ASME V&V 40 Overview

Marc Horner, Ph.D.
Principal Engineer, Healthcare
ANSYS, Inc.
&
Co-Vice Chair
ASME V&V40
Credibility in Modeling

• Verification, validation, and uncertainty quantification (VVUQ) can be used to establish trust in the predictive capability of a computational model.

• How to foster an appropriate level of VVUQ for establishing the predictive capability of a computational model?
Standards Committee

- Provide procedures for assessing and quantifying the accuracy and credibility of computational modeling and simulation.
The ASME V&V 40 Standard

ASME V&V 40 Charter
• Provide procedures to standardize verification and validation for computational modeling of medical devices
• Charter approved in January 2011

Motivating factors
• Regulated industry with limited ability to validate clinically
• Increased emphasis on modeling to support device safety and/or efficacy
• Use of modeling hindered by lack of V&V guidance and expectations within medical device community
"Develop computational modeling technologies to support regulatory decision-making"
V&V 40 Sub-Committee Member Companies
## Terminology

<table>
<thead>
<tr>
<th>Term</th>
<th>Description</th>
<th>Evidence Source</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Verification</strong></td>
<td>Did you solve the underlying mathematical model correctly?</td>
<td>Mathematical Evidence</td>
</tr>
<tr>
<td><strong>Validation</strong></td>
<td>Does the underlying mathematical model correctly represent the reality of interest?</td>
<td>Experimental* Evidence</td>
</tr>
<tr>
<td><strong>Uncertainty Quantification</strong></td>
<td>What is the uncertainty in the inputs (e.g., parameters, initial conditions), and what is the resultant uncertainty in the outputs?</td>
<td>Statistical Evidence</td>
</tr>
<tr>
<td><strong>Applicability</strong></td>
<td>How relevant is the validation evidence to support using the model in the context of use?</td>
<td>Engineering Judgement</td>
</tr>
<tr>
<td><strong>Credibility</strong></td>
<td>Based on the available evidence, is there belief in the predictive capability of the computational model for the context of use?</td>
<td>Engineering Judgement</td>
</tr>
</tbody>
</table>
The V&V40 standard outlines a process for making risk-informed determinations as to whether CM&S is credible for decision-making for a specified context of use.
The **question of interest** describes the specific question, decision or concern that is being addressed.

**Context of use** defines the specific role and scope of the computational model used to inform that decision.
Risk Assessment

Model risk is the possibility that the model may lead to a false/incorrect conclusion about device performance, resulting in adverse outcomes.

- **Model influence** is the contribution of the computational model to the decision relative to other available evidence.

- **Decision consequence** is the significance of an adverse outcome resulting from an incorrect decision.
Model credibility refers to the trust in the predictive capability of the computational model for the COU.

Trust can be established through the collection of V&V evidence and by demonstrating the applicability of the V&V activities to support the use of the CM for the COU.

Goals for each credibility factor are based on model risk.
Credibility Assessment

Establish Risk-Informed Credibility
- Define COU
- Assess model risk
- Establish credibility goals

Credibility Activities
- Establish plan
- Execute plan

Assess Credibility
- Computational model credible for COU?
  - Yes → Documentation and evidence
  - No → Go back to Establish Risk-Informed Credibility

ASME V&V10
ASME V&V20
Credibility Assessment

Figure 7-1 Example Workflow for Assessing Computational Model Credibility

- Define COU
- Assess model risk
- Establish credibility goals
- Establish plan
- Execute plan

Assess Credibility: Computational model credible for COU?
- Yes: Documentation and evidence
- No: Conduct additional credibility activities, change the computational model, reduce influence, and/or modify the COU.
Documentation & Evidence

CM&S Report

I. Executive Report Summary ......................
II. Background/Introduction ..........................
III. Code Verification .................................
IV. System Configuration ............................
V. Governing Equations/Constitutive Laws.....
VI. System Properties ..............................
VII. System Conditions .............................
VIII. System Discretization ........................
IX. Numerical Implementation .....................
X. Validation  ........................................
XI. Results ...........................................
XII. Discussion  ......................................
XIII. Limitations .....................................
XIV. Conclusions ....................................
XV. References .....................................
Illustrations/Examples

Illustrations provide more details about key concepts as they are introduced in the main body of the document.

Examples demonstrate the risk-informed credibility framework for a variety of medical device types and physics. No examples are end-to-end.

