



ADVANCED DIGITAL DESIGN OF PHARMACEUTICAL THERAPEUTICS

A Systems-Based Approach to Digital Design and Operation in the Formulation of Pharmaceuticals

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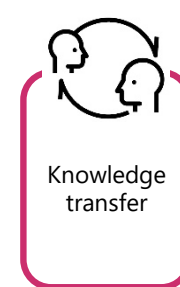
1 Britest Limited, 2 Process Systems Enterprise Limited

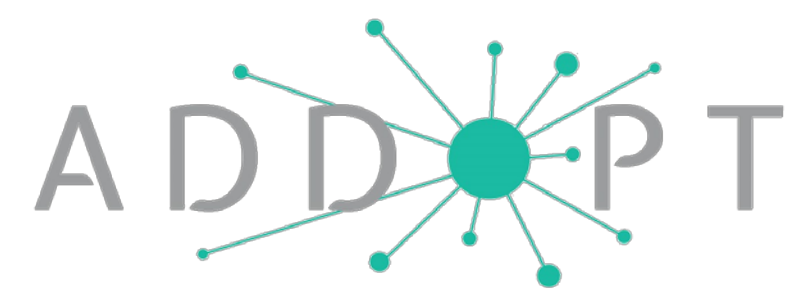


Britest is a highly successful not-for-profit SME. Since its founding in 2001, the application of Britest tools has generated many €millions of productivity gains, driving enhanced business sustainability and competitiveness.

Britest's **expert technical facilitators** use a suite of proprietary tools to help organisations **define, structure, and translate knowledge into process understanding**.

This promotes **effective communication** of the underlying science across disciplines and functions, **enabling knowledge transfer** and allowing organisations to derive tangible **business value**.





The ADDoPT Project

Advanced Digital Design of Pharmaceutical Therapeutics



A £20.4m UK Government-Industry-Academia collaboration

Part-funded under the Advanced Manufacturing Supply Chain Initiative (AMSCI*)

*A BEIS initiative delivered by Finance Birmingham and Birmingham City Council



Department for
Business, Energy
& Industrial Strategy



Instigated by the Medicines Manufacturing Industry Partnership (MMIP)



“This project has the potential to propel the UK to the forefront of medicinal product design and manufacture”

ABPI & BIA



Project Consortium

Pharma Primes:



SMEs:



Research:



Solid oral dose tablets are formulations of:

- The Active Pharmaceutical Ingredient (API)
- Excipients
- Coating

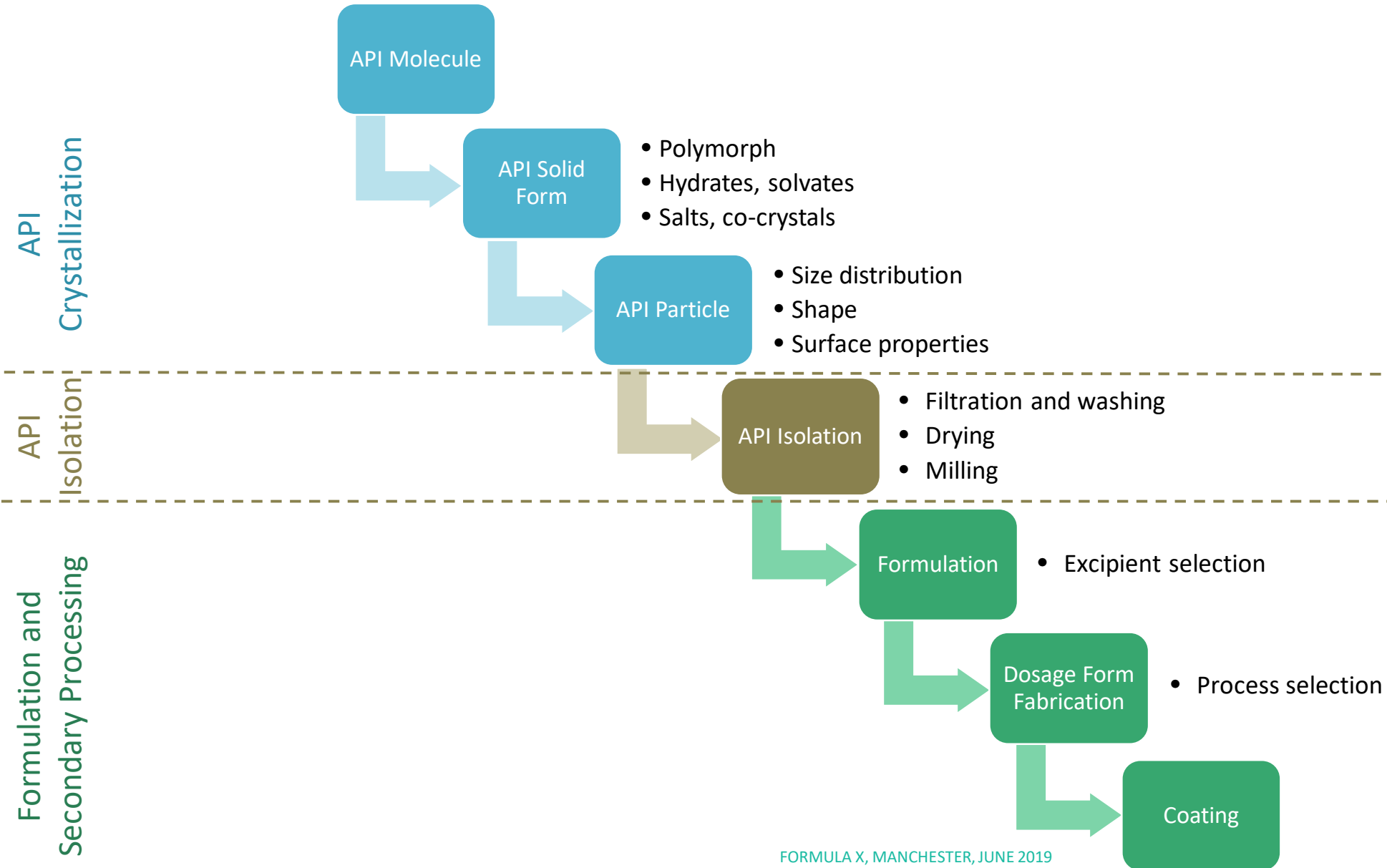
Excipients are present for:

- Function – e.g. disintegrants
- Processing – e.g. lubricants

Material properties and process selection interact to determine:

- Performance
- Stability
- Manufacturability

From Molecule to Dosage Form



Secondary Processing Options

- Direct Compression
- Dry Granulation
- Wet Granulation

Selection Criteria

- Powder flow
- Segregation
- Compressibility
- API sensitivities

Manufacturing Classification System¹

- Secondary process selection based on API particle characteristics and dosage level

1. M Leane, K Pitt, G Reynolds, A Proposal for a Drug Product Manufacturing Classification System (MCS) for Oral Solid Dosage Forms, Pharmaceutical Development and Technology, August 2014

