ADVANCED PROCESS MODELLING FORUM
LONDON
20–21 APRIL 2016

# gPROMS FormulatedProducts

Integrated design of formulated products & their manufacturing processes

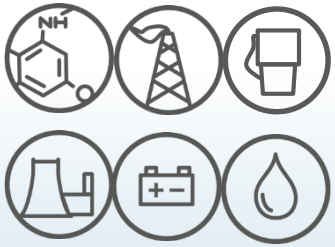
Sean Bermingham, Head of PSE Formulated Products

gPROMS

# A new PSE product …

# … in the gPROMS Product Family

## *"Fluids processing world"*



**g|PROCESS**
gPROMS ProcessBuilder
Process MLs

**g|WATER** — Water MLs

**g|UTILITIES** — Utilities MLs

**g|CCS** — CCS MLs

**g|POWER** — Power MLs

**g|OILFIELD** — Oilfield MLs

## *"Formulated products world"*

**g|FORMULATE**
gPROMS FormulatedProducts

**g|CRYSTAL** — Crystallisation MLs

**g|SOLIDS** — Solids MLs

**g|COAS** — Oral absorption MLs

**g|FLARE** * — Flare & depressurisation MLs

**g|FUELCELL** — Fuel cell MLs

## General mathematical modelling

**g|MODEL**

gPROMS ModelBuilder provides essentially the full platform functionality

## The gPROMS platform

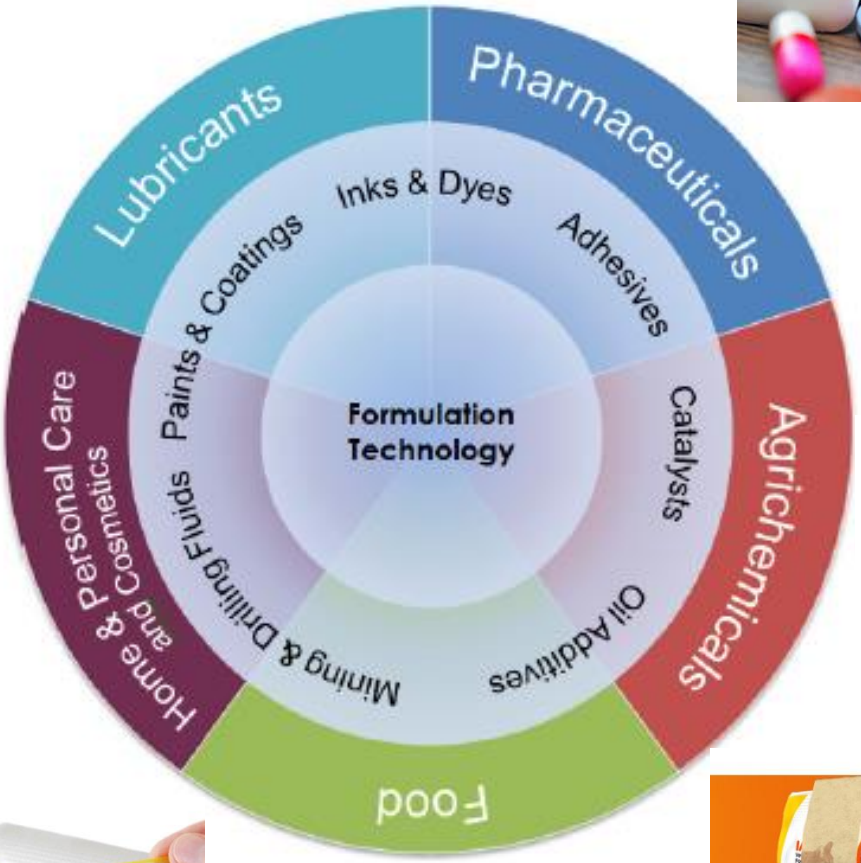
Equation-oriented modelling & solution engine

