Computer Modeling and Simulation (CM&S)

MDIC

MEDICAL DEVICE INNOVATION CONSORTIUM

ALIGN | ACHIEVE | ACCELERATE

Randy Schiestl, Board Champion
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Kyle Myers, FDA PI

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#MDIC2014

Vision

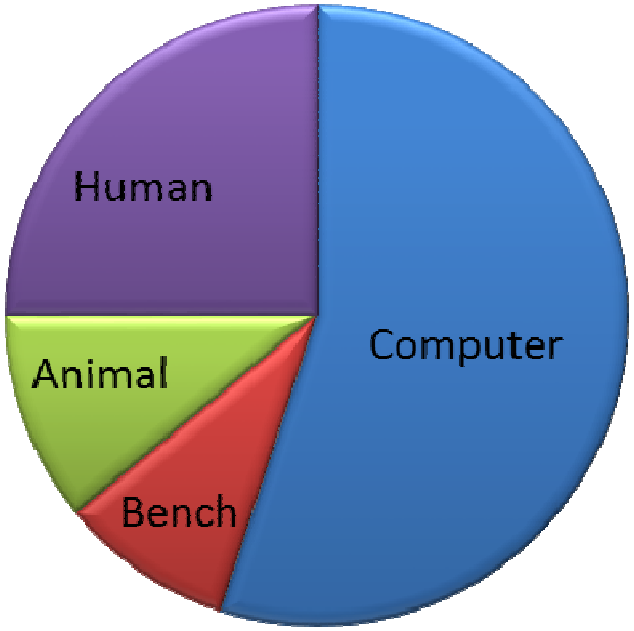
Quick and **Predictable**

access for **Patients** to **Innovative** technologies

enabled by

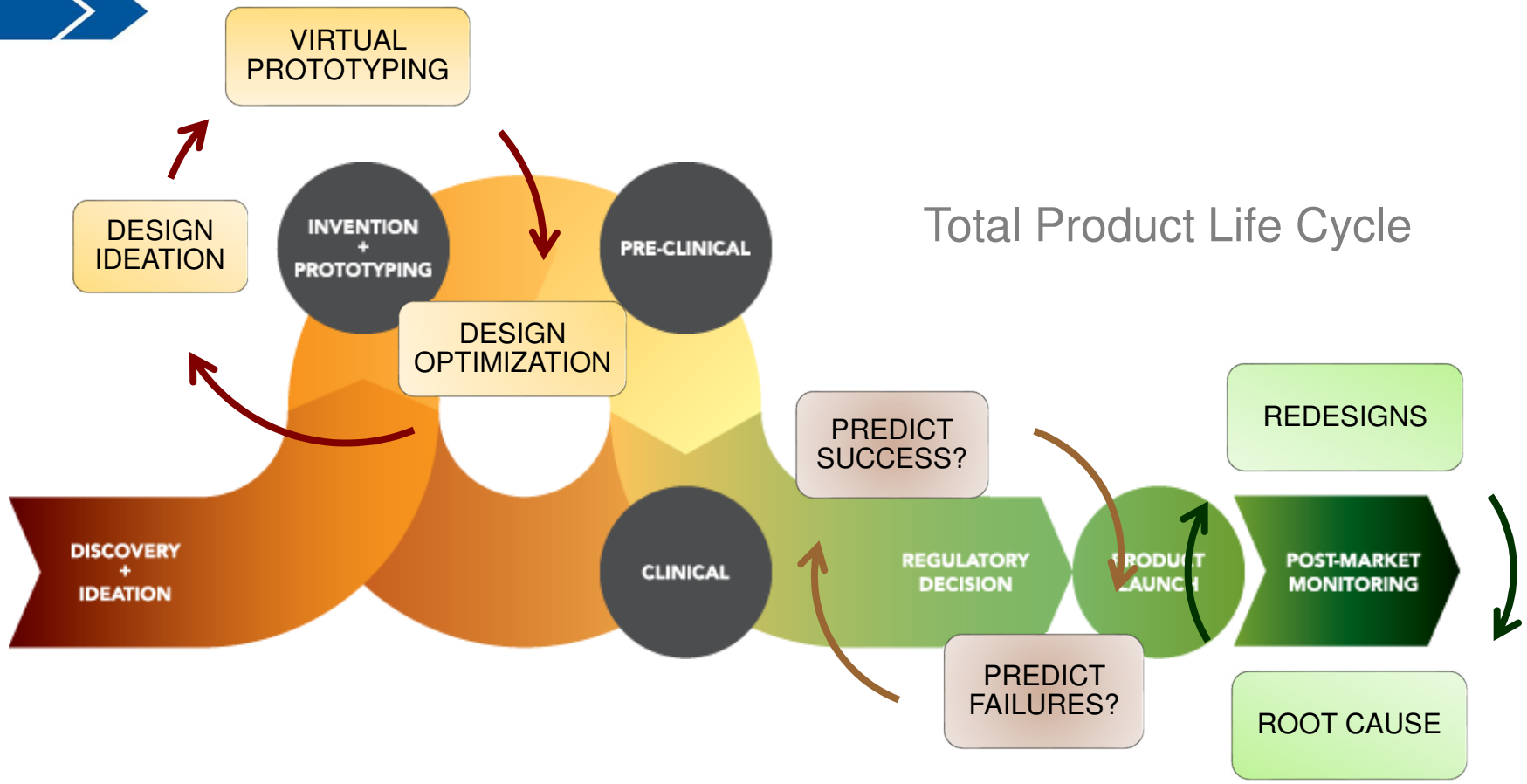
Computation Modeling and Simulation

Evidence of safety and performance



The Future of Evidence

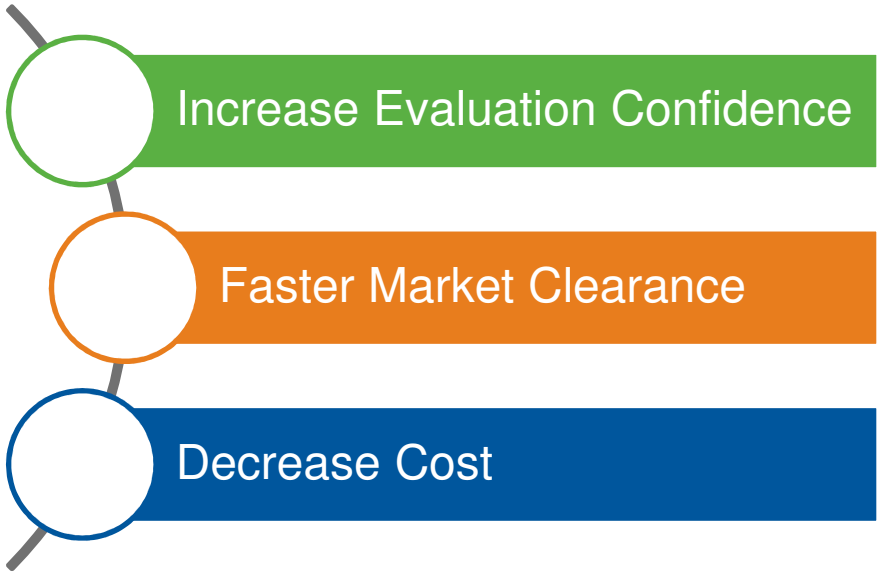
TPLC Use of CM&S Evidence



Source: "Regulatory Science in FDA's Center for Devices and Radiological Health: A Vital Framework for Protecting and Promoting Public Health"
http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHReports/ucm274152.htm