Advantages of a Digital Design Approach

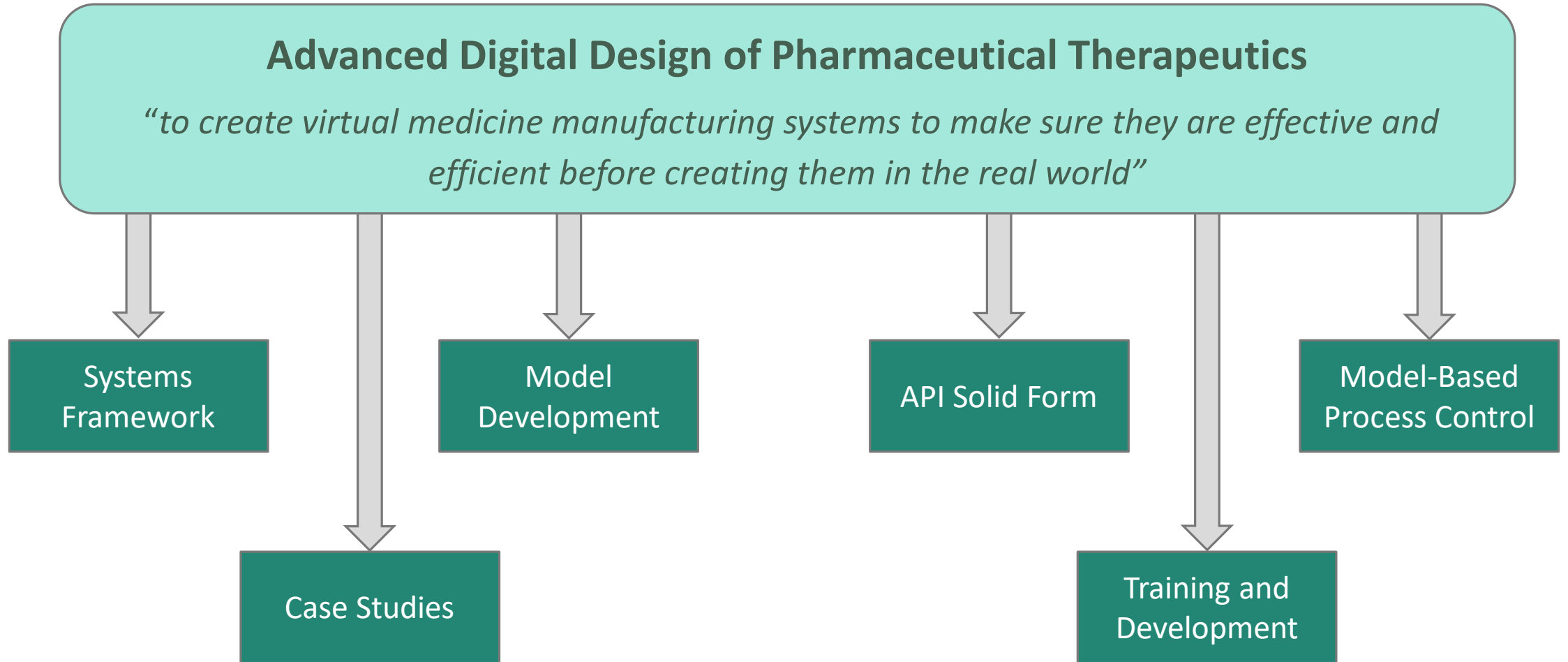
A “Digital Twin” of a product or process is created. Experiments are used to parameterise and validate the model.

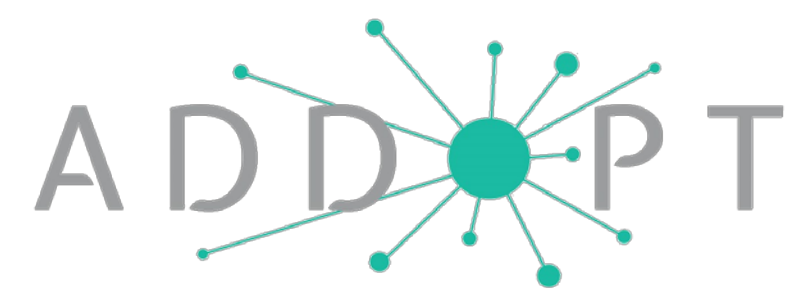
Qualitative systems models can be used to help develop and test the assumptions of the quantitative model, and in the selection of parameters to explore in “virtual DoEs”

Conducting virtual DoEs allows:

- Exploration of a wide range of material attributes and process parameters
- Identification of which parameters are critical to performance
- Assessment and optimisation of the robustness of performance with respect to variability in raw materials, physiology etc.
- Reduction in development time, costs and use of scarce materials

Scope of the ADDoPT Project





Development of the Digital Design Information Flow



Need for a Digital Design Information Flow

There is a need for an overall framework that:

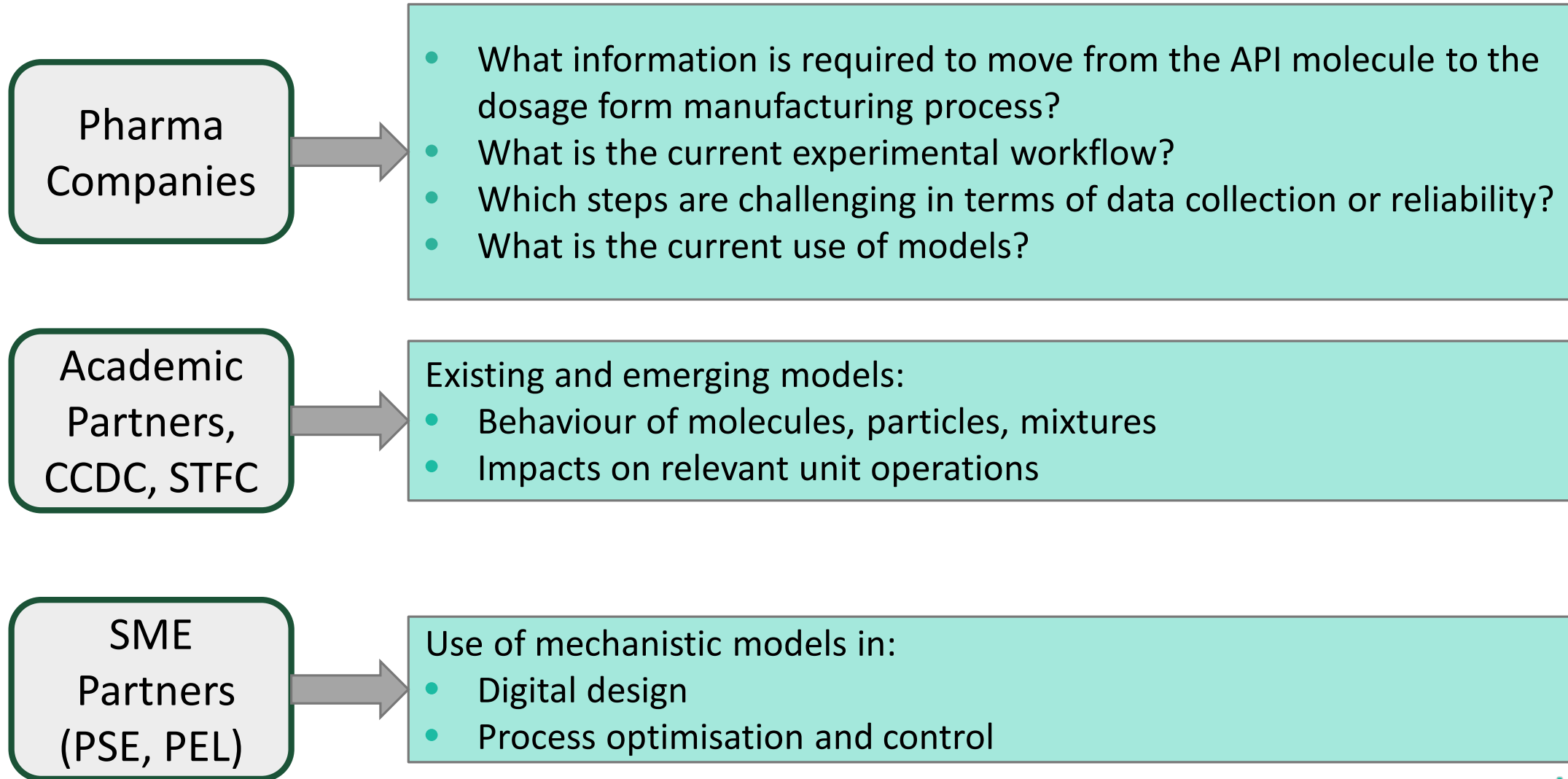


Allows users to understand the current state of models and their data requirements, and identifies potential future developments

Combines the information flows from individual aspects of modelling and experimentation into an integrated structure

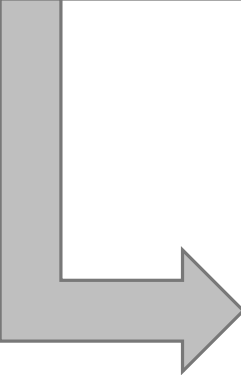
Maps the digital design opportunities to the current product and process development workflows

Links to training materials required to support the approach



Requirements for the Digital Design Information Flow:

