S-01

Data Repository to Enable Organization and Collaboration for Pharmacometric Analysis

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INTRODUCTION

Interdisciplinary research teams encounter both logistical and technical challenges during collaborative pharmacometric analyses projects, especially teams with significant geographic distributions. Because team members are from multiple organizations, each of which utilize a distinct internal workflow, there is often variation in the tools and practices implemented for the organization and storage of data and files. This inconsistency and lack of a universal version-controlled data storage structure can result in miscommunication, duplication of work, or even in the use of outdated or incorrect information.

Three key components for a successful collaborative project are: 1) transparency in work product development, 2) secure permission-based access and use of data, and 3) consistency in data organization and interface with workflows. These key elements allow for the preservation of ownership of the data of an organization, while enabling forward progress on a project with permission-based partner engagement. As the project advances, team members may join, change roles, or depart from an organization, necessitating a structured and well-maintained team management module to direct access to the collaborative research environment.

METHODS

Project Structure and Workflow

Due to the inherent complexity of pharmacometric analyses, the maintenance and utilization of a useful and universal systematically defined project directory structure is paramount. Projects can be broken down into stages, which can further be divided into tasks, providing the ability to design, maintain, and communicate an accurate and comprehensive workflow.

Relationships

In general, drugs, projects, and studies are all treated as singular objects in the Data Repository. Relationship links can be created between these entities in any manner that makes sense to an organization to help users identify relationships and guide navigation. Two scenarios demonstrate relationship links (Figure 1):

Example 1: A user is on a team that has access to Drug A and Study M, but would like to learn what other studies fall within Drug A's domain. The user would be able to see a list of studies in Drug A's relationship link list. While this user would not have access to Study Q, they would see that it exists and could request access from their Team Lead or Project Manager.

Example 2: A user is working on analysis Project Z, and wants to gather more information about the studies used by Project Z. The user could examine the project's relationship link list. The user would be able to view that Study P and Study Q are both used by Project Z and could request access from their Team Lead or Project Manager.

Figure 1

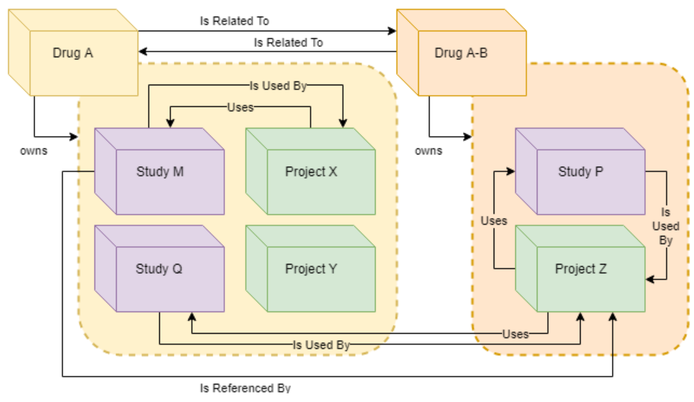
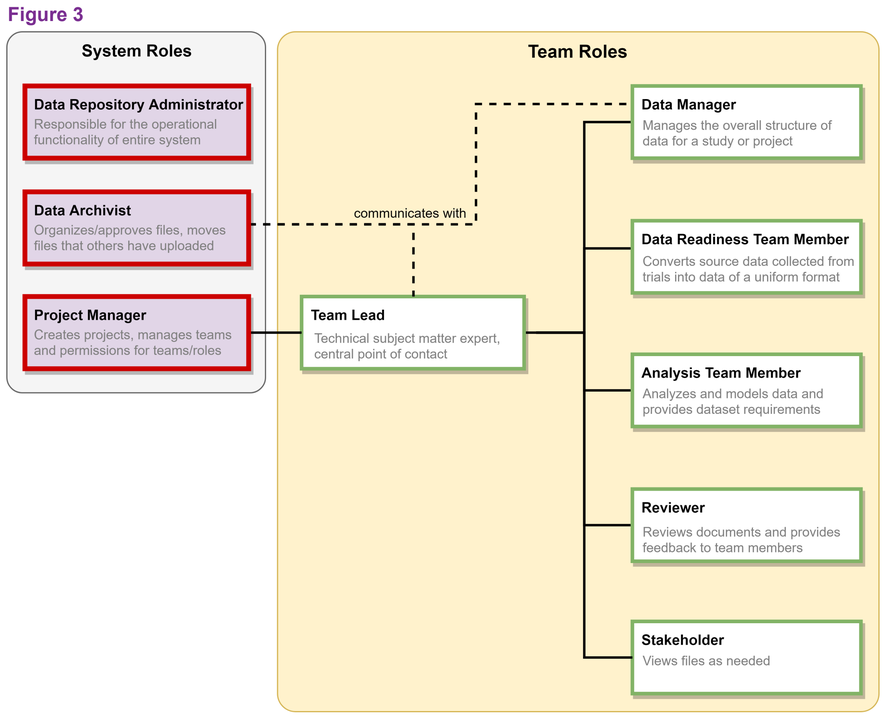