MDIC
Computer Modeling and Simulation Goals

Access to safe and effective medical device technology through Regulatory Grade computer models & simulations



Project Goals

- Advancing medical device innovation, and evaluating new and emerging technologies
- Developing state of the art preclinical methods for assessing device safety and performance
- Developing novel ways to use clinical data in evaluating medical devices – Big Data

Priorities and Tactics

Focus on the now

– Make progress on quick wins

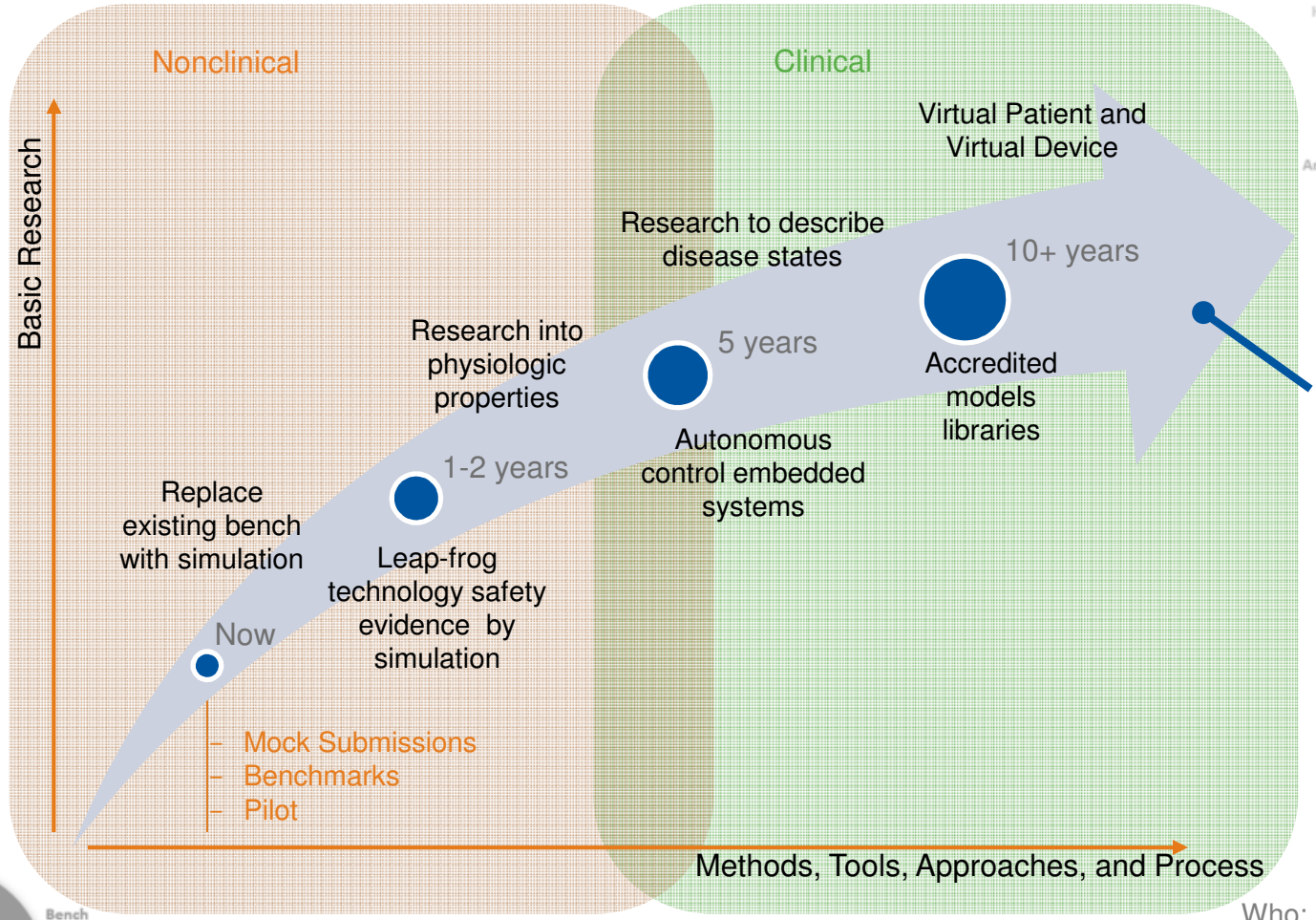
Level-set on CM&S capabilities

– Collaboration, education, and convening

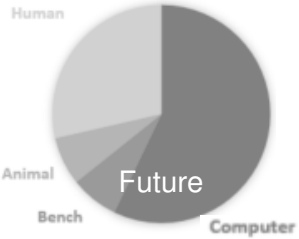
Build the roadmap

– MDIC member consensus action items

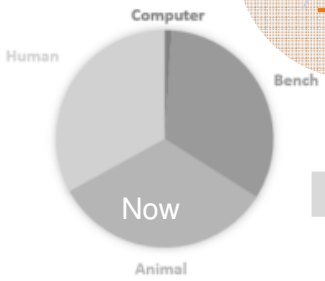
Roadmap: Increasing the use of CM&S evidence



