ASME V&V 40-2018

Assessing Credibility of Computational Modeling Through Verification and Validation: Application to Medical Devices

AN INTERNATIONAL STANDARD

The American Society of Mechanical Engineers

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FOREWORD

Computational models have been used to support the design of medical devices for many years, without any specific guidance on how to assess their credibility. Device manufacturers therefore use internal approaches and best practices for model verification and validation (V&V). This has created challenges for regulatory agencies to develop consistent, structured approaches for evaluating the legitimacy of model results used to support device safety and/or effectiveness.

In recognition of the challenges facing the device industry, the U.S. Food and Drug Administration (FDA) hosted the first in an annual series of workshops on computational modeling for medical devices in 2008. The intent of this series was to bring together researchers, medical device manufacturers, and regulatory agencies to present advanced research, review best practices, and address barriers to the use of computational modeling for the design, development, and evaluation of medical devices. Based on several years of input, it became clear that guidance on V&V for computational models was necessary to support and promote appropriate use of computational modeling in medical device design, development, and evaluation. Due to the growing interest in V&V of computational modeling for medical devices within the ASME V&V subcommittees, the ASME V&V Standards Committee proposed the development of a new subcommittee focused on this area.

The proposal for a new V&V subcommittee focused on medical devices was presented at various device-related conferences over the course of several years, with increasing interest from the medical device community. In 2011, the ASME V&V 40 Subcommittee on Verification and Validation of Computational Modeling for Medical Devices was officially approved. The Subcommittee is composed of members representing a broad cross-section of the medical device community, including device manufacturers, academic groups, consultants, software developers, and government agencies (primarily the FDA). The breadth of knowledge of the Subcommittee members spans solid mechanics, fluid dynamics, electromagnetics, kinematic modeling, and other physics-based modeling.

At the initiation of the ASME V&V 40 Subcommittee, standardization of the V&V process had already been addressed by the first two ASME V&V subcommittees (V&V 10 Verification and Validation in Computational Solid Mechanics, and V&V 20 Verification and Validation in Computational Fluid Dynamics and Heat Transfer). The V&V 40 Subcommittee therefore set out to provide guidance on the application of V&V practices for medical devices. The anticipated guidance would provide a level of standardization for V&V practices that would encourage sound use of modeling to support device development and facilitate objective and consistent evaluation of model credibility by device manufacturers and regulatory agencies.

Medical devices are classified by the FDA based on risk to patients, which requires a greater level of evidence to demonstrate the safety and effectiveness of medical devices that pose a higher risk to patients. Analogously, the V&V 40 Subcommittee focused on developing a risk-based approach to determine the level of V&V needed to support the use of a computational model for evaluating device safety and/or effectiveness. The concept of risk is also foundational to NASA-STD-7009, which predated the V&V 40 Subcommittee and informed the Subcommittee's perspective. However, NASA-STD-7009 explicitly links the required level of V&V activities to each risk level. In contrast, the consensus perspective of the V&V 40 Subcommittee was that the individual organization (e.g., a medical device manufacturer) should have the authority and responsibility to associate a certain level of risk with a certain set of V&V activities, and that the individual organization should justify this association to internal and external stakeholders, including regulatory agencies. Therefore, instead of defining specific credibility criteria, the V&V 40 Subcommittee developed a framework that allows users to determine the appropriate level of credibility required for their computational model.

Several foundational materials for the subcommittee (e.g., NASA-STD-7009, as well as the Predictive Capability Maturity Model introduced in SAND2007-5948) prescribe matrix frameworks. The V&V 40 Subcommittee also started with two matrices: the risk assessment matrix (RAM) and the credibility assessment matrix (CAM). The RAM focused on determining the level of risk for a computational model, while the CAM focused on the level of credibility (achieved through V&V activities) needed to satisfy that level of risk. Case studies conducted in 2013 that used the RAM and CAM exposed a number of practical and functional challenges with these matrices across the spectrum of medical devices, manufacturers, and model applications. Therefore, the V&V 40 Subcommittee revised the RAM/CAM framework, enabling users to define appropriate gradations and levels for risk and credibility. The culmination of these efforts is a risk-informed credibility assessment framework, reflecting the core principle that model credibility is commensurate with the risk associated with decisions influenced by the computational model.

