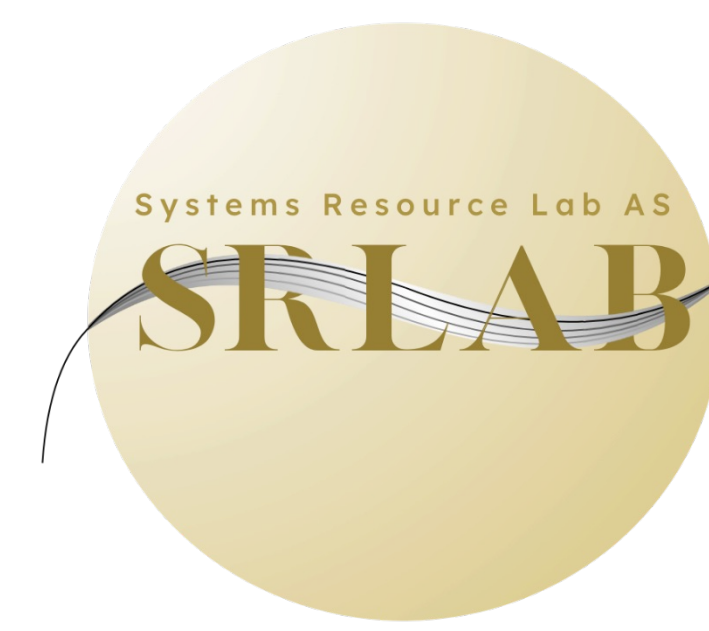




Operationalizing the ERAMET Digital Research Environment (DRE)

Building the Ecosystem



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Ecosystem for Rapid Adoption of modelling and simulation METHODS (ERAMET)

Mission: Pioneer a question-centric approach in orphan and paediatric drug development.

Introduction

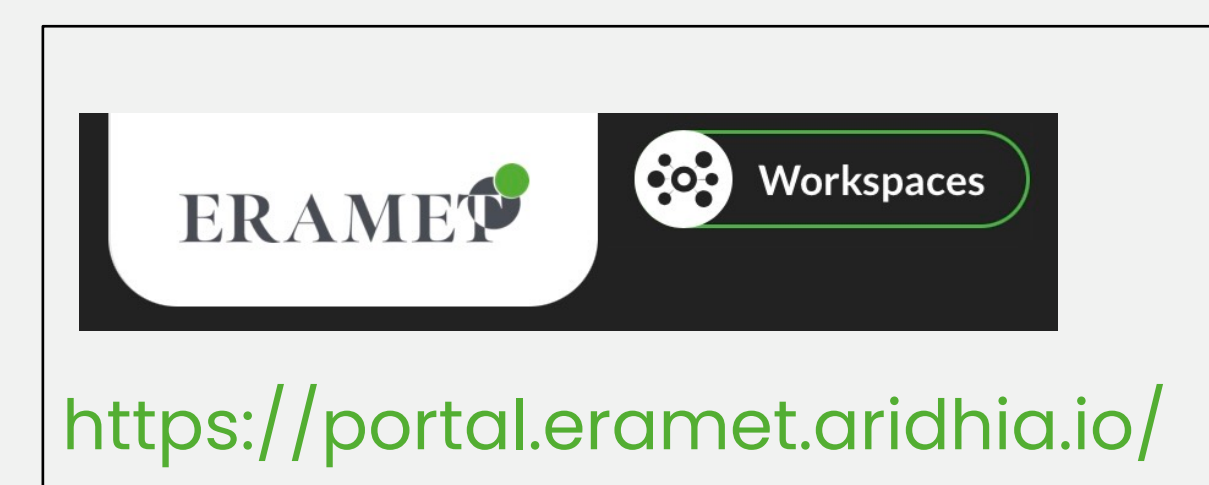
ERAMET (Ecosystem for RAPid adoption of modelling and simulation METHODS) is a funded (HORIZON-HLTH-2023-IND-06-04) initiative to address regulatory needs in the development of orphan and paediatric medicines.

The three key pillars of implementing the Question (Q)-centric approach are:

- creating a repository for drug development and use questions of interest (Qol),
- setting high quality standards for data and analytical methods and
- creating an AI based platform that will provide decision support and support semi-automation of key workflows.

