Constructing the ERAMET Digital Research Environment (DRE)

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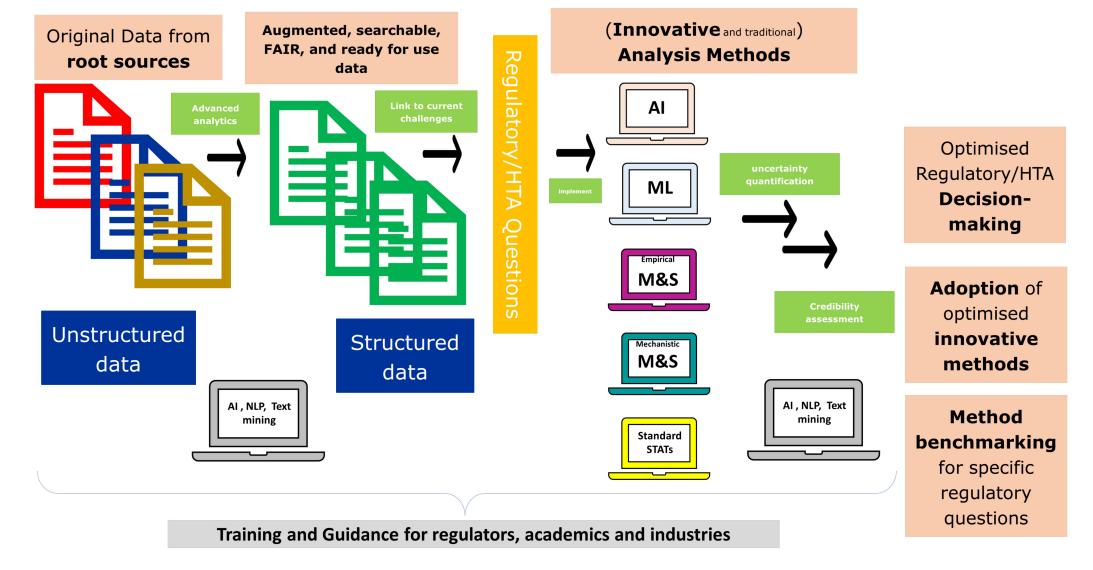


INTRODUCTION

ERAMET (Ecosystem for RApid adoption of modelling and simulation METhods) is a recently funded (HORIZON-HLTH-2023-IND-06-04) initiative to address regulatory needs in the development of orphan and paediatric medicines. This EU-funded project aims at rethinking the assessment and development of orphan and paediatric medicines with a focus on integrating modelling and simulation methods alongside real-world data. The overall objective of ERAMET is to provide and implement a framework for development and establishing the credibility (assessment) of mature modelling and simulation to address regulatory needs in the development and assessment of orphan and paediatric medicines. A key component of work package 7 of the grant is to enable the pediatric rare disease stakeholder community broad access to data and tools particularly in the ecosystem that includes academic researchers, drug developers, regulators, patients, providers and technical partners that focus on solutions to accelerate rare disease treatments. A cornerstone of this work package is a digital research environment (DRE) that provides secure and customized access to global data sources made available to this community via a variety of mechanisms and a portal to ongoing trials across the rare disease space.

The ERAMET project relies on 3 pillars of the ecosystem: 1) a repository connecting questions, data and methods, 2) development and validation of high-quality standards for data and methods and 3) an AI-based approach for automation of data collection and credibility assessment. All aspects of the grant activities including data ingestion, project management, metadata cataloguing, and tool development will be managed through the creation of the ERAMET DRE. The DRE enables stakeholder communities in three different scientific domains (ataxia, transfusion-dependent haemoglobinopathies and drug induced cardiovascular toxicity) broad access to data and tools relevant for their domain. Analytical tools, including AI-driven platforms and computational tools for assessing the methods and data credibility will be developed, refined and applied to the three use-cases to foster improved ability in terms of both basal research on disease characterization and the development of health interventions and supportive methods such as diagnostic methods, risk detection and monitoring tools

Figure 1: ERAMET project vision highlighting the underlying data, methodologies and question-centric approach



OBJECTIVES

- Establish a 3-pillar ecosystem of: (1) A repository connecting questions, data and methods, (2) Development and validation of high-quality standards for data and methods, and (3) An AI-based approach for automation of data collection and credibility assessment.
- As part of ERAMET the ecosystem will be set up and applied to five use-cases
- Enable the pediatric rare disease stakeholder community broad access to data and tools particularly in the ecosystem that includes academic researchers, drug developers, regulators, patients, providers and technical partners that focus on solutions to accelerate rare disease treatments.