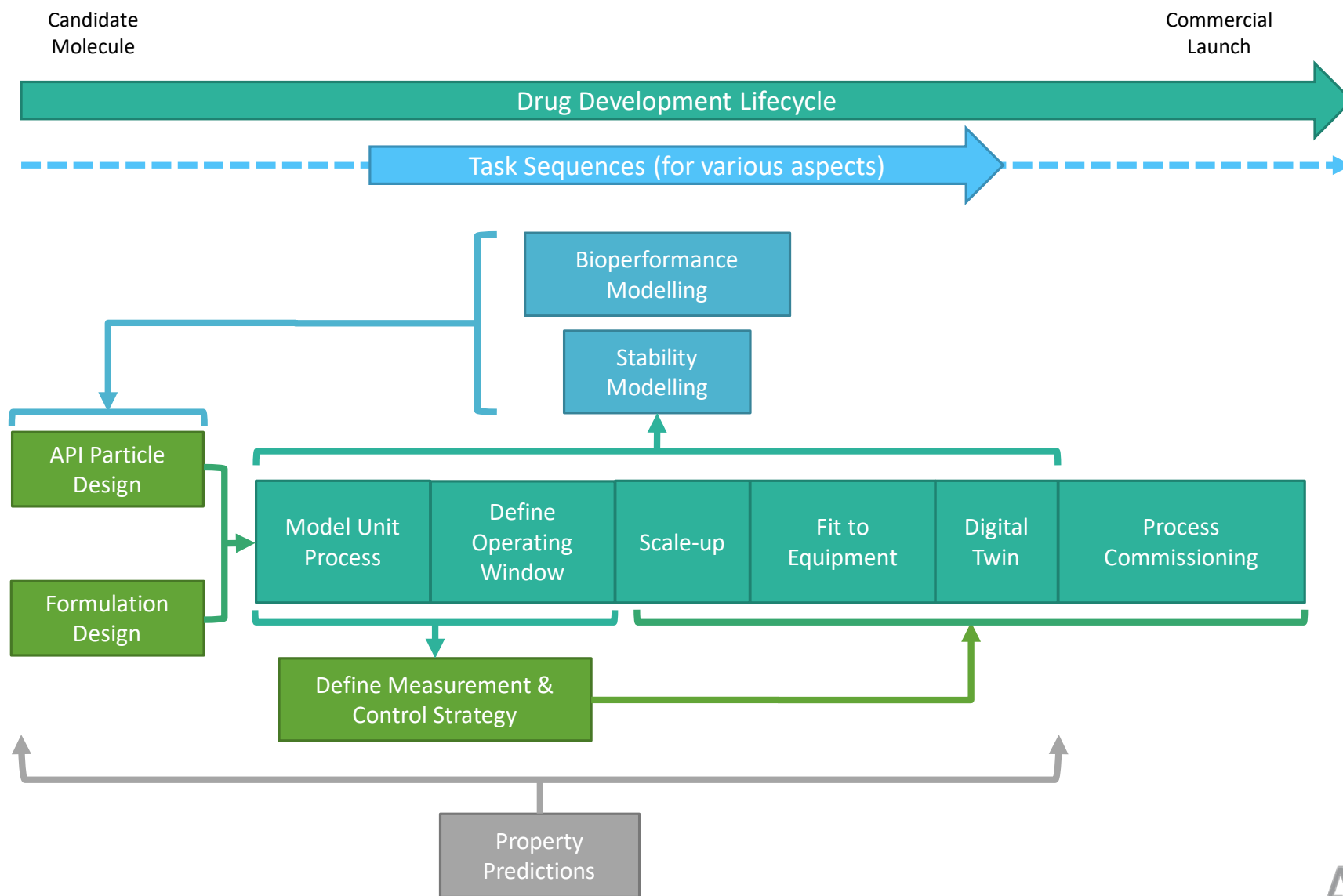
- Start at a high-level and provide layers of information to enable access to increasing levels of detail as required
- Enable the user to select their own navigation path
- Link to external sources of information, including training materials
- Capable of being web-hosted, meaning no new software requirements for the users



Implemented in:

- (a) Articulate Storyline (for main navigation), with links out to
- (b) SharpCloud (for models, providers and training packages)