Figure 3



Teams, Roles, and Permissions

System and Team Roles

Roles that can be assigned to users are divided into 2 categories, system (administrative) roles and team roles.

System roles allow administrators to manage the entire Data Repository system and oversee teams, data storage components, users, and assignments. Team roles are assigned to users on a specific team. Team roles allow users to perform specific actions within the drugs, projects, and studies that have been assigned to their team (Figure 3).

Role Interactions

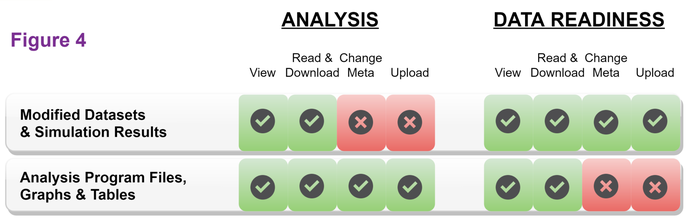
System roles have global access and are not assigned to teams. These roles have the power to assign users and data storage components to teams. Typically, Team Leads communicate with Project Managers regarding the status and needs of their work. The Team Lead serves as the main point of contact for a team and would communicate with the Project Manager to request role and user changes. Any user may have multiple roles.

Role Permissions

The actions each user role can perform vary based on a mapping of permissions for each data storage component. For example, the "analysis team member" role is permitted to create and upload files to new programming language directories within the analysis location in project tasks. The "data readiness team member" is not permitted to do this, but can instead create and upload files to new programming language directories in the assembly location (Figure 4).

Users holding different roles can collaborate in the same project task with a degree of flexibility, but without the risk of accidental or unpermitted changes. Team role permissions are cumulative, and users with both team and system roles must choose to use their elevated role in order to perform administrative actions. The Staging Area provides a list of all files that have been uploaded but have not yet been approved by an authorized user. Once a file is approved, the file will be removed from the Staging Area and committed to the Data Repository in the designated location.

