

Introducing DDMoRe's framework within an existing modelling and simulation environment.



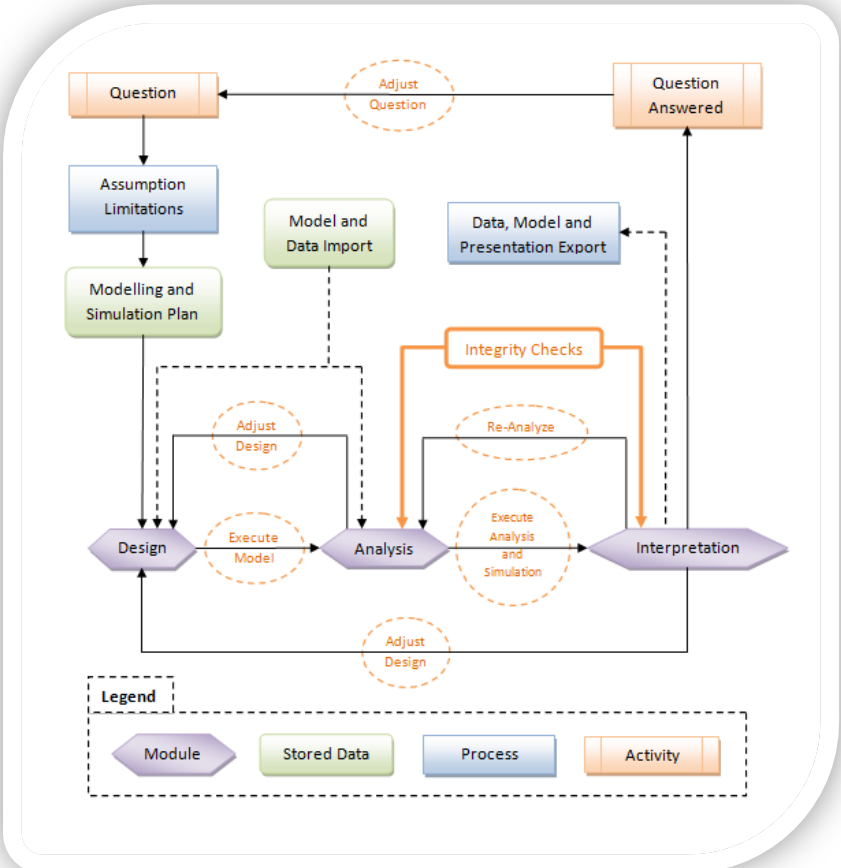
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Introduction

DDMoRe will introduce a new paradigm for model-based data analysis. This implies updating enterprise modelling systems and infra-structure to accommodate the new applications and tools.

Here we review GSK's Predictive Modelling Environment (PME) functionality to illustrate what is required to modify and upgrade validated environments to accommodate the concepts and tools provided by DDMoRe.

This exercise is based on a pre-defined M&S workflow and can be viewed as a model for identifying systems requirements and process changes.