g|SAFT

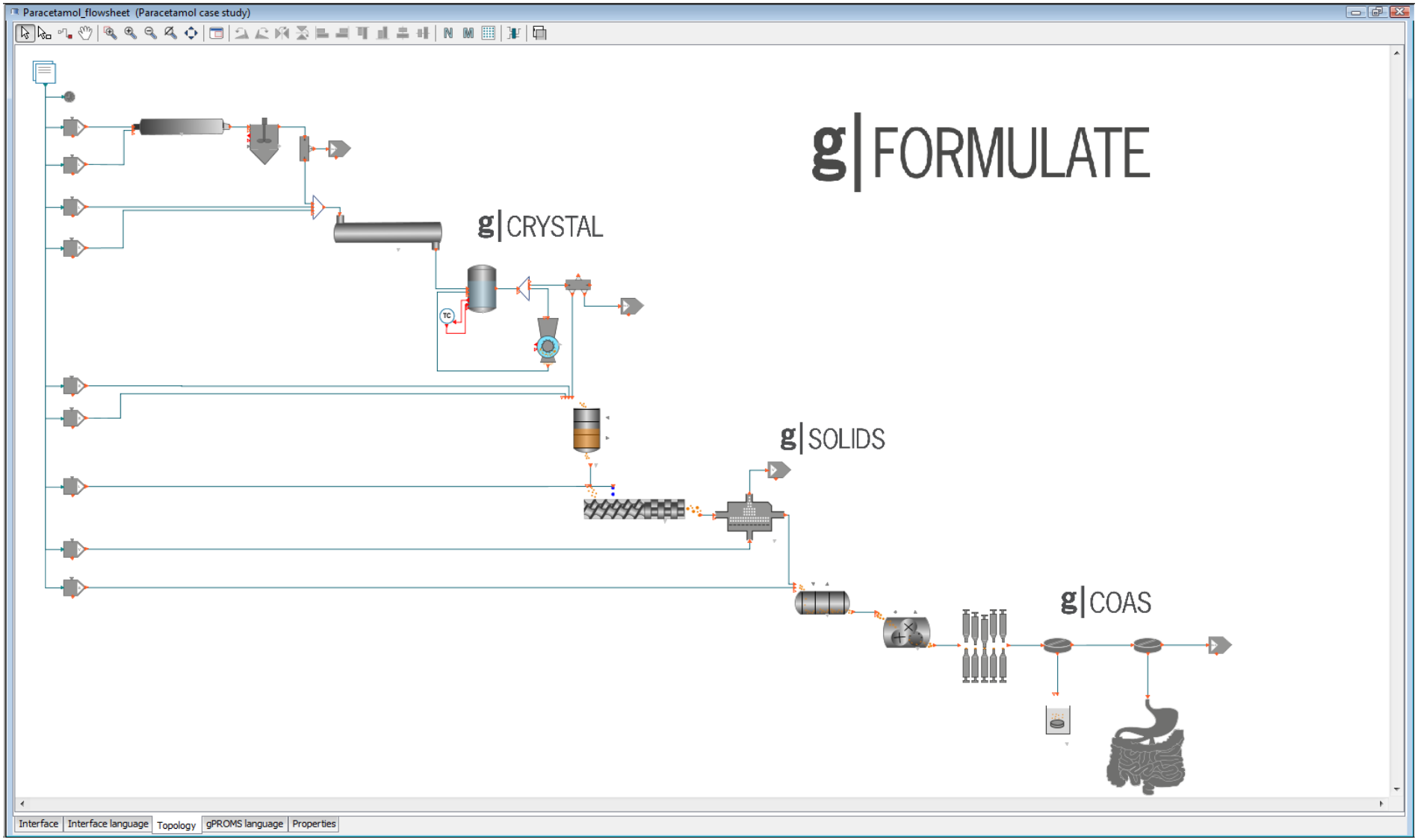


* Primarily used internally by PSE for delivery of services

# Formulated products world?

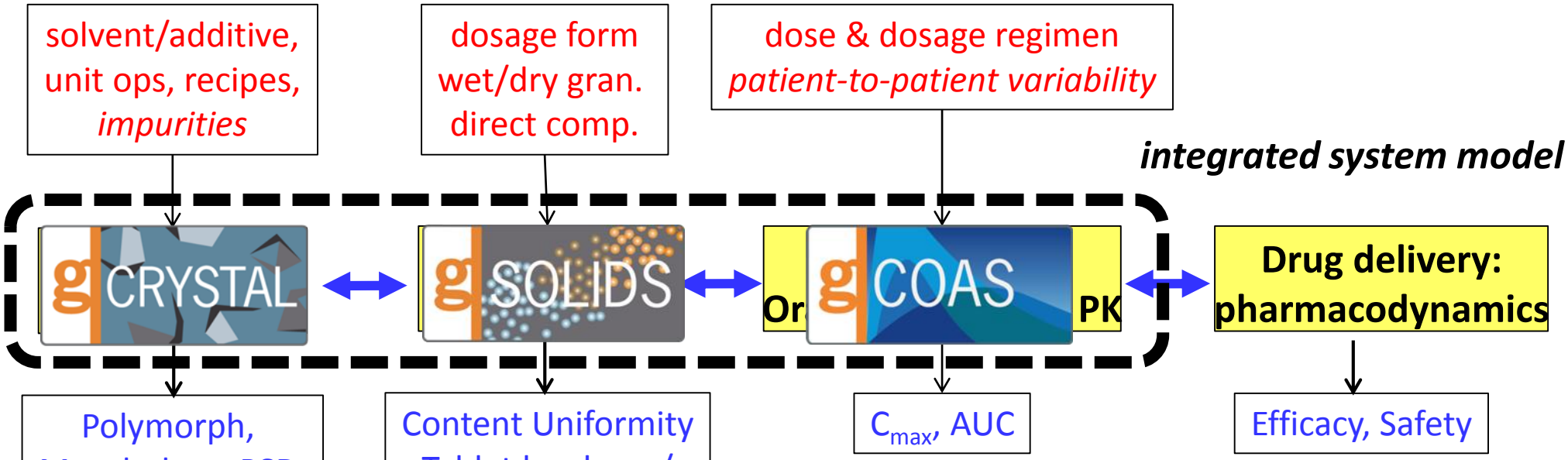



# Holistic, systems-based approach to design of formulated products and their manufacturing processes



An example of such a systems based approach

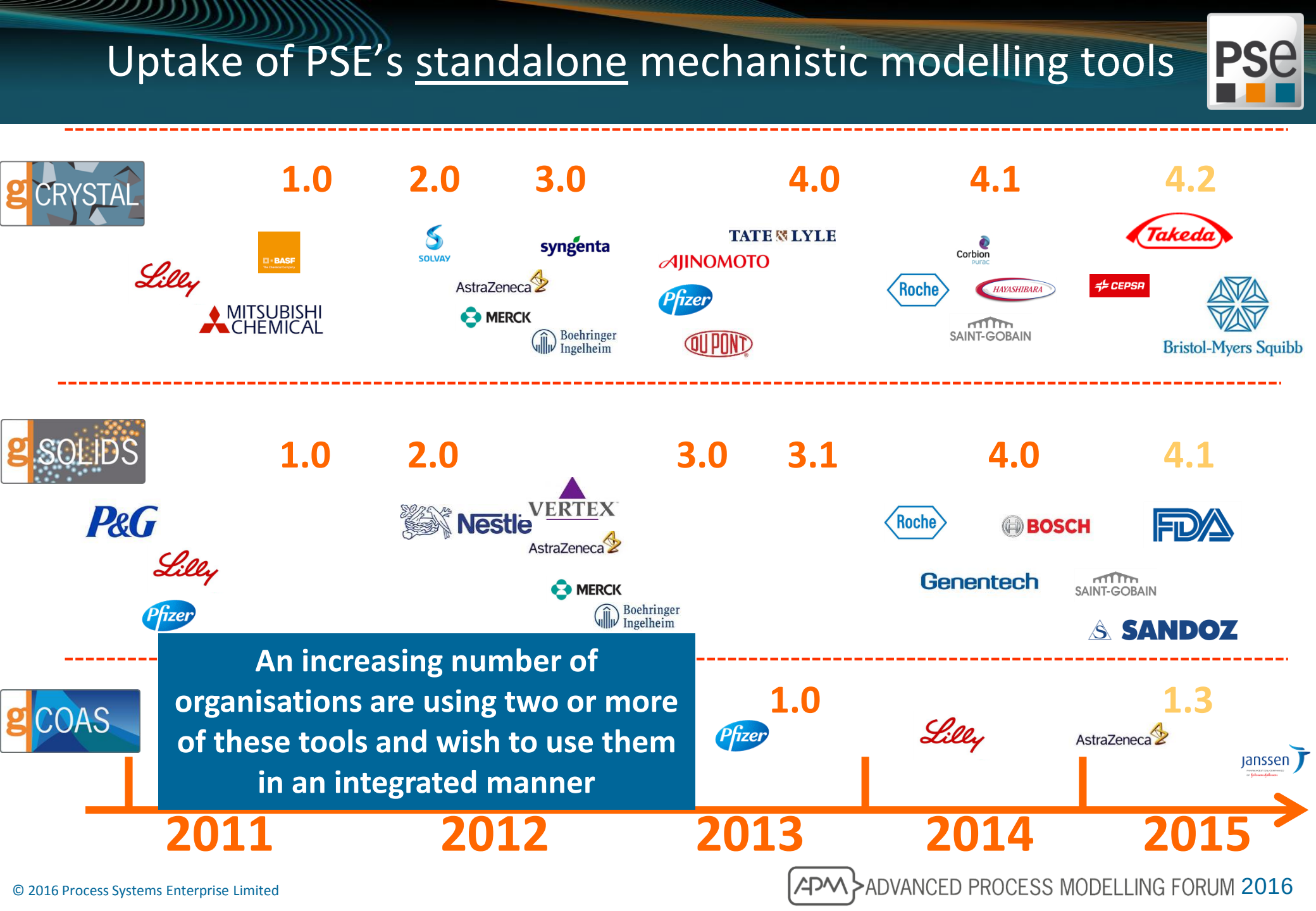
# Systems-based Pharmaceutics



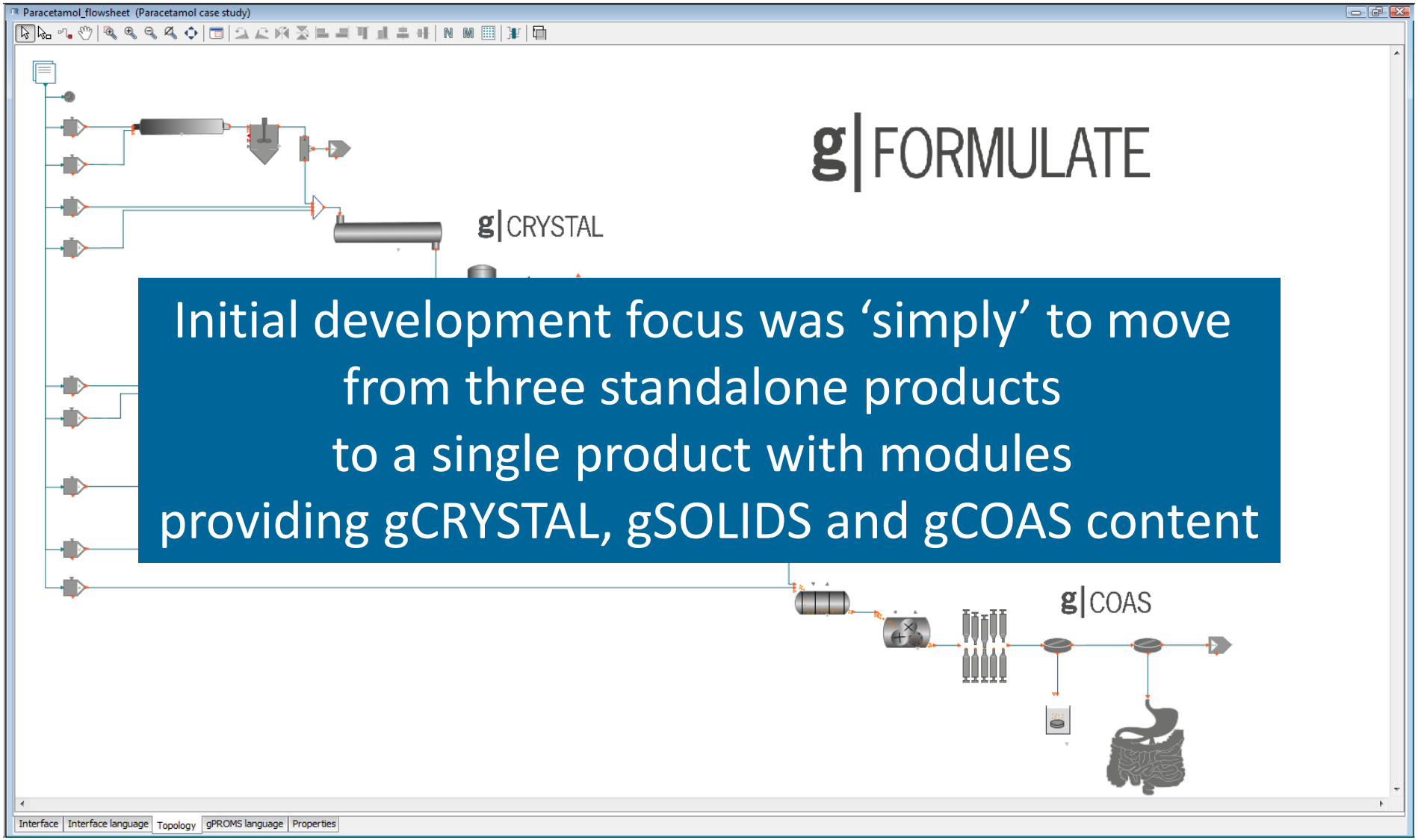

Why? To reduce iterations between product design and manufacturing process design.

- Use an integrated system model to quantify effects of CPPs & disturbances on CQAs, process economics, operability, safety

# Uptake of PSE's standalone mechanistic modelling tools



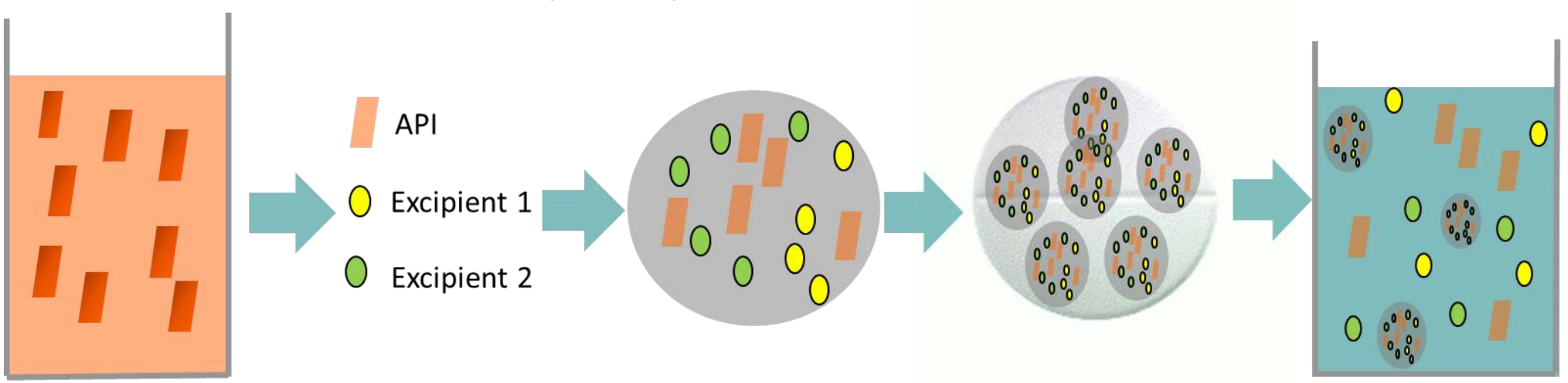
# Development of this product started in 2014




Initial development focus was 'simply' to move from three standalone products to a single product with modules providing gCRYSTAL, gSOLIDS and gCOAS content

# Introduces major architecture changes

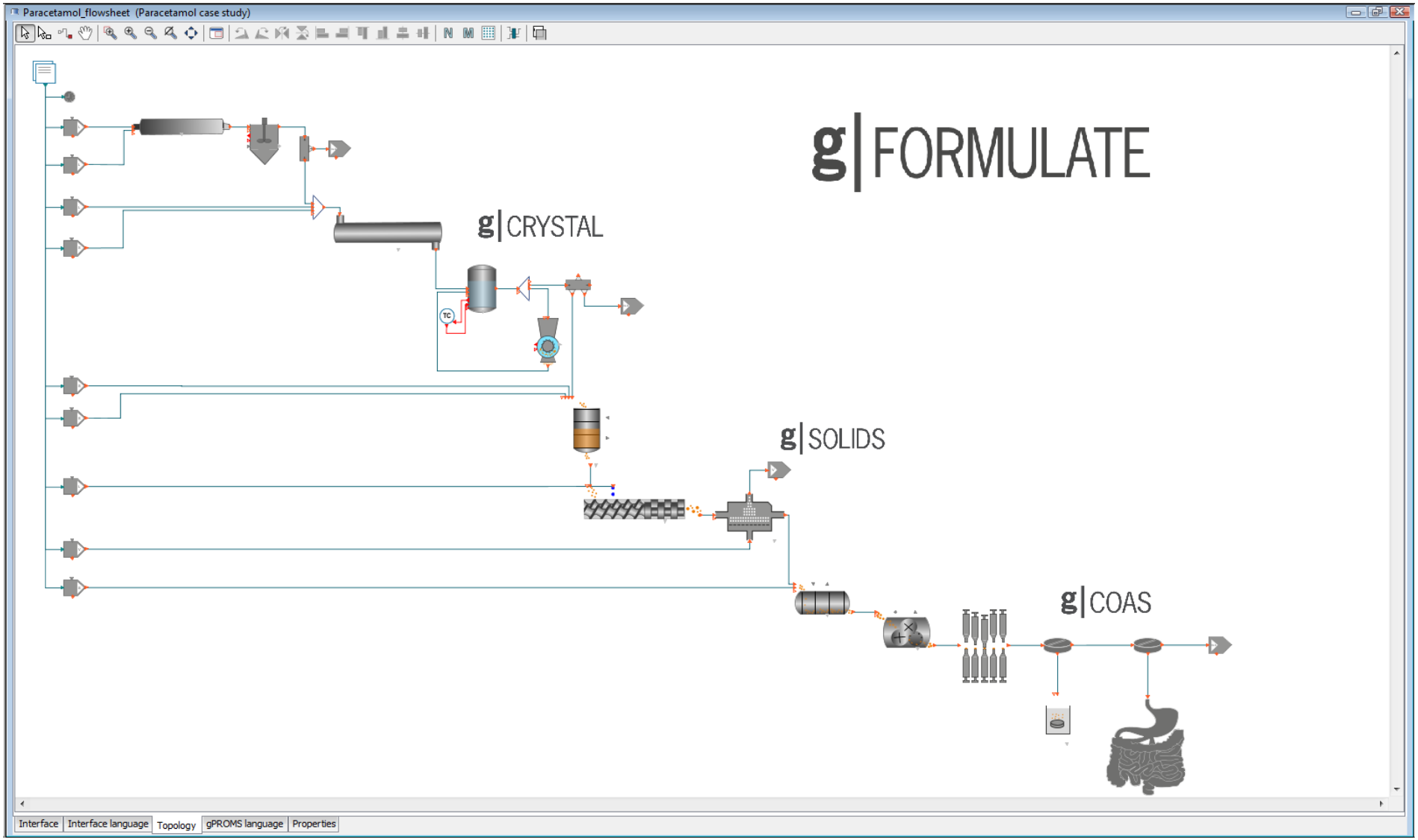
- Superficially: connecting gCRYSTAL, gSOLIDS and gCOAS
- Internally many changes, in particular architecture to describe
  - evolution of distributed phases
  - existence of composite phases



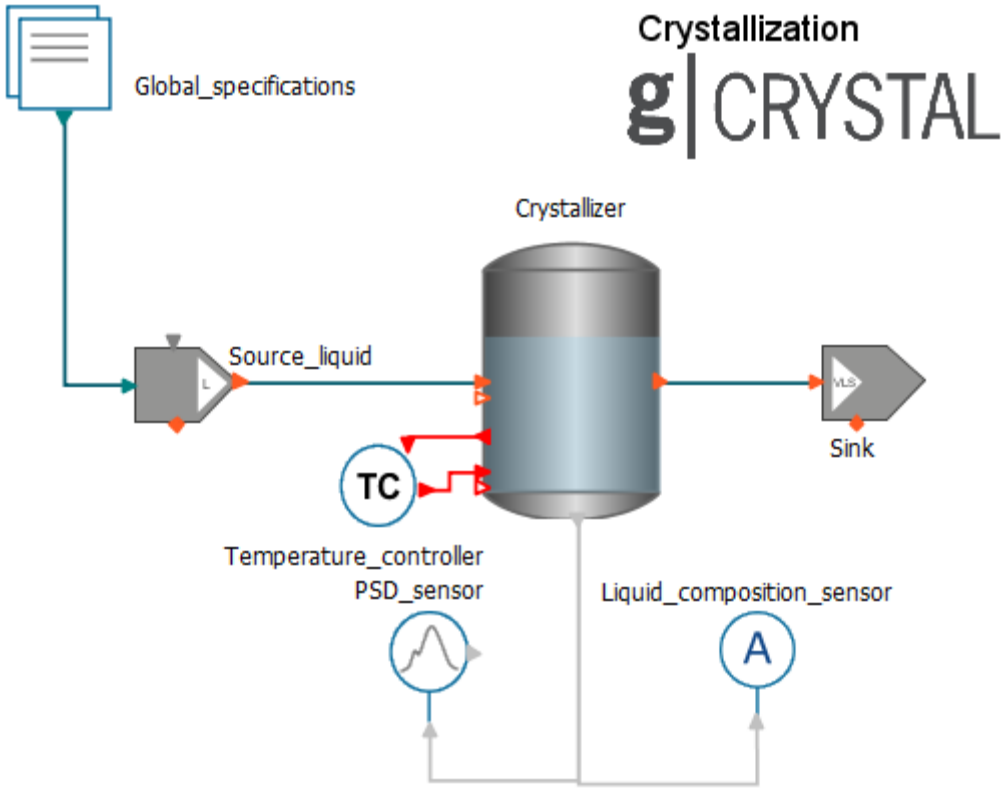

Crystallization Blending Granulation Tabletting Disintegration and dissolution

  - This handling of distributed and composite phases is not limited to solid phases