ERAMET Digital Research Environment (DRE)

A cornerstone of the project is the creation and operationalisation of a Digital Research Environment (DRE) to provide a secure and customized access to data sources and tools made available to this community via a variety of mechanisms.



- Trusted Collaborative Research Environment
- Digital analysis of data
- Connection to a wide variety of different tool open access to shared datasets
- Controlled individualized access to restricted parts of the DRE such as protected or proprietary datasets

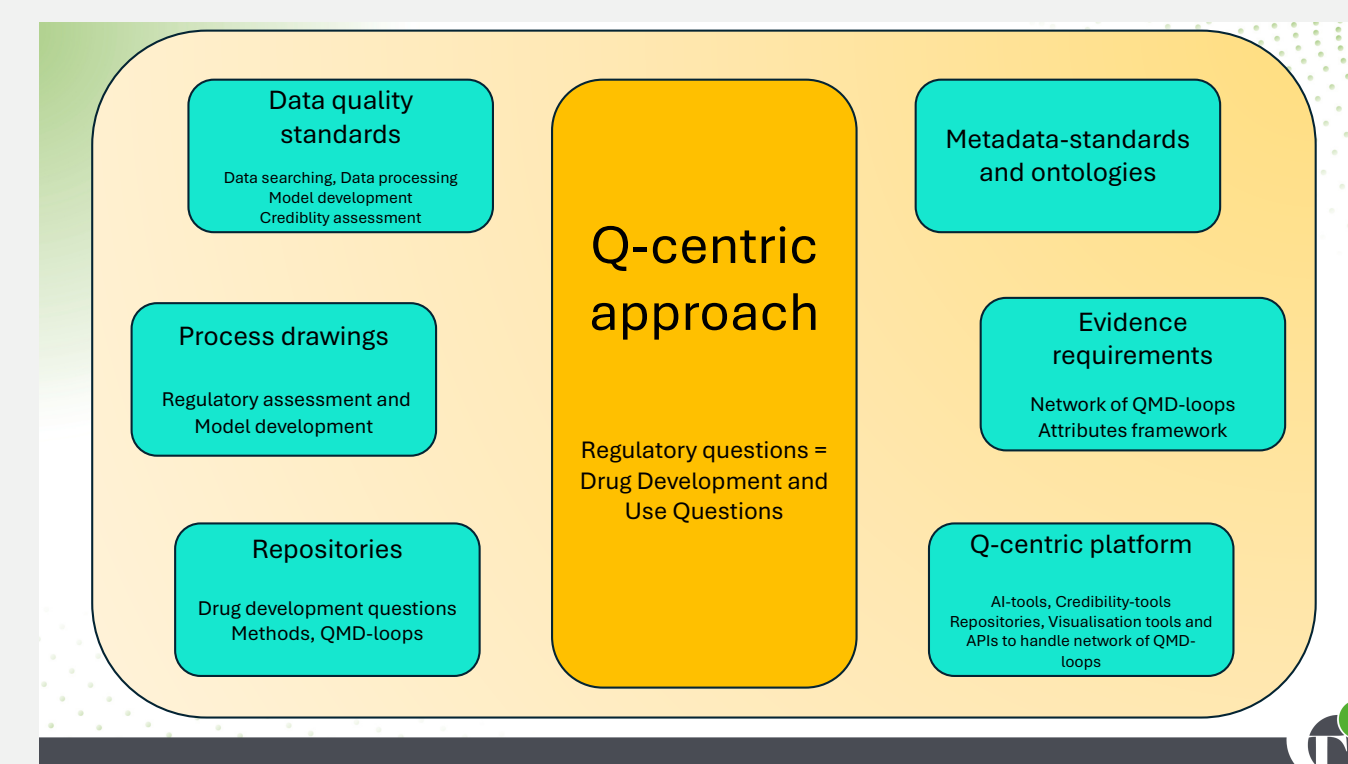
Results

The DRE infrastructure is in place.