Figure 4

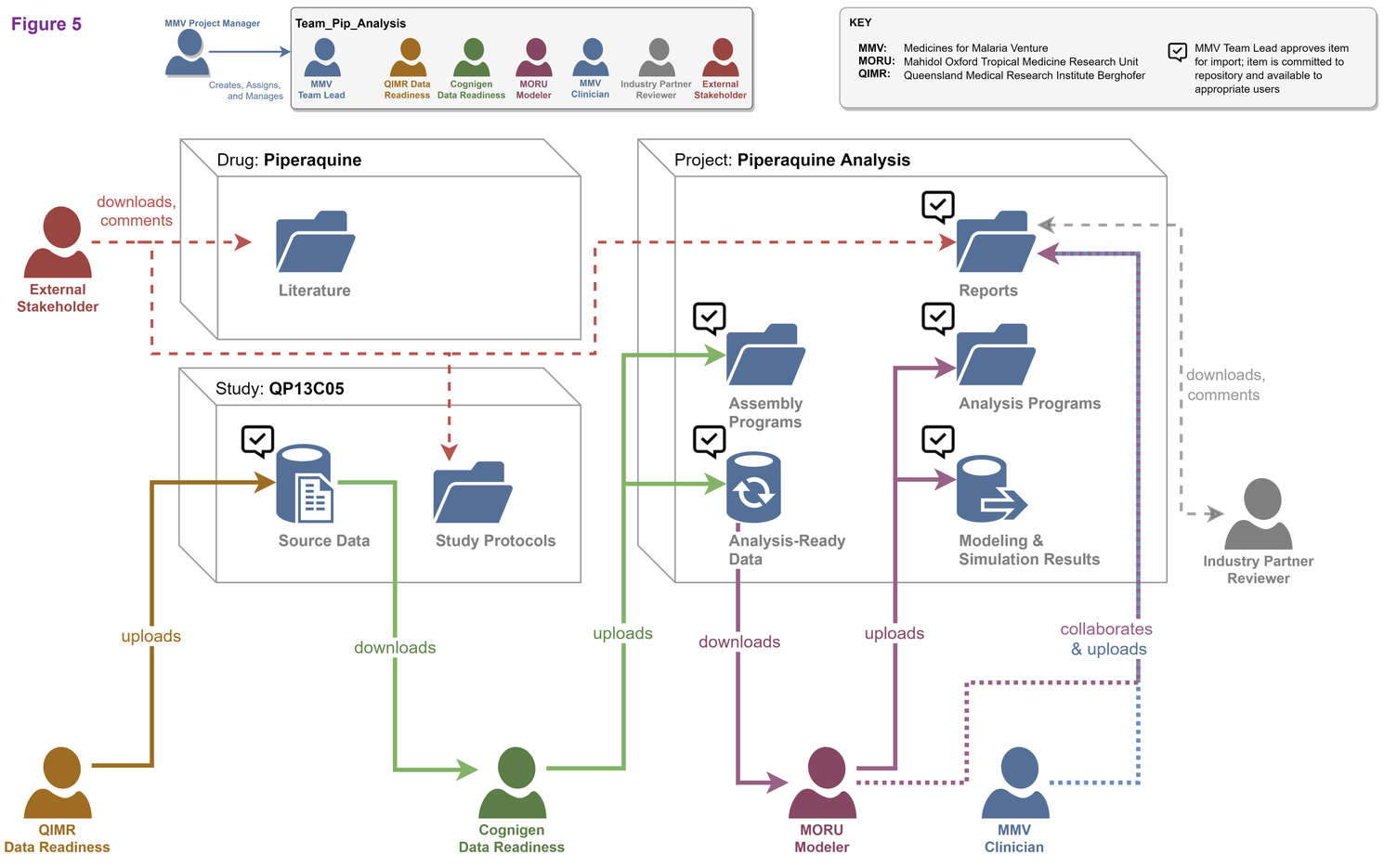


RESULTS

Case Study - Malaria Therapeutics Pharmacometric Analysis

Drug development for malaria therapeutics often involve collaboration between scientists, stakeholders, clinicians, and project managers across multiple organizations. A case study is outlined below to demonstrate the workflow of the Data Repository and interactions of team members during a pharmacometric analysis (Figure 5).