# Holistic, systems-based approach to design of formulated products and their manufacturing processes



# Also supports optimal design of system components



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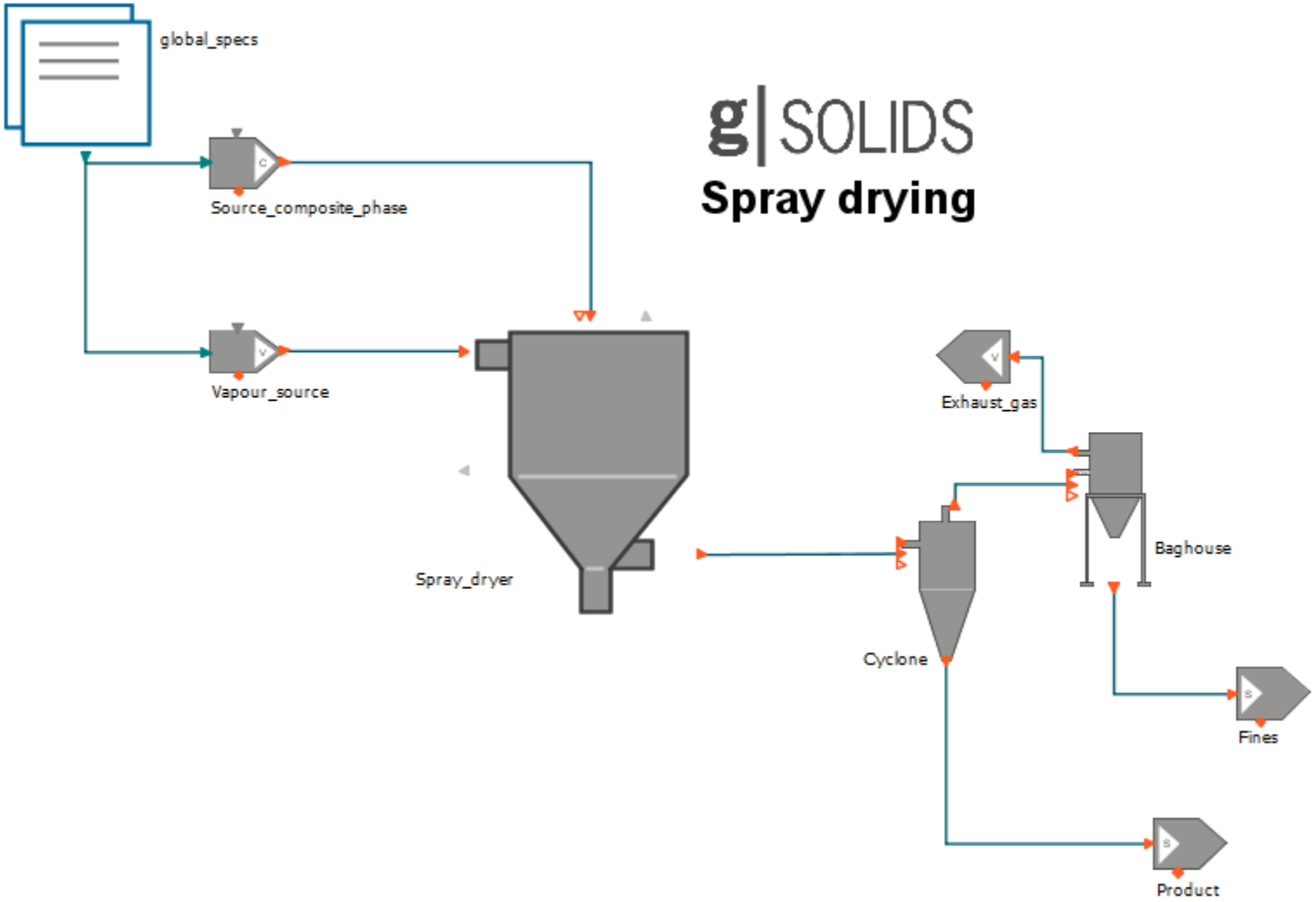

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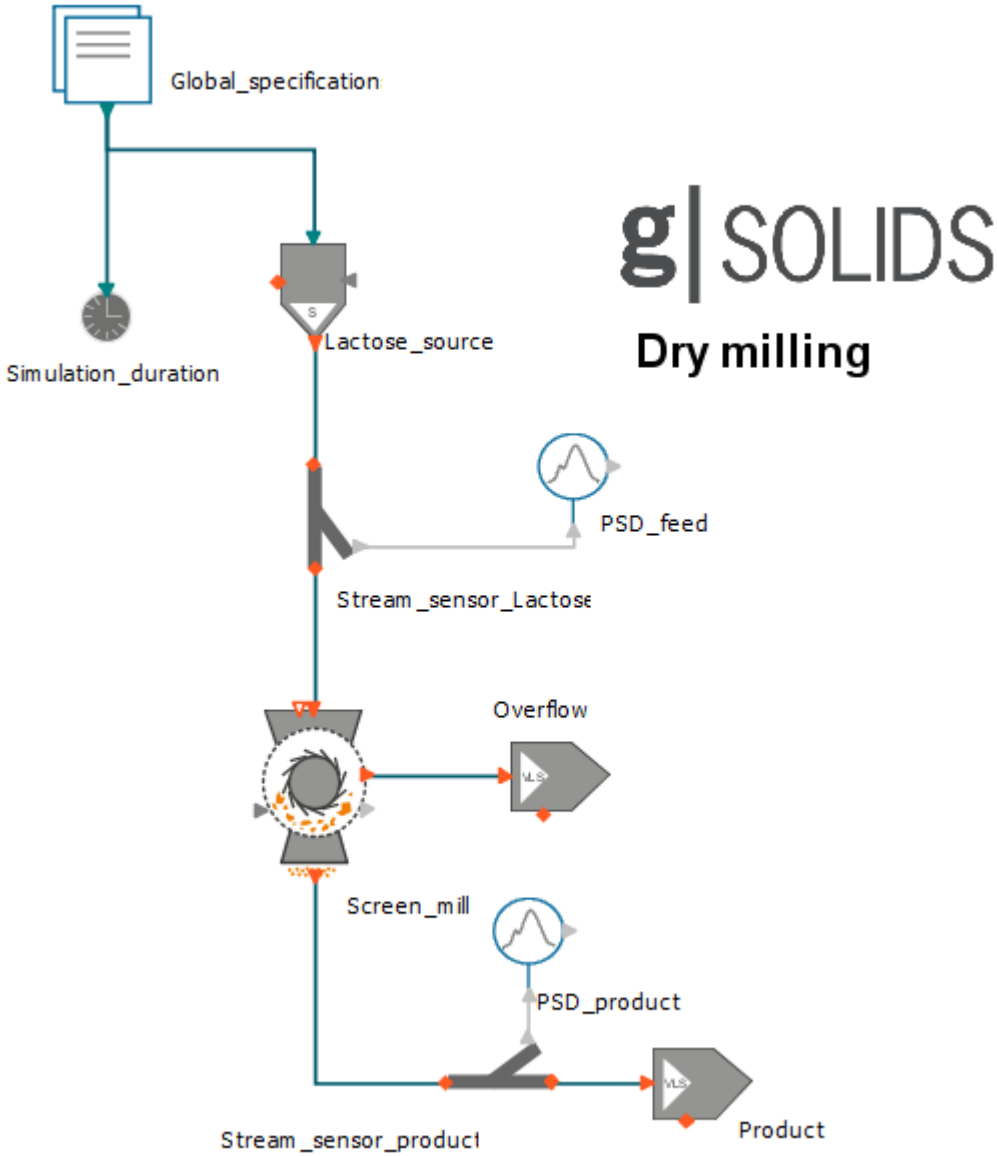

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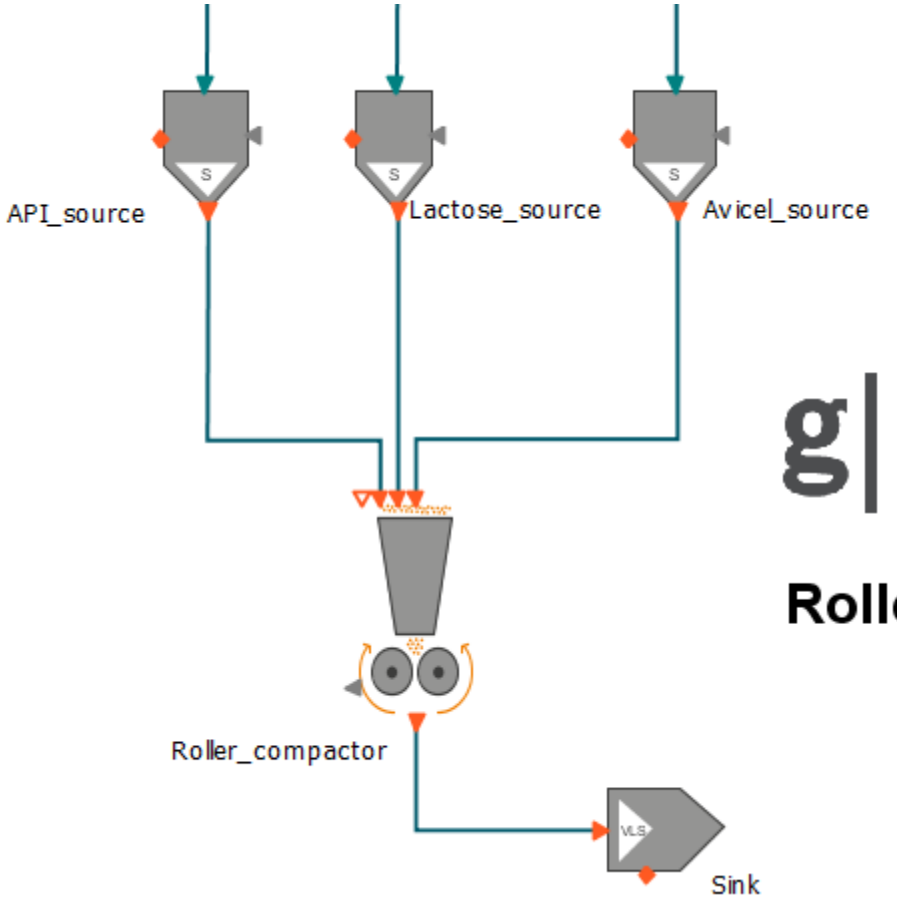
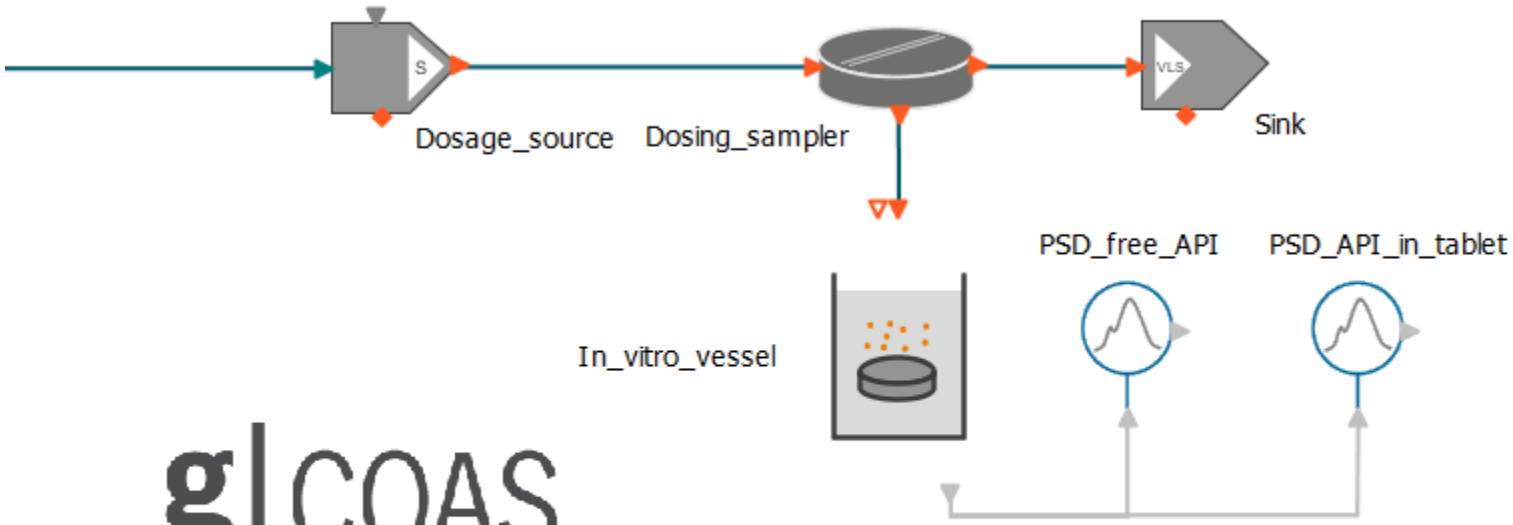



g|SOLIDS

**Roller compaction**

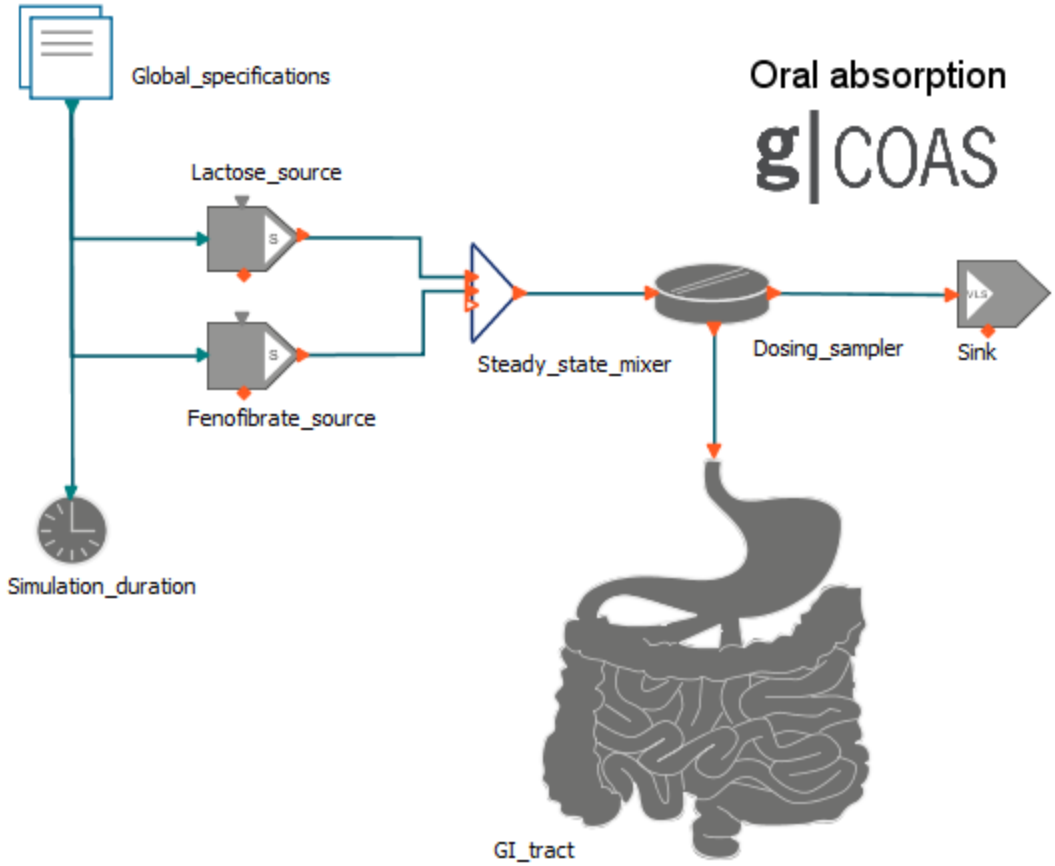
# Also supports optimal design of system components



