REQUEST FOR PROPOSAL _ RFP-2026-001

Services for Critical Path Institute Quantitative Disease Modelling activities

Document 1: Technical Specifications

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1 INTRODUCTION

1.1 Purpose of the Request for proposals

The Critical Path Institute (C-Path) intends to establish a strategic scientific partnership with one or more qualified contractors to support the design, development, validation and implementation of regulatory-grade quantitative disease models.

The procurement seeks to identify contractors capable of providing high-level scientific, methodological and technical expertise across multiple disease areas and therapeutic indications. The selected contractor(s) shall contribute to the development of fit-for-purpose modelling solutions that support regulatory decision-making, clinical drug development and evidence generation throughout the medicinal product lifecycle.

The services procured under this Request for Proposal (RfP) are intended to establish a long-term collaboration supporting the delivery of disease modelling projects from initial concept development through regulatory engagement and implementation. Activities may include, but are not limited to, disease progression modelling, clinical trial simulation, extrapolation methodologies, real-world evidence integration, advanced statistical and machine learning approaches, and the development of reusable regulatory-grade analytical tools.

The contractor shall work in close collaboration with C-Path multidisciplinary teams, international scientific experts, patient organizations, academic partners, industry participants and regulatory authorities, including but not limited to the European Medicines Agency (EMA), the U.S. Food and Drug Administration (FDA) and other health authorities, as appropriate to individual projects.

The procurement is structured to ensure scientific excellence, methodological transparency, reproducibility, and alignment with internationally recognized regulatory standards and good modelling practices.

1.2 Legal and Regulatory Framework

The services performed under this contract shall support C-Path's mission as an independent, non-profit organization dedicated to accelerating medical product development through collaborative regulatory science.
Activities undertaken under this procurement shall be conducted in accordance with applicable international scientific and regulatory principles, including, where relevant:

- International Council for Harmonisation (ICH) guidelines applicable to model-informed drug development and quantitative methodologies, including ICH E11A (Pediatric Extrapolation) and ICH M15 (General Principles for Model-Informed Drug Development);

- EMA and FDA guidance documents relevant to quantitative methods, clinical outcome assessment and regulatory qualification of Drug Development Tools (DDTs); and internationally recognized statistical standards;
- applicable European Union legislation governing data protection, including Regulation (EU) 2016/679 (General Data Protection Regulation - GDPR) and the European Health Data Space (EHDS) Regulation;
- where applicable, the U.S. Health Insurance Portability and Accountability Act of 1996 (HIPAA), including relevant privacy, security and breach-notification requirements;
- applicable information security standards, including ISO/IEC 27001 and related requirements; and
- applicable ethical, scientific and governance requirements relating to the handling of clinical trial data, real-world data and patient-level information.

The contractor shall ensure that all methodologies, analyses, software development and documentation are sufficiently transparent, reproducible and documented to support scientific review, regulatory interactions and independent verification where required.

1.3 Strategic Objectives

The overall objective of this RfP is to establish a strategic scientific capability that supports the development of regulatory-grade disease modelling tools. Specific objectives include:

1. **Develop regulatory-grade quantitative disease models** that are scientifically robust, fit for their intended Context of Use (CoU), and suitable for supporting regulatory decision-making.
2. **Support the development and qualification of Drug Development Tools (DDTs)** by generating the scientific evidence, documentation and technical outputs required for interactions with global regulatory authorities.
3. **Promote scientific transparency and reproducibility** through rigorous documentation, version control, validation procedures and adherence to recognized best practices in quantitative sciences.
4. **Contribute to the long-term sustainability of the C-Path Disease Modeling Coalition (CP-DMC)** by developing transferable methodologies, reusable software components and knowledge assets that support future disease modelling initiatives (cf section 2.1 for context).
5. **Stakeholders:** Relevant participants in CP-DMC activities, including, as appropriate, regulatory authorities, industry, academia, clinicians, patient organizations, and other scientific or technical partners.

1.4 Definitions

For the purposes of this procurement, the following definitions shall apply.