Figure 5

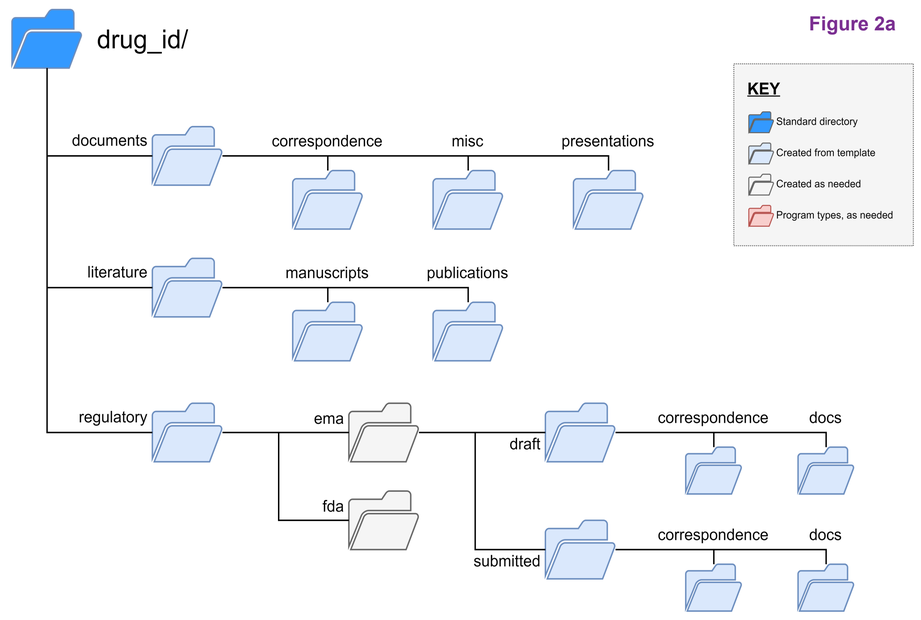


Data Storage Components

Data storage components are logical units with pre-specified templates designed to organize and store data and documents.

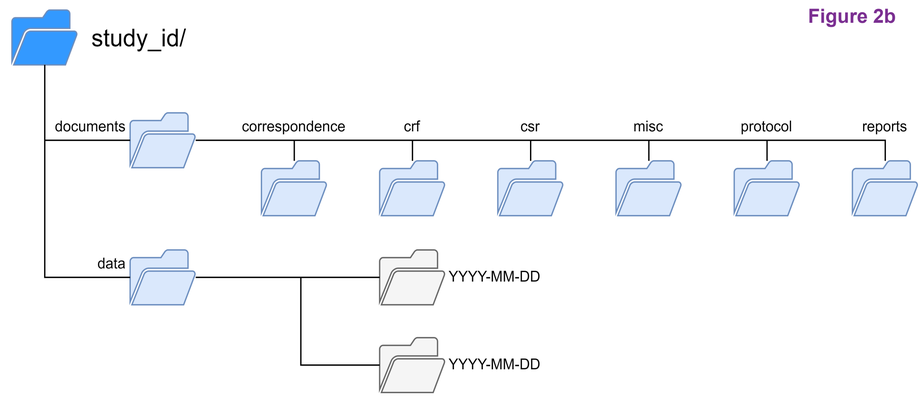
Drug: The drug component contains drug-specific information, such as an investigator's brochure, literature, and regulatory correspondence (Figure 2a).

Figure 2a



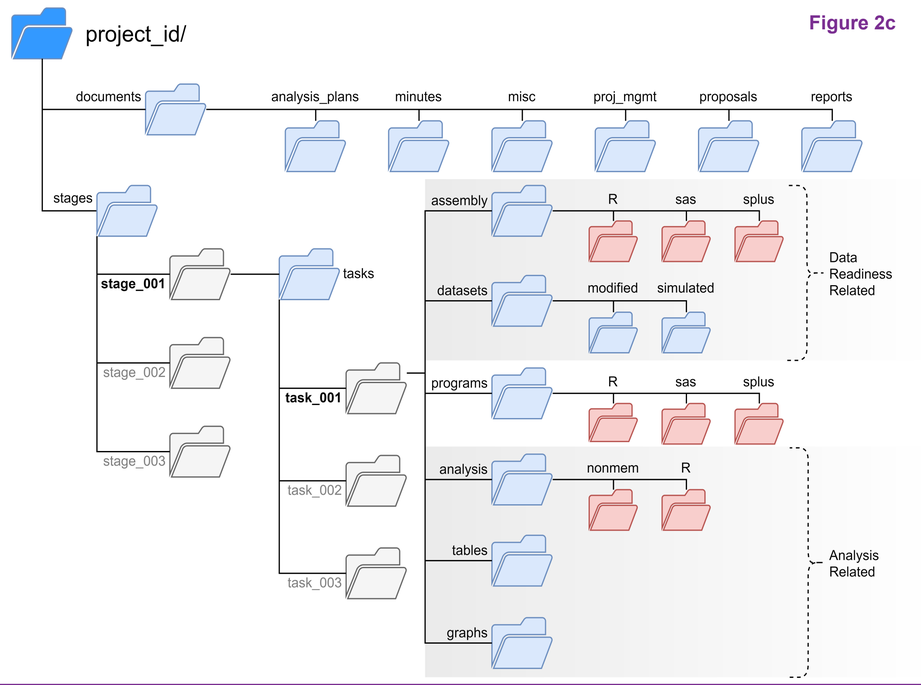
Study: The study component contains data and documents from a specific study, such as a protocol, case report form, clinical study report, and source data. The storage of source data is always located under "data" inside a date-stamped sub-folder with the transfer date of the data (Figure 2b).