Overview of a Potential Integrated Workflow



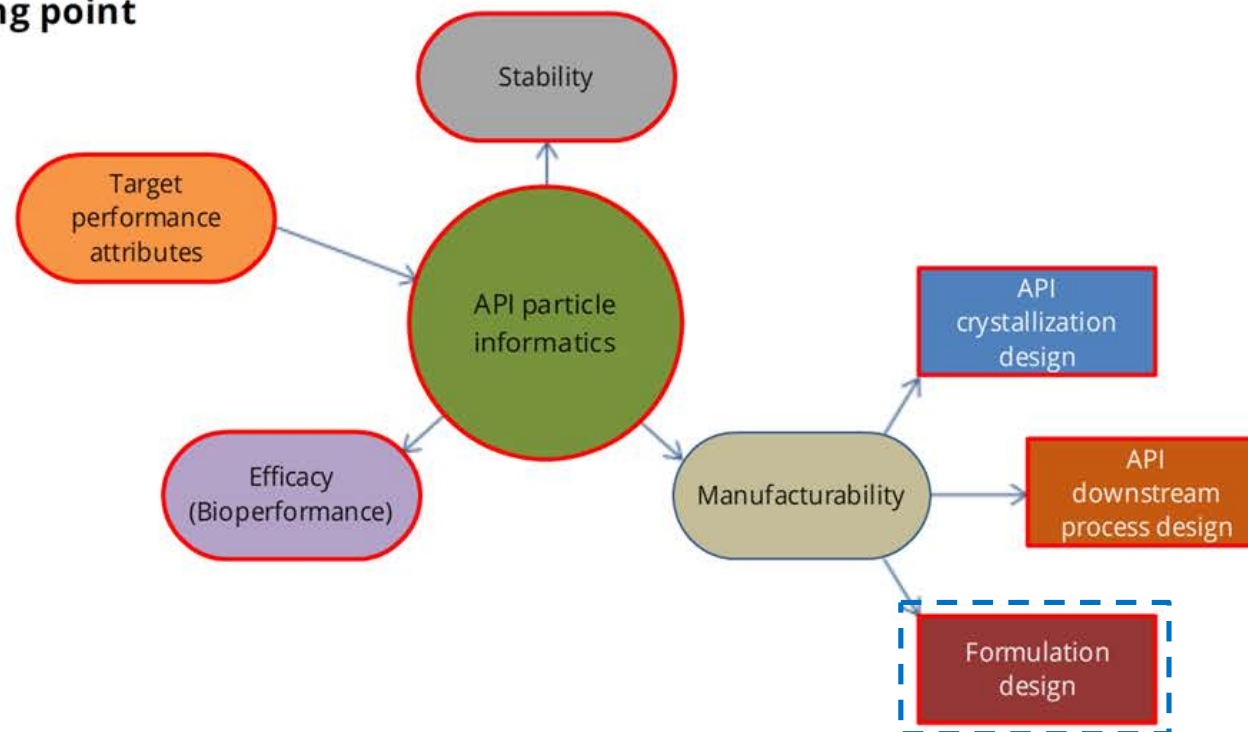
ADDoPT Guide to Pharmaceutical Digital Design and Manufacture

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Overview and starting point



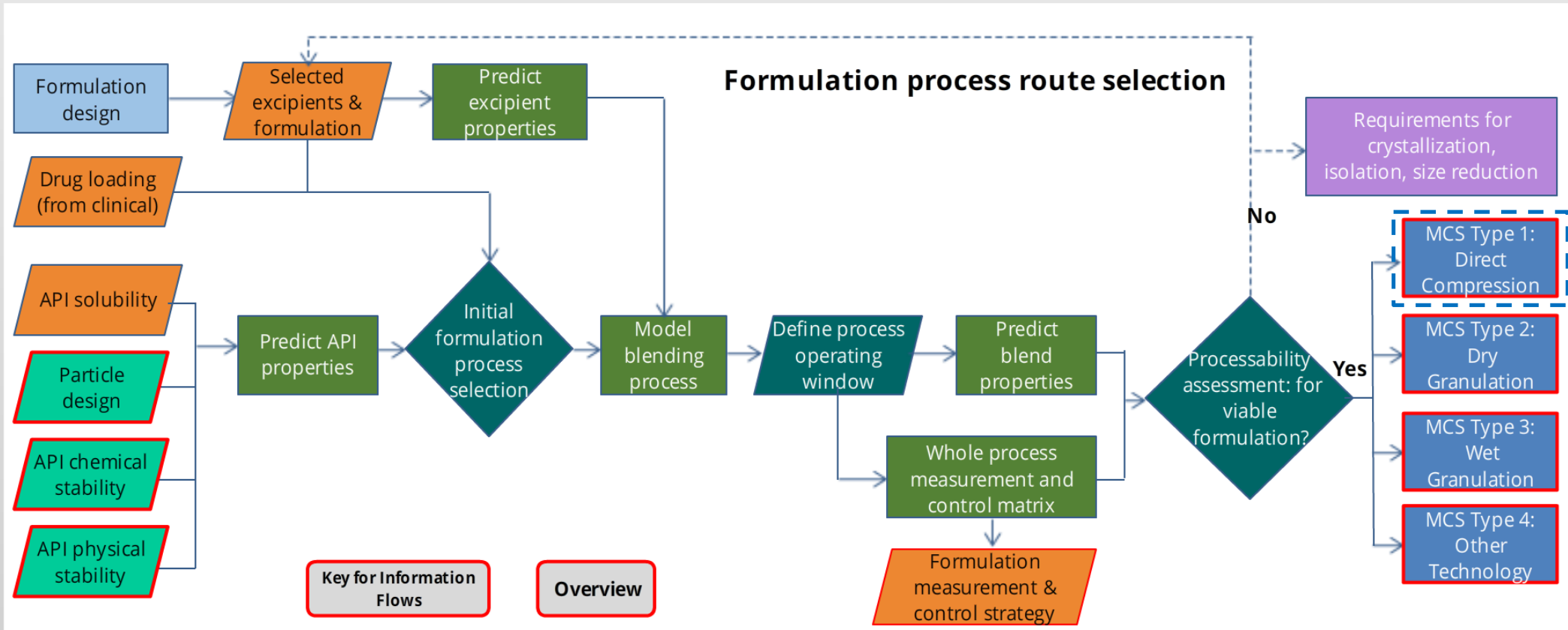
- Introduction
- What is ADDoPT?
- What is Digital Design?
- What is this Guide?
- How do I use the Guide?
- Training and Support
- Glossary of Terms