Context of Use (CoU): A concise description of the specific decision, application or regulatory purpose for which a disease model or Drug Development Tool is intended to be used.

Disease Model: A quantitative mathematical or statistical representation of disease progression, treatment response, patient characteristics or clinical outcomes developed to support biomedical research, drug development or regulatory decision-making.

Drug Development Tool (DDT): A method, model or measurement intended to facilitate drug development and regulatory evaluation through a clearly defined Context of Use.

Regulatory-Grade Model: A model developed, documented and validated according to recognised scientific and regulatory standards such that it may support interactions with health authorities and, where appropriate, qualification activities.

Validation: The process of demonstrating that a model is scientifically sound, performs as intended within its defined Context of Use, and produces reproducible and credible results.

Real-World Data (RWD): Data relating to patient health status or healthcare delivery routinely collected from sources other than traditional interventional clinical trials.

Clinical Trial Simulation (CTS): The application of quantitative models to simulate clinical trial scenarios in order to evaluate alternative trial designs, dosing strategies, eligibility criteria or development decisions.

2 Context

2.1 The CP-DMC

The CP-DMC is a pre-competitive, multi-stakeholder initiative established to develop quantitative disease models and related Drug Development Tools (DDTs) that support more efficient, evidence-based drug development and regulatory decision-making in high unmet needs areas.

The CP-DMC brings together expertise from regulatory authorities, academia, industry, clinicians, patient organizations, and technology partners to address common scientific and methodological challenges that cannot be efficiently solved by individual organizations acting independently.

The CP-DMC develops disease modelling frameworks across multiple therapeutic areas using a common scientific, methodological, and governance approach. Individual disease programmes may differ in their scientific objectives, available data, and intended applications; however, all programmes follow a framework developed by C-Path for model development, validation, regulatory engagement, and lifecycle management.

2.2 Regulatory Science Context

Increasing complexity in drug development, combined with the growing availability of clinical trial data, real-world data (RWD), and advanced quantitative methodologies, has led regulatory authorities to encourage greater use of model-informed approaches throughout the medicinal product lifecycle.

International regulatory initiatives, including ICH E11A (Pediatric Extrapolation) and ICH M15 (General Principles for Model-Informed Drug Development), recognize the role of quantitative methods in reducing uncertainty, integrating multiple sources of evidence, optimizing clinical development programmes, and supporting regulatory decision-making.

The CP-DMC aims to develop modelling frameworks that are scientifically robust, transparent, reproducible, and aligned with these evolving regulatory expectations.

2.3 Drug Development Tools (DDTs)

DDTs are scientifically validated methods, models, or measurements developed for a clearly defined regulatory purpose. When supported by an appropriate evidence package, DDTs may be used to inform drug development decisions and, where appropriate, may be submitted to regulatory authorities for qualification or other forms of regulatory endorsement.

Within the CP-DMC, quantitative disease models are developed as potential DDTs capable of supporting applications such as disease characterization, clinical trial simulation, model-informed drug development, pediatric extrapolation, external control strategies, and optimization of clinical development programmes.

Each modeling framework developed within the CP-DMC is driven by a clearly defined **Context of Use (CoU)**. The Context of Use specifies the intended application of the model, the regulatory or scientific question it is designed to address, the target population, the proposed users, and the decision(s) the model is intended to inform.

The Context of Use defines the evidence requirements, validation strategy, model acceptance criteria, and regulatory engagement plan. Consequently, model development is not undertaken as a generic scientific exercise but as a targeted activity designed to support a predefined decision-making context. Individual disease programmes may have different Contexts of Use depending on the specific development challenges and regulatory questions being addressed.

2.4 Regulatory Engagement

Regulatory engagement is an integral component of the CP-DMC development process.

The CP-DMC follows an iterative approach in which interactions with regulatory authorities are initiated early in model development and continue throughout the project lifecycle. These interactions are intended to facilitate scientific discussion on the proposed Context of Use, modelling strategy, data sources, validation approach, uncertainty quantification, and evidence generation plan.

