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Assessing Credibility of Computational Models Using a Risk-Based Framework: Application to Hemolysis in a Centrifugal Blood Pump

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June 14, 2018

Slides will be on figshare

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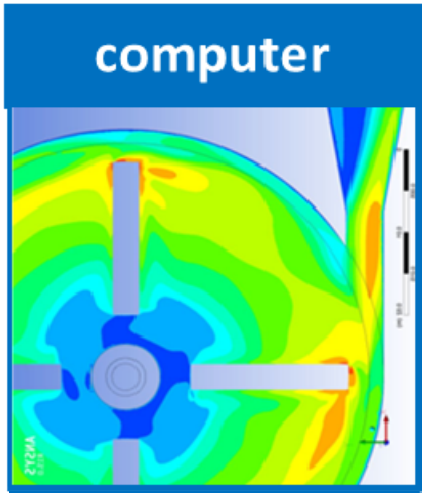
Medical Device Evaluation



Digital Evidence

Ref: *Morrison, et al., (2017). The Role of Modeling and Simulation in the Total Product Life Cycle of Peripheral and Vascular Surgery Devices, J Med Dev.,* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5823268/

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Toxicology & Biocompatibility

Fluid Dynamics

ASAIO Posters: #117, 144, 151, 189, 219, 224

Clinical Trial Design and Image Analysis

Medical Imaging

Medical Devices biocompatibility

Optics

Microbiology and Infection Control

Solid Mechanics

Software Reliability

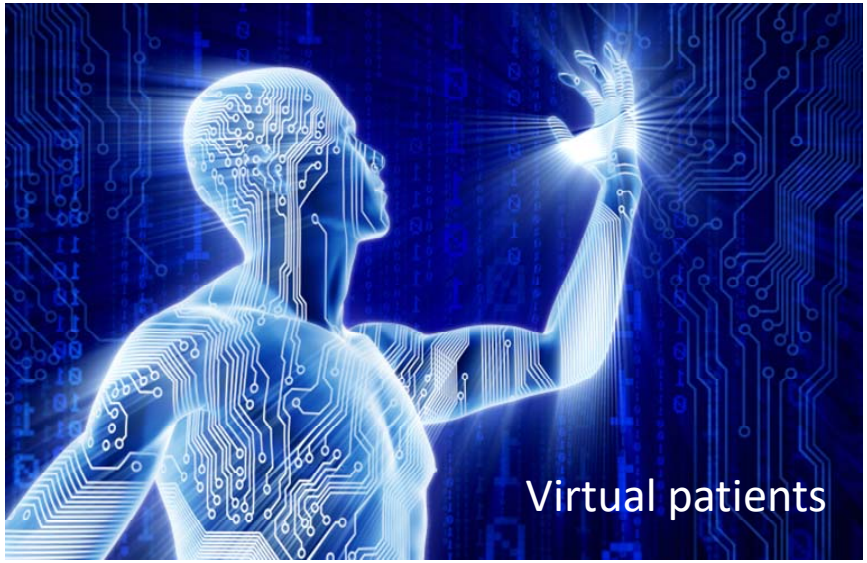
Materials Performance

Diagnostic & Therapeutic Ultrasound

Biophysics

Electromagnetics

OSEL has more than 3 dozen research projects with computational modeling & digital evidence.



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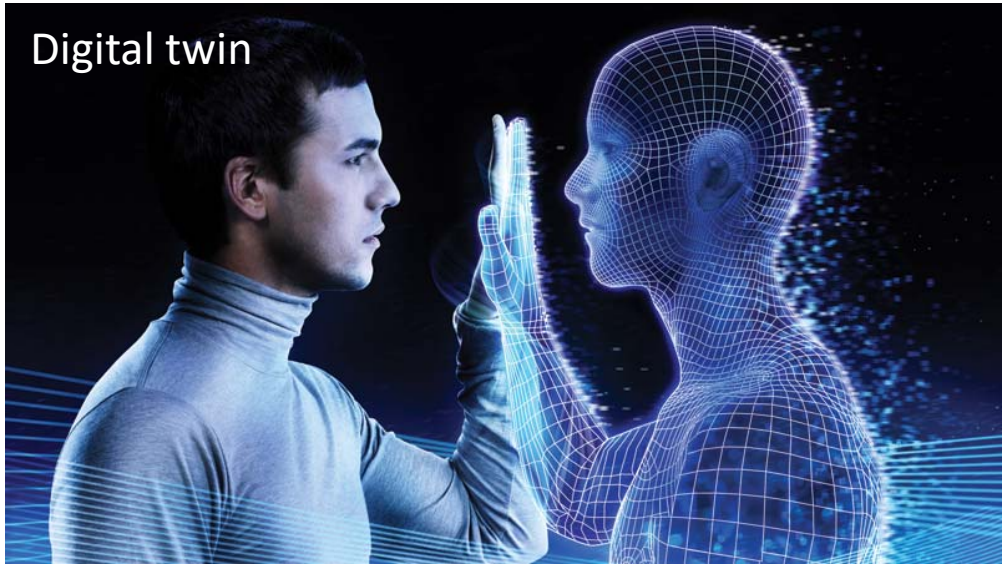

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What is the evidentiary bar for digital evidence?


ANSYS
SIMULIA
MAYO CLINIC
SimuTech Group
FDA
SYNOPSYS
Ethicon Endo-Surgery
Baxter
stryker
Edwards
MDIC
MEDICAL DEVICE INNOVATION CONSORTIUM
Exponent
BD
GORE
COOK RESEARCH
VEXTEC
Abbott Vascular
4WEB
Google
ZIMMER BIOMET
Medtronic
DePuy Synthes SPINE
COMPANIES OF Johnson&Johnson
ASME
SETTING THE STANDARD
Alere
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complex problems inspired solutions
EMBRY-RIDDLE AERONAUTICAL UNIVERSITY

ASME V&V 40 Standard

Credibility: the **trust**, obtained through the collection of evidence, in the predictive capability of a computational model for a context of use

ASME V&V 40-2018

Assessing Credibility of Computational Models through Verification and Validation: Application to Medical Devices

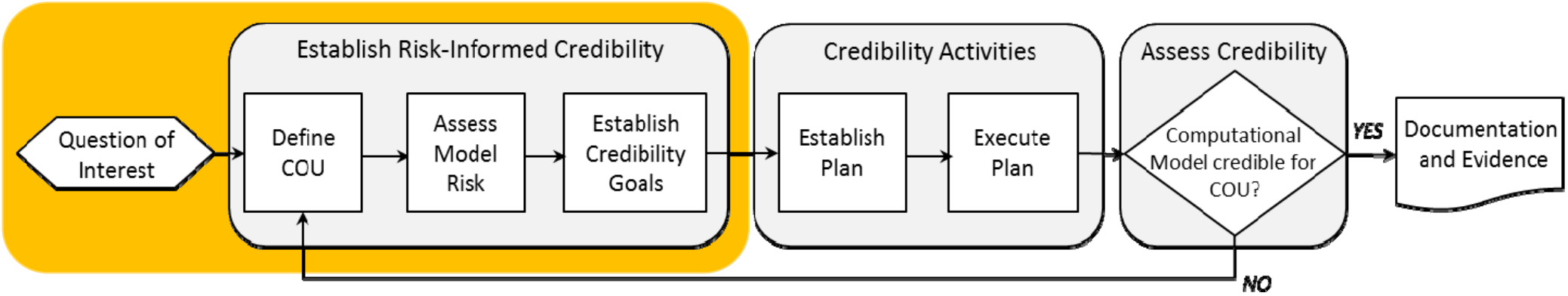
Coming Summer 2018!