Who: Academia informed by Industry and OSEL/OSB



Computer Modeling and Simulation Roadmap



Who: Industry and OSEL/OSB informed by ODE

Model Credibility

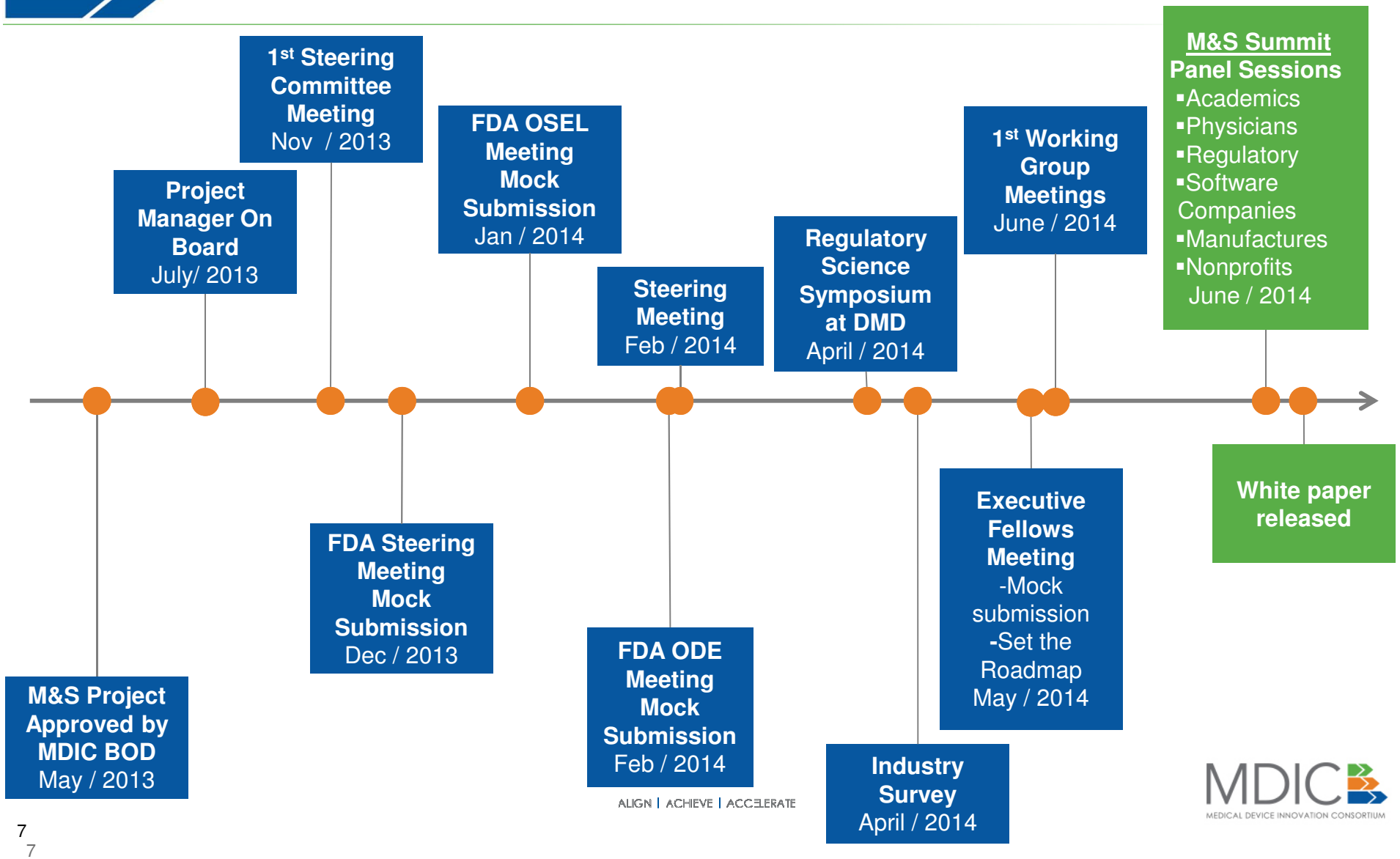
Data Archival

Interoperability

??

Standards & MDDT

Activity Timeline



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Recent accomplishments in detail

MDIC conducted two brainstorming sessions with ODE and OSEL

- Brainstorming Topic was: identify potential devices for which modeling might serve a significant role in a mock submission (510k, IDE, PMA)
- Over 30+ participants identified 50+ ideas

On May 2nd, MDIC held an Executives and Fellows meeting at the FDA with 70 members present from industry, nonprofits, NIH, and FDA