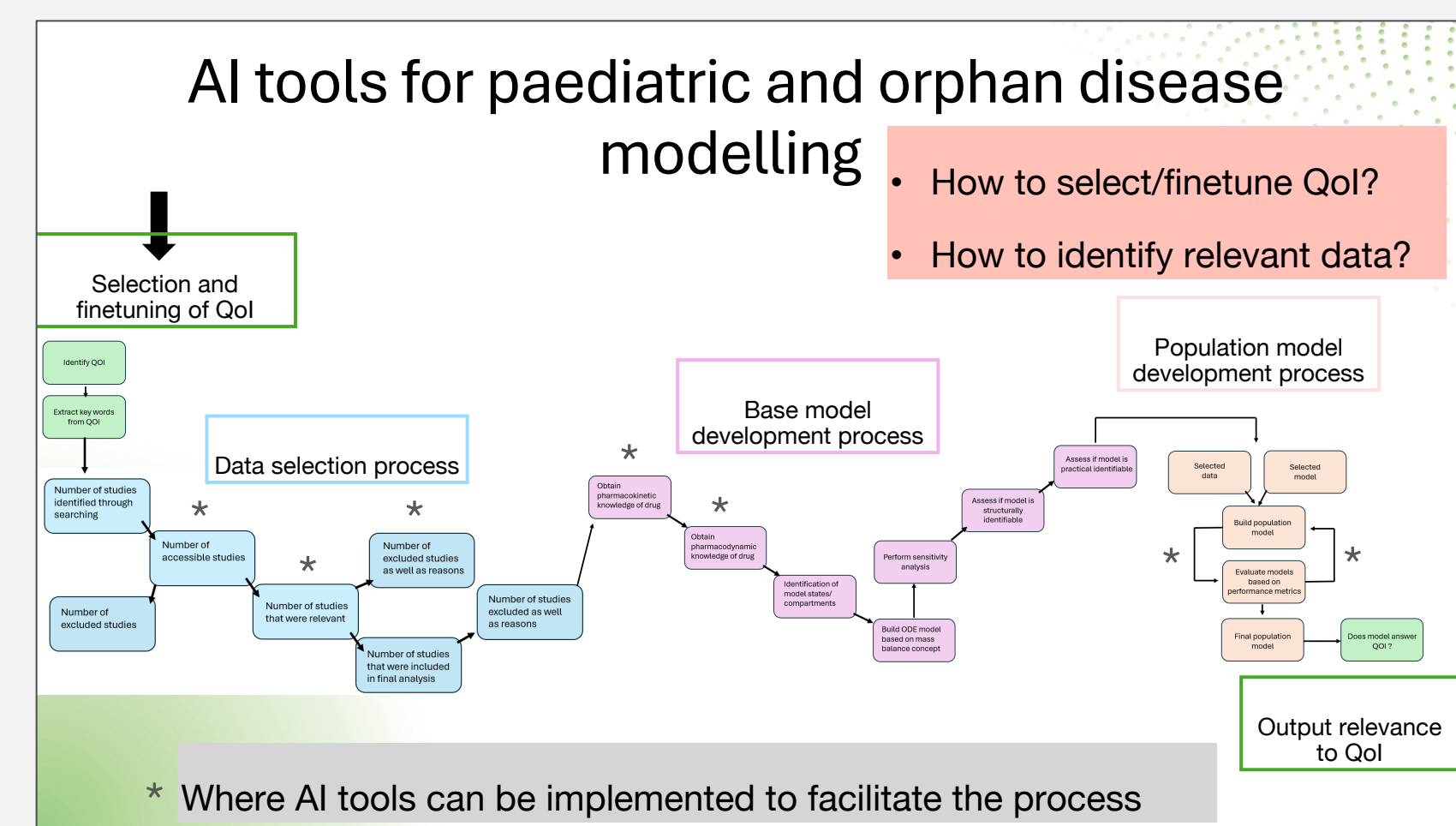
- Early progress on the ERAMET DRE has focused on the implementation of open-science tools into the workspace environment such as R studio and PK as well as commercial MIDD solutions including Phoenix and Nonmem.
- Researchers from WP2 (The University of Namur) and WP3 (The University of Warwick and Systems Resource Lab AS) have been successfully onboarded to their Workspaces to explore the connectivity between their respective research projects in developing the various elements of the Q-centric approach.
- For the use-case WP partners, WP5 (Certara) have been successfully onboarded to initiate exploring the environment for collaboration on the ERAMET use-cases.