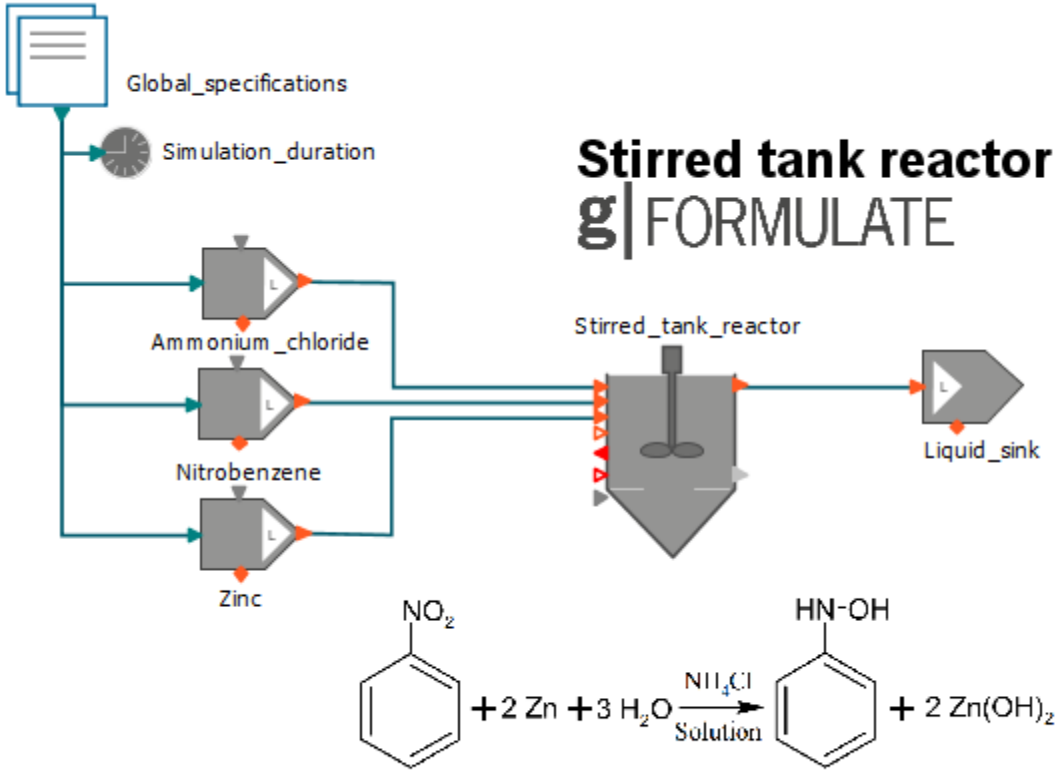

gCOAS

**In vitro dissolution**

# Also supports optimal design of system components



# And introduces many new models



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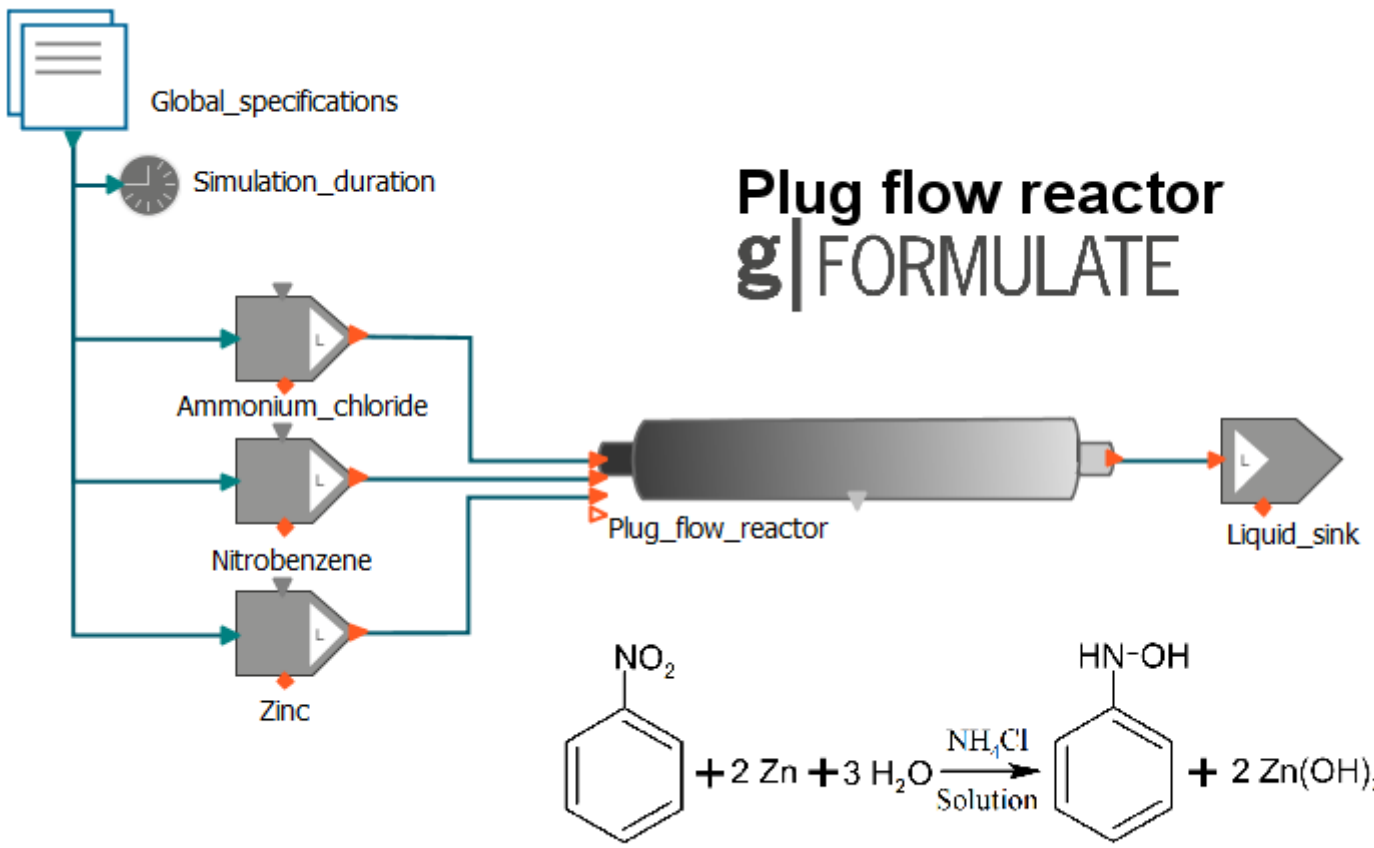

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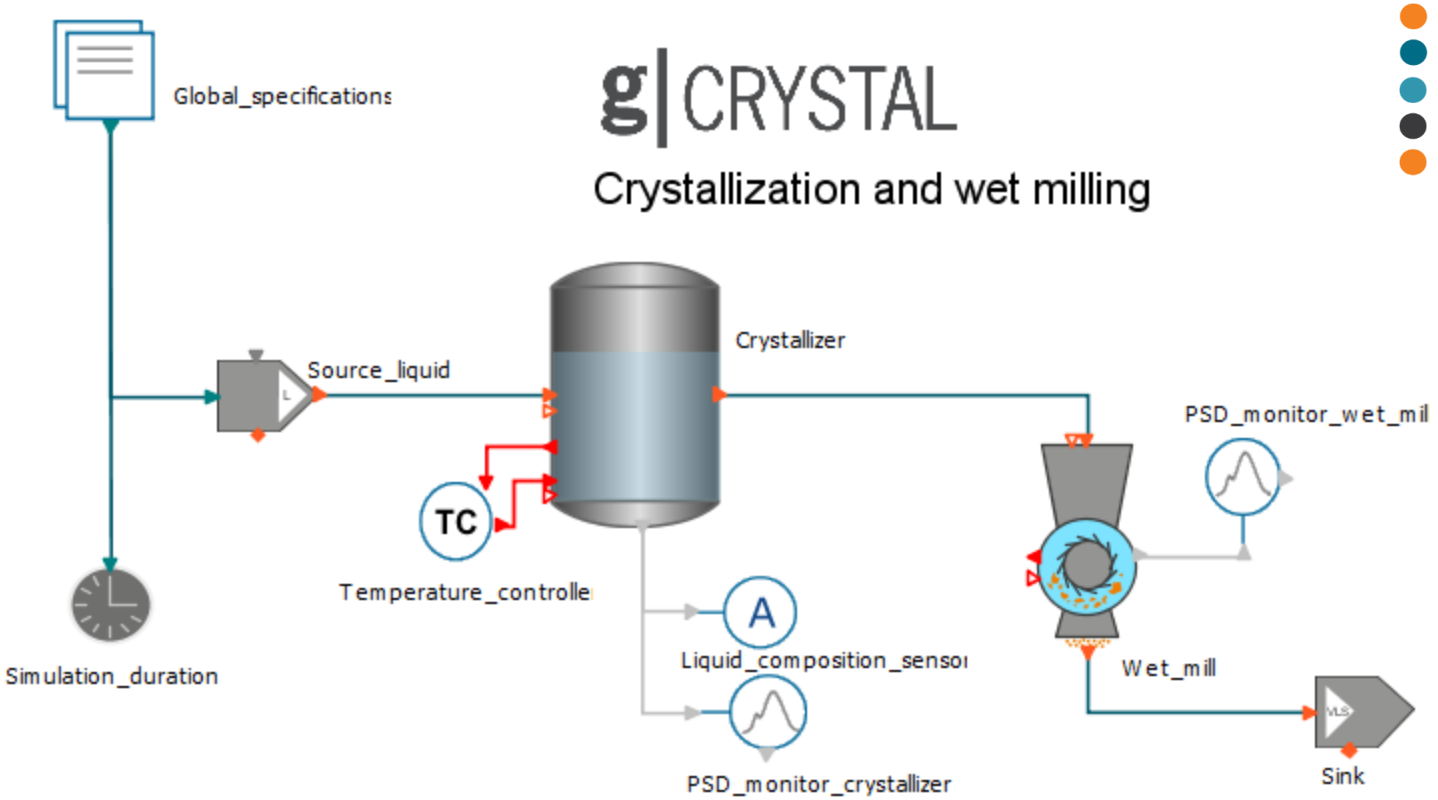