AN AMERICAN NATIONAL STANDARD

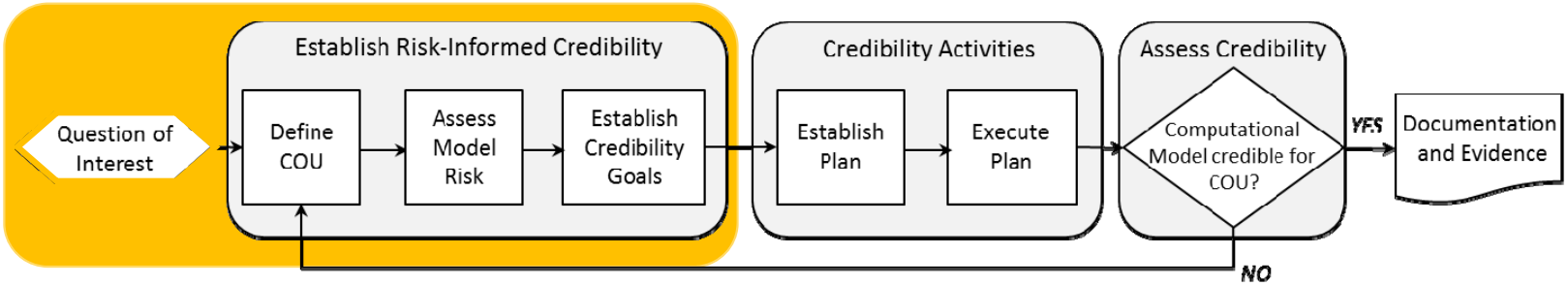
The American Society of Mechanical Engineers

http://go.asme.org/VnV40Committee

ASME V&V40 Framework Overview

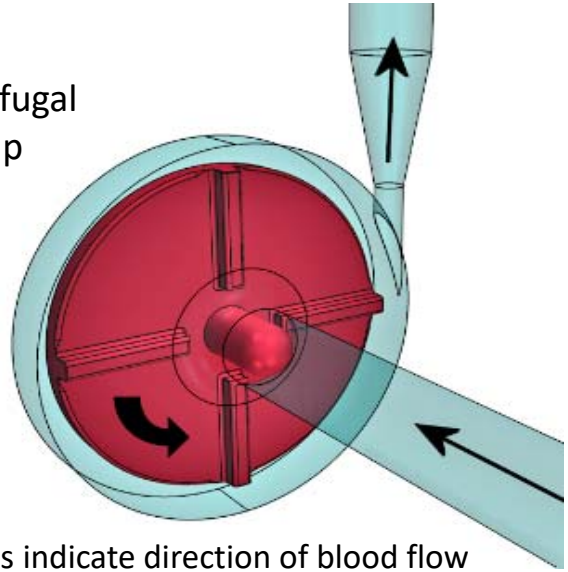


ASME V&V40 Framework with Blood Pump Example



1. State the ***decision or question of interest*** that is being informed by the computational model.

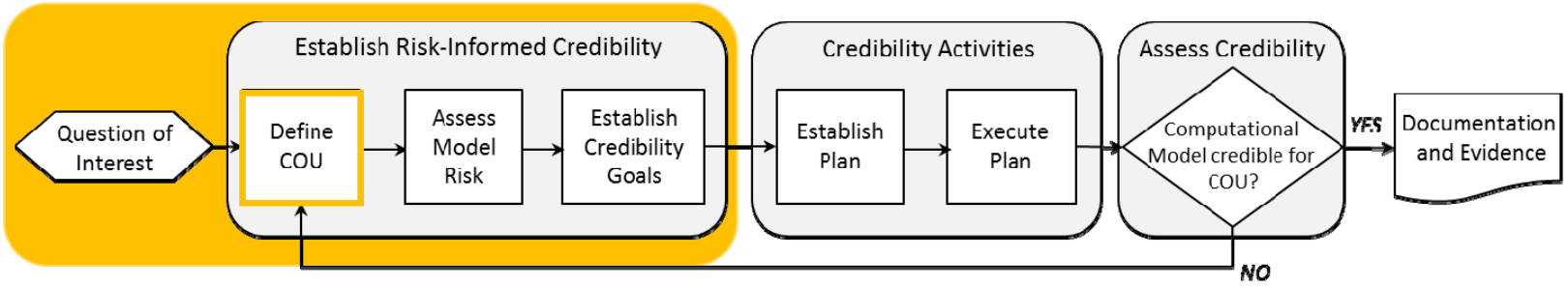
FDA Centrifugal Blood Pump



Arrows indicate direction of blood flow

Question of Interest: Are the flow-induced hemolysis levels acceptable for the intended use?