NONMANDATORY APPENDIX B
EXAMPLES OF RISK-INFORMED CREDIBILITY ASSESSMENT CONCEPTS

<table>
<thead>
<tr>
<th>Example [Note (1)]</th>
<th>Device Type</th>
<th>Governing Physics</th>
<th>Of Special Interest</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Centrifugal blood pump</td>
<td>Fluid mechanics</td>
<td>Risk assessment</td>
</tr>
<tr>
<td>2</td>
<td>Aneurysm flow diverter</td>
<td>Fluid mechanics</td>
<td>In vitro test data and preclinical evidence</td>
</tr>
<tr>
<td>3</td>
<td>Hospital bed</td>
<td>Rigid body mechanics</td>
<td>Single computational model supports multiple COUs</td>
</tr>
<tr>
<td>4</td>
<td>Implanted plate/screw system</td>
<td>Electromagnetics</td>
<td>Different comparators</td>
</tr>
<tr>
<td>5</td>
<td>Total knee arthroplasty system</td>
<td>Solid mechanics</td>
<td>Family of designs</td>
</tr>
<tr>
<td>6</td>
<td>Interbody fusion device</td>
<td>Solid mechanics</td>
<td>Comparator testing per industry standard</td>
</tr>
</tbody>
</table>

NOTE: (1) See paras. B-2.1 through B-2.6 for the examples.

Table B-1-2 Mapping of Examples to Device Type and Modeling Approach

Illustration 1: Context of Use

Medical Device: A new posterior-stabilized total knee arthroplasty assembly (see Nonmandatory Appendix B, paras. B-2.5)

Question of Interest: Does the proposed locking mechanism have sufficient strength to prevent liftoff?

Context of Use: Finite element analysis (FEA) will be used to determine if the locking mechanism is sufficient. The design of the implant will be reviewed and optimized with a focus on durability. Finite element analysis will be used to test the locking mechanism. The test will be conducted with a maximum load of 1000 lbs.

Illustration 2: Model Risk

Medical Device: Centrifugal blood pump for circulatory support (see Nonmandatory Appendix B, paras. B-2.1)

Question of Interest: How is pump-related hemolysis affected by component dimensional tolerances?

Context of Use: A computational fluid dynamics (CFD) model will be used to evaluate the sensitivity of pump-induced hemolysis to variations in component dimensions, with the goal of identifying the dimensional tolerances that most likely contribute to increased hemolysis levels. Based on the CFD results, physical pumps with components of varying dimensions will be fabricated and tested.

Model Influence: The model influence is MEDIUM because testing will be used to confirm some of the results.

Decision Consequence: An incorrect decision to alter the key pump feature’s dimensional tolerances could impact hemolysis levels during clinical use. Patient injury could result and require immediate intervention of the clinician to monitor patient hemolysis levels and/or replace the pump. Therefore, the decision consequence is HIGH.

Model Risk: The model risk is determined to be MEDIUM-HIGH.

Figure B-2.1-1-2 Model Risk Matrix for Example 1

<table>
<thead>
<tr>
<th>Decision Consequence</th>
<th>High</th>
<th>Medium</th>
<th>Low</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIGH</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>MEDIUM</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>LOW</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>
Please Remember….

HOW TO DO V&V

HOW MUCH V&V
# New Subcommittee Work Items

<table>
<thead>
<tr>
<th>NUMBER</th>
<th>TITLE</th>
<th>LEADER(S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>V&amp;V 40.1</td>
<td>Using (Historical) Clinical Data as a Comparator</td>
<td>Paul Briant, Exponent</td>
</tr>
<tr>
<td>V&amp;V 40.2</td>
<td>End-to-End Example</td>
<td>Sudeep Sastry, WL Gore</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Brandon Lurie, WL Gore</td>
</tr>
<tr>
<td>V&amp;V 40.3</td>
<td>Patient-Specific Models</td>
<td>Mark Goodin, Simutech</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Shumin Cheng</td>
</tr>
<tr>
<td>V&amp;V 40.4</td>
<td>Verification Best Practices (Code and Calculation)</td>
<td>Marc Horner, ANSYS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ismail Guler, Boston Scientific</td>
</tr>
<tr>
<td>V&amp;V 40.5</td>
<td>Mock Submission: V&amp;V 40 Practice in Regulatory Applications</td>
<td>Tina Morrison, US FDA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Brent Craven, US FDA</td>
</tr>
<tr>
<td>V&amp;V 40.6</td>
<td>V&amp;V 40 Revisions</td>
<td>V&amp;V 40 Chair</td>
</tr>
</tbody>
</table>
ASME V&V 40.1: Using (Historical) Clinical Data as a Comparator

- **Question:** Can we leverage historical clinical data to validate a model?

