NAMSA is a Medical Research Organization (MRO), accelerating product development through integrated laboratory, clinical and consulting services. Driven by our regulatory expertise, NAMSA's MRO® Approach plays an important role in translational research, applying a unique combination of disciplines—consulting, preclinical, toxicology, microbiology, chemistry, clinical and quality—to move client’s products through the development process, and continue to provide support through commercialization to post-market requirements, anywhere in the world.
Mike Bravo
Director, Preclinical Strategy
NAMSA

Mike’s role is to assist clients in developing preclinical strategies for testing, from proof-of-concept through GLP as well as marketing and physician training studies. Mike also works cross-functionally with colleagues in regulatory, biostatistics, and clinical to add value to clients’ development plans. In addition, he performs a large number of surgical and interventional procedures for clients. He has authored several publications and posters, with a focus on model development. With 19 years of experience in preclinical research, Mike’s background includes experience in academia, industry, and contract research labs. He earned his Surgical Research Specialist (SRS) certification from the Academy of Surgical Research and is a member of the Society of Interventional Radiology (SIR).
Preclinical Work at Each Stage of the Product Development Life Cycle

Mike Bravo
Director, Preclinical Strategy
The medical device development pathway from discovery and ideation to product launch and post market monitoring is shown. The regulatory process affects a significant portion of the device development pathway and should accommodate the iterative, cyclical nature of device design and development.

Discovery/Ideation
I have an idea for a device!!!!

I have this **device**

I want to put **here**

**Disease**

**To treat/monitor this**

**Ailment**

**Anomaly**

**Other**
Discovery/Ideation

» This is where you may have a solid idea on what your device may be, or you even have your napkin sketch.

A small preclinical study could have large value to vet even an idea on physiologic response, before moving forward with the expense of device builds.
Discovery/Ideation

Example:

- Neurostimulation
  - Use off-the-shelf stimulators to identify which nerve gives a desired response or if any stimulation will…
  - Identify ease of access and suitability for chronic implantation. (How would you even get access and tunnel/secure your device?)

The scope would be very small—an acute study to prove that you can elicit the desired response. A small chronic study may also have merit, if you are looking for certain responses over time (blood chemistry/hormone changes, etc.).

Can start with a cheaper small animal model to stretch your dollar.

Very early stage start-ups can then use this data to begin/continue fundraising.

These can be referred to as ‘fundraising’ studies.
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Invention/Prototyping

This stage can be independent of the previous stage, or built directly upon it.

For example, a start-up who was able to raise seed money from their fundraising study, and build a prototype to continue development.

Or

You begin with a prototype that you made in-house or built in your basement, garage, or kitchen.
Invention/Prototyping

Examples of studies:

» Acute / Non-GLP

- May be able to remain in the cheaper rabbit model, but need to start thinking about applicable large animal models. Cadaveric models can also be used at this stage.
- Does your (potentially) crude prototype show promise? Did it work?
- Narrow your objective and endpoints to capture as much data as possible to show feasibility.
  - ECG/Pressure data
  - Imaging (fluoro/angio/ultrasound/etc.) stills
  - More specific endpoints…..

Stills/summary tables of this data can be put into PowerPoint presentations for management review (for more funding) or presentations to investors (for more funding).
Preclinical
Preclinical

This is the most familiar stage, and where most activity occurs.

The idea/prototype is vetted and development is underway.

The common study types in this stage are:

» Model Development (non-GLP)
» Pilot/Feasibility (non-GLP)
» Chronic Feasibility (non-GLP)
» GLP
There are a multitude of animal models that can be suitable. It really depends on your device and desired outcome…….

Device size, target anatomy similar to humans, experience with a particular model, animal amenability to any follow-up procedures, regulatory precedence, etc. are all taken into account.
Which animal model is best for me?

» A few examples of use for each model:

Canine: Cardiovascular, heart rhythm management, heart failure, urinary, neurostim
Sheep: Heart valves, peripheral vascular, orthopedic, ocular, neurostim
Goat: Orthopedic, neurostim
Swine: Cardiovascular, peripheral vascular, heart failure, wound healing
Rabbit: General effects of implantation (SQ/IM), vascular, orthopedic, tendon repair
Rat: General effects of implantation (SQ/IM)
Chicken: Tendon repair

***This list is a very brief overview and there are many, many other uses for these models.
Pilot/Feasibility (Non-GLP) Studies

These studies seek to test early stage prototypes or iterations. These studies are acute and involve very basic science and research.