ASME V&V40 Framework with Blood Pump Example

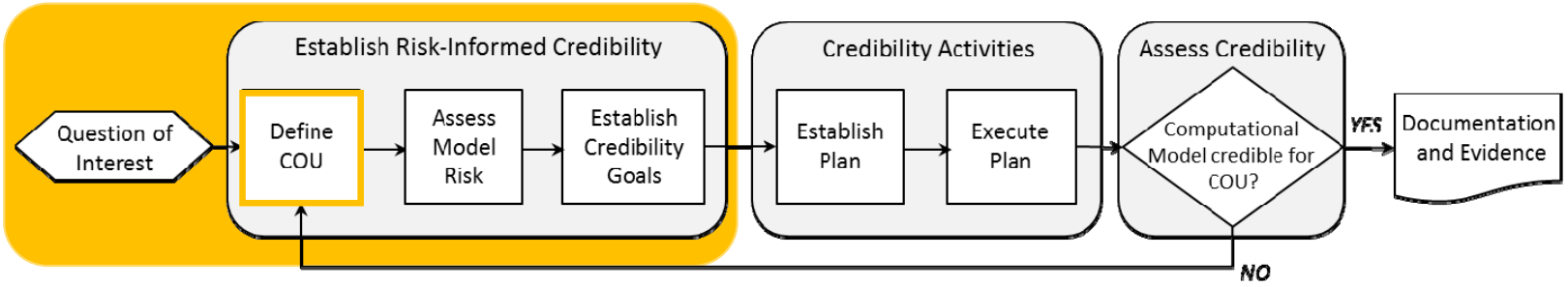


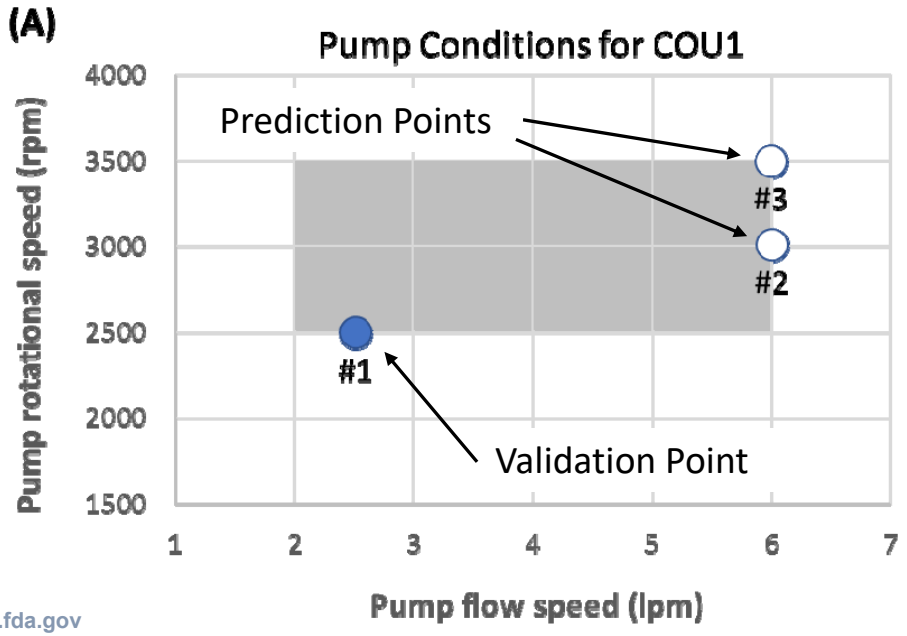
2. Define the ***Context of Use*** for the computational model.

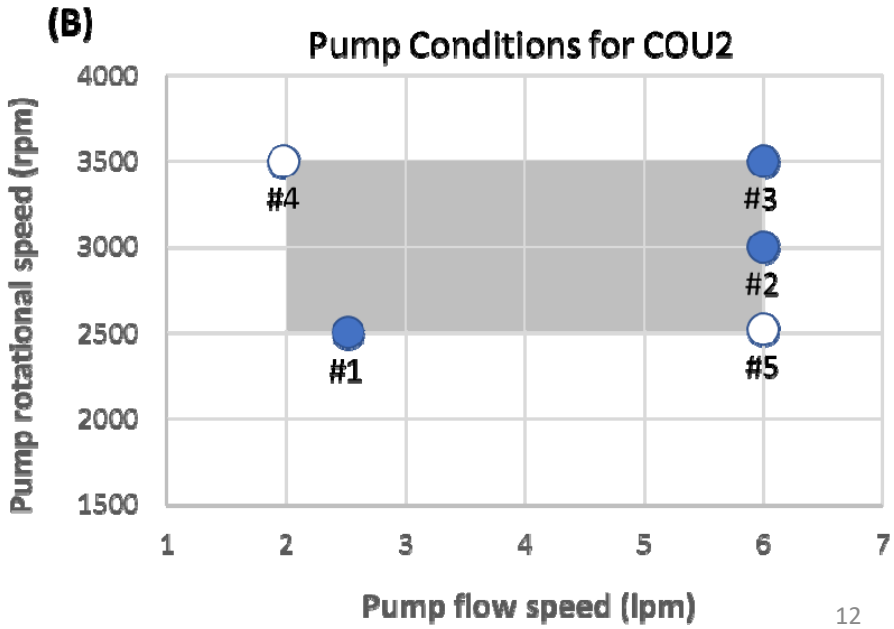
KEY ELEMENTS OF THE COUs	
COU1	**COU2**
• Cardiopulmonary Bypass Device • Class II Indication for Use • CFD model* will identify pump operating conditions at risk for hemolysis • Final hemolysis assessment will be made with *in vitro* testing only	• Ventricular Assist Device • Class III Indication for Use • CFD model* will identify pump operating conditions at risk for hemolysis • Final hemolysis assessment will be made with *in vitro* testing & computational predictions

**CFD model includes the Eulerian power-law model*

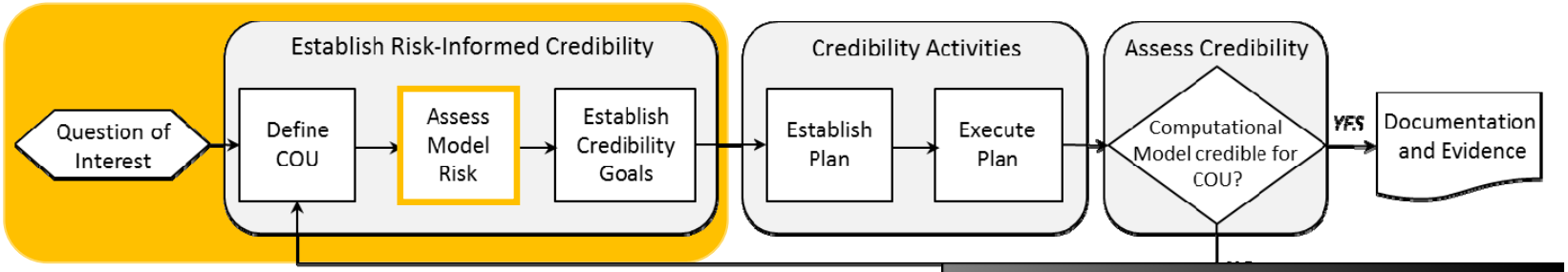
ASME V&V40 Framework with Blood Pump Example