Data on regulatory decision-making informed by a MIDD-based approach is iteratively collected from a variety of data sources to inform the elements needed for operationalizing the Q-centric approach and developing the Q-centric platform:

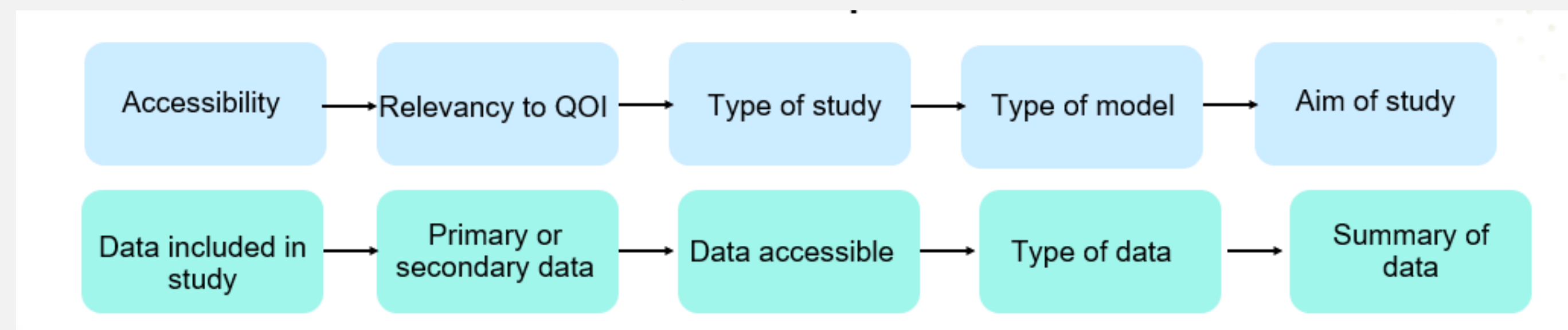
Elements needed for operationalizing the Q-centric approach (Generalised outline based on exemplars)



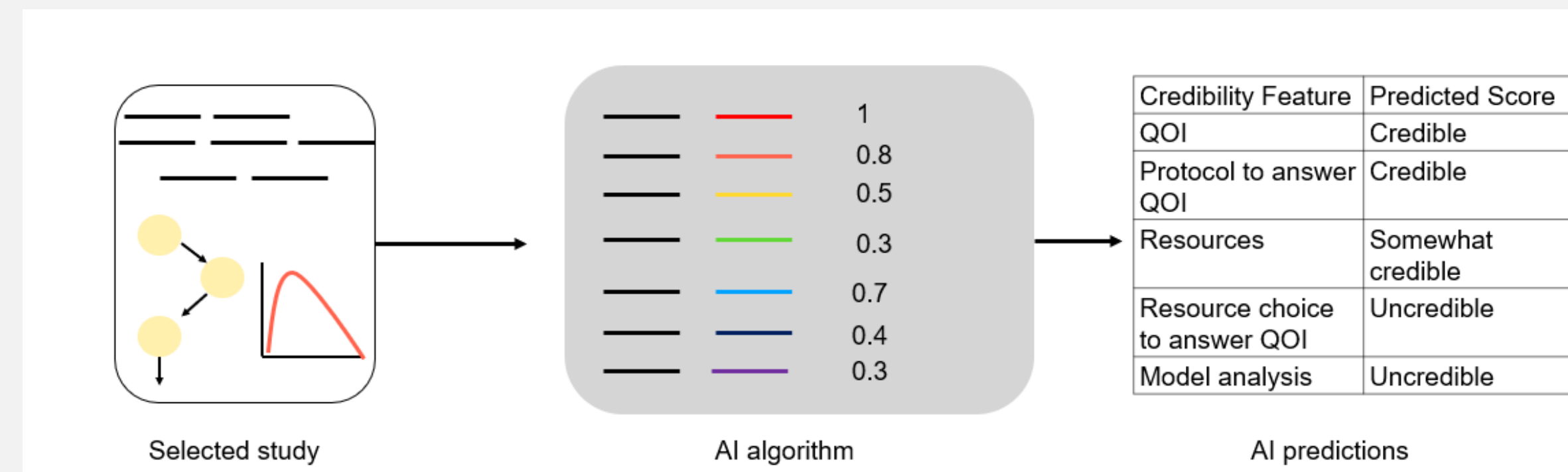
Process drawing (Pop-PK exemplar)



Process drawing (Data searching – Clinical study exemplar)



AI tool development (generalised outline based on dose Qol exemplar)



These elements are key to designing the structure and core components of an automated or assisted decision-supported workflow in this regulated domain.