- **Background:** Two primary types of historical clinical data can be considered
  - Registry data = broad statistical data that provides overall rates or device specific rates
  - Clinical reports = published case studies that describe specific device failures

- **Objective:** Develop case studies that demonstrate the appropriateness of using registry and/or clinical reports for validation

- **Status:**
  - The working item will focus on using tibial tray facture to motivate discussion and examples
  - An initial example with several discussion points has been created and reviewed with the group
  - The example and discussion are being fleshed out for use in the deliverables.
ASME V&V 40.2: End-to-End Example

- Tibial Tray Fatigue

• Motivation: Provide an example that walks through every part of the standard, including comparing simulation data to empirical and assessing the credibility of the model. Also want to illustrate that levels within the risk assessment and credibility assessment are user dependent and may be modified from the standard.

• Progress Update:
  – Settled on device to investigate
  – Determined Question of Interest, Context of Use and Assessed the Risk
  – Working through determining each verification and validation goal based on the risk
  – Up next: Write up the V&V plan prior to generating data

https://jointreplacementtherapists.com/understanding-the-different-types-of-knee-prosthetics/
ASME V&V 40.3: Patient-Specific Models

• **Motivation:** To advance new technologies related to the clinical evaluation of Software as a Medical Device (SaMD), thereby supporting safer, more effective and quicker SaMD regulatory evaluations and introductions by developing an example that demonstrates the process for using patient-specific computational modeling in support of the clinical evaluation of SaMD.

• **Progress Update:**
  - Defining the workgroup scope, objectives, work items, plan, roadmap and deliverables;
  - Re-evaluating the robustness of potential clinical application. The clinical applications under review are:
    • Mandibular repositioning device for treating obstructive sleep apnea;
    • Virtual deployment of stent graft for treating short-neck abdominal aortic aneurysms;
    • Stability of a patient-specific orthopedic bone implant to support reconstruction of femur.
ASME V&V 40.4: Verification Best Practices

- **Motivation:** The fundamentals of code and calculation verification are thoroughly reviewed in the ASME V&V 10, 10.1, and 20 standards. However, the computational models used in the evaluation of medical devices can be quite complex and have their own subtleties. The objective of the ASME V&V 40.4 working group is to explore, learn, and employ code and calculation verification best practices on representative examples from the medical device space.

![Diagram of Verification Best Practices]

- **Code Verification** Best Practices
  - 1) Poiseuille flow example problem (complete)
  - 2) Womersley flow example problem (active)

- **Calculation Verification** Best Practices
  - 1) Nitinol stent FEA example problem (active)
  - 2) Hip stem FEA example problem (active)
Additional Learning Opportunities

• AABME Webinar Series
  – May 9, 2019, M&S in Healthcare
  – June 4, 2019, Introduction to the ASME V&V 40 Standard

• Recent Manuscript on V&V 40 applied to blood pumps

Overview

Title: Modeling and Simulation in Healthcare – Opportunity for Transformation

Date: Thursday, May 09, 2019

Time: 01:00 PM Eastern Daylight Time

Duration: 1 hour

Summary

Modeling and simulation has been beneficial in the automotive and aerospace, and it is increasingly used in the device industry. Combined with strict regulations, it increases patient safety, boosts innovation, and reduces the time to market.

Speakers

Mark Palmer, MD, PhD
Senior Principal Scientist, Corporate Core Technologies
Medtronic

Mark Palmer is a Senior Principal Scientist leading Biomechanics and Modeling in the Core Technologies Group for Medtronic. His current role focuses on the development and application of computational models for medical devices, particularly blood pumps.
In Review

• VVUQ provides the user with mathematical, experimental and statistical evidence that support model credibility.
• The ASME V&V 40 risk-informed credibility assessment framework can be used to determine the appropriate level of rigor required of the V&V activities.
• V&V activities should be commensurate with model risk for a specific context of use.
• Model risk is a combination of model influence and decision consequence and drives the credibility requirements of the V&V activities.
• Applicability and credibility rely on sound engineering and clinical judgement for computational models for medical devices.
Thank You!

Marc Horner

marc.horner@ansys.com