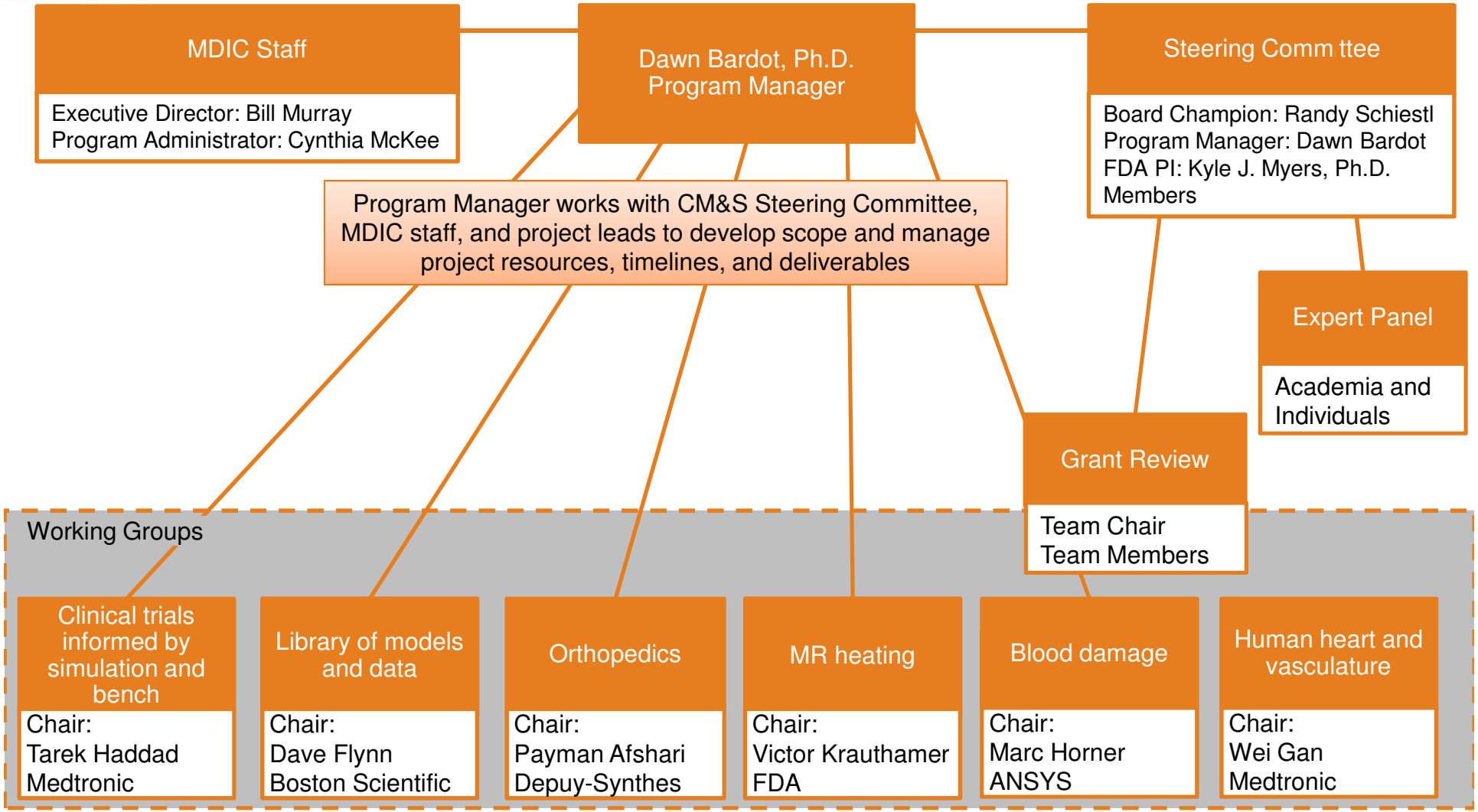
- Pre-meeting survey cataloged areas of opportunity and interest to forward the regulatory science of modeling and simulation (M&S), current uses of M&S, and pain points with the use of M&S (35 of 40 industry members participated)
- Meeting focused on expanding on survey findings through break-out group discussion
- Break-out groups reported on high-level findings, these will be incorporated into a white paper
- Six break-out groups identified to continue as MDIC working groups

Six working groups initiated and 1st group telecons scheduled

- Clinical trials powered by simulation and bench
- Library of models and data
- Orthopedics
- MR heating
- Blood damage
- Leads and human heart

CM&S Team Structure

Computer Modeling & Simulation Team



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CM&S Steering Committee

Randy Schiestl, Vice President, Global Technology, Boston Scientific Corporation, MDIC Board Champion
Dawn Bardot, Senior Program Manager, Modeling and Simulation, MDIC
Kyle Myers, Director, Division of Imaging and Applied Mathematics, OSEL, FDA PI to MDIC

Medical Device Manufacturers

Matt Waninger, President, Cook MED Institute
David Flynn, R&D Manager, Virtual Engineering, Team Boston Scientific Corporation
MorrisMilton, Vice President, R&D, Cyberonics
Dave Anderson, Sr. Vice President, R&D, St. Jude Medical
Anita, Bestelmeyer, Director of Corporate Computer-Aided Engineering, BD
Rich Thomas, Vice President, R&D, Endovascular Therapies, Medtronic