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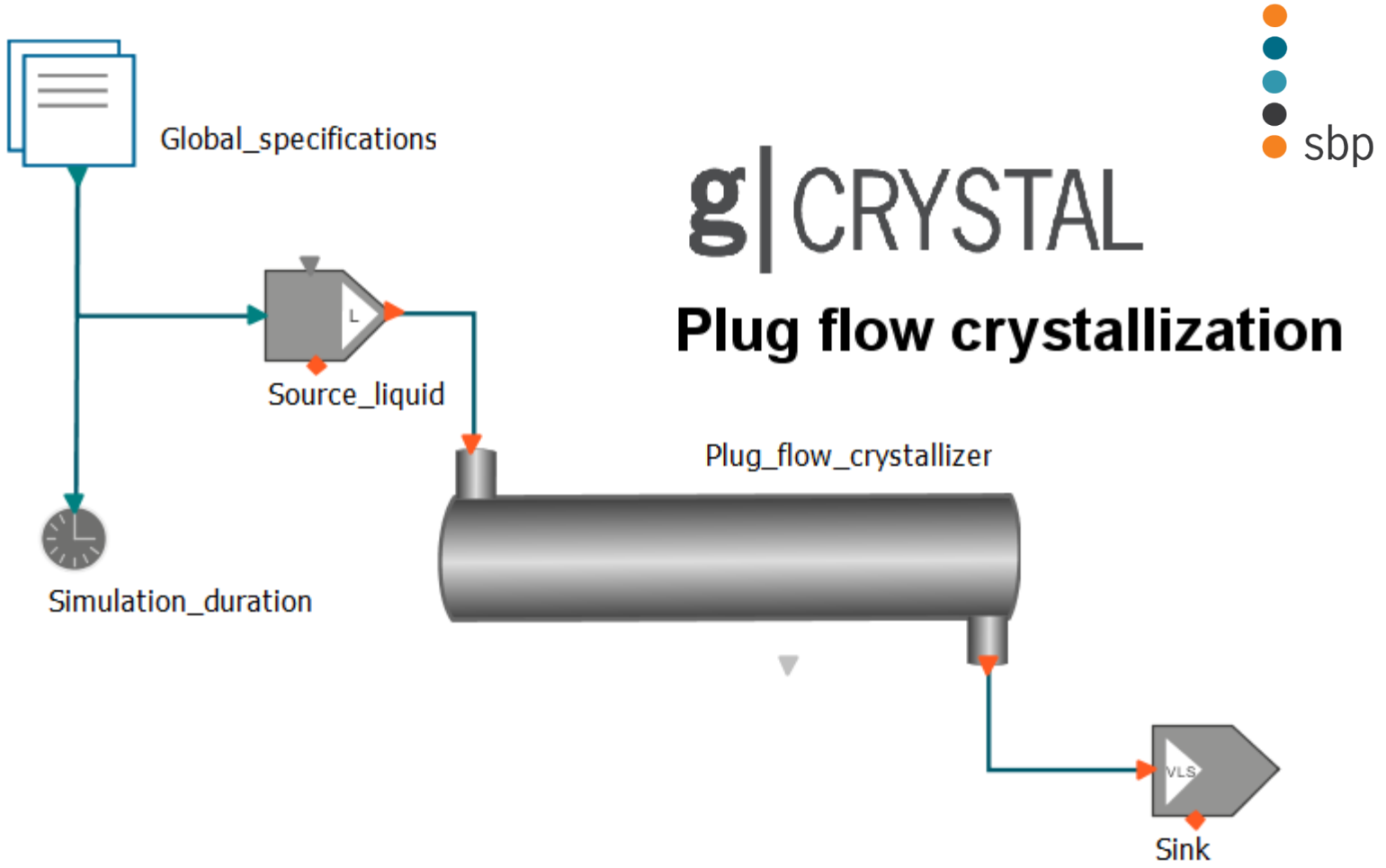
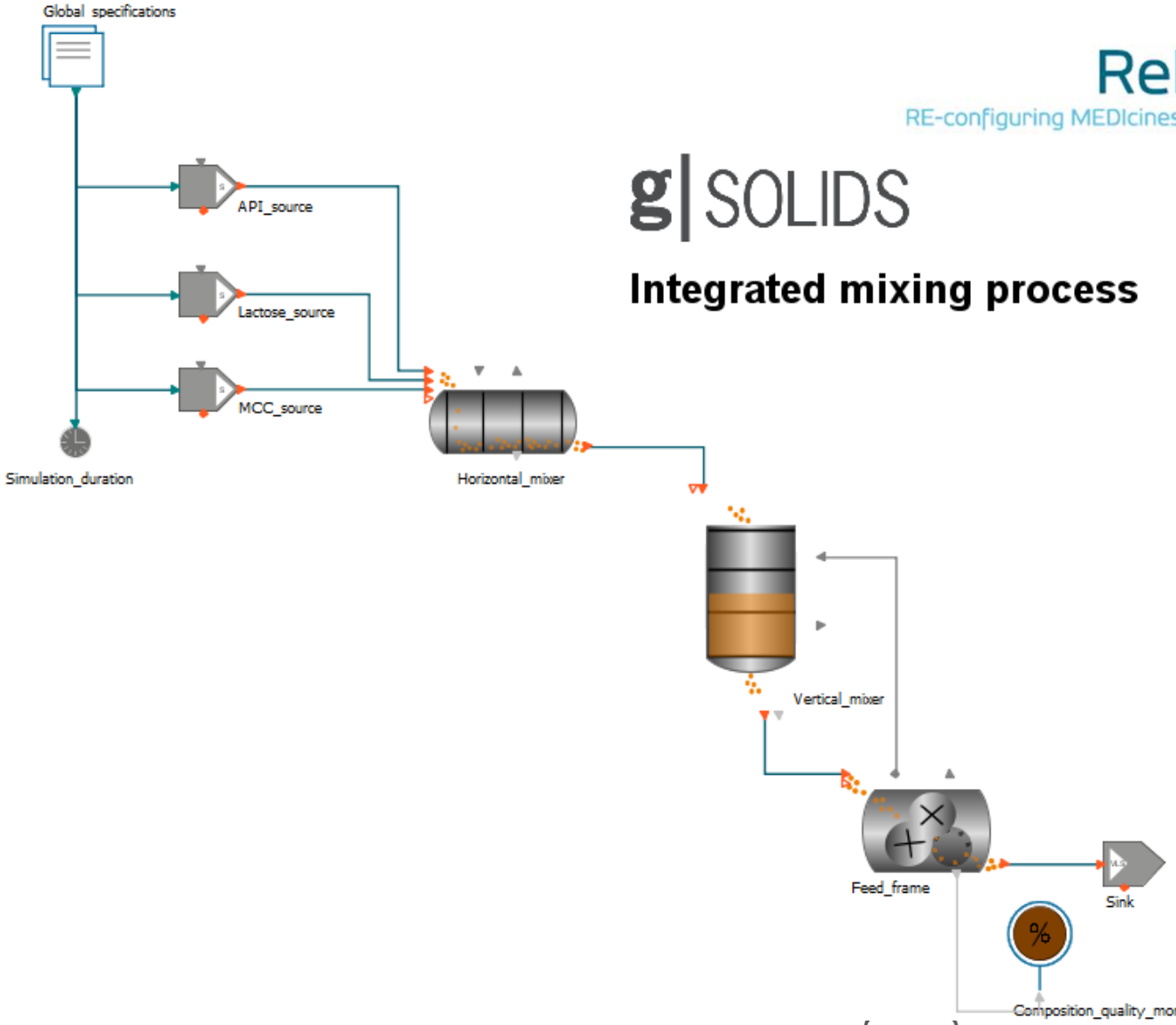


# And introduces many new models

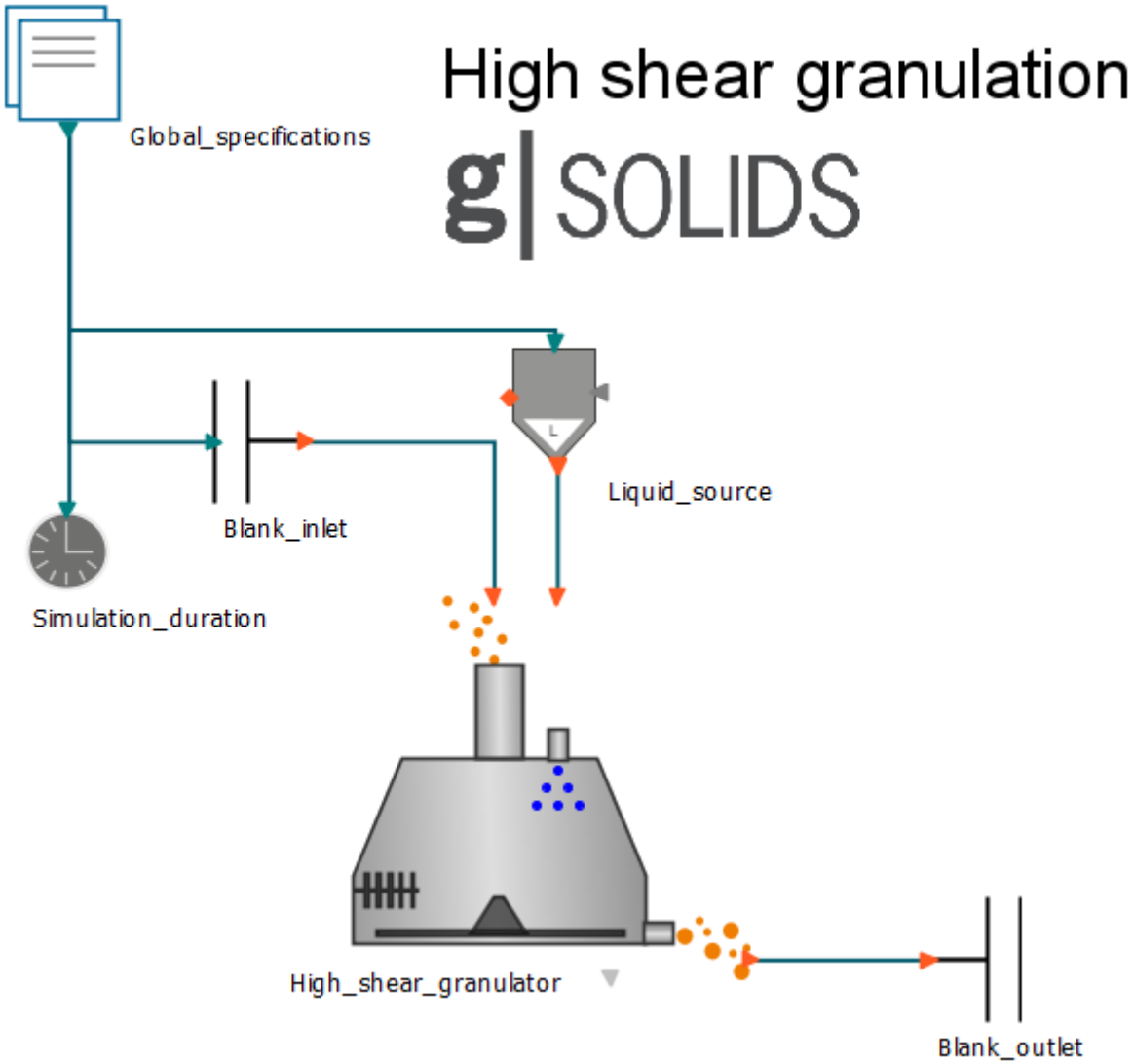
ReMediES
RE-configuring MEDIcines End-to-end Supply

g|SOLIDS

**Integrated mixing process**



# And introduces many new models



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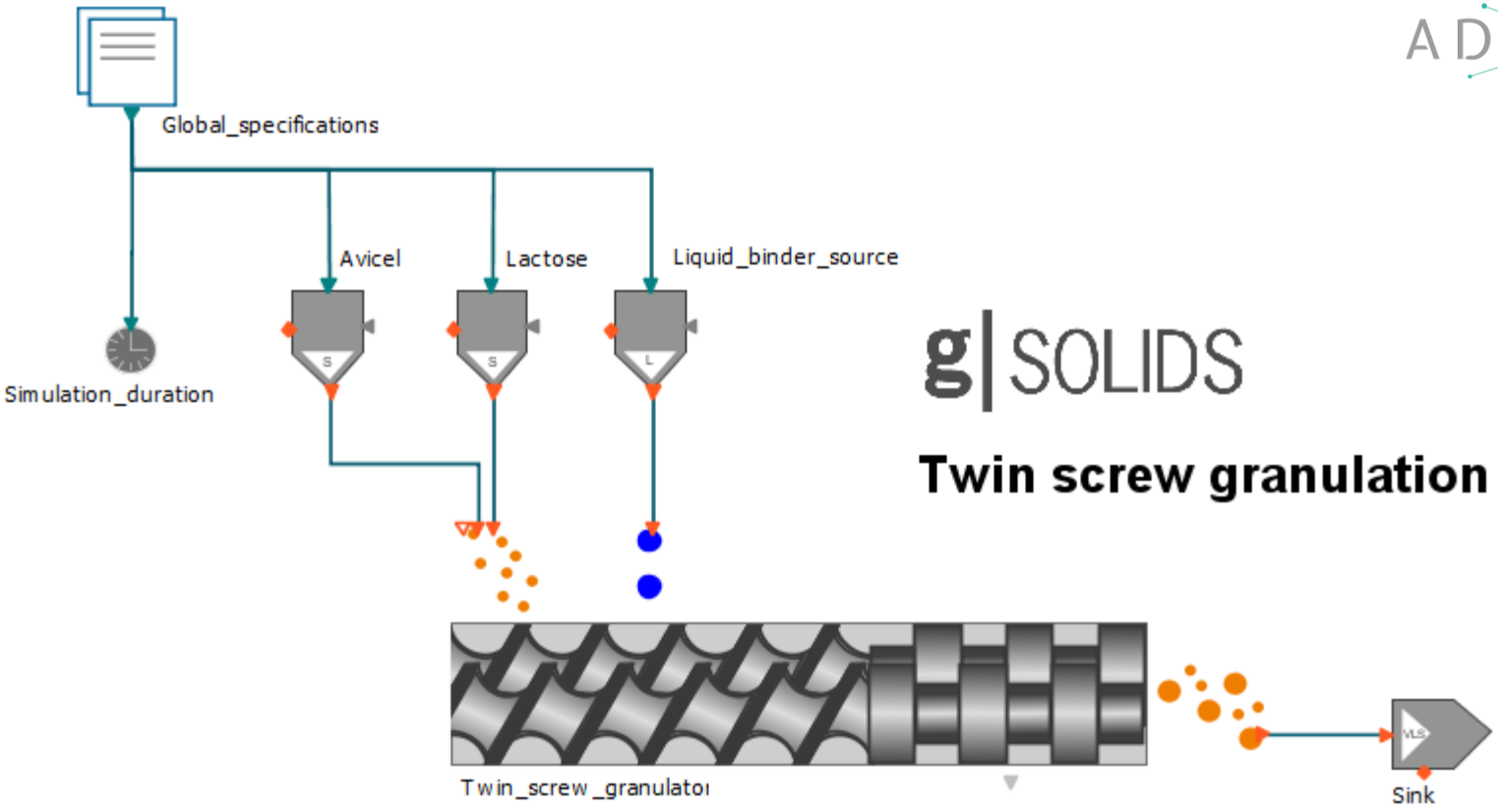


# Brings new features

- FormulatedProducts specific developments
  - Property package for species that may exist in solid (and fluid) phases
  - Databases
    - Material properties
    - Equipment dimensions and operating conditions
    - Physiology

- gPROMS platform developments
  - Switching units of measurement
    - Support for parameter estimation and optimisation
  - Global System Analysis
    - Uncertainty analysis
    - Sensitivity analysis

# Databases

- Flexible database structure compatible with
  - PSE provided databases
  - 3rd party databases
  - corporate databases, etc.