Examples:

» Overall device performance during deployment/implant.
  - Do all aspects of the device work?
  - Is it too stiff or floppy? Is it too short or long?
  - What needs to be improved?

» Interaction with the anatomy/particular organ system.
  - Does it appropriately traverse, cut, grasp, etc. the target environment?
Chronic Feasibility

Your acute work has demonstrated positive results and given you confidence that you are on the right path!

Acutely, your device is performing well. Now you need to evaluate the effect of chronic implantation/deployment.

» Does it fail?

» Does it perforate/dissect/embolize/cause thrombosis/cause large amounts of inflammation at the implant site?

» Is your stimulation paradigm too intense?

» What is the physiologic response to implant over time?

Important endpoints of these studies are: implant procedure notes, daily observations, and necropsy.
Chronic Feasibility

These studies are non-GLP as well. All prep work for your GLP study, which occurs when you are comfortable with safety and performance of your device.

- A device that works (or shows even hints of efficacy) in an animal model, but causes harm or even death, is a show stopper.

GLP

Your acute work is done and looks good!

Your chronic work so far looks good and you are seeing expected results!

Now it’s time for your most important study before submission: GLP.

This study is to confirm your belief that your device is ready to help the human population.
GLP studies should have little to no research being performed. It should be to confirm that your device is ready to help humans in need.

There is a tremendous amount of momentum with your device at this point.

And you don’t want to derail due to any surprises. All questions should be answered and risks addressed by now.
Clinical

U.S. Food and Drug Administration. (2011, February). Figure 2. [The medical device development pathway from discovery and ideation to product launch and post market monitoring is shown. The regulatory process affects a significant portion of the device development pathway and should accommodate the iterative, cyclical nature of device design and development]. Retrieved March 28, 2016, from http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHInnovation/ucm242067.htm
Clinical

» At this stage, your IDE has been submitted

» You are either planning for or enrolling for your clinical trial (for PMA products, and an increasing number of 510(k) products).

» Acute Physician Training Studies can be an important activity at this stage.

- Both animal and human cadaveric models can be used.

- You are training your current/future clinical trial PIs and end users on implant/deployment technique, and performing a dry run of the clinical protocol, which can make your clinical trials run smoother.

- Also gathering additional feedback from your KOLs and high users for future iterations/claims.
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You receive a deficiency letter that addresses preclinical data. Maybe you submitted non-GLP data and received negative feedback from FDA/other regulatory bodies. Maybe your GLP study missed key endpoints or there were unexpected results.

Engage regulatory and preclinical experts to work together to develop a strategy to justify/address it.

- Get that plan started **early**.
- Engage FDA in dialogue (with Regulatory experts).

An additional study or studies may be necessary to address FDA.

- Will have very specific objective and endpoint(s).
- This is a great time for a pre-sub with FDA (with a regulatory expert involved) to discuss the deficiency/questions and lay out your plan to address it.
Product Launch

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Product Launch

Congrats! You were approved!

Now you may have to scale up your sales force to go out and sell the device to generate revenue.

Additionally, you will want to generate market awareness to capture as much of the market as you can.

This is a great place for Sales Force Training and Marketing Studies.
Product Launch

» Sales Force Training Studies

- Animal or human cadaveric models
- Introduce sales team to the device and its timeline in the OR/cath lab
- A proctor will treat the study as a live case in the clinic
  - Surgical/interventional access, opening the package, describing prep and handling, implant/deployment, and posing troubleshooting questions to the sales force
    - All aspects of device use
  - The sales team will also get a chance to prep and to implant/deploy the device to gain first-hand knowledge of behavior—very important aspect

» You want your sales force to be very comfortable in the field, and know the device inside and out!
Product Launch

» Marketing Studies

- Acute and non-GLP
- Animal or human cadaveric models
- Often involves physicians and gathering feedback/testimonials via repeated implants/deployments
  - KOLs, high users, and physicians new to the device
- Focus is to produce images, testimonials, statistically significant data sets—showing the device provides an edge.
- The data from these studies will end up on presentations at meetings, brochures, and in the hands of the sales force
- Think as if you were making a magazine about your device—what would you have in there to advertise?
Post-Market

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Post-Market

» Next-generation development occurring:
   - During clinical trials, and
   - After approval.

» Are you looking for additional indications? They will need additional animal studies.
   - Often non-GLP feasibility work to gain confidence it works, followed by GLP work.

» Continued marketing studies to grow/maintain market share:
   - Often involve physicians, but could also be non-physician (engineer-led) studies that are very image and data driven to produce bulletins, flyers, slideshow material for tradeshows, etc. <same as described in previous slide>
Thank you!!