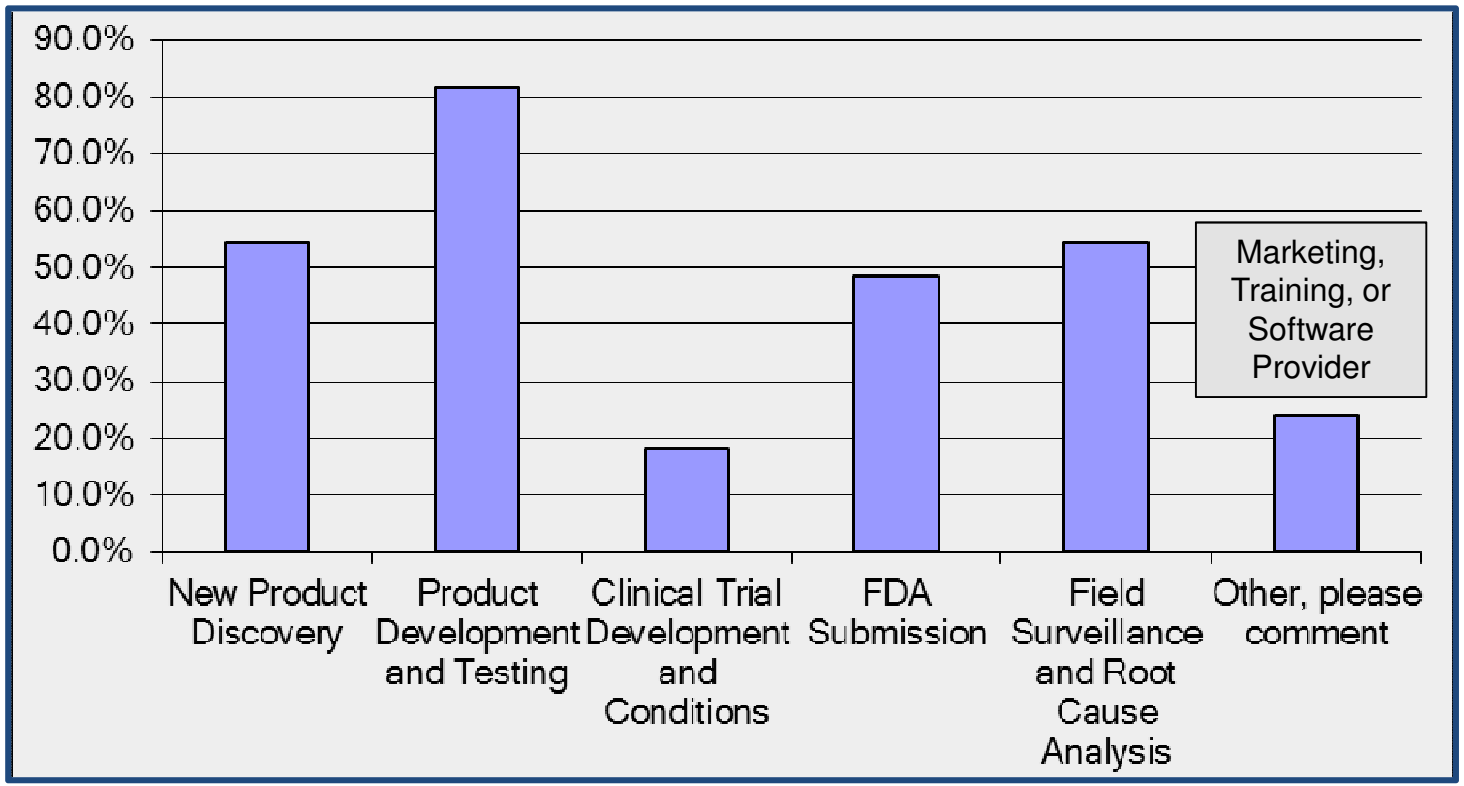
FDA

Tina Morrison, Advisor of Computational Models, Office of Device Evaluation
Donna Lochner, Assistant Director, Office of Science and Engineering Laboratories
Aldo Badano, Imaging Physics, Division of Imaging and Applied Mathematic, OSEL
Gerry Gray, Deputy Director, Division of Biostatistics, OSB
Matthew Myers, Computational Modeling, Division of Solid and Fluid Mechanics, OSEL
Pras Pathmanathan, Computational Biology, Division of Physics, OSEL

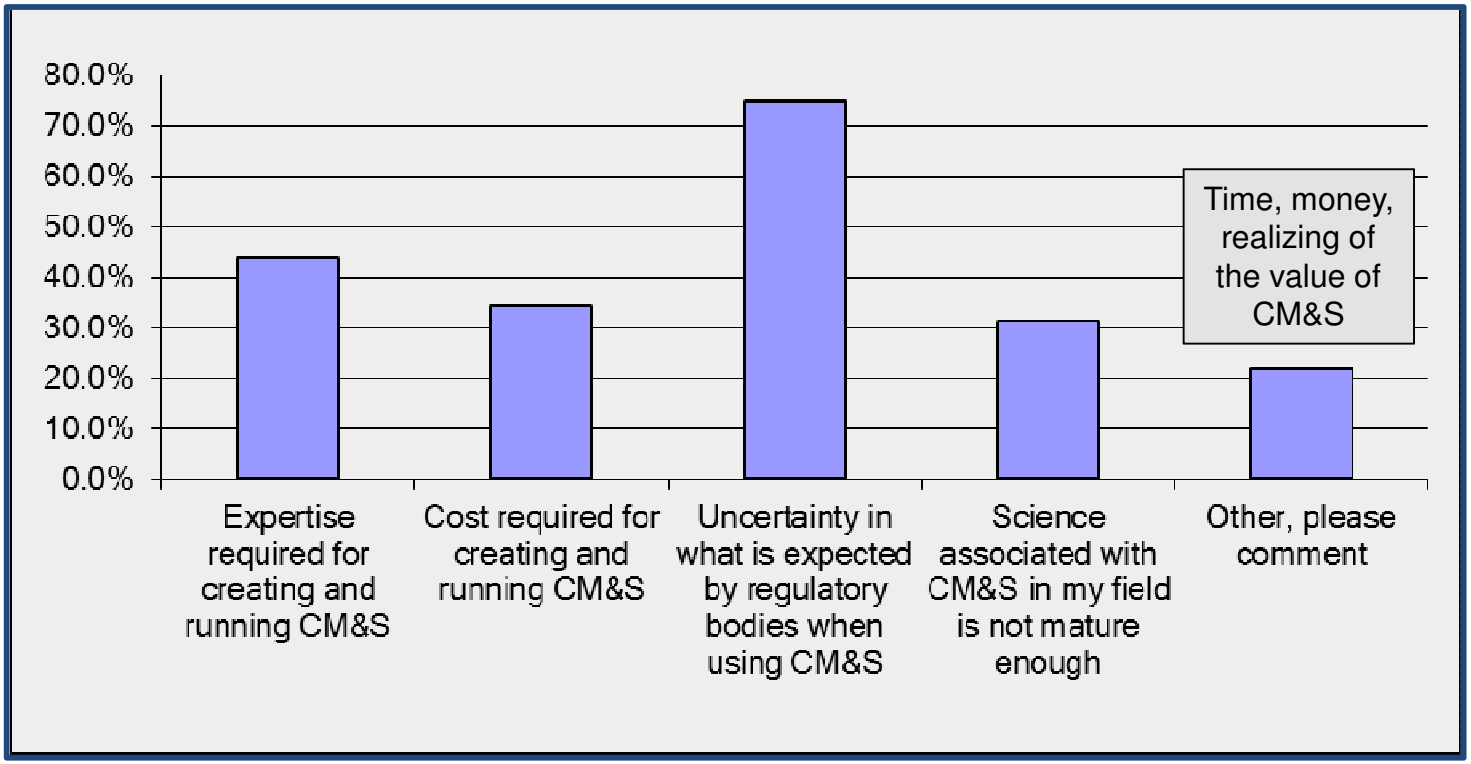
Non Profits and CM&S Expert Organizations