Under the jurisdiction of the ASME Board on Standardization and Testing, ASME V&V 40-2018 was approved by the ASME V&V 40 Subcommittee and the ASME V&V Standards Committee on November 29, 2017. It was approved as an American National Standard by the American National Standards Institute (ANSI) on August 16, 2018.

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Verification and Validation in Computational Modeling and Simulation

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Secretary, V&V Standards Committee
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Two Park Avenue
New York, NY 10016-5990
http://go.asme.org/Inquiry

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The Committee welcomes proposals for revisions to this Standard. Such proposals should be as specific as possible, citing the paragraph number(s), the proposed wording, and a detailed description of the reasons for the proposal, including any pertinent documentation.

Proposing a Case. Cases may be issued to provide alternative rules when justified, to permit early implementation of an approved revision when the need is urgent, or to provide rules not covered by existing provisions. Cases are effective immediately upon ASME approval and shall be posted on the ASME Committee web page.

Requests for Cases shall provide a Statement of Need and Background Information. The request should identify the Standard and the paragraph, figure, or table number(s), and be written as a Question and Reply in the same format as existing Cases. Requests for Cases should also indicate the applicable edition(s) of the Standard to which the proposed Case applies.

Interpretations. Upon request, the V&V Standards Committee will render an interpretation of any requirement of the Standard. Interpretations can only be rendered in response to a written request sent to the Secretary of the V&V Standards Committee.

Requests for interpretation should preferably be submitted through the online Interpretation Submittal Form. The form is accessible at http://go.asme.org/InterpretationRequest. Upon submittal of the form, the Inquirer will receive an automatic e-mail confirming receipt.

If the Inquirer is unable to use the online form, he/she may mail the request to the Secretary of the V&V Standards Committee at the above address. The request for an interpretation should be clear and unambiguous. It is further recommended that the Inquirer submit his/her request in the following format:

Subject:	Cite the applicable paragraph number(s) and the topic of the inquiry in one or two words.
Edition:	Cite the applicable edition of the Standard for which the interpretation is being requested.
Question:	Phrase the question as a request for an interpretation of a specific requirement suitable for general understanding and use, not as a request for an approval of a proprietary design or situation. Please provide a condensed and precise question, composed in such a way that a "yes" or "no" reply is acceptable.
Proposed Reply(ies):	Provide a proposed reply(ies) in the form of "Yes" or "No," with explanation as needed. If entering replies to more than one question, please number the questions and replies.
Background Information:	Provide the Committee with any background information that will assist the Committee in understanding the inquiry. The Inquirer may also include any plans or drawings that are necessary to explain the question; however, they should not contain proprietary names or information.

Requests that are not in the format described above may be rewritten in the appropriate format by the Committee prior to being answered, which may inadvertently change the intent of the original request.

Moreover, ASME does not act as a consultant for specific engineering problems or for the general application or understanding of the Standard requirements. If, based on the inquiry information submitted, it is the opinion of the Committee that the Inquirer should seek assistance, the inquiry will be returned with the recommendation that such assistance be obtained.

ASME procedures provide for reconsideration of any interpretation when or if additional information that might affect an interpretation is available. Further, persons aggrieved by an interpretation may appeal to the cognizant ASME Committee or Subcommittee. ASME does not "approve," "certify," "rate," or "endorse" any item, construction, proprietary device, or activity.

Attending Committee Meetings. The V&V Standards Committee regularly holds meetings and/or telephone conferences that are open to the public. Persons wishing to attend any meeting and/or telephone conference should contact the Secretary of the V&V Standards Committee. Future Committee meeting dates and locations can be found on the Committee Page at http://go.asme.org/VnVcommittee.