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Formulation Process Route Selection

ADD OPT Guide to Pharmaceutical Digital Design and Manufacture

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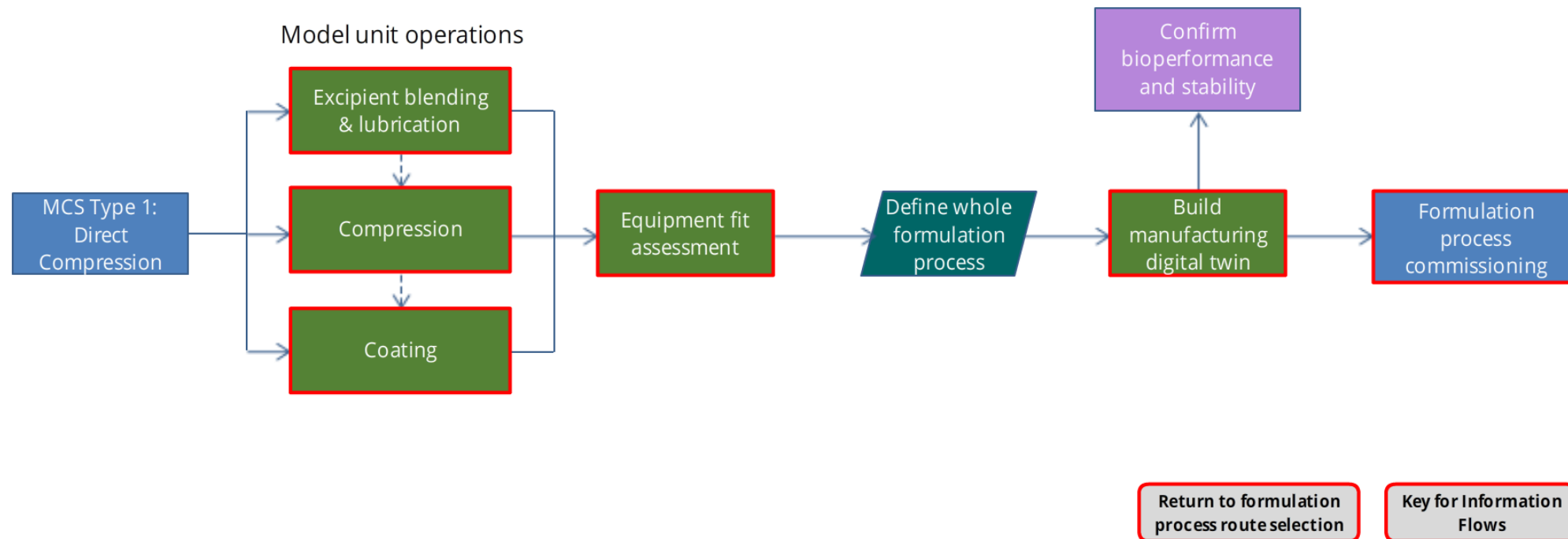