Cheryl Liu, Life Sciences Engagement Manager, SIMULIA
Marc Horner, Lead Healthcare Specialist, ANSYS
Kristian Debus, Director for Life Sciences, CD-adapco
Grace Peng, Program Director, Division Of Discovery Science & Technology, NIBIB/NIH
Niels Kuster, Founding Director, Foundation for Research, IT'IS

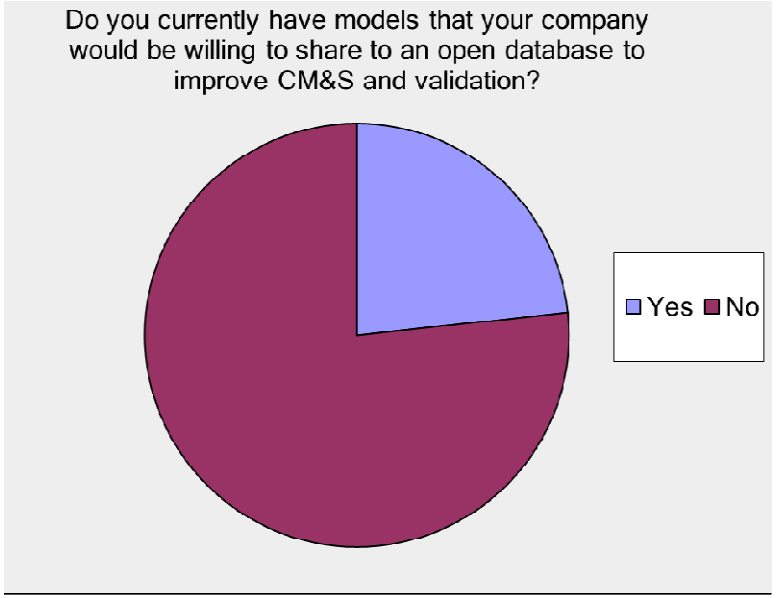
Survey question:
How does your organization use CM&S today?

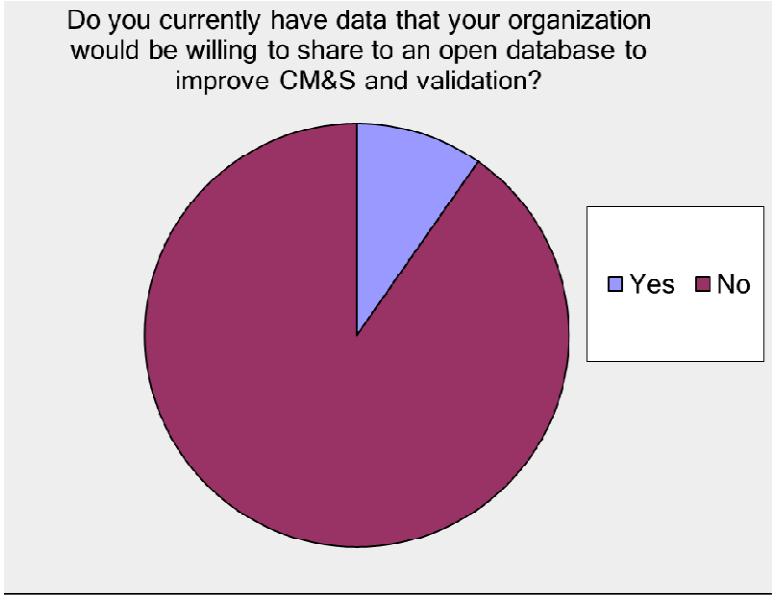


Survey question:
What are the obstacles in using CM&S?



Survey question:
Do you currently have model/data that your company would be willing to share to an open database?





Yes No

Next steps:

1.) Working Groups, 2.) White Paper, 3.) M&S Summit, 4.) Opportunity Series

1.) **Working groups**

- 6 working groups, open to all MDIC members
- 1st deliverable: per working group, 1-page white paper report out
- communication and collaboration portal provided by MDIC

2.) **White paper**

- 2nd draft distributed by July 11th
- publication options: Journal of Medical Devices (8-pages max) & MDIC webpage

3.) **June 26 & 27 MDIC M&S Summit**

- hosted in DC at the Pew Center and open to all: Academics, Industry, FDA
- podium and panel presentations
- **goal** engage a broader audience of subject matter experts
- **build** on the content from the Executive and Fellows meeting
- **include** working group members as track chairs

