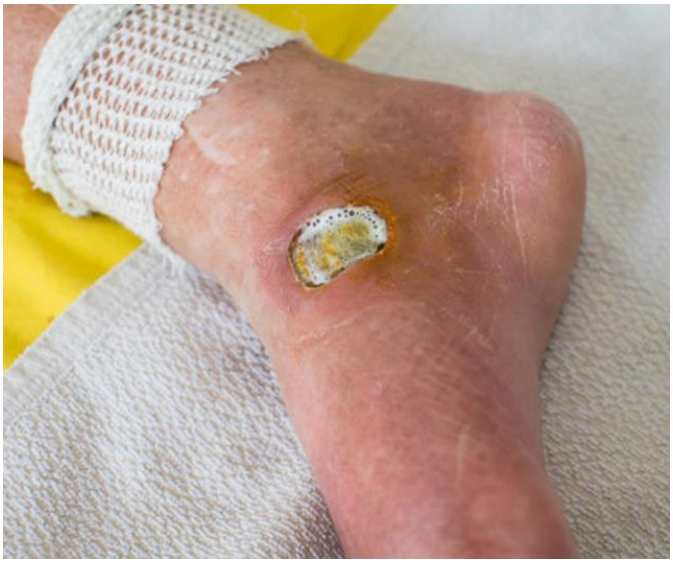
differences between multiple locations on the same foot and between feet to detect a future diabetic foot ulcer before it occurs. Actionable information is then provided via a smart device to patients and doctors to prevent a foot ulcer from occurring ("Podimetrics SmartMat").

Podimetrics RTM System ("Podimetrics SmartMat") and Software (Killeen)



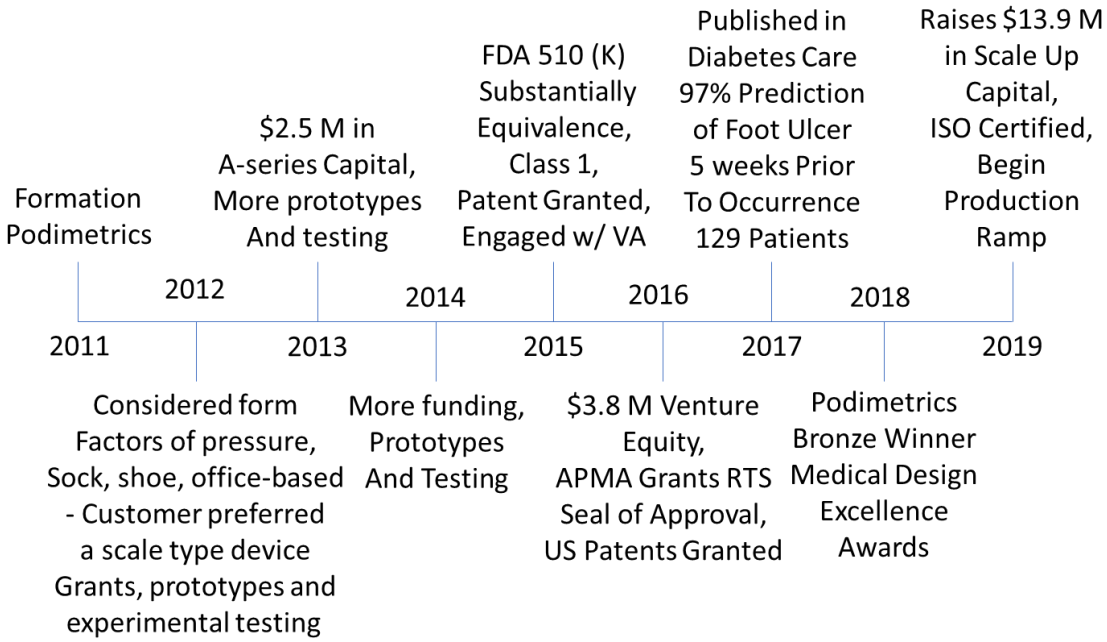
Diabetics are at risk of developing neuropathy (numbness in the extremities) resulting in uneven foot pressure distribution and resulting foot ulcers. The need for the RTM system is immense in that foot ulcers effect 3.6 Million diabetics in the US alone (CDC) and the cost of treatment for a foot ulcer, the leading cause of below knee amputations, is $30,000 post initial two years or $11 billion annually in US alone for diabetic foot care management and treatment (Raghav, Alok et al. 1099-1100).