Early regulatory dialogue is expected to support alignment on scientific expectations, identify potential methodological gaps, and inform the progressive development of regulatory-grade modelling frameworks. Depending on the maturity and intended application of individual models, subsequent interactions may support regulatory qualification or other appropriate regulatory pathways.

3 Objectives of the Contract

3.1 Overall Objective

As mentioned in section 1.1, the overall objective of this contract is to establish a long-term strategic scientific partnership capable of supporting the development, validation, maintenance, and continuous evolution of regulatory-grade quantitative disease models across multiple therapeutic areas within the CP-DMC.

The selected Contractor shall contribute scientific, technical, and methodological expertise to develop fit-for-purpose modelling frameworks that support model-informed drug development, regulatory decision-making, and the development of Drug Development Tools (DDTs). The Contractor shall work collaboratively with C-Path and the broader CP-DMC stakeholder community to ensure that all activities are scientifically rigorous, reproducible, transparent, and aligned with evolving regulatory expectations.

The Contractor is expected to act as a long-term scientific partner rather than solely as a technical service provider, contributing to the strategic evolution of the CP-DMC's quantitative medicine activities. The successful bidder should view this engagement as participation in a collaborative regulatory science initiative rather than the delivery of modelling services alone.

3.2 Specific Objectives

3.2.1 Objective 1 – Develop Regulatory-Grade Modelling Frameworks

Develop scientifically robust, fit-for-purpose quantitative disease and care models capable of addressing clearly defined Questions of Interest and Contexts of Use across multiple disease areas. The Contractor shall implement appropriate procedures to ensure:

- presentation and discussion of modelling progress in internal and external meetings;

- identification and resolution of scientific and technical challenges; including quantification of uncertainty;
- supporting the preparation and conduct of regulatory interactions and lifecycle management at therapeutic area level; and
- continuous refinement of modelling strategies based on stakeholders feedback.

3.2.2 Objective 2 – Ensure Scientific Quality, Transparency and Reproducibility

Ensure that all modelling activities are conducted according to recognized scientific standards and good modelling practices. The Contractor shall implement appropriate procedures and be able to adapt its approach to common methodological principles agreed with C-Path during the relevant work package, notably:

- complete documentation of model assumptions;
- version control of models and code;
- independent review of modelling outputs; and
- appropriate uncertainty quantification.

3.2.3 Objective 3 – Generate Innovative, Decision-Relevant Quantitative Solutions

The Contractor shall integrate multiple sources of evidence provided through C-Path, including clinical trial data, real-world data, natural history studies, and other relevant data sources to contribute to the development and application of state-of-the-art quantitative approaches, selecting and integrating methodologies according to the scientific question, available evidence, and intended regulatory application.

4 Scope of Services

The Contractor shall provide scientific, technical and strategic support to the CP-DMC for the development, validation and maintenance of regulatory-grade quantitative disease modelling frameworks. Services shall be delivered through a collaborative, multidisciplinary and iterative approach, supporting the complete lifecycle of model development from project initiation through regulatory engagement and scientific dissemination.

The services described below represent the minimum requirements. Depending on the disease area, Context of Use, and project maturity, additional activities may be agreed during contract implementation.

4.1 General Requirements

The Contractor shall:

- provide scientific leadership in quantitative medicine, disease modelling and model-informed drug development;
- allocate appropriately qualified personnel throughout the duration of the contract;
- perform activities according to internationally recognized scientific and operational standards such as quality-management-system (QMS)-like systems;
- ensure all work is reproducible, transparent and adequately documented;
- work collaboratively with C-Path project teams and external stakeholders;
- proactively identify scientific, technical and operational risks and propose mitigation strategies;
- support multiple disease programmes simultaneously where required;
- maintain flexibility to adapt work plans as scientific priorities and regulatory expectations evolve;
- contribute to the continuous development of reusable methodologies across the CP-DMC portfolio;
- actively participate, as appropriate, in CP-DMC multi-stakeholder workshops, scientific working groups, Steering Committee meetings and regulatory interactions;
- present project progress, explain modelling methodologies and assumptions, discuss scientific and technical challenges, contribute to consensus building, respond to stakeholder feedback, and support the timely preparation of scientific publications, presentations and regulatory briefing materials.

