Notes from FDA/NIH/NSF Public Workshop on Computer Methods for Medical Devices

Day 2: June 12, 2013

A Strategy to Assess Model Credibility

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Overview of the Agenda

- ASME V&V 40 Subcommittee Introduction
- Exercise #1 from pre-workshop assignment
- Discussion Panel #1 – Risk Assessment Matrix
- Adapting NASA-STD-7009 to Assess the Credibility of Biomedical Models and Simulations
- Discussion Panel #2 – Structure and Function of the Credibility Assessment Matrix (CAM)
- Presentation of Illustrative Example with CAM
- Discussion Panel #3 – Credibility Level Determination
- Next Steps

Panel #1 - Risk Assessment Matrix

Key Comments/Questions:

- Scatter in homework possibly reflective of imprecise definitions, not differing viewpoints.
- Would an expected value function better capture risk/benefit calculation? Potentially problematic because the values associated with each category are not combinable in linear fashion.
- Should we think about “patient consequence” as consequence to the end-user?
- Modeling isn’t always about the end device, but sometimes it’s about a method to test/reduce testing of device.
- How about using the RAM for each decision, then assess each decision and determine a range? The user can make multiple assessments and determine a range of possible consequences, then determine the different levels of influence and have a range of risk. The user can then determine which “level” of credibility they’re able to achieve with their resources and can determine “how to use the model for supporting regulatory decision making”.
  - If your patient consequence is too high, then you can lower your “risk” by lowering the influence in the decision making.
- The assessment of risk will naturally include thresholds and probabilities – no need for a third axis.
- Revising the name to “Benefit assessment matrix” might help with messaging.
- Sponsors would like to have some idea of an acceptable level of risk (at least clear guidelines) for using a computational model within a submission
- “Risk consideration tool” as new name??
- The RAM can also be used to justify what you did and why you thought that was sufficient – could be useful for industry/FDA interactions

Panel #2 - Structure and Function of the CAM

Key Comments/Questions:

- The level of justification (explanation) needed for the determination of a credibility value within a factor (column) is not well defined.
  - Please note that this is being developed by the ASME Subcommittee
- Inconsistency in scoring goes back to definitions (will need iterating)
- Complexity and quality appear to be used interchangeably – this should not be so
  - Need some examples
  - "Robustness of analysis" is important – how do we distinguish what is appropriate
- Useful for a discussion between decision maker and analyst about model credibility and what factors are important; however, it's not clear that this process will define the 'actual' credibility of the model/ V&V process
- Maybe the numbers are not necessary because rank is implied regardless
- Applicability column should be kept in the CAM as this ties in the Context of Use
  - The comparator factors might need some revision
- Maybe the factors (columns) could be rearranged in some semblance of order of importance (model relevance 1st)
- Regime changes (laminar to turbulent) are particularly worrisome when using a model beyond range (extrapolation): aspects that affect credibility when extrapolating/ interpolating because the domain of validity should be identified/explicit
- It might be beneficial for the advancement of this methodology/strategy to have a study that identifies what factors are most important for a particular context of use
  - Maybe this could be accomplished with a prospective pilot study
  - It's possible we could establish a baseline from a retrospective study

Panel 3 - Credibility Level Determination

Key Comments/Questions:

- Breaking down to a matrix indicating how much the modeling applies to a specific risk is useful.
- Is it useful to condense the factors down to a single number?
  - Perhaps not for a specific submission
  - There are multiple ways to establish, say, a level 2 – what does that really mean about credibility? (e.g., verification)
  - Each factor value is not the same (a level 2 for solution verification is not the same as level 2 for sample size) – thus they cannot be “averaged”, per se
- “Validated“ is not a useful description, "adequately validated for (a specific context of use)“ is better
- Revisiting old cases and assessing their credibility could be useful for learning, and then we could implement the process for upcoming submissions
  - Lessons learned can be shared without discussing specifics
- An example case (additional) would be appreciated by industry
  - Data for it can be fabricated
- The Context of Use is central to evaluating the CAM and RAM, and it ought to be captured clearly
- Industry would like clarity on when they should come to FDA to start the process (early, late, throughout); this process is iterative – how best to communicate this?
- What are the regulatory implications of a low credibility score?
  - Depends on the context of use
- How does the RAM influence/establish the requirements of the CAM? This is not clear.
- Should the level of documentation be commensurate of the level of risk?

Computational Modeling for Medical Devices

The development of the V&V activities and usage of computational models in medical device submissions are clearly inter-related but different groups are working on different aspects:

- V&V of computational model (ASME V&V40 subcommittee)
  - There are aspects particularly noteworthy for medical devices (physiologic boundary conditions, growth and remodeling, how physiological variations are reduced/represented, geometry from medical image data)
  - The guide will focus on V&V methodolgoy and planning for aspects of modeling and simulation that are more broad than regulatory submissions, e.g., industry decision making, economic decision making, establishing credibility of research

- Computational modeling in a medical device submission as valid scientific evidence for regulatory decision (FDA)
  - A big step forward is to improve documentation
    - Setting expectations about:
      - What can be said
      - What should be said
      - What must be said
      - How to say it so it is understood
  - Another aspect is to clarify expectations of underlying models & simulations (credibility (validation, performance, use, limitations))

Next Steps

- The ASME V&V40 Subcommittee plans on completing the first draft of the Guide (Verification and Validation of Computational Modeling for Medical Devices) by the end of 2013
- Could FDA in conjunction with ASME develop an sample submission of a computational modeling (maybe from ASTM standards data – hip stem or stent) focusing on documentation and the credibility strategy?
  - We could fabricate the experimental data for demonstration purposes
- FDA Guidance (Reporting of Computational Modeling Studies in Regulatory Submission) is expected to be out for public comment in Q4 of 2013
- FDA is thinking of putting together a pilot study to support
  - the Medical Device Development Tools (MDDT)
    - the Credibility Strategy could be a first possible MDDT
  - Implementing the credibility strategy for regulatory submissions
- The Medical Device Innovation Consortium (MDIC) is launching its first program area – computational modeling and simulation is one
  - Is this a possible arena to develop test cases or run a pilot program with industry?
  - How can we better leverage expertise from academia?