Dibetic Foot Ulcers: Why You Should Never Ignore Them ("Diabetes & Endocrinology")



The benchmark time to market for a substantially equivalent FDA Class 1 device is 3 – 5 years. Let's consider a rough timeline for the Podimetrics RTM System.

Time to Market RTM System (Medgadget, "Clinical Evidence" and "News")



What we quickly see is Podimetrics has developed a high-performance system being able to identify 97% of observed diabetic foot ulcers with and average lead time of 37 days, temperature asymmetry of 2.22°C and false-positive rate of 57% in a clinical study of 129 patients. At a temperature threshold of 3.20°C, diabetic foot ulcer prediction decreased to 70% with 32% false positives in a lead time of 35 days (Frykberg et al. 973). When this product comes to market, it will drastically change a diabetics life for the better in this at-risk group by reducing risk of this debilitating injury. However, let's consider some of the areas they could have improved and expedited time to market.

Design for commercialization involves consideration of manufacturing and quality in addition to testing and measurement of the device and subcomponents at the forefront. Podimetrics brought their manufacturing partner into game very late (8 years after start). In design for commercialization, you would have selected your manufacturing partner early in the process, after initial validation, and involved their feedback into the design of the device to make it easier to manufacture and lower cost. You would also use the same manufacturing processes as the preferred partner in development to understand how production variation effects device performance beyond acceptable limits. This would prevent an expensive design change or yield loss when scaling the product. It also appears a quality plan may have been developed prior to FDA determination of substantially equivalence but Podimetrics did not receive ISO certification until 2019. In design for commercialization, quality is considered up front with

development of a manufacturing control plan, failure modes and effects analysis, dimensional capability studies and a plan for design and pilot validations. Furthermore, it appears some changes were made in the system after clinical studies and this increases risk of introducing a new variable that changes performance or can introduce a quality problem. For example, the external envelop, display and possibly materials changed.

Prototype Design (975)

Production Design ("Podimetrics SmartMat")

In design for commercialization, the product design and materials are iterated 2 – 3 times to the final production intent prior to clinical studies. In addition, production manufacturing processes and tools are used for manufacture of both the device and subcomponents in each of these iterations. I am often challenged that a startup cannot afford production equipment in the early stages. This is where commercialization centers come into play. Hesse Mechatronics, a top wirebonding company, is creating centers of excellence for wirebonding development and low volume runs. This is an excellent way to get access to extensive wirebonding expertise and test how production variation affects the performance of your product. Another company, SMART Commercialization Center, also has wirebonding, automated measurement, die attach and underfill capabilities that can be used for production development prior to scaling. Startups can use the production equipment at these centers at a fraction of the cost of an equipment purchase in the early stages of product development and then purchase the same equipment when ready to scale.

The Saliva Glucose Biosensor by GBS, Inc is another medical device being developed for scale commercialization. This is the first non-invasive, saliva-based glucose test for diabetes management ("The Saliva Glucose Biosensor").

How it Works ("The Saliva Glucose Biosensor")

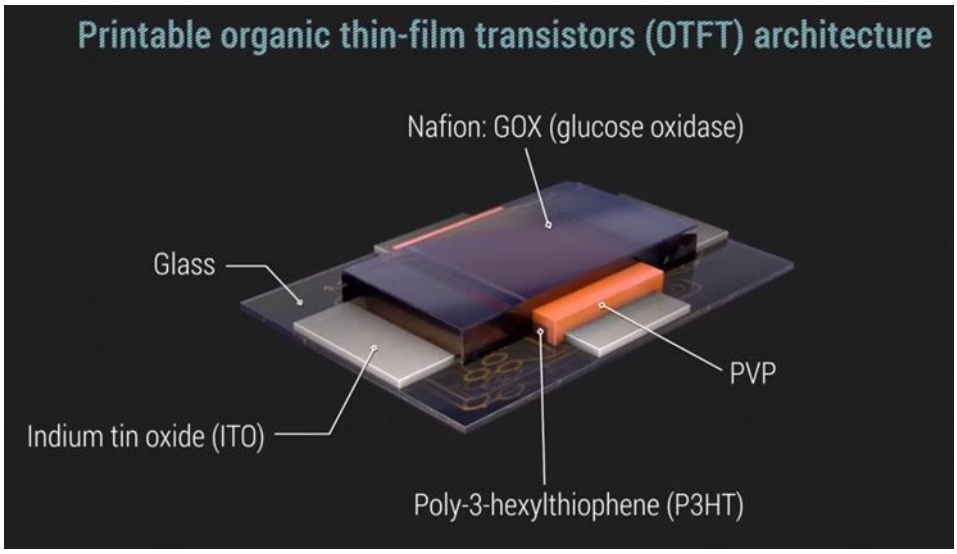
Place Saliva Glucose Biosensor in contact with saliva