4.2 Scientific Support

The Contractor shall provide scientific expertise to support the design, development and evaluation of quantitative disease models and related Drug Development Tools.

Activities may include, but are not limited to:

- disease progression models;
- clinical trial simulation tools;
- patient stratification algorithms;
- external control methodologies;
- machine learning and artificial intelligence;
- novel statistical methodologies including Bayesian;
- other innovative evidence generation approaches.

Expected outputs may include, as appropriate:

- quantitative disease and care models;
- simulation scenarios supporting drug development and regulatory decision-making;
- scientific reports and publications;
- reusable computational tools and analytical workflows; and
- regulatory-facing technical documentation.

Consistent with C-Path's mission as a neutral, non-profit organization, the outputs developed under this contract are intended to contribute to the broader scientific community through open-science principles, maximizing transparency, reproducibility, and reuse while respecting confidentiality, intellectual property rights, and contractual obligations related to proprietary data. The achievement of these outputs will be assessed against the agreed deliverables, acceptance criteria, and performance indicators defined throughout the contract.

4.3 Technical Support

The Contractor shall provide the technical capabilities necessary to implement, validate and maintain quantitative modelling frameworks. Technical support shall include, as appropriate:

- assessment of data readiness and fitness-for-purpose;
- data harmonization strategies;
- exploratory data analyses;
- statistical programming;
- software development and code management;
- model verification and validation;
- version control and documentation;
- generation of simulation outputs;
- development of reusable computational components;
- preparation of technical reports and analytical documentation.

The Contractor shall ensure that all analytical workflows are reproducible, auditable and suitable for independent scientific review.

C-Path will retain responsibility for data acquisition, data-access permissions, Data Contribution Agreements, central platform operations and central data ingestion or preparation, unless otherwise agreed in writing. The Contractor will be responsible for defining modelling-driven data requirements, assessing data readiness and fitness for purpose, identifying data gaps, advising on disease-area harmonisation needs, and conducting authorised analyses within the applicable secure analytical environment.

4.4 Regulatory Support

The Contractor shall support the regulatory strategy associated with each disease programme and contribute to the development of regulatory-grade evidence packages. Activities may include:

- support for the preparation of regulatory briefing packages;
- documentation of modelling assumptions and limitations;
- preparation of responses to regulatory questions;
- participation in scientific advice meetings and other regulatory interactions;
- incorporation of regulatory feedback into model development;

The Contractor shall ensure that modelling activities remain aligned with evolving international regulatory expectations, including relevant EMA, FDA and ICH guidance by monitoring advances in quantitative medicine and regulatory science and identifying opportunities to leverage emerging analytical techniques (e.g., AI, Bayesian methods) where scientifically justified;

5 Deliverables

The Contractor shall deliver the outputs described below. The exact timing and content of individual deliverables may be refined during project initiation to reflect the specific disease area, Context of Use (CoU), and project priorities. Any modifications shall be agreed in writing between C-Path and the Contractor. All deliverables shall be submitted in English in editable electronic format and shall be subject to scientific and technical review by C-Path before formal acceptance.

5.1 General Deliverable Requirements

As the CP-DMC portfolio spans multiple therapeutic areas and regulatory applications, the nature and timing of deliverables will vary between projects. The detailed scope, milestones, and acceptance criteria for each assignment will be specified and mutually agreed at contract or work package level. A general framework for expected outputs is provided as an example in Annex 1.

Unless otherwise agreed, each deliverable shall include:

- Executive summary;
- Scientific rationale;
- Methods and assumptions;
- Results;
- Limitations;
- Uncertainty assessment;
- Conclusions;
- References;
- Supporting analytical code (where applicable);
- Version history.