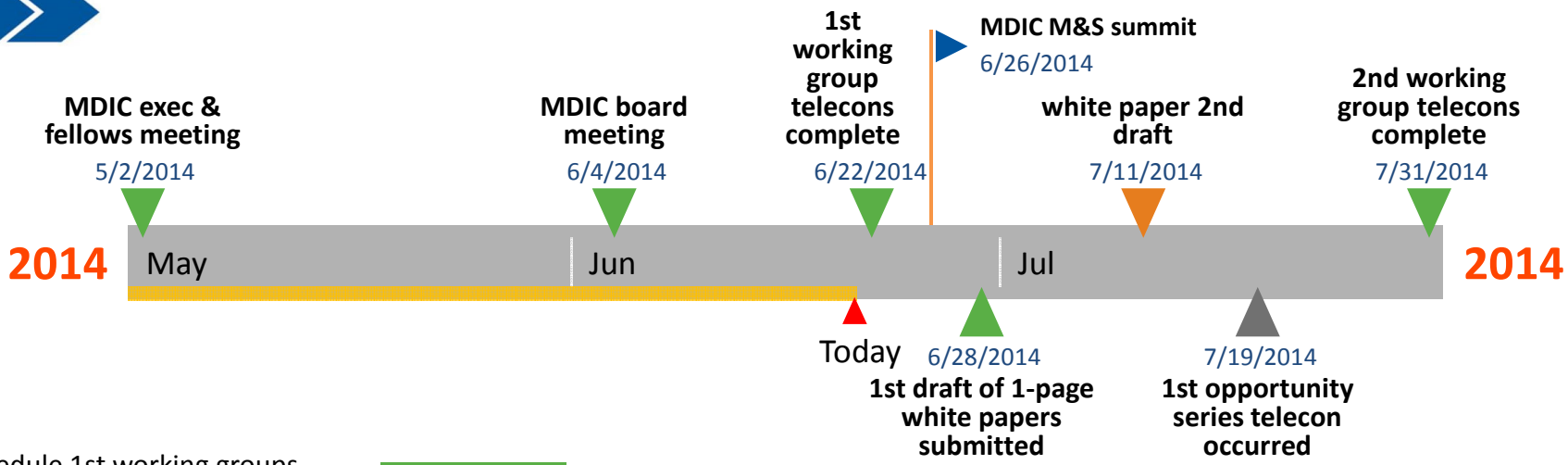
4.) **Opportunity Series**

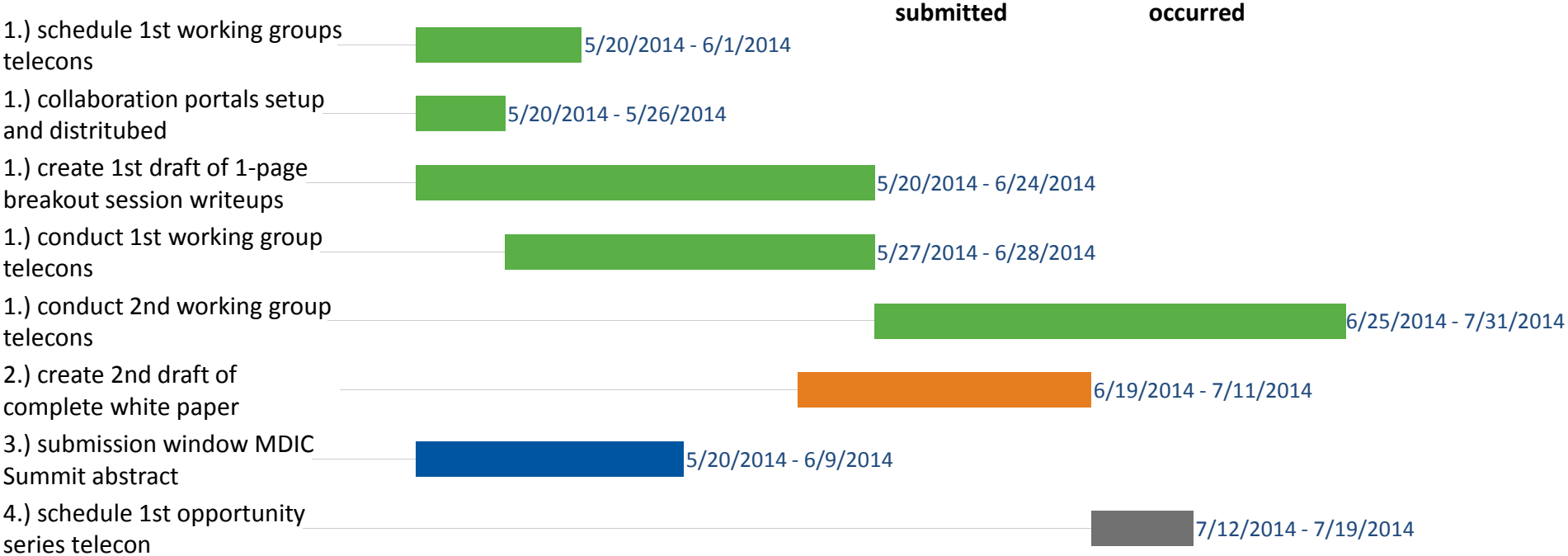
A series of telecons showcasing current success stories and discussing the future of Regulatory Science where Modeling and Simulation is used to demonstrate safety and efficacy of medical devices

- one hour long telecons with two half hour presentations per telecon, hosted by MDIC once per month
- 1st telecon to discuss: what is a PPP and how to accomplish goals in the precompetitive space?

Next steps:

1.) Working Groups, 2.) White Paper, 3.) M&S Summit, 4.) Opportunity Series





1st MDIC CM&S working group telecons

dates, times and connection information below (central time)*

Working group	Date and time
Combining bench and simulation to impact/inform clinical trials	Tuesday, June 17th @ 10am CT
Repository for models, inputs, validation data	Friday, June 13th, @ 12pm CT
Leads & human heart	Friday, June 13th, @ 2pm CT
MR heating	Tuesday, June 17th @ 11pm CT
Orthopedic	Monday, June 16th @ 10am CT
Blood damage	Monday, June 16th @ 2pm CT

Agenda for the 1st working group telecons

- Discuss 1-page breakout session write up
- Discuss M&S Summit
- Identify members for recruitment to the working group
- Begin brainstorming on working group scope and statement of work
- Identify times for next telecon

Working Group:

Combining bench and simulation to impact/inform clinical trials

The intent of this group is the incorporation of numerical prediction models into the clinical trial development.

There exists highly predictive numerical models that have the ability to predict safety and efficacy outcomes, as well as numerically quantify the uncertainty in the prediction (i.e. confidence intervals).

This groups will focus on methods to augment a clinical trial with these numerical predictive models. This would allow for a smaller more cost-efficient clinical trial.

Examples of potential clinical trials could be cardiac lead trials were the end point of the trial is lead reliability. Use a mock submission to demonstrate and develop a framework for this kind of example.