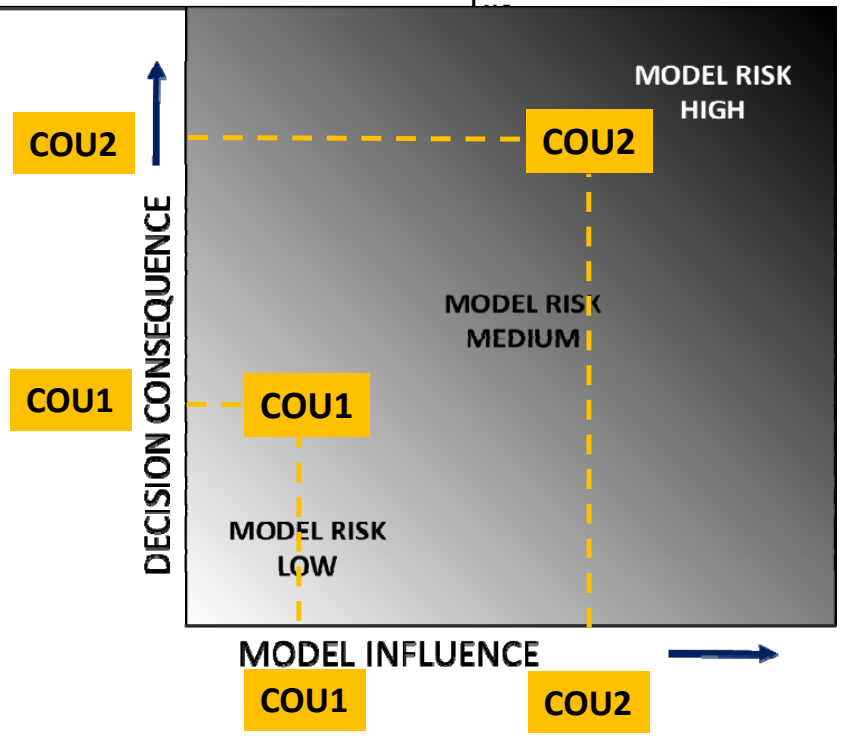


ASME V&V40 Framework with Blood Pump Example

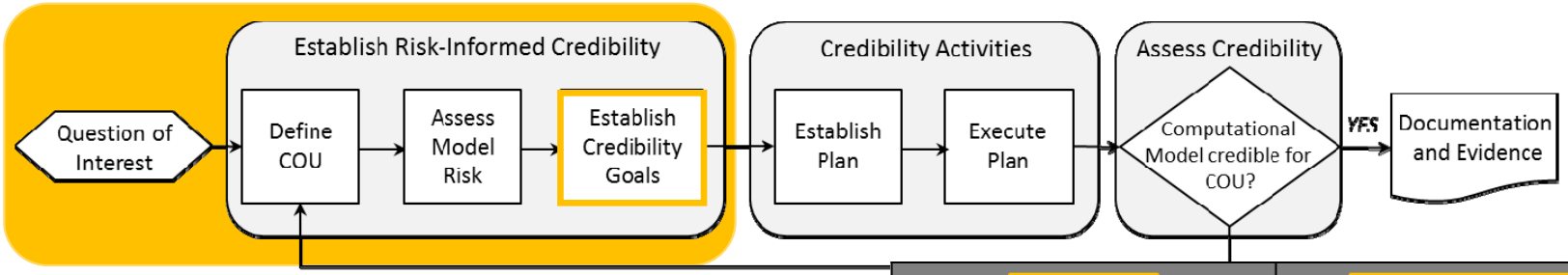


3. Determine ***model risk***

KEY ELEMENTS OF THE COUs	
COU1	**COU2**
• **Final hemolysis assessment will be made with *in vitro* testing only** • **Class II Indication for Use**	• **Hemolysis assessment will be made with *in vitro* testing and computational results** • **Class III Indication for Use**



ASME V&V40 Framework with Blood Pump Example



4. Establish ***credibility goals***

KEY ELEMENTS OF THE COUs	
COU1	**COU2**
• **Lower model risk** • **Less rigor needed** • **Level of agreement: within 20%**	• **Higher model risk** • **More rigor needed** • **Level of agreement: within 5%**

<u>Output Comparison for</u>

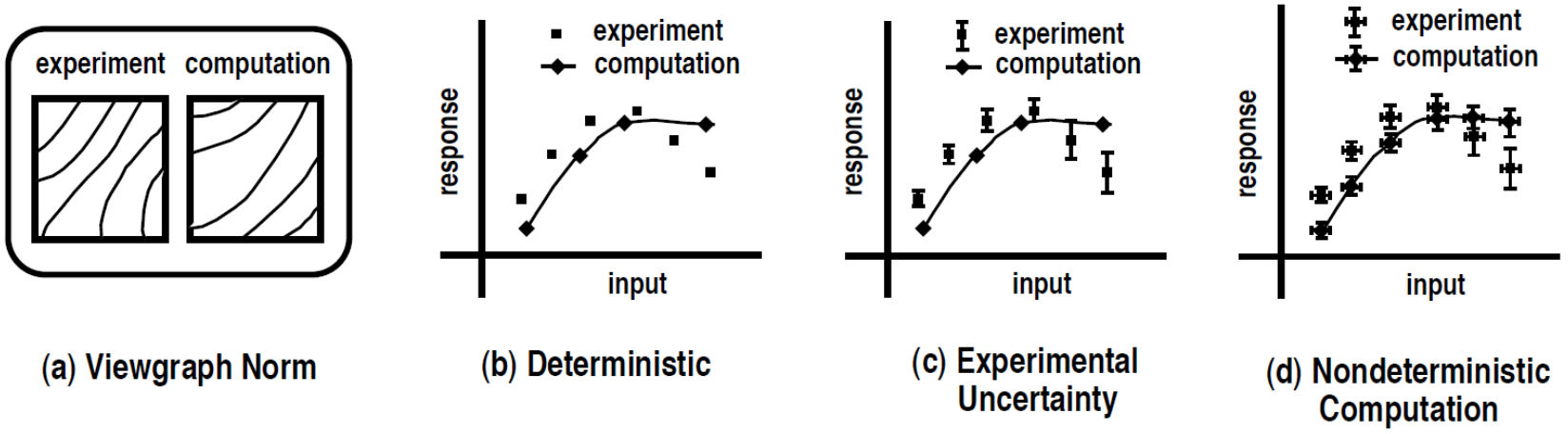
- Velocity
- Relative Hemolysis

Activities		Credibility Factors
Verification	Code	Software Quality Assurance
		Numerical Code Verification
	Calculation	Discretization Error
		Numerical Solver Error
		Use Error
Validation	Computational Model	Model Form
		Model Inputs
	Comparator	Test Samples
		Test Conditions
	Assessment	Equivalency of Input Parameters
		Output Comparison
Applicability		Relevance of the Validation Activities to the COU
		Relevance of the Quantities of Interest

Output comparison

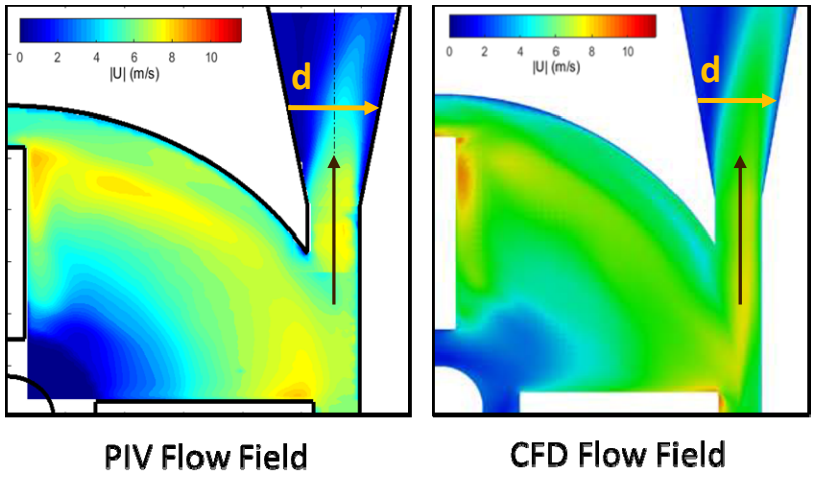
Components of Output Comparison

- Quantity
- Equivalency of output parameters
- Rigor of output comparison → ***How did you do the comparison?***
- Agreement of output comparison