Conclusions and Future Work

- ERAMET's vision is to operationalise a Q-centric approach within orphan and paediatric drug development and deliver a Q-centric platform implemented within a secure DRE to allow secure sharing of data and tools.
- The approach will be tested on ~5 use-cases (WP4-6) covering different quantitative models informing orphan and paediatric drug development that will be brought to the EMA for ITF briefing meetings, SA/PA, QAs/QOs.
- The objectives for this year's efforts are to promote individual workspace owners to participate in collaborative research activities to iteratively test the Q-centric workflows, the AI-search tools and the credibility tools, in effect creating small ecosystems which share questions, methods and data in a secure environment.
- The next steps, scheduled for completion, are to train these teams on how to collaborate effectively across secure Workspaces.

Methods

- The finalised data in the DRE will be comprised of results obtained from Q-centric approaches to answering key drug development and use questions.

- To reach this stage the Q-centric approach has to be well defined and established.

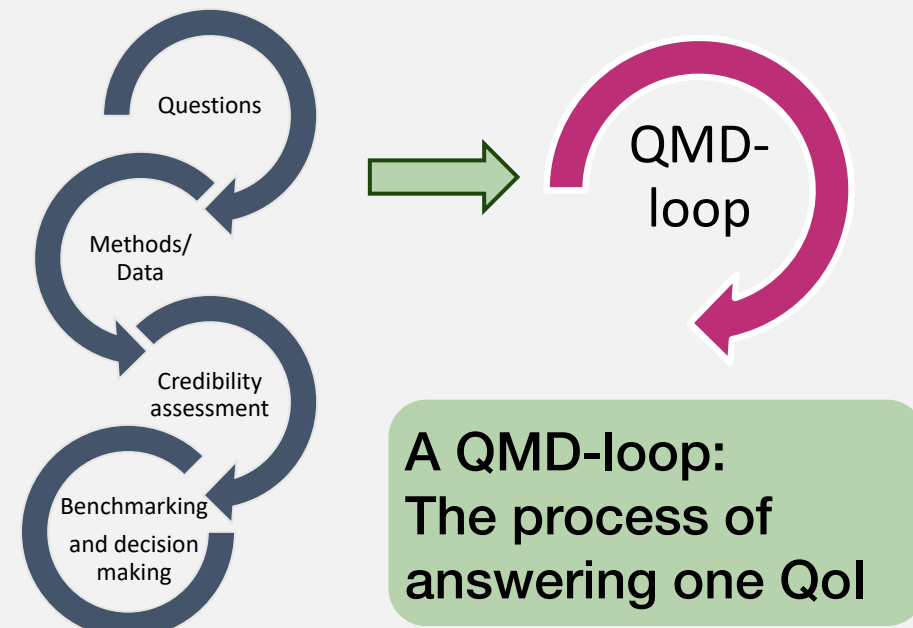
- The Q-centric approach in orphan and paediatric drug development is based on a series of pragmatic qualitative casus studies exploring and describing the elements present in each case exemplar.

- These research processes are needed for developing the workflow standards underpinning the AI-based decision support and and for developing semi-automated workflows for data searching, model development and credibility assessment.