Assessing Credibility of Computational Modeling Through Verification and Validation: Application to Medical Devices

1 EXECUTIVE SUMMARY

Computational modeling can be used throughout the product life cycle to provide information about technical performance, safety, and effectiveness of medical devices. Computational models can also be used to assess aspects of in vivo performance without subjecting patients (or animals) to potential harm or unnecessary risk. Establishing the credibility of a computational model to assess performance is important because of the potential risk a device presents to patients and/or healthcare providers.

Model credibility can be established through verification and validation (V&V) activities. Although methods for V&V are becoming well established, guidance is lacking on assessing the relevance and adequacy of the V&V activities for computational models used to support medical device development and evaluation. Given the inherent risk of using a computational model as a basis for predicting medical device performance, the ASME V&V 40 Subcommittee has developed a risk-informed credibility assessment framework. The framework centers on establishing that model credibility is commensurate with the risk associated with the decisions influenced by the computational model. Thus, the intent of this Standard is to provide guidance on how to establish and communicate risk-informed credibility of computational models used in the evaluation of medical devices.

2 INTRODUCTION

2.1 Motivation

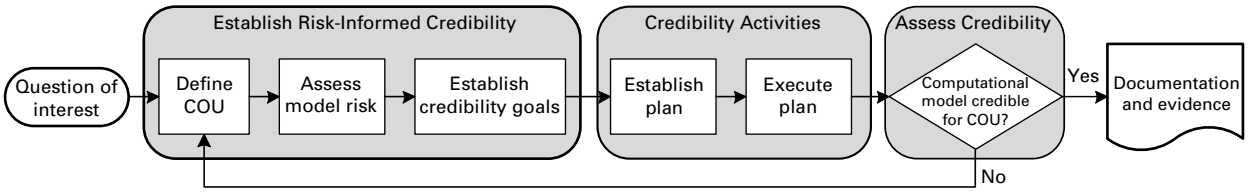
Computational modeling can be used to provide information that supports decisions related to the technical performance, safety, and/or effectiveness of medical devices. Computational models can be used throughout the total product life cycle of medical devices, from validating initial concept, design, and development, to supporting nonclinical and clinical activities, to providing postmarket surveillance. Medical device manufacturers may use computational models to augment in vitro and in vivo evaluations or to simulate such evaluations when they are unjustifiably invasive or prohibitive, and/or are deemed unreasonable. Moreover, computational models may also be used for evaluations that are not possible experimentally or clinically.

Decisions about the performance and/or safety of medical devices have potentially significant consequences, such as patient harm. Because computational modeling plays an increasingly important role in these decisions, there is an increased need to ensure that computational models appropriately represent reality. This can be accomplished through V&V. A considerable body of work on V&V and uncertainty quantification exists and continues to mature. ASME V&V 10 (ref. [1]) presents a general framework for V&V for computational solid mechanics. Additionally, ASME V&V 20 (ref. [2]) outlines a V&V procedure for computational fluid dynamics and heat transfer, both of which are generally applicable to physics-based computational models. As described in the referenced standards, the aim of V&V is to assess the degree to which the computational model is an accurate representation of the reality of interest through the comparison of simulation results with theory, carefully designed and controlled experiments, or other sources of relevant information. However, the relevance and adequacy of the V&V activities, and thus the computational model credibility, are subjective. This can create a lack of common understanding of expectations between stakeholders on what constitutes a *sufficiently* verified and validated computational model. Moreover, while ASME V&V 10 and ASME V&V 20 mention credibility, neither offers guidance on how to establish credibility.