Working Group:
Library of models and data

Needs a library could solve

- Knowledge Sharing
- Expectations and Standards
- Clinical Relevance
- Communication
- Business Case

- The library can offer a means to
  - Peer review/rate models and input data
  - Enriched this peer review/rating over time by a community of FDA/academia/committee/validated members
- Library will help increase confidence and consistency in models, may allow a quality stamp

Working Group:
Orthopedics

Common Ground Needs for M&S

- Product Development (Concept Evaluation to Optimization)
- Postmarket Data Analysis (success and failure field feed back)
- Regulatory Submission
  - 510 K (Ways to harmonize process and virtual testing procedures)
  - IDE/PMA (Ways to impact/interact with the clinical study cycle to reduce cost and duration)

- Class III, for PMA supplements such as minor design changes and/or use of new materials, M&S can predict clinical outcomes without having to provide extensive clinical data to establish that safety and effectiveness has remained unchanged.
- Class II devices which require clinical data to establish substantial equivalence to marketed devices is another area for computer models.
- Can the concept of substantial equivalence be extended to validation data?

Working Group:
MR heating

- MR heating simulation is already highly used at the FDA. In the precompetitive space immediate work is possible since so much of this data is already in the public domain.
- Standards have a 3yr plus timeline. We want to focus on quicker items and have FDA, academics, and industry involved.
- Create a few generic examples, An EM safety example that gets published in various forms, papers, models, complementary data.
- Identify and validate software to define validation need in submissions. A mock submission is an example of what we can do here.
- Coil modeling is a possible tool for the MDDT path.

Working Group:

Blood damage

- Dual need: how a blood damage model might be utilized at a regulatory stage, are these models clinically relevant.
- Often we just use clinical data is a submission, but behind the scene much other descriptive work is done via modeling, would this add to a submission.
- Even characterizing: what is blood damage, from a validation perspective, what correlative measures imply blood damage. How to we know the model in clinically predictive.
- What do we specifically mean by blood damage. What markers do we validate against.
- Challenge: can qualitatively compare blood damage, how do we make this quantitative.

Working Group:

Human heart and vasculature

- Need to focus on bang-for-the-buck. High value targets.
  - In the leads space, the AMII work on a high fidelity lead test standard is a high value target
  - Human models or clinically relevant use conditions that bench does not capture
  - Consider inclusion of simulation to supplement/replace bench in a mock submission
  - Define end goals/scope for simulation usage in mock submission

White paper outline (draft)

1. **Executive Summary**
2. **The role of a public-private partnership (MDIC)**
   a. What is precompetitive space
   b. What can be done in this space
3. **The evolution of the use of M&S in medical devices**
   a. Current M&S
      i. Simulation of the device
      ii. Simulation of the anatomy/physiology
      iii. Simulation becomes a 3D printed device
      iv. Simulation embedded in the device
      v. Simulation as the device
      vi. Simulation to predict device treatment effects
      vii. Simulation modeled from big data
   b. Emerging M&S
   c. Future M&S
   d. Methods, tools, procedure development needs
   e. Research challenges
4. **Establishing model credibility metrics**
   1. Achieving model credibility: V&V
   2. Demonstrate and evaluate 'Regulatory Grade'
   3. Infrastructure needs
5. **Creating certainty in the use and confidence in the evaluation of M&S**
   1. Precompetitive space activities
   2. Product life-cycle activities
   3. Community of practice and education opportunities
6. **May 2nd breakout groups report outs** (one section for each of these groups to answer the following questions)

   Questions
   a. What can we do well, what is working well?
   b. Why can't we declare victory?
   c. What are the next steps for this community?
   d. Is this an area where a mock submission should be conducted, if yes please describe?
   e. Is this an area that should progress as an MDIC Working Group?

   Groups
   a. Combining bench and simulation to impact/inform clinical trials
   b. Repository for models, inputs, validation data
   c. Business use case for CM&S and metric
   d. Leads & human heart
   e. MR heating
   f. Orthopedic spine, hip, and other
   g. Blood damage assessment, hemolysis
7. **Call to action**
   a. Road map to establish computer modeling as a fundamental pillar in the existing bench-animal-human paradigm
   b. Funding considerations

CM&S ANNUAL SCORE CARD

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Approach	Deliverables	Comments
Remove risk and increase the certainty in using CM&S in regulatory submissions by - Socializing CM&S validation requirements - Using mock submissions to create consensus examples of the use of CM&S - Conduct workshops and telecon to promote and discuss CM&S - Explore creating MDDTs and Model Libraries to make available qualified CM&S tools	☑ Regulatory Science symposium ☑ Executive and Fellows meeting ☑ Working groups initiated ● M&S Summit ● White paper with road map ● Library project plan ● Working group work statements ● Identify funding for larger working group projects, i.e. Library of Models	• Working groups are actively discussion their statement of work and identifying core team members. • White paper write-ups are in progress

Q1 activities	Q2 activities	Q3 activities	Q4 activities
2 brainstorming meetings at FDA with OSEL & ODE on mock submission topics Steering committee meeting Survey	Regulatory Science symposium, DMD conference Executives and Fellows meeting at FDA 1st working group telecons M&S Summit at Pew Center	White paper drafted Working group statements of work (to include white papers, libraries, mock submissions, MDDTs) Library of models project plan	White paper published Working group projects scoped and initiated Identify funding for working group projects

MDIC is the place to make positive change to the benefit of industry and patients

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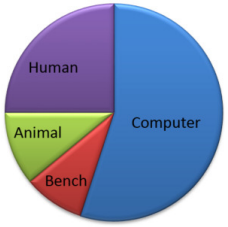
Vision



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Evidence of safety and performance

Structure

Board champion: Randy Schiestl

Program manager: Dawn Bardot

FDA PI: Kyle J. Myers

Steering committee:
- 20 members from 13 organizations
- Representation from OSEL/ODE/OSB

Working groups initiated in 6 areas

Priorities and Tactics

Increase Evaluation Confidence

Faster Market Clearance

Decrease Cost

Focus on the now
- Make progress on quick wins

Level-set on CM&S capabilities
- Collaboration, education, and convening

Build the roadmap
- MDIC member consensus action items

Accomplishments from Past Quarter

- OSEL and ODE brainstorming session on prime areas of use for M&S mock submission
- Executive and Fellows meeting held May 2nd
- Survey of CM&S use and pain points complete
- White paper initiated
- Working groups initiated

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