

Supporting ICH M15 Principles Through a Platform for Good Simulation Practices



Clear, transparent documentation

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Drive regulatory-ready M&S projects with a secure, collaborative platform built for traceability and transparency

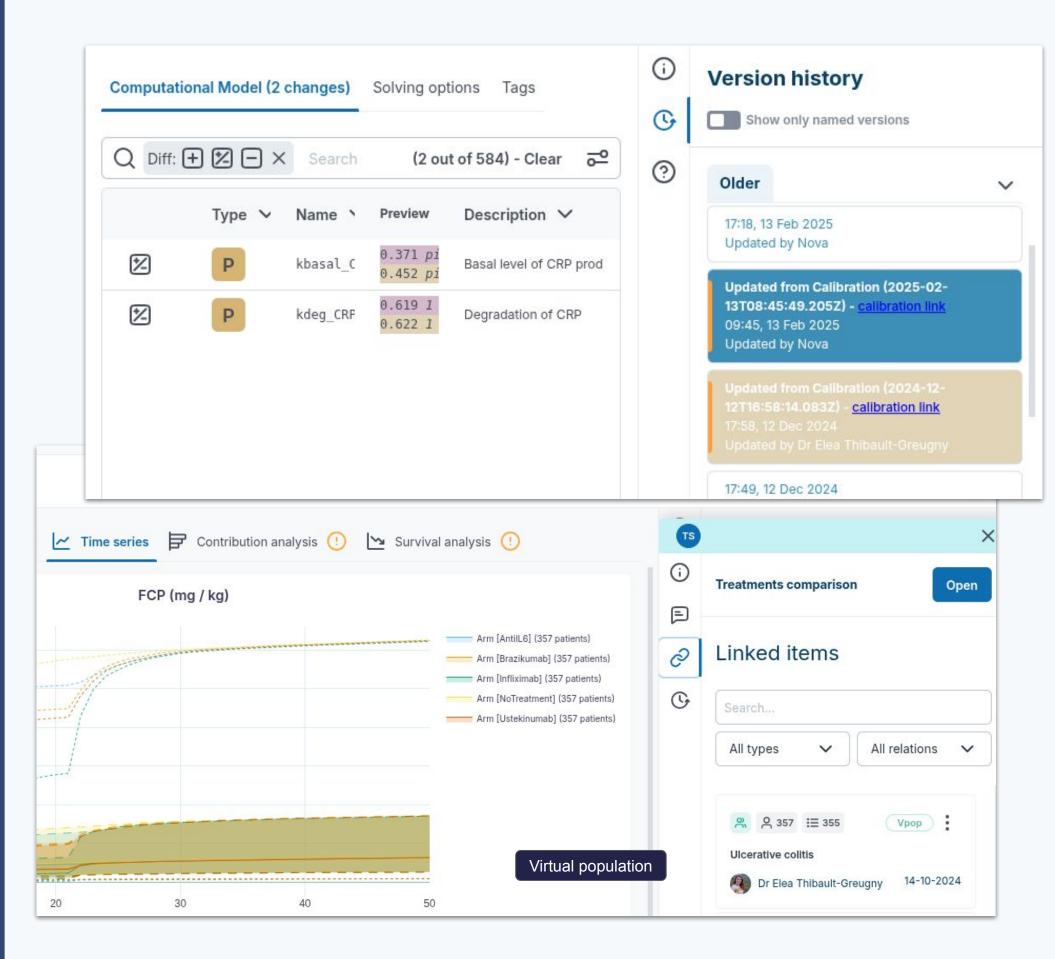
Jinkō¹, an M&S platform that enables confident interactions for multi-disciplinary teams

P Liver.CRP General Advanced Graph Edit Preview V **Inflammatory Bowel Disease** Advanced options VmProtSynth * Liver * (1.0 - antiIL6) * Liver.IL6 ^ 2.0 / {x} () type Biomarker (2) Manage tags ((KmProtSyn * Liver) ^ 2.0 + Liver.IL6 ^ 2.0) Inflammatory bowel disease (IBD) is a heterogeneic disease with a variety of treatments Add link(s) Extract targeting different mechanisms. Here we focus on key clinical biomarkers following five 1 picomol different treatment options for Crohn's disease. Intestinal Lumen Louis 10 months ago @Claire the Liver.CRP component is A Dynamic Quantitative Systems Pharmacology N now ready for review (see extract attached as well), any chance you Transform to Con \ominus

Pinpointed content from assets can be commented on, discussion threads are archived for traceability.

Accessible equations, linked to knowledge

Traceable versioned assets, from kickoff to simulations



Related items are interlinked automatically for ease of navigation / traceability between key assets. Here for instance we can see the virtual population the results are tied to.

Fig. 1: Illustration of key elements in the jinkō platform allowing for the support of ICH M15 recommendations. The features illustrated are interconnected, built for accessibility and transparency for all M&S projects.

BACKGROUND

Illustration

The ICH (International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use) aims at harmonizing the regulatory expectations in regions around the world, working with key Bodies such as the FDA and the EC. To this effect, the organization published in November 2024 a Draft Guidance documentation 'M15: General Principles for Model Informed Development², with key recommendations.