The aim of this Standard is to present a framework for assessing the credibility of a computational model. The framework integrates concepts from two foundational documents: SAND2007-5948 (ref. [3]) and NASA-STD-7009 (ref. [4]). The predictive capability maturity model (PCMM) method of SAND2007-5948 describes different levels of model maturity but does not link maturity with how the computational model could be used to support a decision. NASA-STD-7009 defines the risk associated with using a computational model as a combination of the influence the simulation results have on the decision and the consequence of making a wrong decision. Based on the risk assessment results and programmatic priorities, NASA-STD-7009 specifies a quantitative and/or qualitative level of credibility that needs to be achieved for each modeling and simulation activity.

This Standard provides a risk-informed credibility assessment framework to empower the medical device industry to determine and justify the appropriate level of credibility for using a computational model to inform a decision. The decision could be internal to an organization or part of a regulatory activity, e.g., research or review. Therefore, this

Figure 2.4-1 Process Diagram of the Risk-Informed Credibility Assessment Framework



Standard may also be used by regulatory bodies to evaluate the appropriateness and adequacy of credibility activities and the overall model credibility.

2.2 Purpose

The purpose of this Standard is to provide a framework for assessing the relevance and adequacy of completed V&V activities that establish credibility of a computational model. The credibility should be commensurate with the degree to which the computational model is relied on as evidence of device performance, functional characteristic, and/or safety to support a decision, and the consequences of that decision being incorrect. This Standard will help users communicate the value of the completed V&V activities and establish the associated credibility of the computational model to support a decision.

2.3 Scope

The scope of the Standard encompasses physics-based computational models used for medical device applications. This Standard augments other standards that present V&V methodologies, such as ASME V&V 10 and ASME V&V 20. Therefore, this Standard is intended for the practitioner who is familiar with V&V terminology. It does not present a method for incorporating user expertise or modeler pedigree, nor does it describe the specific V&V activities and rigor that are needed to establish credibility for a particular application and/or device. Instead, this Standard presents a framework for the practitioner to make that assessment using sound engineering judgment. This Standard is not a step-by-step guide, nor is it intended to present a quantitative method for establishing model credibility. While the framework was developed specifically for medical devices, the V&V 40 Subcommittee considers this Standard to be general enough to be applied to other disciplines.

2.4 Overview of the Risk-Informed Credibility Assessment Framework

This Standard presents a framework for establishing and assessing model credibility, which is the trust, obtained through the collection of evidence, in the predictive capability of a computational model for a *context of use* (COU). The COU is the specific role and scope of the computational model used to address a question of interest. The framework, referred to as the risk-informed credibility assessment framework, is presented in Figure 2.4-1. The foundational element of the framework is *model risk*, which is the possibility that the computational model leads to an incorrect decision that results in an adverse outcome, such as patient harm or device malfunction. Model risk is a combination of the influence of the computational model relative to other contributing evidence for making a decision, and the consequence for the patient or end users if a decision is incorrect. Model risk is then used to establish the required level of adequacy of the credibility activities for the COU.

The risk-informed credibility assessment framework begins with *identifying a question of interest*, which describes the specific question, decision, or concern that is being addressed. The next step is to *define the COU*, which is a statement that describes the role and scope of the computational model used to inform that decision in relation to other evidence (see section 3). Then, *model risk is assessed* for the COU, which takes into account the role of the computational model to inform the decision and the potential consequence of an incorrect decision (see section 4). Model risk is then used to *establish the goals for each credibility factor*. The credibility factors are elements of the process used to establish the credibility of the computational model for a COU; the factors include verification, validation, and applicability (see section 5). The goals for the credibility factors are used to *plan the activities that establish credibility* (see section 6). Once the activities are defined, the *plan is executed*. After the credibility activities are completed, an assessment is performed to determine if the computational model is *credible for the COU* (see section 7). If sufficient credibility is not achieved, then the risk-informed credibility portion of the framework can be revisited, as indicated by the return arrow in Figure 2.4-1. If sufficient credibility is not achieved, corrective actions may be taken as outlined in section 7. If sufficient credibility is achieved for the COU, then the computational model can be used to inform the decision. Finally, the credibility activities and findings should be