RESULTS

- Users are invited to the platform by the ERAMET Tenant Administrator (TA). The platform assigns Multi-Factor Authentication (MFA) and Role-Based Access Control (RBAC) to each user. Only users with an assigned role and an invitation to a Workspace have access to the data in that Workspace. Similarly, only users approved in FAIR and assigned the appropriate role by the TA can access datasets or Data Access Requests (DARs) in FAIR. Additionally, a user must be a member of a Workspace before they can request data through the DAR process.
- Early progress on the ERAMET DRE has been focused on the implementation of open-science tools into the workspace environment with nlmixr, nlmixr2 and PK Sim / MOBI already operational (see Figure 2).
- Virtual machine deployment of ICON's NONMEM and CERTARA's commercial MIDD solutions including Simcyp and Phoenix are in progress and custom AI algorithms from EMA and the University of Warwick are being tested by platform developers for workspace qualification against simulated data (see Figure 3). A demonstration of the workspace environment will be made available at the meeting. Data use agreements from the 3 scientific domains are in various stages with the expectation that ingestion can occur prior to the end of year 1.
- Code assessing data quality and credibility linked to models and tools developed are being integrated into the workspace environment presently and will be used to test the contributed data upon ingestion.
- The DRE will be utilized prospectively for targeted pediatric extrapolation use cases (Work package 5) in subsequent years.

RESULTS

Figure 2: nlmixr2 being used in RStudio inside a DRE workspace and plots generated in a DRE workspace using the nlmixr2 algorithm