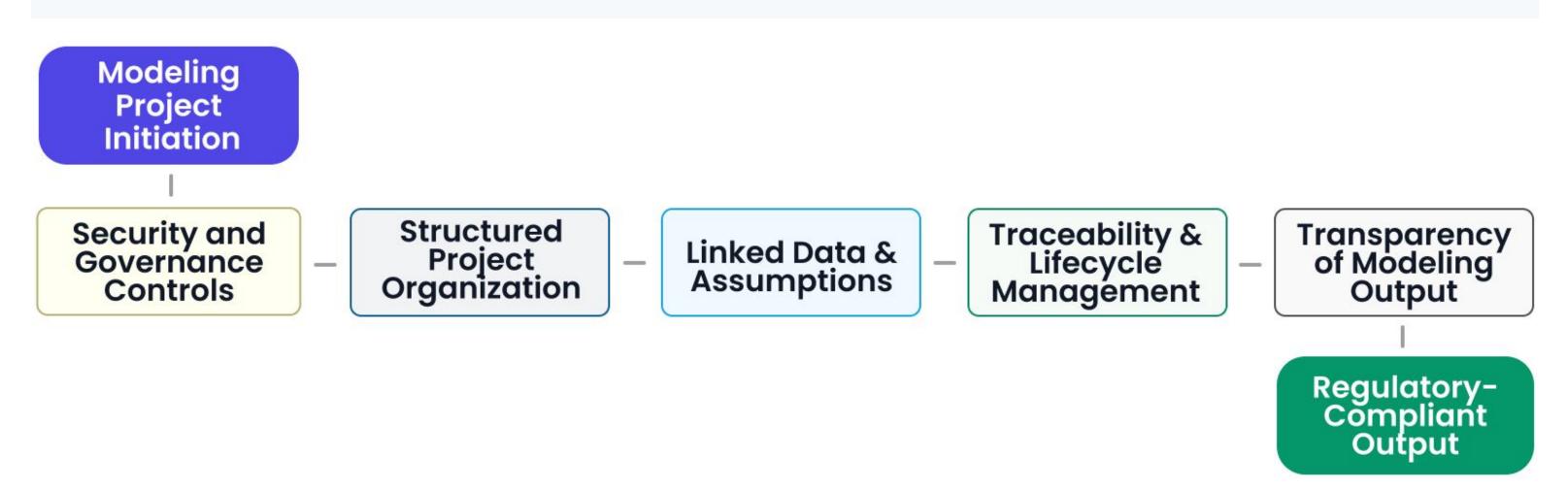
Fig.1 - Model structure overview, including major cells, cytokines, biomarkers, and connections

The model consists of 2 major compartments (gut and blood), immune cells, cytokines, and

biomarkers (CRP and FCP). Dotted lines indicate that the species in the model impacts the

A Modeling & Simulation platform designed to support these recommendations must inherently incorporate robust security, interdisciplinary collaboration, transparency, traceability, and auditability across all its modules.

METHODS



Role-based access, secure authentication and alignment with regulatory standards (such as GDPR, HIPAA and ISO/IEC 27001), coupled with a clear hierarchized project organisation, automatic interlinking of assets and versioning, ensure that modeling workflows are implemented in a compliant and auditable manner. Intuitive interfaces further promote universal access of assets even for non-modelers.

RESULTS

production of IL-6 through cells not currently included in the

model but included as factors influencing the basal rate of

IL-6 production.²³ Neutrophils can lead to cleavage of sol-

uble IL-6R and production of IL-6, although the latter is still

under debate.²⁴ IL-6 regulates the balance of Th17 and Treg

cells by inducing Th17 differentiation and inhibiting Treg differentiation.²⁵ The commonly measured biomarker CRP is

produced through an IL-6 stimulus mainly in hepatocytes and is often upregulated in inflammation.²⁶ IL-8 (CXCL8) is

a chemoattractant leading to migration of neutrophils from

Specific section of interest from the

scientific literature and data sources

can be selected and used in various

context in a project, here for instance

to link the knowledge behind this

particular model component.

Regular exchanges and edition are secured, pinpointed and transparent throughout the life-cycle of a project, for both internal and external stakeholders. A greater interactivity with key elements (models, results, assumptions, data..) allows for thorough reviews and traceability.

Early interactions with Regulatory Agencies are facilitated

Users are encouraged, notably via a documentation module and assets linking features, to follow the ICH M15 framework for Key Assessments Elements (and MIDD planning stage), thus enabling early interactions and review with Regulatories Agencies. The generation of of the Model Analysis Plan (MAP) and Model Analysis Reports (MAR) are also facilitated.

Model evaluation and auditability are by design

Model verification and validation activities are facilitated by an accessible model interface that clearly shows the model structure, equations used and link to knowledge. Model applicability is also easily assessed via fast calibration, real-life data overlay, simulations and traceable results.

CONCLUSION

- → We illustrate here how a collaborative platform with traceability and transparency at its core can support R&D teams in leading M&S projects that follow Good Simulation Practices, in particular tied to the ICH M15 early recommandations.
- This 'white-box' approach is a foundation that paves the way to further the structural readiness of M&S projects for Regulatory audit and acceptance. It is already in line with the first ICH M15 Draft Guidance document and ready to adapt as it evolves.



REFERENCES

[1] https://www.jinko.ai

[2] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/m15-general-principles-model-informed-drug-development