



Avicenna Alliance Glossary

Terms for Computer Modelling and Simulation

Introductory Remark

*There are occasional confusions and diverging opinions possibly leading to misunderstanding in the use of some in silico concepts in the literature. To clarify **our** message, a team of academic and industry members of the Avicenna Alliance is proposing a definition of words regularly used in the 'in silico' literature. The definitions in this glossary, results of a consensus within our members, clarify the meaning of the terms we are using in our publications. We understand that different definitions may exist and we welcome any comment as these definitions may evolve.*

This Glossary is a first release with a first short list of definitions; more concepts will be defined and existing definitions may be adjusted in future updates of this document. Therefore, comments and inputs are welcome to enrich this glossary. You are encouraged to share your comments or suggestions for modification with Roberta Maggi, manager@avicenna-alliance.com.

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DEFINITIONS:

Absolute benefit

Difference between the rate or risk of event between the untreated / control individuals and the corresponding treated individuals in the same group or cohort. Instead of the event rate, it can also be the value of a marker.

Adequacy assessment

Process of evaluating the evidence in support of credibility of a computational model, for a given context of use, and making a determination on whether the evidence is sufficient.

Agent-Based models (ABM)

Computational representation of a physical reality that utilizes a large number of autonomous discrete particles (called Agents) that move in space and time, interact with each other and change their internal state according to a set of rules. ABMs are capable of re-creating macro-level phenomena by the actions and interactions of micro-level individual agents (emergence).

Example: "A multi-step and multi-scale bioinformatic protocol to investigate potential SARS-CoV-2 vaccine targets", Briefings in Bioinformatics, Volume 23, Issue 1, January 2022, bbab403, <https://doi.org/10.1093/bib/bbab403>

Applicability

Relevance of the credibility assessment of the computational model (e.g. verification and validation activities, uncertainty quantification) for a given context of use. (Adapted from FDA, source "Assessing the Credibility of Computational Modeling and Simulation in Medical Device Submissions - Draft Guidance for Industry and Food and Drug Administration Staff", <https://www.fda.gov/media/154985/download>).

Assertion

Principal feature (e.g., Chemical or biological entities and their functional relation(s) between these entities) of a piece of knowledge (scientific extract, Figure, Table) that carries scientific information in the form of plain language that will be assembled into a Knowledge Model.

Base model

Hypothetical, abstract representation of the object's properties, in particular, its behaviour, which is valid in all possible contexts, and describes all the object's facets. (H. Vangheluwe, McGill University, 2001).

Calculation verification (i.e. solution verification)

The process of estimating the numerical error in the output of a computational model due to the use of numerical methods to solve the mathematical model (including the post-processing) specific to the context of use. It aims to estimate the magnitude of the numerical errors in the estimated solutions. (Based on M. Viceconti et. al.).

Calibration (Model) (i.e. tuning or fine-tuning)

The process in which a priori unknown and estimated parameters are refined through a numerical procedure in order to achieve a desired behavior of the model regarding given criteria.

Clinical outcome

Measurable change in patient's health, function or quality of life at specific time point.

Clinical score

A standardized quantitative or qualitative indicator of the severity of a disease, or other variables for a particular patient, at a particular instant in time. The clinical score may be obtained on the basis of a series of clinical and/or biological and/or imaging and/or pathological factors.

Code verification

The process of ensuring the quality (including correctness, reproducibility and good standards practices) of the algorithm and its source code via minimization of weaknesses and errors, when translating the chosen mathematical model.

Comparator

Test data that are used for comparison with computational results as part of the validation, which may be data from bench testing or in vitro, ex vivo, in silico, and in vivo studies.

Compartment

Specific subsection or structure of a biological system in a computational model. The level of granularity depends on the Context of Use. Compartment may be also called "**part**" depending on the field of application.

Computational modelling

Numerical representation of the mathematical model performed by means of computational implementation in order to simulate and study complex systems. (Based on FDA: *Frontiers in Medicine*, September 2018, Volume 5, Article 241 by Tina Morrison (FDA) et. al.)

Context of Use (CoU)

Defines the specific role and scope of the computational model used to address the question of interest. It should include a detailed statement of what will be modelled and how the outputs from the computational model will be used to answer or inform the question of interest. It is important to note that the CoU is distinct from the "indications for use" or "intended use" of a medical device, which are descriptions of how a device is intended to be used in clinical practice. [Assessing Credibility of Computational Modeling through Verification and Validation: Application to Medical Devices V&V 40 – 2018. ASME, 2018. 60p. ISBN: 9780791872048.]

Digital Evidence (i.e., in silico evidence)

Results of computational modelling and simulation submitted as part of a (regulatory) evaluation process provided in a prescribed format, that encompass in silico trials and in silico tests.

Digital twin

A computational model of physical assets (or processes or systems) that learns and is updated from multiple sources, in real time or not, depending on the context of use. It acts as a bridge between the physical and virtual world, allowing analysis (e.g. simulations) that can help to anticipate problems and plan for the future.

Personal Digital Avatar (PDA)

Digital twin of a specific human connected with its physical counterpart (physical twin) to regularly collect data about his/her evolution and predict likely evolution of his/her health.

Risk analysis

Analysis based on a combination of a model influence and decision consequence.