All modelling deliverables shall include:

- complete model documentation;
- traceable data provenance;
- clear data management processes, including documentation of choices made during the analysis leading to reproducible analytical workflows; appropriate sensitivity analyses to test deviations from key assumptions made during model construction
- validation results;
- computational code in a pre-agreed language;
- software version information;
- user guidance where appropriate.

6 Decision-Making

Scientific and strategic decisions shall be made collaboratively. C-Path shall retain final responsibility for decisions relating to:

- project priorities;
- Context of Use;
- regulatory strategy;
- stakeholder engagement;
- publication strategy;
- acceptance of deliverables.

The Contractor shall provide scientific recommendations to support these decisions.

7 Risk Management and Escalation

The Contractor shall proactively identify scientific, technical, operational, and resource-related risks that may affect project delivery. A risk register shall be maintained throughout the contract and reviewed regularly with C-Path.

Where significant issues arise, the Contractor shall:

- notify C-Path promptly;
- assess the potential impact;
- propose mitigation measures;
- provide revised timelines where necessary.

Issues that cannot be resolved at project level shall be escalated for review and resolution.

8 Key Personnel

The Contractor shall propose a multidisciplinary core team with the expertise and availability required to deliver the scientific, technical, regulatory, and operational scope of the contract.

The proposed team shall collectively provide:

- scientific and regulatory leadership in quantitative medicine, disease modelling, machine learning and artificial intelligence
- quantitative and technical expertise relevant to the applicable Use Case, including statistical modelling, simulation, validation, uncertainty quantification, scientific programming and reproducible analytical workflows;
- project-management capability covering work planning, timelines, budget, risks, dependencies, reporting and escalation.

Scientific leadership, technical leadership and project-management responsibilities may be assigned to different individuals or combined where appropriate. The Bidder shall clearly describe how responsibility for scientific quality, technical delivery, project coordination and timeline adherence will be allocated across the team.

The team shall include both technical experts and senior profiles with experience engaging with industry executives, regulatory evaluation bodies, health technology assessment (HTA) experts and funders, and shall collectively demonstrate experience leading multidisciplinary quantitative-medicine or regulatory-science programmes.

Key personnel shall remain available throughout the relevant work package, any material replacement shall be notified to C-Path and may require prior approval.

9 Annex 1: Examples of deliverables

The deliverables presented below are illustrative examples of the types of outputs that may be requested under this framework agreement for a single use case. The final scope, content, sequencing, and timing of deliverables will be defined for each individual work package, taking into account the therapeutic area, scientific objectives, data availability, agreed Question of Interest (QoI) and Context of Use (CoU), as well as the overall regulatory strategy.

As described in Section 2.4 (Regulatory Engagement), the CP-DMC follows an iterative regulatory science approach in which interactions with regulatory authorities are initiated early and continue throughout model development. Consequently, the timing of specific deliverables may need to be adapted to support planned regulatory interactions, incorporate

agency feedback, or address evolving scientific and regulatory priorities. Deliverables should therefore be considered as part of a flexible, milestone-based development process rather than a fixed sequence of contractual outputs.

Bidders should identify any material assumptions, dependencies or potential pitfalls, including those related to data availability or access, that could affect the indicative timeline, and describe how they would propose to manage these through appropriate mitigation measures and flexibility in the project plan.

Deliverable	Description	Indicative Due Date
D1	Project Initiation Plan	Month 1
D2	Preliminary Question of Interest (QoI) and Context of Use (CoU)	Month 2
D3	Data Landscape, Readiness and Gap Assessment	Month 3
D4	Modelling Strategy and Analysis Plan	Month 4
D5	Initial Data Characterization Report	Month 8
D6	Proof-of-Concept Quantitative Model (Version 1)	Month 10
D7	Model Validation Report	Month 12
D8	Scenario exploration of potential model impact	Month 13
D9	Model Documentation and Computational Package	Month 14
D10	Regulatory-Ready Technical Report	Month 15
D11	Final Project Report and Knowledge Transfer Package	Month 16

Model maintenance, and lifecycle-management activities may be commissioned through subsequent work packages following completion of the initial base scope.