With biosensor nearby, the digital app displays glucose measurement

App provides real time comparison and flags attention when needed

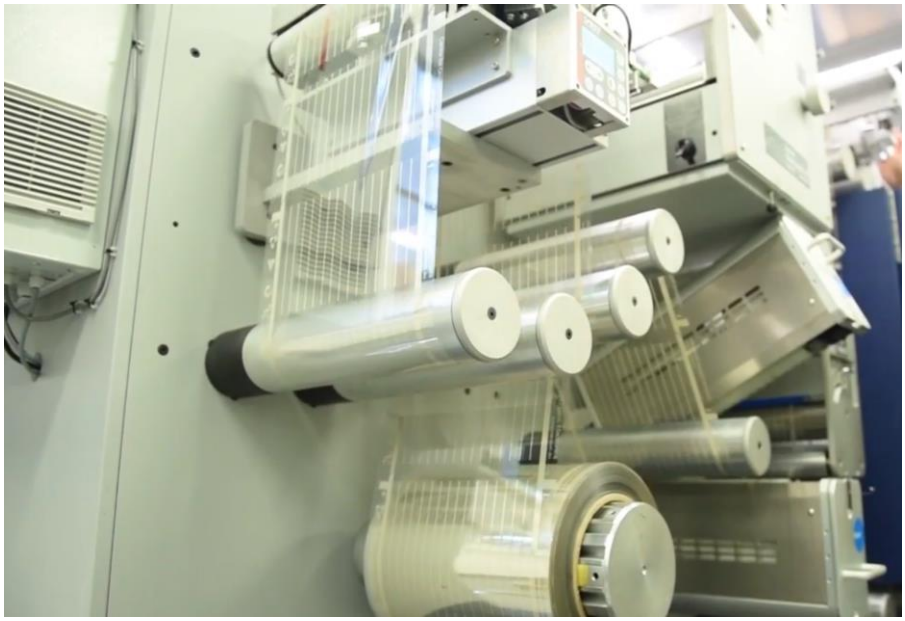
The Saliva Glucose Biosensor, started with an idea and a specification (the gold standard of glucose detection in blood) and developed a proof of concept prototype.

Proof of Concept for Saliva Glucose BioSensor ("Behind the Technology")



After proof of concept, the product quickly transitioned into design for commercialization using reel to reel printing very early in the development. A printable enzymatic glucose sensor based on organic thin film transistors was developed using an inkjet printing process. This design could be scaled quickly to service the approximate 422 million diabetics in the world ("Diabetes"). It is important to note this manufacturing strategy was developed prior to clinical studies for regulatory approvals so the clinical studies would not have to be repeated a second time costing more and lengthening time to market.

Reel to Reel Printing Process of Saliva Glucose BioSensor ("Behind the Technology")



In the case of the saliva glucose sensor, the design validation prototypes closely represented the production device that could then be fine-tuned through 2-3 design validations off tools capable of low volume production. This enabled testing of performance and failure to environmental exposure as it relates to expected variation in materials, dimensions and manufacturing. Scaling is then accomplished by adding capacity through tool replication and automation that is validated in the pilot phase with limited fine tuning.

Another great attribute of this technology is it is a platform technology (or core building block) where much of the product can be replicated in derivative products keeping manufacturing and component costs low by volume scale. For example, the organic thin film transistors can be adapted to detect a variety of substances that identify a range of diseases. Hence many derivative products beyond glucose sensing can be developed using the reel to reel printing process, substrates, electrical components, wireless communications and software. Currently work is being done to create substances that identify cancer, heart disease and allergies. One area this company needs to be careful of is project creep and defocus, resulting in drained capital and delayed timelines.