Materials

Dosage forms

Equipment

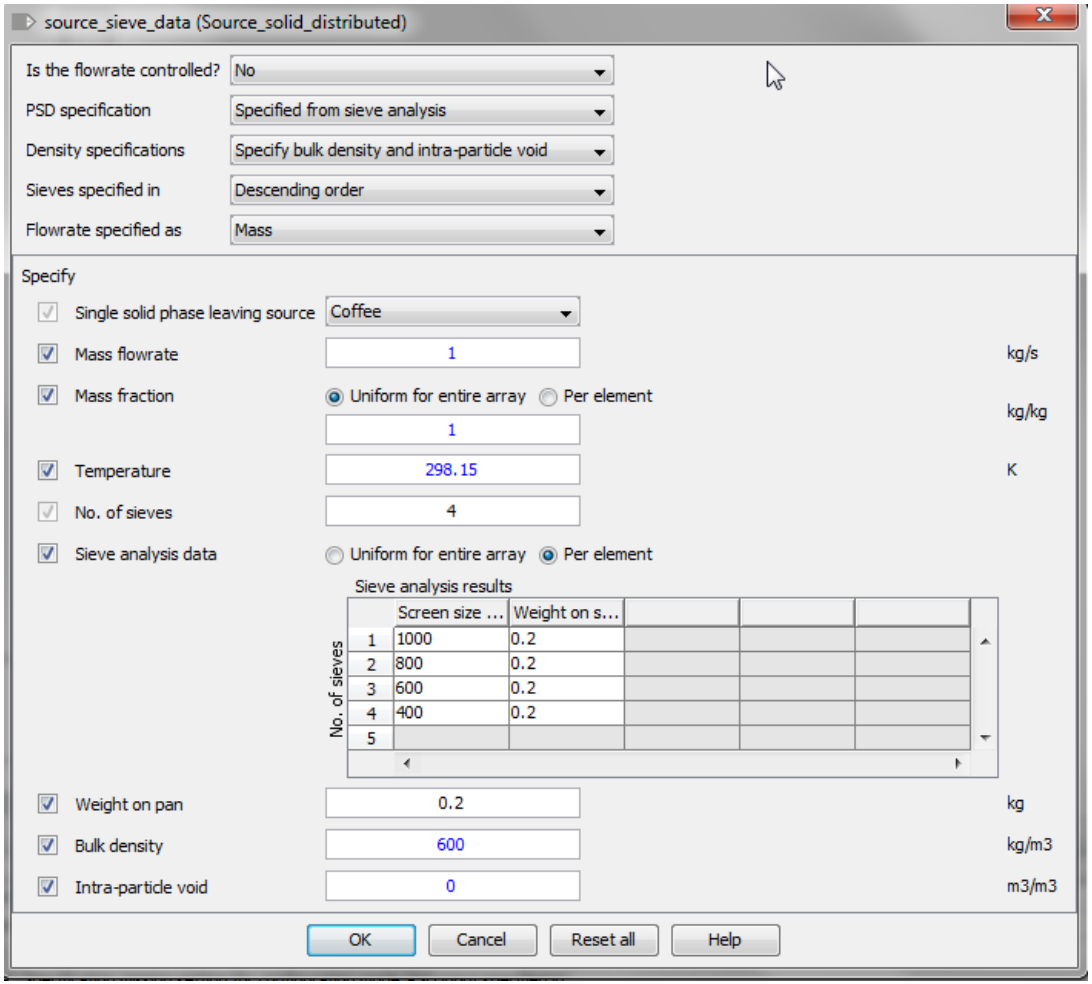
Physiology

- Significant increase in usability
  - single repository for validated data
  - less looking up of data
  - fewer transcription errors

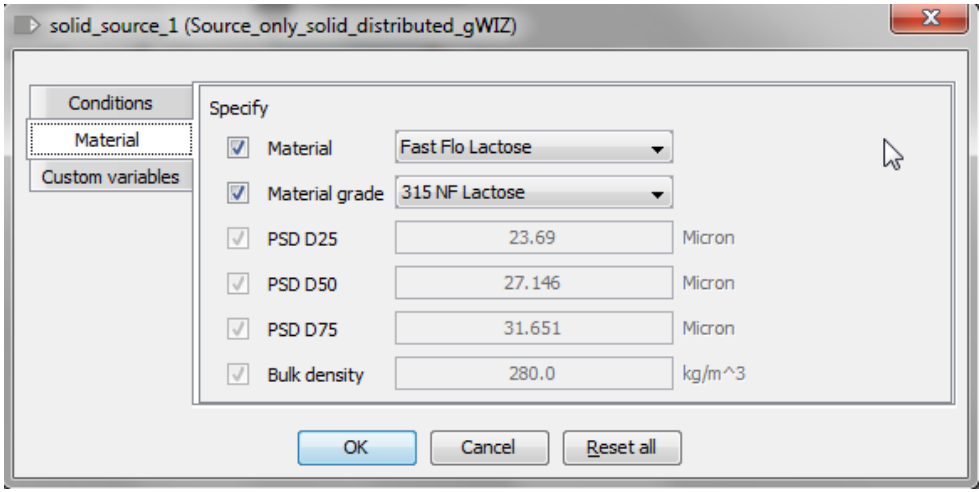
Significant increase in usability

# Material database

## Pre-database




## Using database

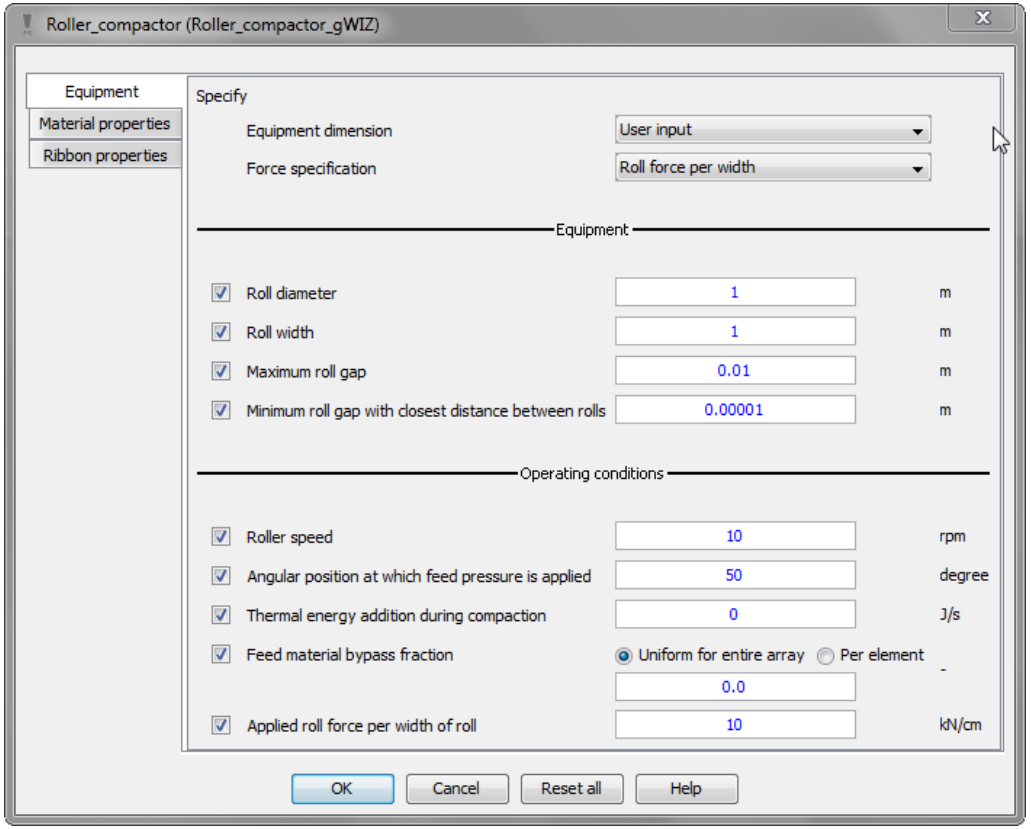



- Material list filtered by species available
- User now only needs to specify values for flowrate and temperature
- Custom material still a possibility: pre-database functionality

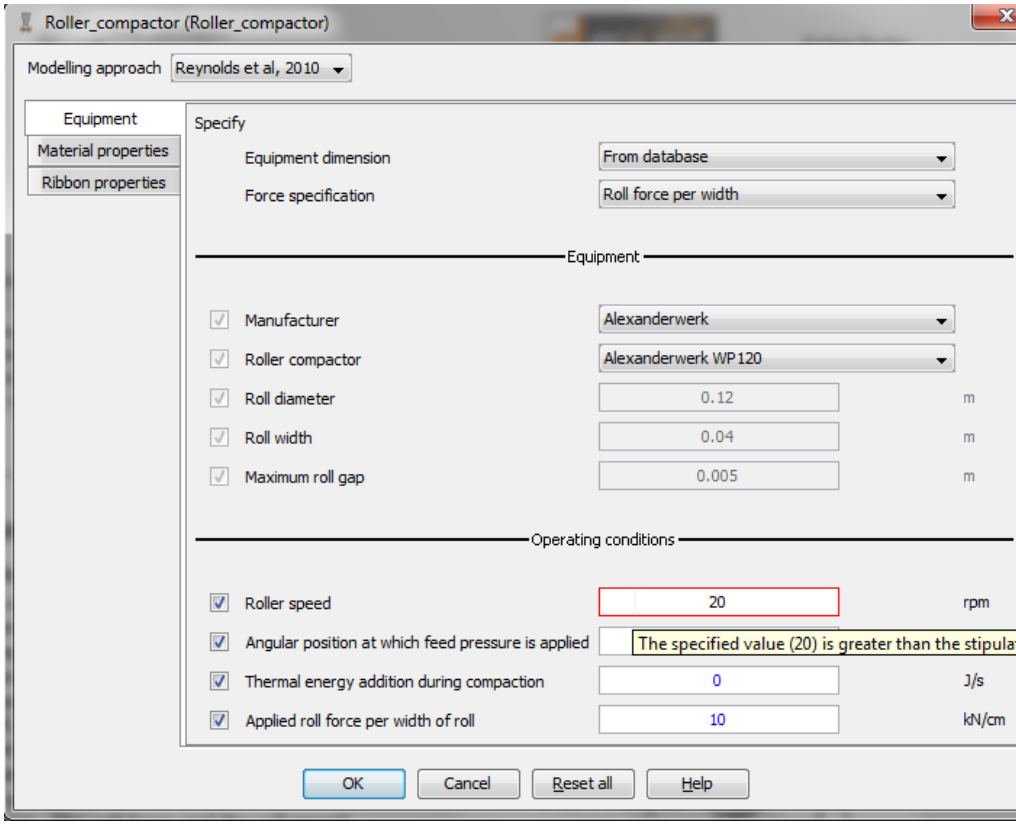
Significant increase in usability

# Equipment database

## Pre-database




## Using database

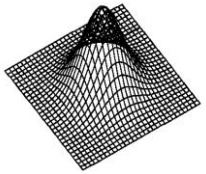



- User now only specifies operating conditions, which are verified against bounds also provided by the database
- Custom equipment still a possibility: pre-database functionality

# Manage risk by quantifying impact of uncertainty

Innovate UK collaborative R&D project on
**Global Systems Analysis**
AstraZeneca, Britest, GSK, Pfizer, PSE
2014/06 – 2016/05

**Environmental inputs**
External disturbances
Commercial environment



*Variability*

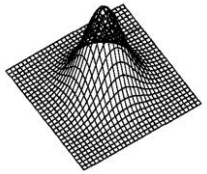
**Decisions**
- Design
- Operational

**System**

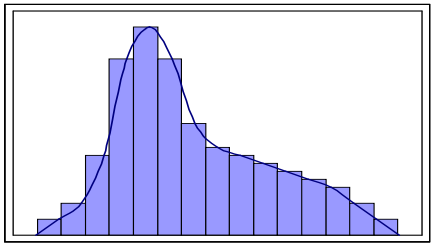
**Model**

*Uncertainty*

**Model parameters**



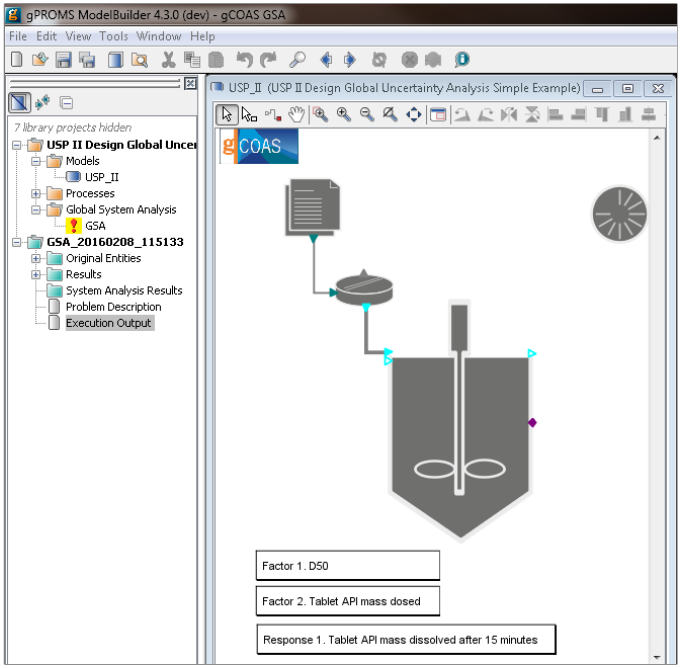
**KPIs**
- CQAs
- Process operability
- Process safety
- Environmental impact
- Economic performance



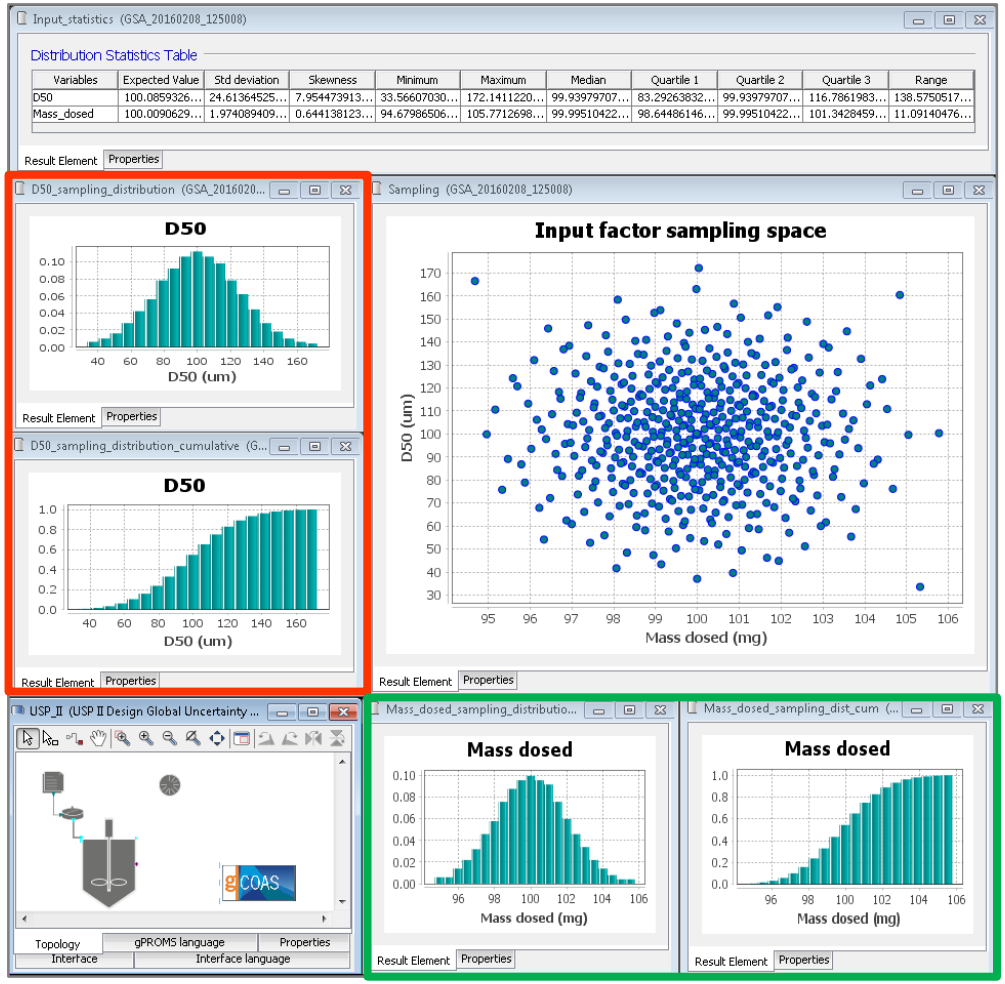
**Risk associated with model-based decisions**