Figure 3: PK Sim and NONMEM inside a DRE workspace VM

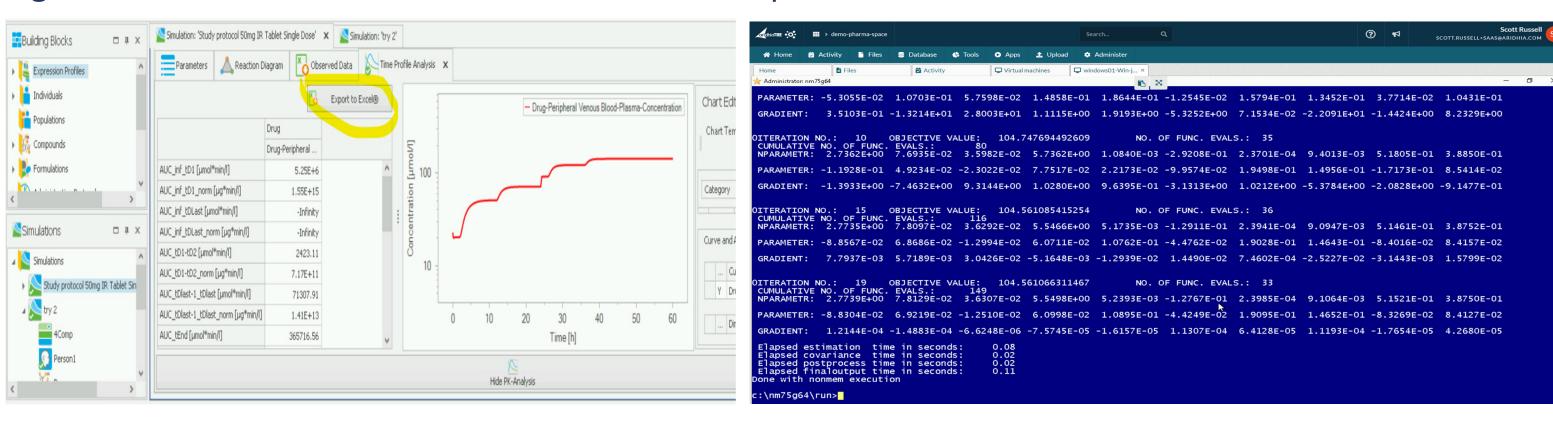
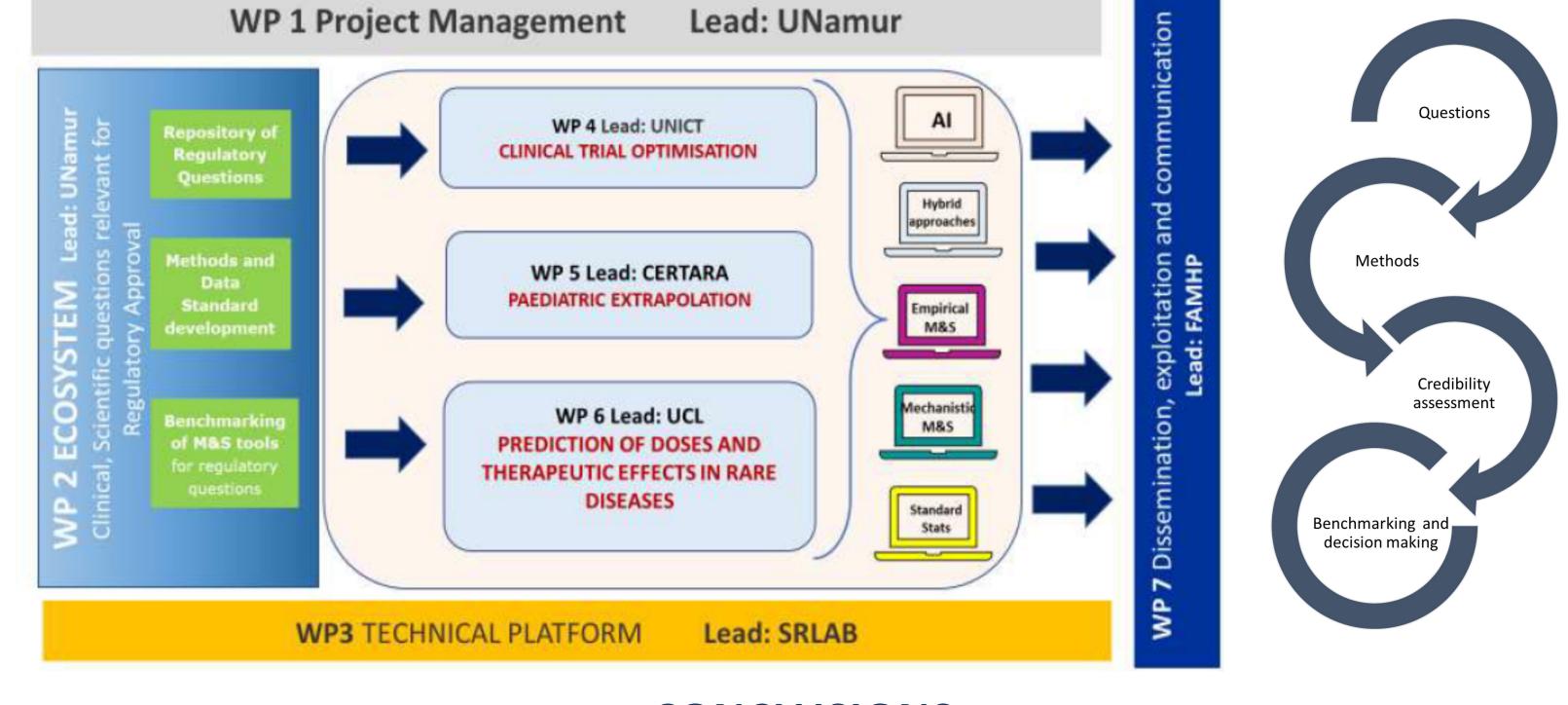


Figure 4: ERAMET stakeholders, work package relationships and reliance on the DRE as the technical platform (WP3)



CONCLUSIONS

- A trusted research environment (TRE) has been established to support the ERAMET grant
- The current TRE contains workspaces for pharmacometric applications (both commercial and open-source solutions) along with an R and R console development environment from which user-written code including AI/ML applications can be run.
- Additional functionality will be added to the Workspace environment throughout the lifetime of the grant with the intention to achieve MIDD deliverables for the various work packages
- A library of trusted analytics has been established with connectivity to Gitea and Git Hub
- Contributed data will be ingested into the TRE once data use agreements are in place
- Additional connectivity to external services (e.g., Metworx, Pumas AI) will be a feature of future workspaces once agreements are in place.

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For more information, see https://www.erametproject.eu/