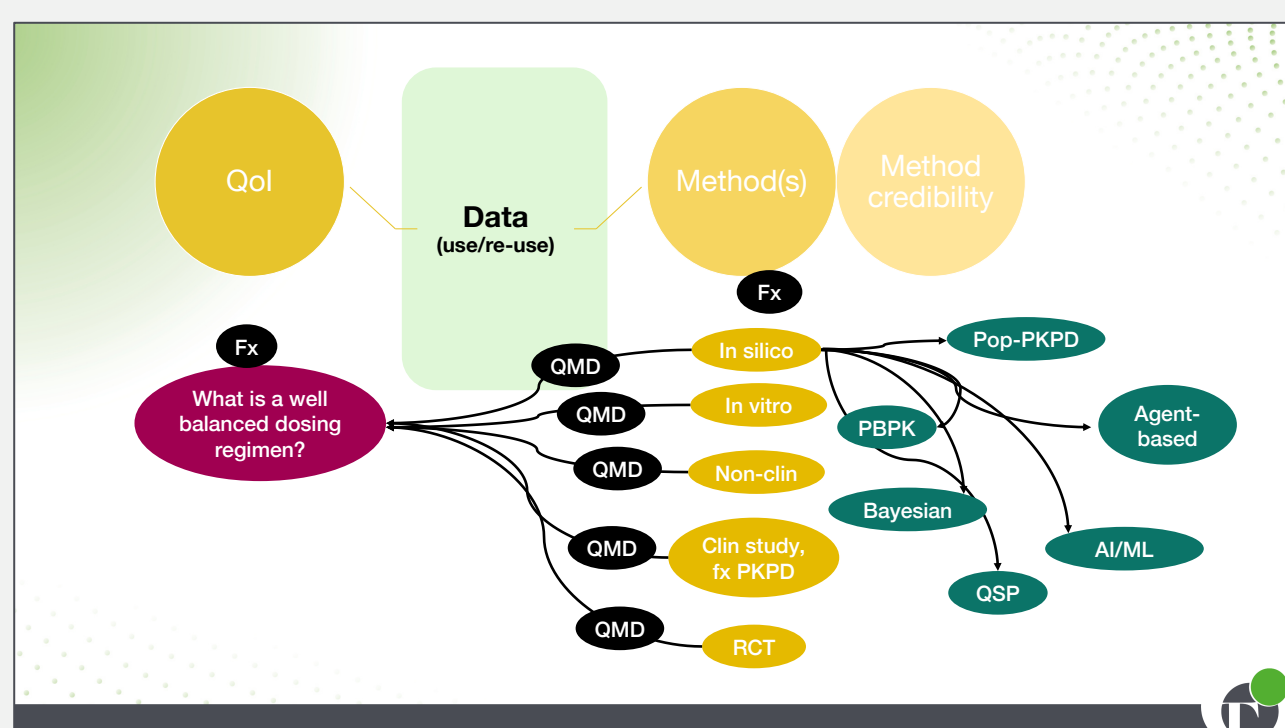
The standards and tools developed within the project will be iteratively refined on exemplars and will be applied to the project's use-cases within the ERAMET DRE.