# Tablet dissolution

## Biorelevant dissolution testing



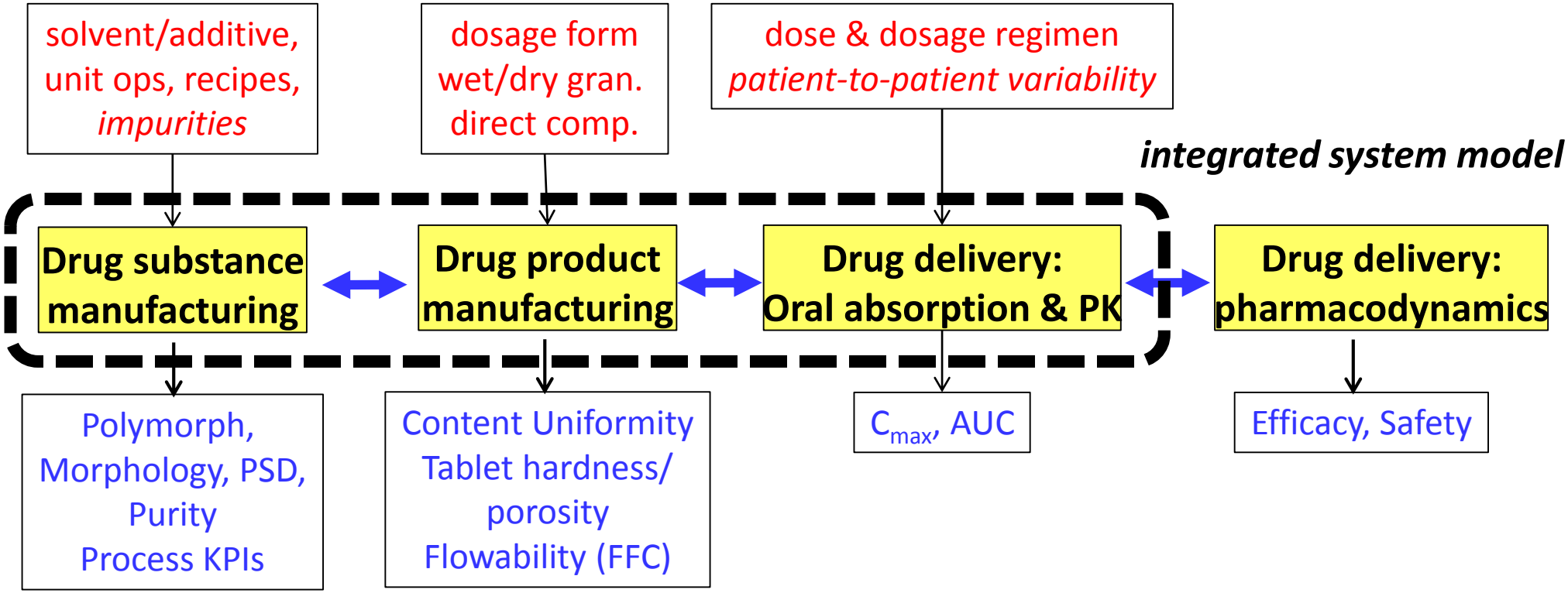

## Factor sampling space – D50 and dose mass



# Tablet dissolution

## Response space – showing effect of **D50** and **dose mass** on fraction dissolved

# Systems-based Pharmaceutics



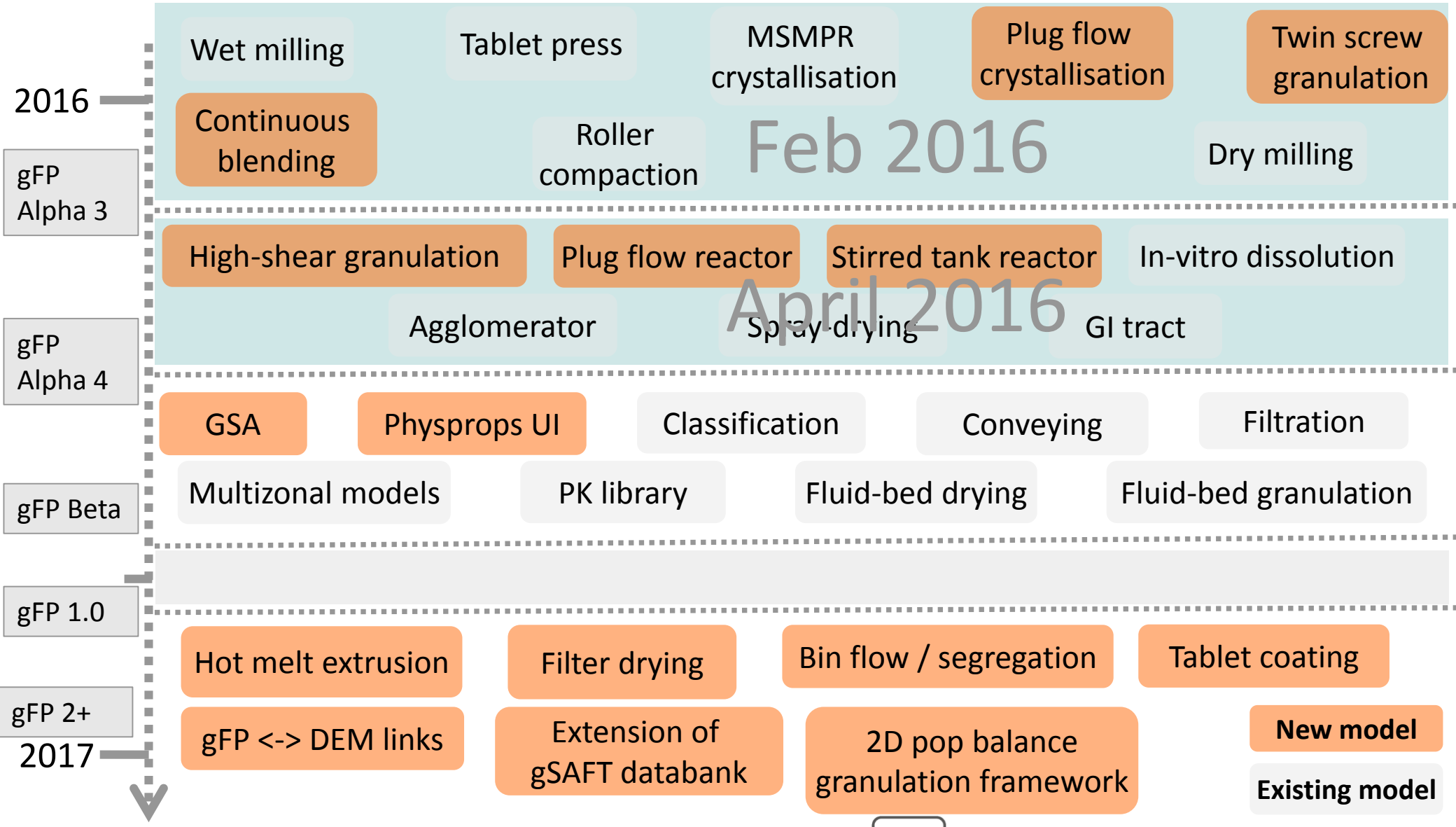

- Explore decision space effectively & efficiently
  - formal optimisation to eliminate trial-and-error
- Manage risk by quantifying impact of uncertainty

How? Use sensitivity analysis to quantify effect of upstream disturbances on variability in downstream performance.

# Roadmap

## gPROMS FormulatedProducts

# Scope and timelines

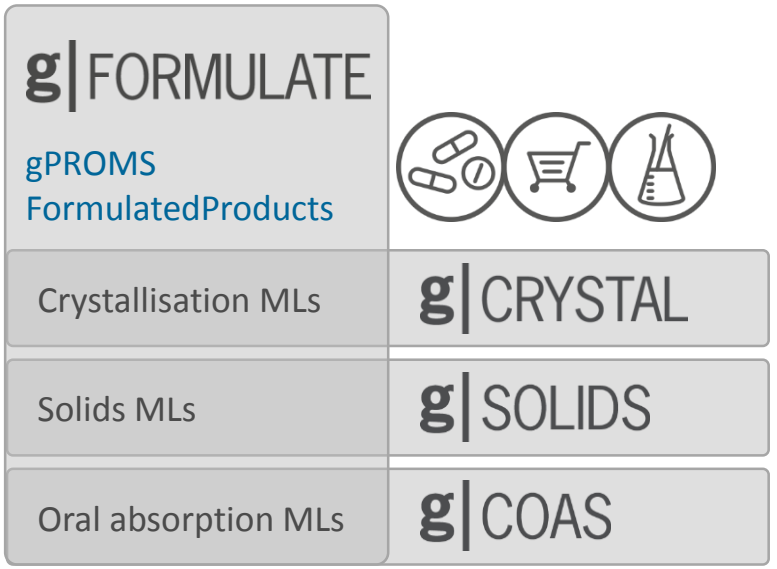


# Conclusions

gPROMS FormulatedProducts

# gPROMS FormulatedProducts contains functionality previously offered by four different PSE products

- gCRYSTAL, gSOLIDS and gCOAS
  - no longer standalone products
  - now modules (libraries, examples and documentation) within gPROMS FormulatedProducts




- Custom modelling
  - and other ModelBuilder functionality
- Hence reduces number of (installers for) PSE products from four to one, with significant advantages to both
  - users of these products
  - IT departments

# An extendible platform for realising the vision of systems-based approaches for formulated products

- Systems-based Pharmaceutics Alliance
  - Phase 1: Eli Lilly and Pfizer; $1,200k; Oct 2013 – Oct 2015
  - Phase 2: Eli Lilly, Pfizer, … ; $1,200k+; Dec 2015 – Dec 2017

sbp

- Digital Design: £444k; 3 FTE over 2 years till Jun 2016
  - Global System Analysis
  - AstraZeneca, Britest, GSK and Pfizer

- ReMediES
  RE-configuring MEDIcines End-to-end Supply
  £400k; 1.6 FTE over 4 years till Jan 2018
  - Continuous drug product manufacture
  - AstraZeneca, GSK, GEA, Britest, Perceptive Engineering and ~20 others

- ADD-P-T £3,600k; 10 FTEs over 4 years till March 2019 – 480 person-months
  - Multi-scale modelling, Solubility, Sensor models, Big data and support for Operations
  - AstraZeneca, BMS, GSK, Pfizer, Britest, Perceptive Engineering, CCDC, STFC, U. Leeds, U. Strathclyde, Cambridge U.

# An extendible platform for realising the vision of systems-based approaches for formulated products

- Increased focus on models for food industries
  - Manufacture (Thu PM meeting)
  - product performance


- Complex liquids: emulsions, dispersions, gels, …
- Other product performance aspects
  - e.g. product stability

# Acknowledgments

gPROMS FormulatedProducts

# Acknowledgments


- Formulated Products team
- Software Technology Group
- Formulated Products Advisory Board

# Thank you

# Transitioning from gCRYSTAL, gSOLIDS and gCOAS

## gPROMS FormulatedProducts

# Transitioning from gCRYSTAL, gSOLIDS and gCOAS

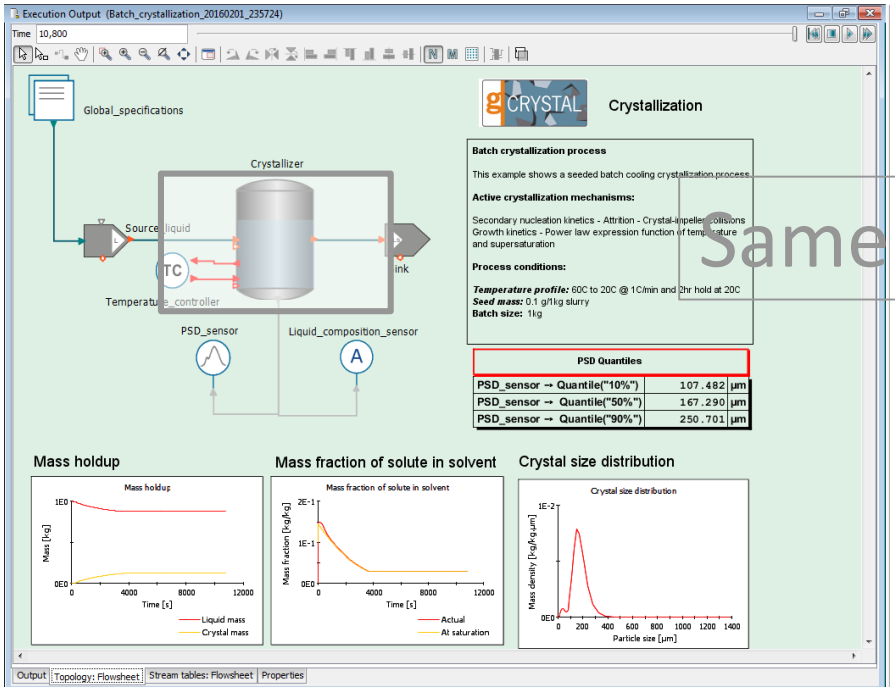
- Licensing
  - existing customers will be issued with a new set of licences covering their existing functionality
- Backward compatibility
  - physical property specifications – yes
  - specifications of unit operation and other models – partial
- PSE's recommendation
  - use FormulatedProducts 1.0 for new applications
  - for existing applications
    - continue using gCRYSTAL, gSOLIDS or gCOAS until we have introduced necessary platform functionality to fully address backward compatibility
    - Work with the Formulated Products team to manually convert models