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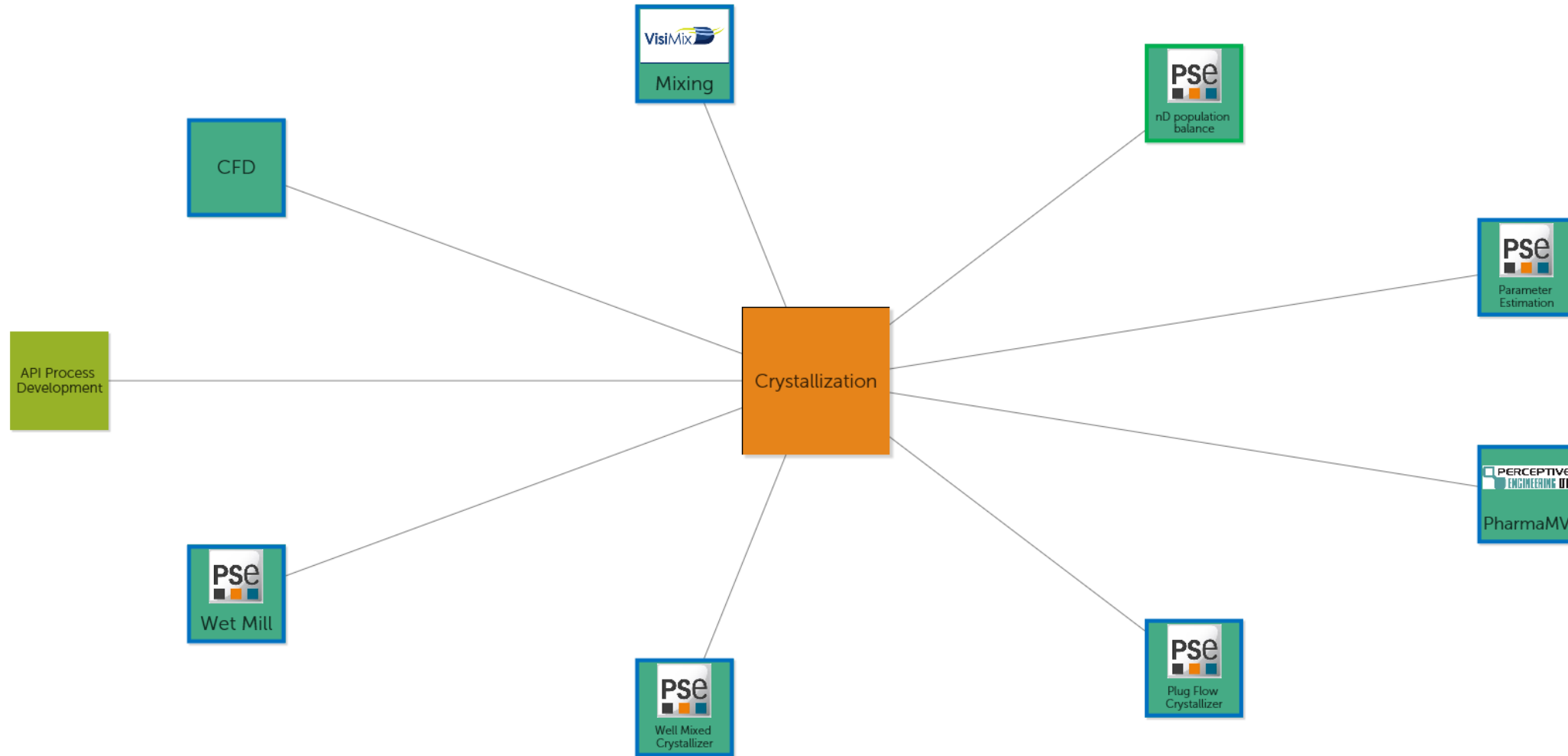
Direct Compression Information Flow

MCS Type 1: Direct Compression Process Design



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SharpCloud Display of Crystallization Models



Summary

1 Digital Design approaches offer a number of advantages in drug product design and manufacture

2 The ADDoPT project has led to the development of new quantitative models for property predictions and manufacturing processes

3 Britest has worked with the consortium partners to integrate these modelling approaches into an overall interactive information flow

4 The information flow maps digital design opportunities to development workflows, and links to supporting training materials

5 Specific information flows have been developed for pharma partners

6 The approach could be extended to other sectors