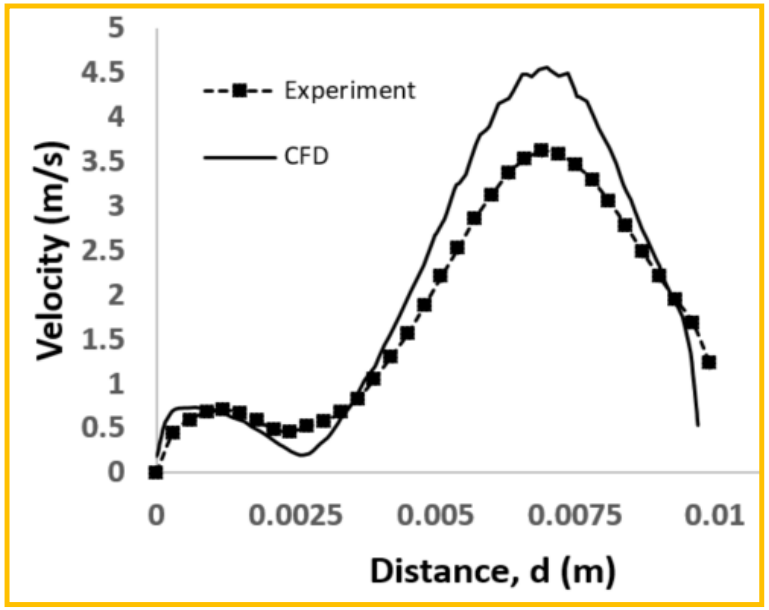


Ref: Adapted from Figure 12, Trucano T.G. *et al., General Concepts for Experimental validation of ASCI Code Applications*, SAND2002-0341, 2002.

Output Comparison – Velocity



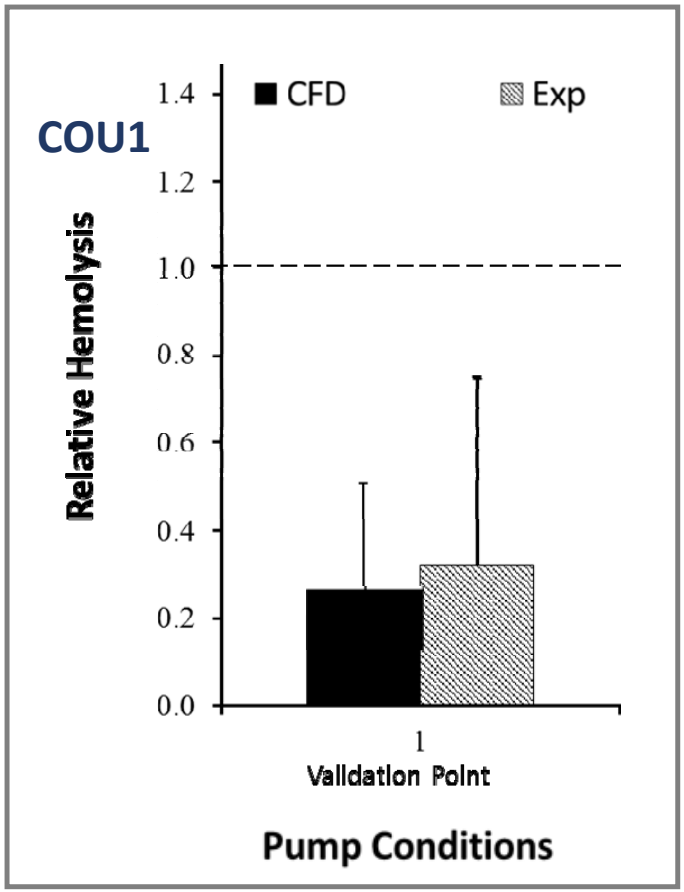
PIV Flow Field CFD Flow Field

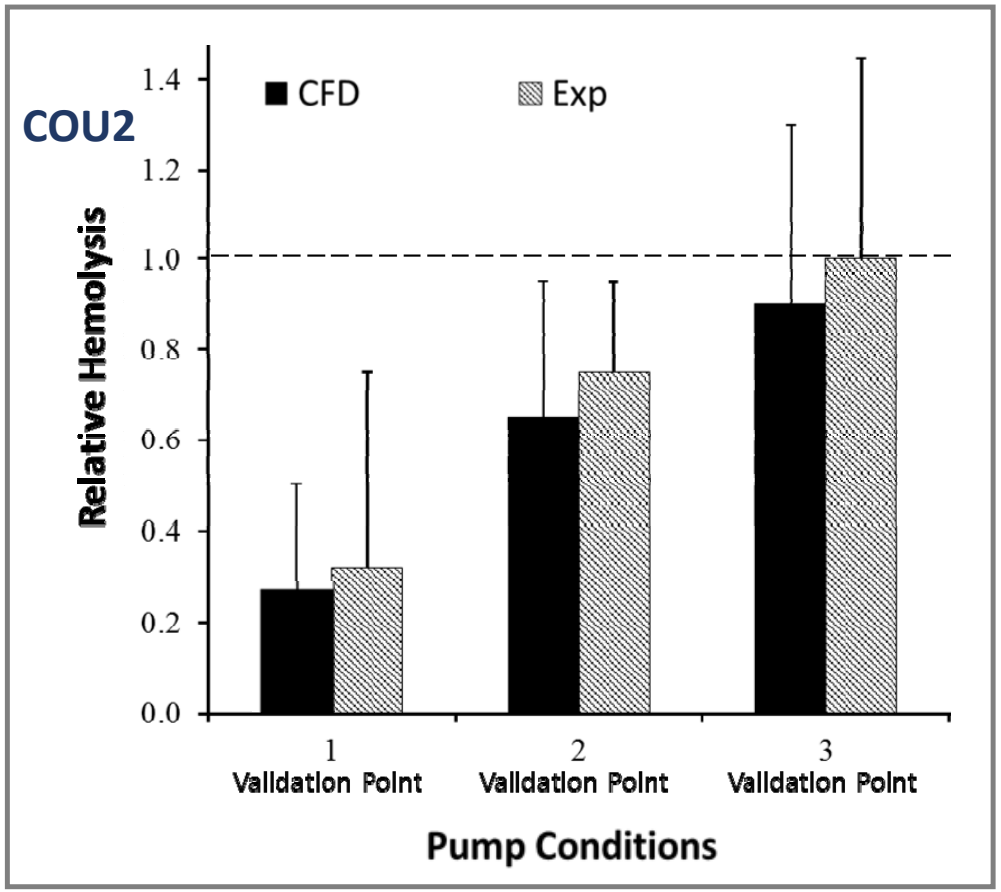


Ref: *Malinauskas, et al., (2017). FDA benchmark medical device flow models for CFD validation. ASAIO Journal, 63(2), 150-160. doi:10.1097/MAT.0000000000000499*