Results

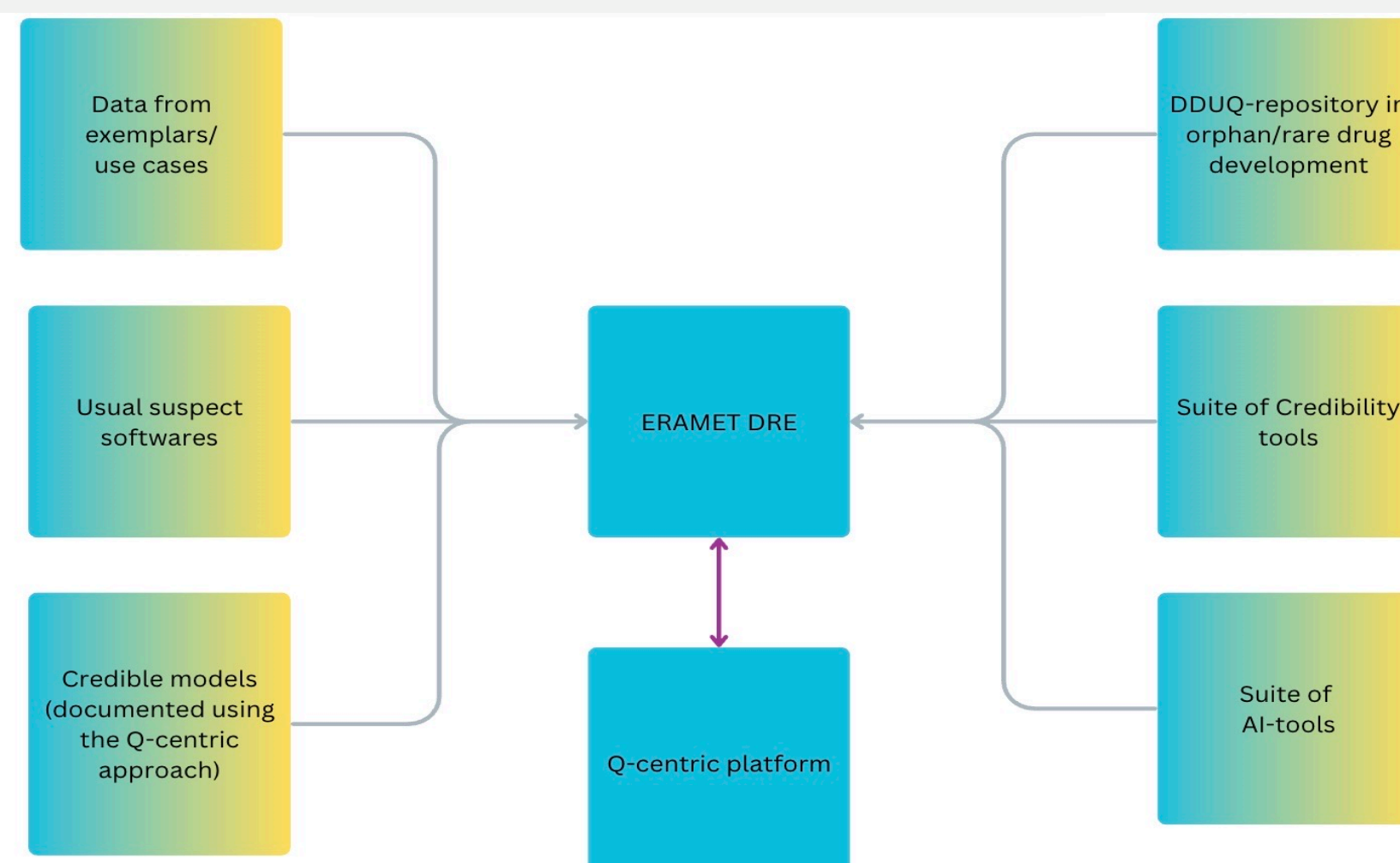
QMD-loops form a key part of the **credibility activities** needed for assessing and documenting the overall credibility of a **quantitative model** as well as **the safety and efficacy of medicinal products**. The Qols are related across the drug development plan and can top-down be seen to branch depending on methods and datatypes used and from a bottom-up perspective be seen to connect by the outcome (answer) of one QMD-loop being re-used as input values for the next QMD-loop.



Schematic illustration (based on dose Qol exemplar)



Resources to be made available within the ERAMET DRE



Resources directly useful for data processing are made available within the ERAMET DRE, whereas as the implementation of the Q-centric platform will allow semi-automated workflows for data searching, model development and credibility assessment.

Applications for drug developers and regulatory assessors:

Repositories:
Find relevant and/or finetune your Qol(s)
Find potentially relevant methods, datasources and datasets

Data quality standards:
Find process support (standardization) for the knowledge work:

- Credibility assessment
- Data quality assessment
- Model development

Evidence requirements:
See how the current Qol is connected to other Qols in the overall development plan and the evidence requirements at the various levels and transition points.

Automation and knowledge assisted process and decision support:

- Perform credibility assessment activities, including UQ
- Identify (extract, format as relevant) and perform credibility assessment of potential data for planned CoU
- Identify and perform credibility assessment of methods for the planned CoU, including UQ

References: Musuamba Tshinanu F, Cheung SYA, Colin P, Davies EH, Barrett JS, Pappalardo F, Chappell M, Dogne JM, Ceci A, Della Pasqua O, Rusten IS. Moving towards a Question-centric approach for regulatory decision-making in the context of drug assessment. Clin Pharmacol Ther. 2023 Jan 27. doi: 10.1002/cpt.2856. Epub ahead of print. PMID: 36708100. Barrett JS, Eradat Oskoui S, Russell S, Borens A. (2023), Digital Research Environment (DRE)-enabled Artificial Intelligence (AI) to facilitate early-stage drug development. Front. Pharmacol. 14:1115356. doi: 10.3389/fphar.2023.1115356.

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