In conclusion, a great technical product alone is not enough to successfully launch a medical device at scale; design for commercialization is a necessity. Before one starts, it is important to have a clear plan of the timeline to market. The benchmark for FDA substantially equivalent medical devices is 3 – 5 years and competitors will take advantage of your missteps and investors will get impatient. Delayed time to market will also result in unnecessary cash burn. Design for commercialization should be considered at

the start of a project. This will minimize performance and quality issues that arise in production that are extremely expensive to fix and can terminate your product. Scaling is most efficient when tool replication and automation is implemented not changes to the design of the product. Have a plan for regulatory approval and engage early with the FDA for guidance. Lastly, platform technology building blocks are great for derivative products and growing the business at healthy margins. It is highly encouraged to use these lessons to assess your own products from the very beginning to maximize your success rate.

To learn more about this subject, you may contact David directly and attend COMS2020 in Washington DC Capital Region. This year's theme is: *Commercialization of Converging Technologies to Enhance Quality of Life – Health, Security & Environment*. There will be four session tracks; 1) Advanced Systems, 2) IT, AI and Computer Integration, 3) MEMS, NANO and Sensors, and 4) Business Development, Education and Sustainable Infrastructure. For more information you can visit https://www.mancef.org/.

Works Cited

"Podimetrics SmartMat." *Podimetrics*, Jan 2020, podimetrics.com/index.html

Killeen, Amanda, DPM et al. "Remote Temperature Monitoring in Diabetic Foot Ulcer Detection." *VA Health Care Defining Excellence in the 21st Century*, 2017. podimetrics.com/wp-content/uploads/2019/10/Killeen-2017-Remote-Temperature-Monitoring-in-Diabetic-Foot-Ulcer-Detection.pdf

"The study device was an in-home, wireless, thermometric mat designed for remote temperature monitoring of patients at risk for inflammatory foot diseases." *Diabetes Care*, vol. 40 no. 7, July 2017, p. 975. care.diabetesjournals.org/content/40/7/973.long.

"History of Foot Ulcer Among Persons with Diabetes --- United States, 2000—2002." *Morbidity and Mortality Weekly Report (MMWR)*, November 14, 2003, Vo. 52 no. 45, p.p. 1098-1102. *Center for Disease Control and prevention (CDC)*, cdc.gov/mmwr/preview/mmwrhtml/mm5245a3.htm

Raghav, Alok et al. "Financial burden of diabetic foot ulcers to world: a progressive topic to discuss always." Therapeutic advances in endocrinology and metabolism vol. 9,1 (2018): 29-31. doi:10.1177/2042018817744513

"Diabetic Foot Ulcers: Why You Should Never Ignore Them, Cleveland Clinic." *Diabetes & Endocrinology*, April 24, 2018, health.clevelandclinic.org/diabetic-foot-ulcers-why-you-should-never-ignore-them/

"Clinical Evidence", *Podimetrics*, Jan 2020, podimetrics.com/clinical-evidence.html

"News", *Podimetrics*, Various, https://www.podimetrics.com/news.html

"Podimetrics System Helps Prevent Diabetic Foot Ulcers: Interview." *Medgadget*, July 17, 2017, medgadget.com/2017/07/podimetrics-system-helps-prevent-diabetic-foot-ulcers-interview.html

Frykberg, Robert G. et al. "Feasibility and Efficacy of a Smart Mat Technology to Predict Development of Diabetic Plantar Ulcers" *Diabetes Care,* vol. 40 no. 7, July 2017, pp. 973-980. doi.org/10.2337/dc16-2294

"The Saliva Glucose Biosensor." *Replacing Finger-Pricks Monitoring diabetes from the tip of your tongue,* The iQ Group Global, glucosebiosensor.com/

"Diabetes." *World Health Organization*, 30 October 2018, who.int/news-room/fact-sheets/detail/diabetes

"Behind the Technology: Meet the team behind the biosensor technology." *The Saliva Glucose Biosensor*, The iQ Group Global, Jun 28, 2018, glucosebiosensor.com/saliva-glucose/

About the Author:

David DiPaola is Managing Director of DiPaola Consulting. As an engineer / entrepreneur, David specializes in providing inspiration, design and commercialization for his customers. Through inspiration he provides leadership and business consulting to startups and existing corporations. David also provides design and commercialization services helping customers bring their electromechanical products from concept to high volume production and all the steps in between. David is also Chairman of the Operations Board at MANCEF specializing in Emerging technology commercialization and is Chairman of the COMS2020 conference in Washington D.C. Capital Region being held Oct 19-22, 2020. Previously, David held technical staff and leadership positions at Texas Instruments and Sensata Technologies and was VP of Global R&D for TT Electronics, PLC. To learn more visit: dceams.com.