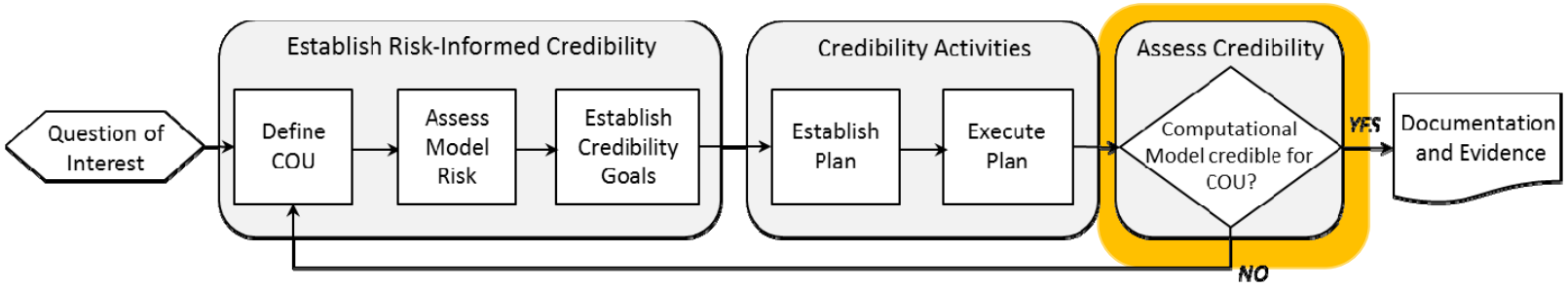
Output Comparison – Relative Hemolysis

$$\text{Relative hemolysis} = \frac{\text{Estimated or measured Hemolysis index}}{\text{Acceptable level of hemolysis}}$$