Figure 2b



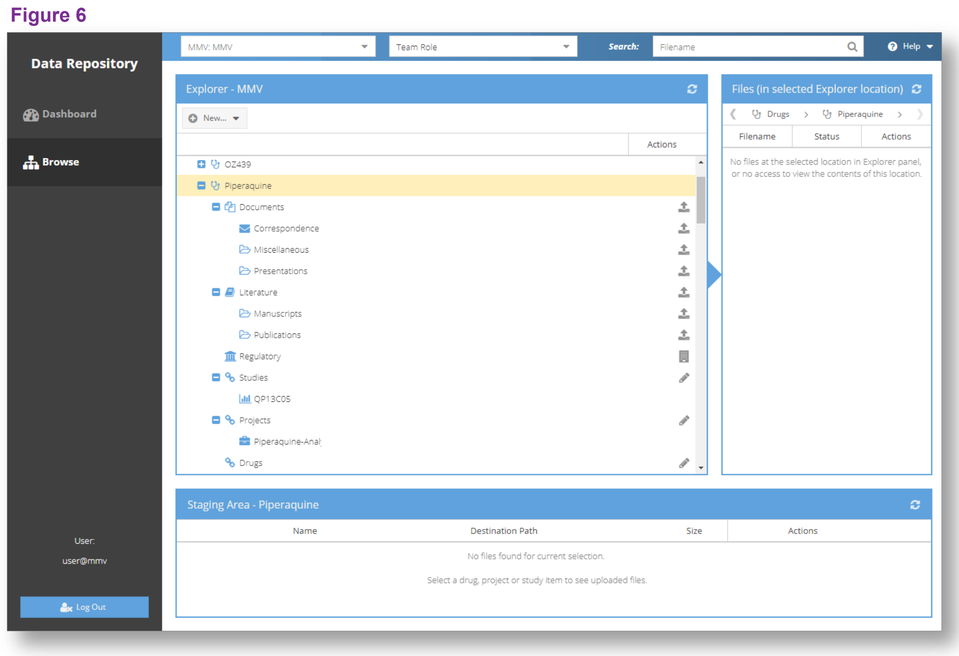
Project: The project component is at the heart of all file sharing within the Data Repository and is the location where most actions are performed by the pharmacometric team members (Figure 2c).

Figure 2c



The Data Repository user interface (Figure 6) and supporting team management application were used during the case study. An Explorer panel allows hierarchical navigation of directory structures. The Staging Area panel displays files pending approval, and the Files panel shows approved documents for a selected directory depending on the permissions of the current user.

Figure 6



CONCLUSIONS

The Data Repository is a highly permissioned, cloud-based storage space for confidential documents produced or used by pharmacometric analyses. The application does not restrict the tools used by any team member throughout any project, and provides an organized space for long-term storage of programs and results. Functionality within the application facilitates an efficient workflow for team members to accomplish their responsibilities. The Data Repository accommodates teams working on multiple projects where cross-team security is a requirement. Safeguards have been put into place to guard against inadvertent disclosure of confidential information.

The repository offers an environment for a global collaborative library for sharing data and models transparently with traceability to source data and models. The repository offers a structure to minimize duplication of effort, increase communication between team members, and streamline the development of new medicines for diseases which disproportionately affect the poor in low- and middle-income countries.

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