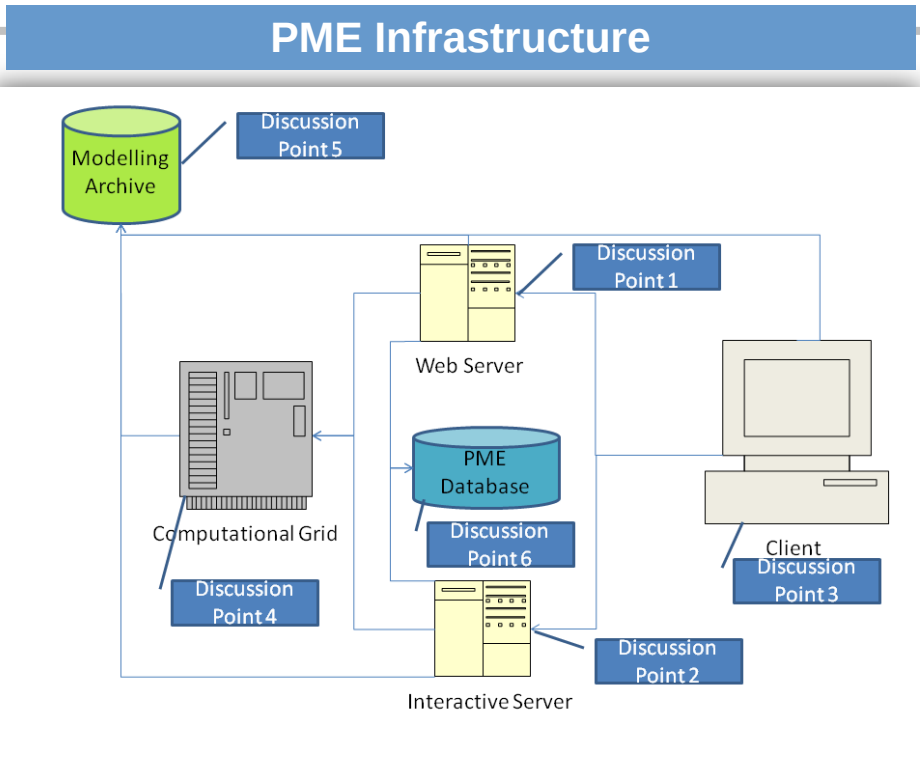


Modelling & Simulation Workflow

Methods

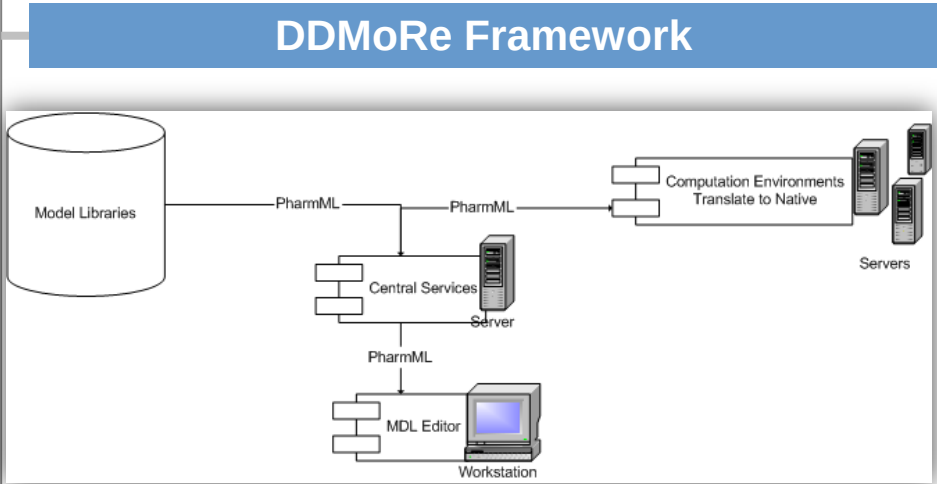
M&S infrastructure and functionality should be the result of a well-thought system design and available "computer architecture". This allows one to identify the components that can be re-used, and those that need modification. The resulting architecture is then assessed for the problem areas (e.g., re-execution of previous analyses). Moreover, system specifications need to consider different applications of M&S tools, i.e., both as an exploratory and as an inferential tool for regulatory submissions.

Here we assume a whole-scale change of the modelling environment provided by DDMoRe. The MDL framework provides a front-end editor in the Model Definition Language, with data transferred between components in a new computer-understandable language PharmML. DDMoRe will provide the specifications of these languages as well as tools to operate with these within a modelling environment.



DDMoRe – Preparing for Expansion

- DDMoRe provides an extendable design.
- The PharmML specification will be publicly available to allow developers to build on the framework.
- New tools can be plugged in as they come along.



Results

PME is predominantly a NONMEM- and R-centric application. Currently other tools are available – but limited to the command line.

The impact of DDMoRe will be discussed for each component – as per the diagram below.

New Functionality

- Models can be written in target-neutral language.
- Access to library of accepted models.
- Additional tools available for use by modellers
- Models can be shared with other communities

Reduced Functionality

- PME allows for data transformation and storage during the preparation phase
- DDMoRe framework will allow R and other language specific processing – but without an intermediate data repository

Overview of Changes

The upgrade to a new environment can be viewed based on the following sections.

Point 1: The Web Interface

- The existing web-interface will need to be replaced.
- Existing functionality will either be replaced, or no longer available.

Point 2: The Command Line Interface

- The command line itself is reasonably application independent.
- Users will still require direct access to tools.
- This will need to be updated to remove customisation to include existing PME-based functionality.

Point 3: The Client

- Although we are considering a web-based application, users ("the client") will need training.
- A complete work-stream within DDMoRe is dedicated to this element – as the key uptake of a new tool is acceptability within the community.

Point 4: The Computational Grid

- Existing tools are independent of the application itself. Changes here are more likely to be addition of new tools to provide more capability for the user.

Point 5: The Modelling Archive

- The archive is intended for interaction by the existing tools. This will need to be migrated to be accessible by new tools.

Point 6: PME Database

- The PME database will be redundant in a new environment.
- Functionality within this component will either be non-existent or managed by other components.

Component	Degree of Change
Web Interface	High
Command Line	Low
Client	High
Computational Grid	Low
Modelling Archive	Medium
PME Database	Low

Conclusions Frameworks

- The availability of a framework is aimed at facilitating and improving the efficiency of M&S activities. It does not itself provide all of the components. Instead, it provides places to allow these to be embedded.

- DDMoRe's aim is to provide both a framework and tools to fulfil the aforementioned objectives in a structured manner which had previously not been achieved by any initiative to date,

Planning for the Future

- The last development of PME removed tight relationships between components. Most R&D organisations do not have such a system architecture

- Providing an environment which can allow addition and removal of individual components allows flexibility and facilitates future development to enhance the system.

- The key component for change is user training. Without adequate training, the new environment will not gain the traction needed

Impact of Change

- A correctly prepared environment is critical to limit the changes to the visible components.
- Strategies have to be put in place to determine how existing analyses are stored or accessed

- In most cases, successful implementation of a new system will demand user education

Application to Other Interfaces

- The same basic analysis and results can be applied if a different solution were implemented.

- The underlying grid infrastructure provides a robust and re-usable structure for other systems.

- Decoupling of core components (e.g. NONMEM) allows these to be managed on their own and to limit impacts of changes to these components.