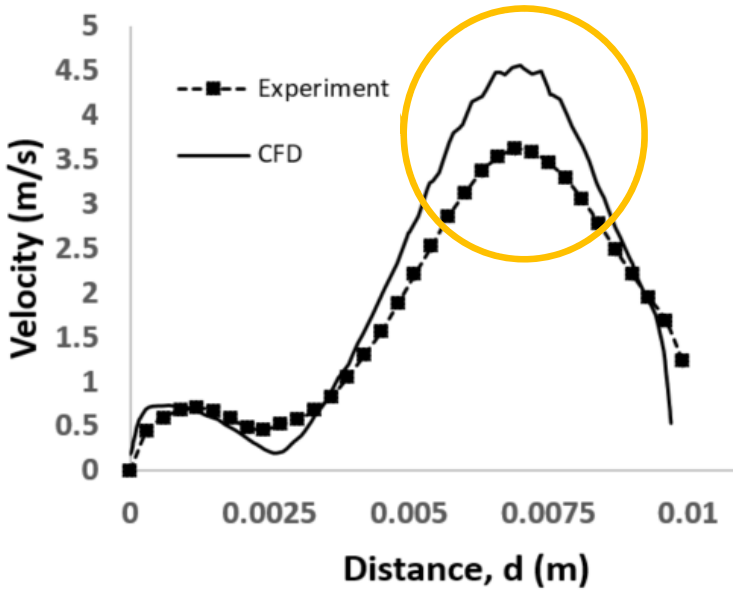


ASME V&V40 Framework with Blood Pump Example



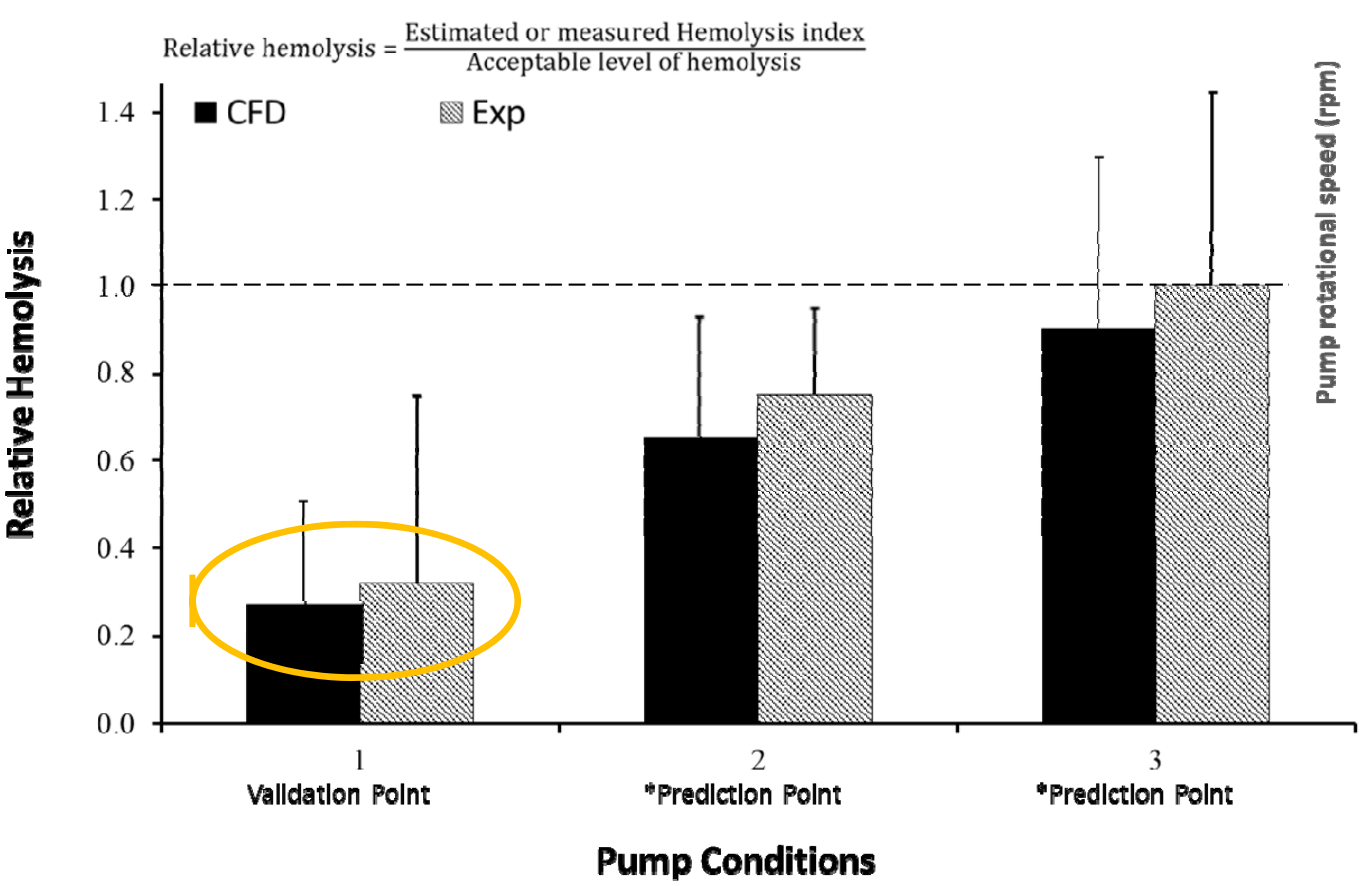
Output Comparison Credibility Factor

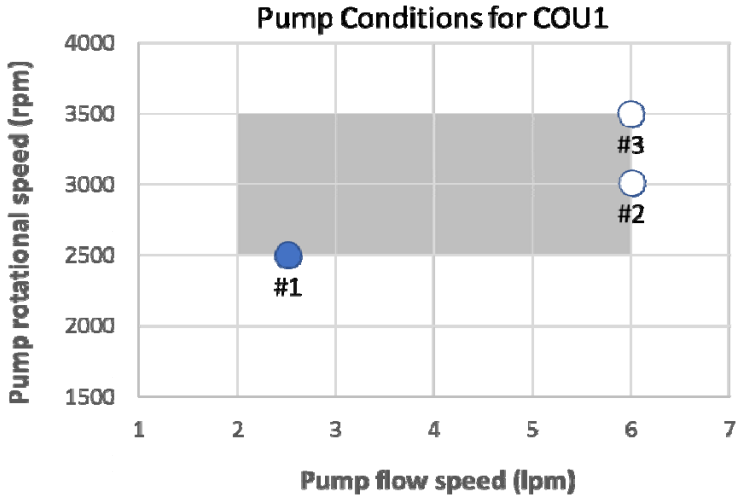
KEY ELEMENTS OF THE COUs	
COU1	**COU2**
• Lower model risk • Less rigor needed • Level of agreement: within 20%	• Higher model risk • More rigor needed • Level of agreement: within 5%



Credibility Assessment – Relative Hemolysis COU1

Output Comparison Credibility Factor

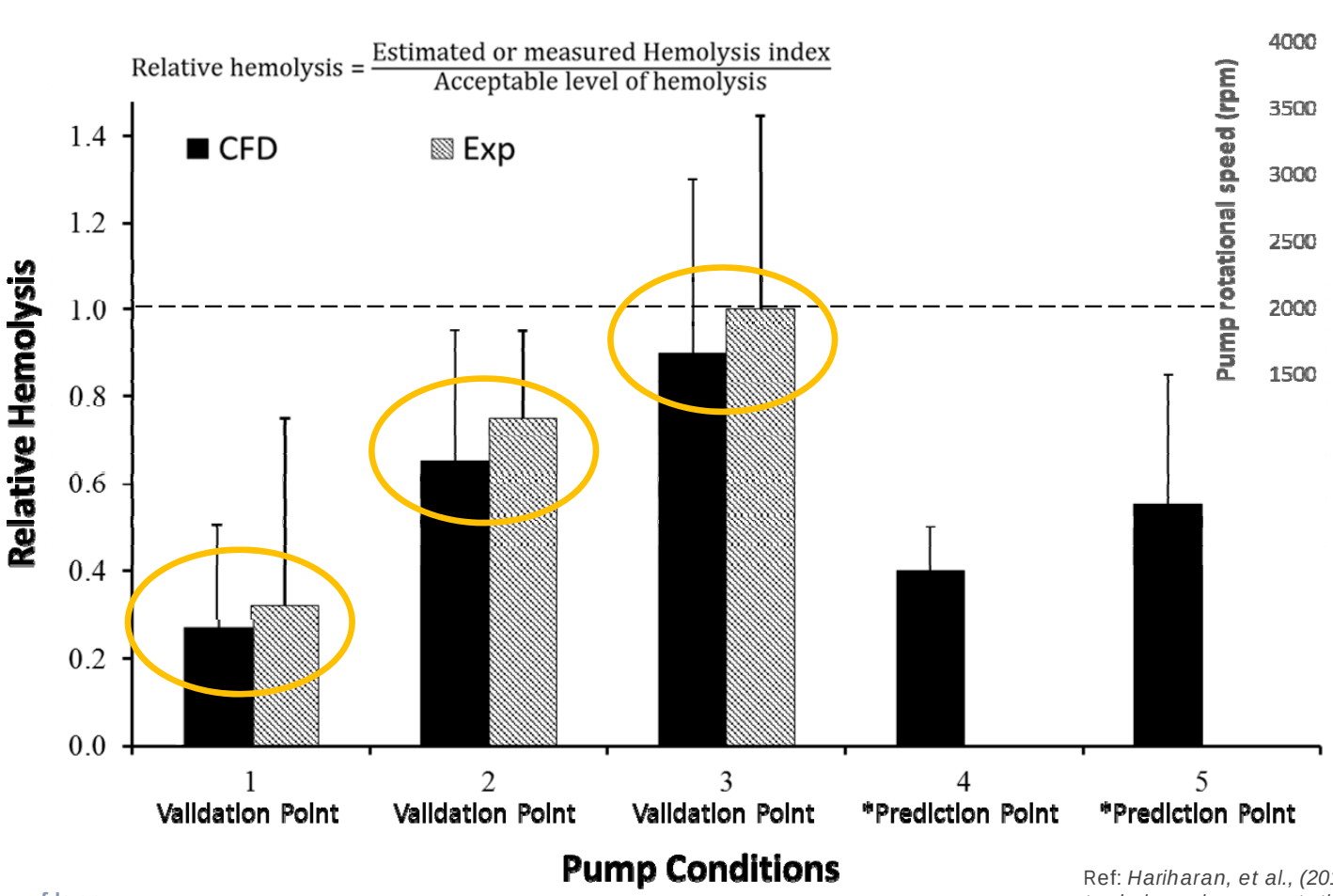


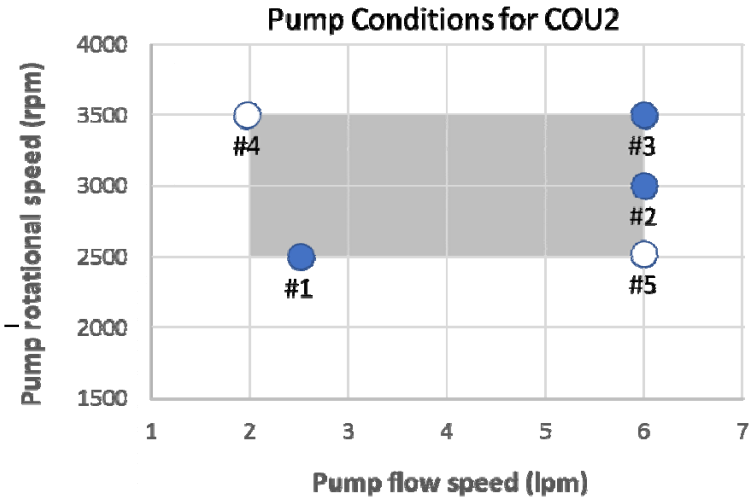


COU1:
For class II indication, rely on *in vitro* testing for final hemolysis assessment – output comparison is within 20%.

Credibility Assessment – Relative Hemolysis COU2

Output Comparison Credibility Factor





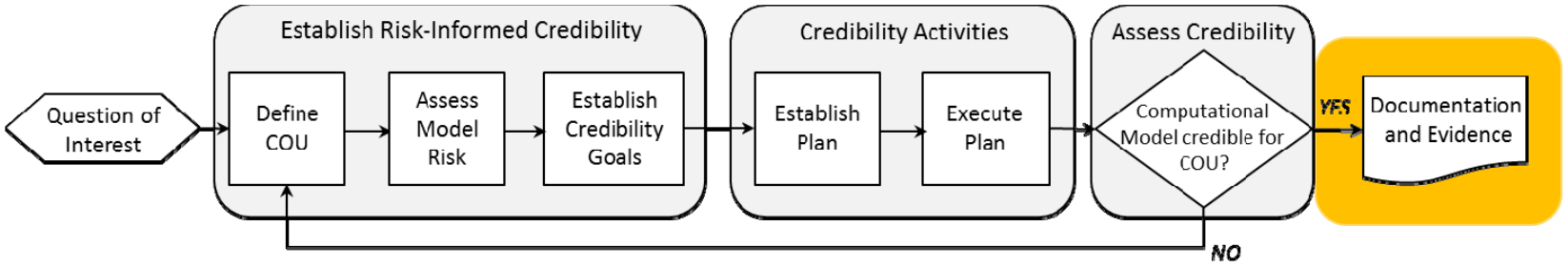
COU2:
For class III indication, rely on CFD results for final hemolysis assessment – output comparison is within 5%.

*

**maybe it is with the threshold-method – see backup slide*

Ref: *Hariharan, et al., (2017). Use of the FDA nozzle model to illustrate validation techniques in computational fluid dynamics (CFD) simulations. PLOS ONE, https://doi.org/10.1371/journal.pon.0178749*

ASME V&V40 Framework with Blood Pump Example



- FDA Final Guidance, Reporting of Computational Modeling Studies for Medical Device Submissions, September 21, 2016

Other V&V Resources:

- ASME V&V 10-2006, V&V for Computational Solid Mechanics
- ASME V&V 10.1-2012, V&V for Computational Solid Mechanics (Illustrative Example)
- ASME V&V 20-2009, V&V for Computational Fluid Dynamics & Heat Transfer

Conclusions

- With the same CFD model and same data for two COUs, demonstrated the concept of credibility requirements based on a risk assessment
  - Context of use matters!
- The ASME V&V 40 Standard provides a framework for establishing the credibility requirements for digital evidence.
  - Large, successful collaboration between FDA and Industry to foster broad adoption
  - The standard is critical for advancing the use of modeling in a broad range of regulatory applications, such as:
    - virtual patients, digital twins, in silico clinical trials, software as a medical device
- No cookie-cutter recipes → assessing credibility relies on sound engineering and clinical judgement, as appropriate.

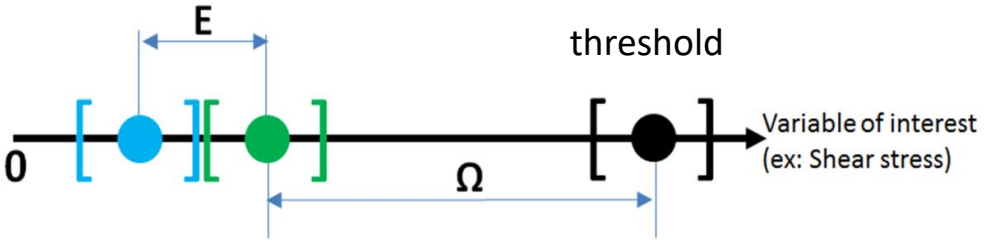
Slides will be on figshare

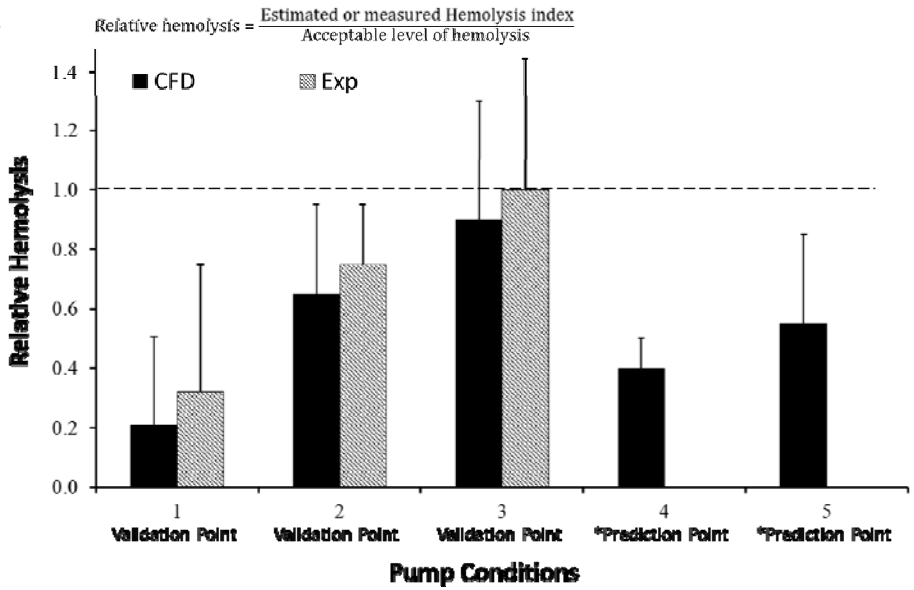
Ref: *Morrison, et al., (2018). Assessing Credibility of Computational Models Using a Risk-Based Framework: Application to Hemolysis in a Centrifugal Blood Pump; submitted to ASAIO J for this Top Abstract*

Threshold-based validation method

Risk-based approach for establishing Model credibility

- Acceptance criterion: acceptable difference between computational output and validation experiments
- Acceptance criteria is a function of Model Risk
  - Risk to patient safety because of Error, E





Ref: *Hariharan, et al., (2017). Use of the FDA nozzle model to illustrate validation techniques in computational fluid dynamics (CFD) simulations. PLOS ONE, https://doi.org/10.1371/journal.pon.0178749*