# Features

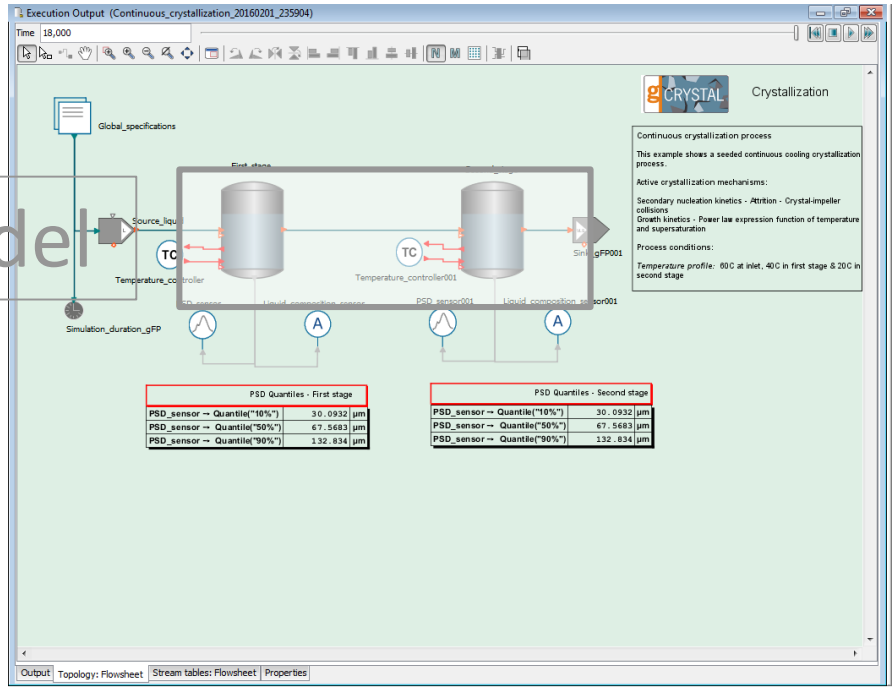
## gPROMS FormulatedProducts

# Batch and continuous operation

## Batch crystallization

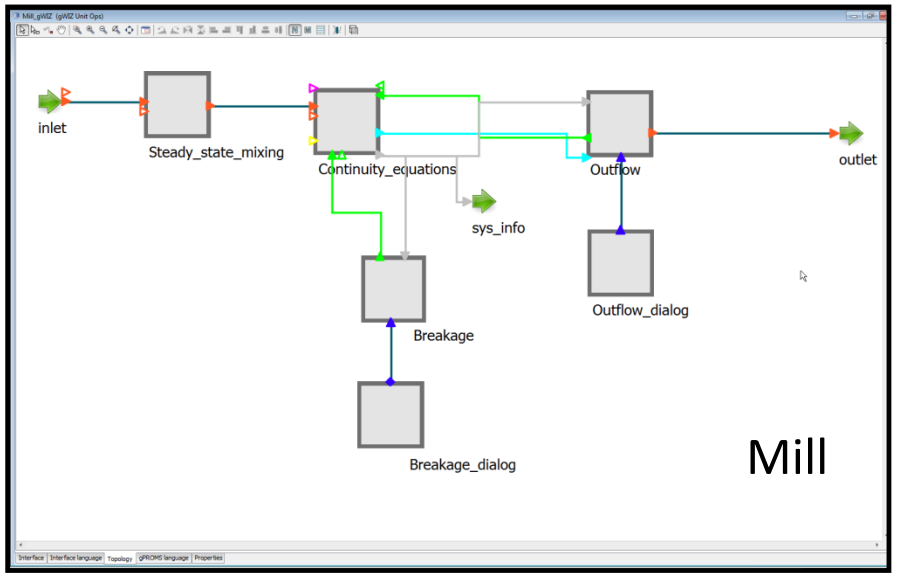


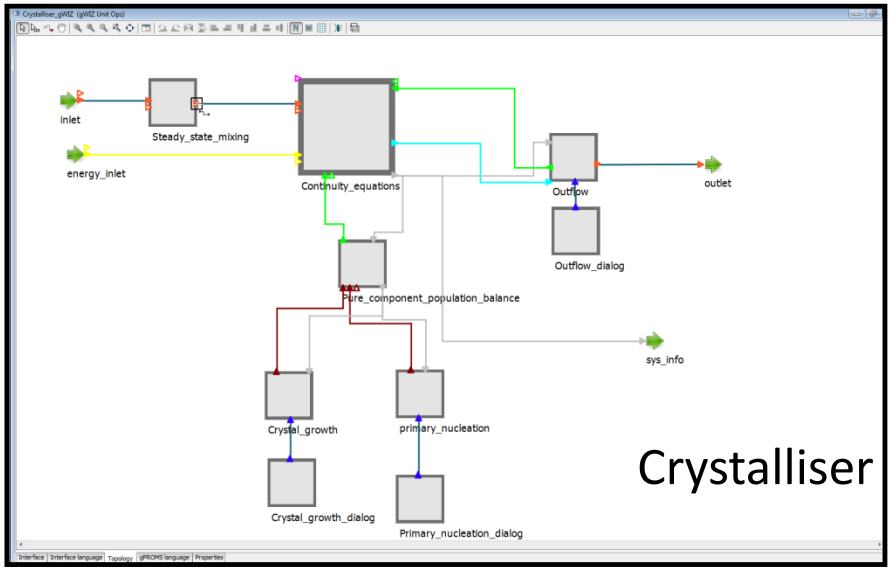

## Continuous crystallization




Same model

# Consistent internal structure across all models



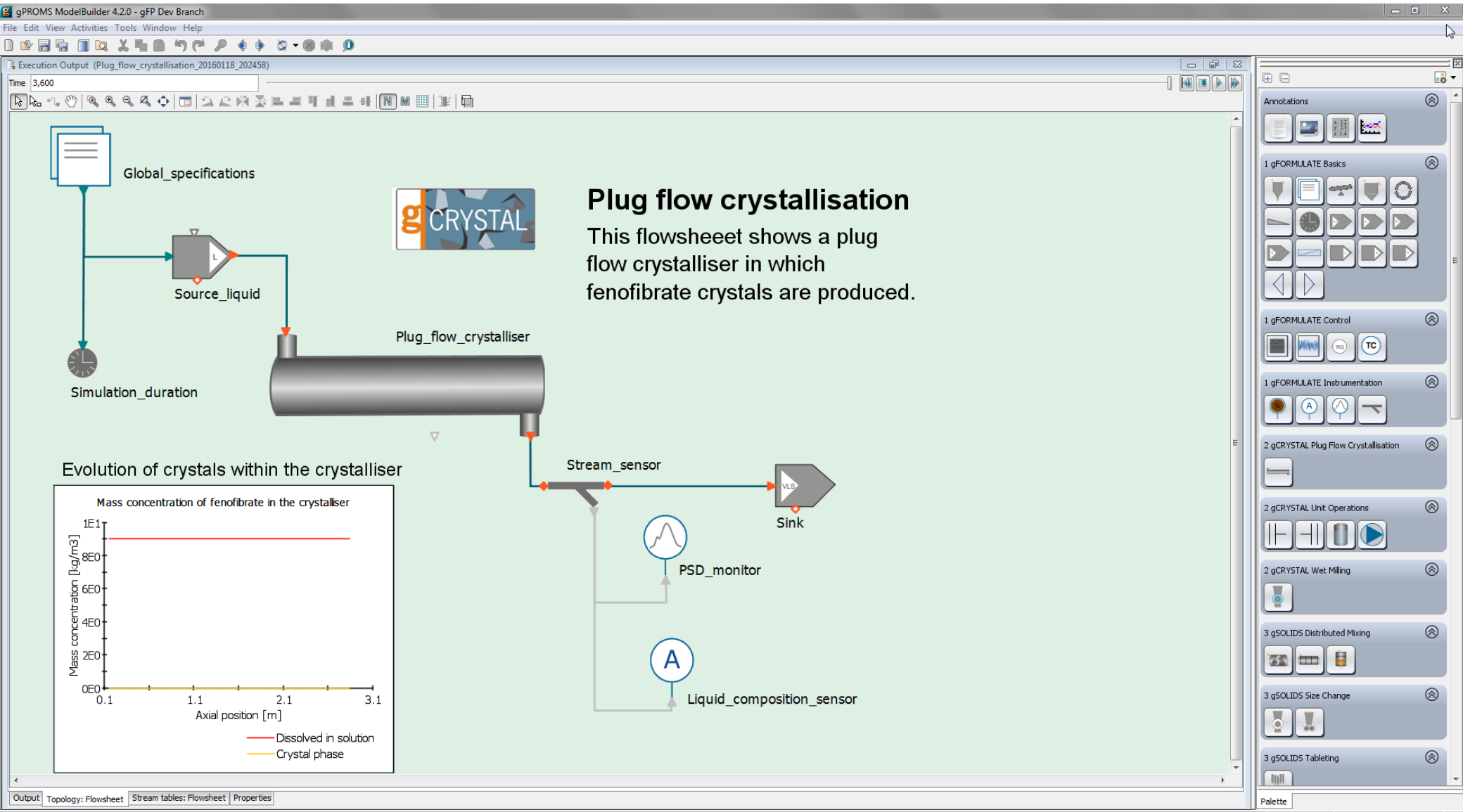




- "Mix and match" physical phenomena between different library models
- Consistency in code base, user interfaces and databases

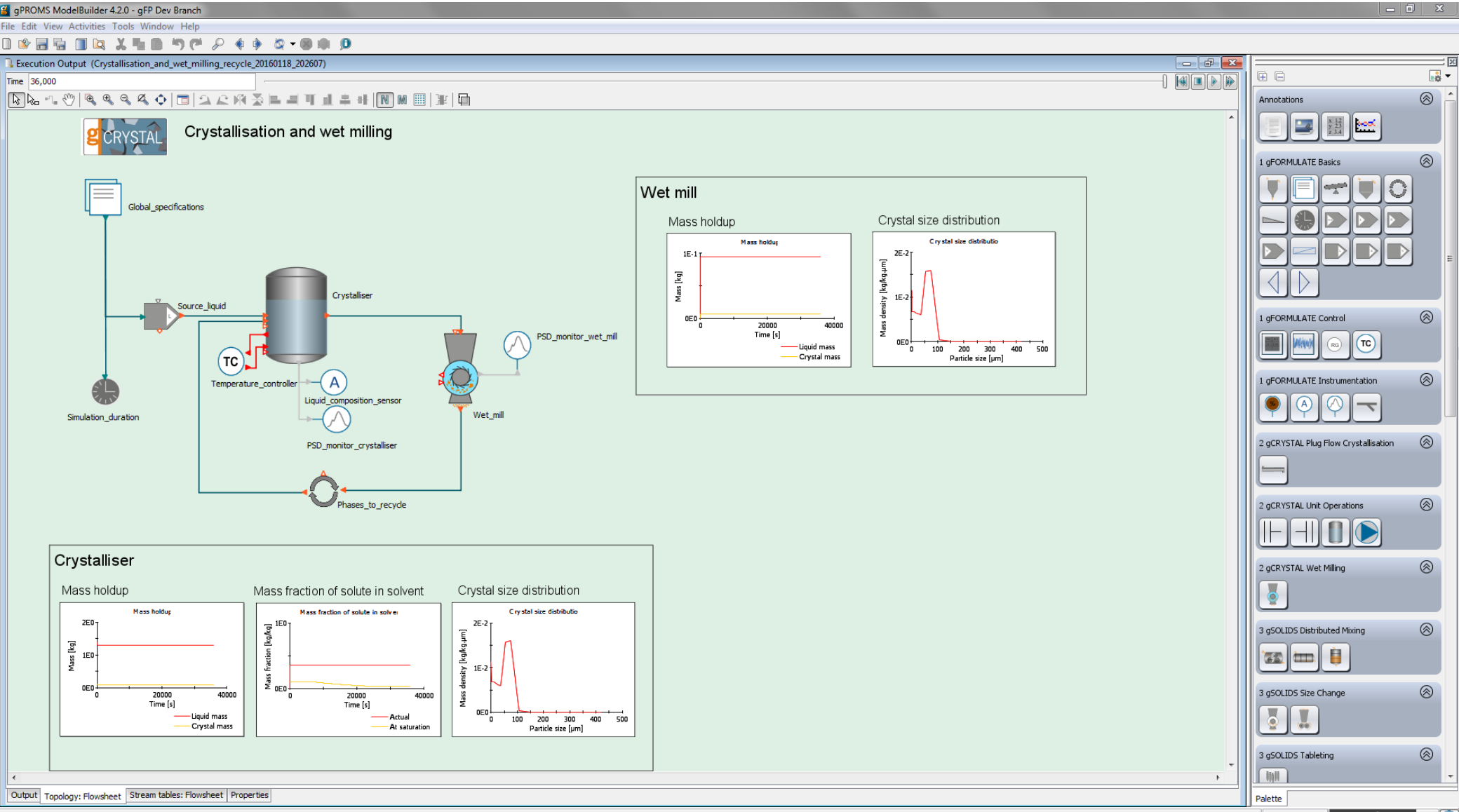
# Example applications

## gPROMS FormulatedProducts

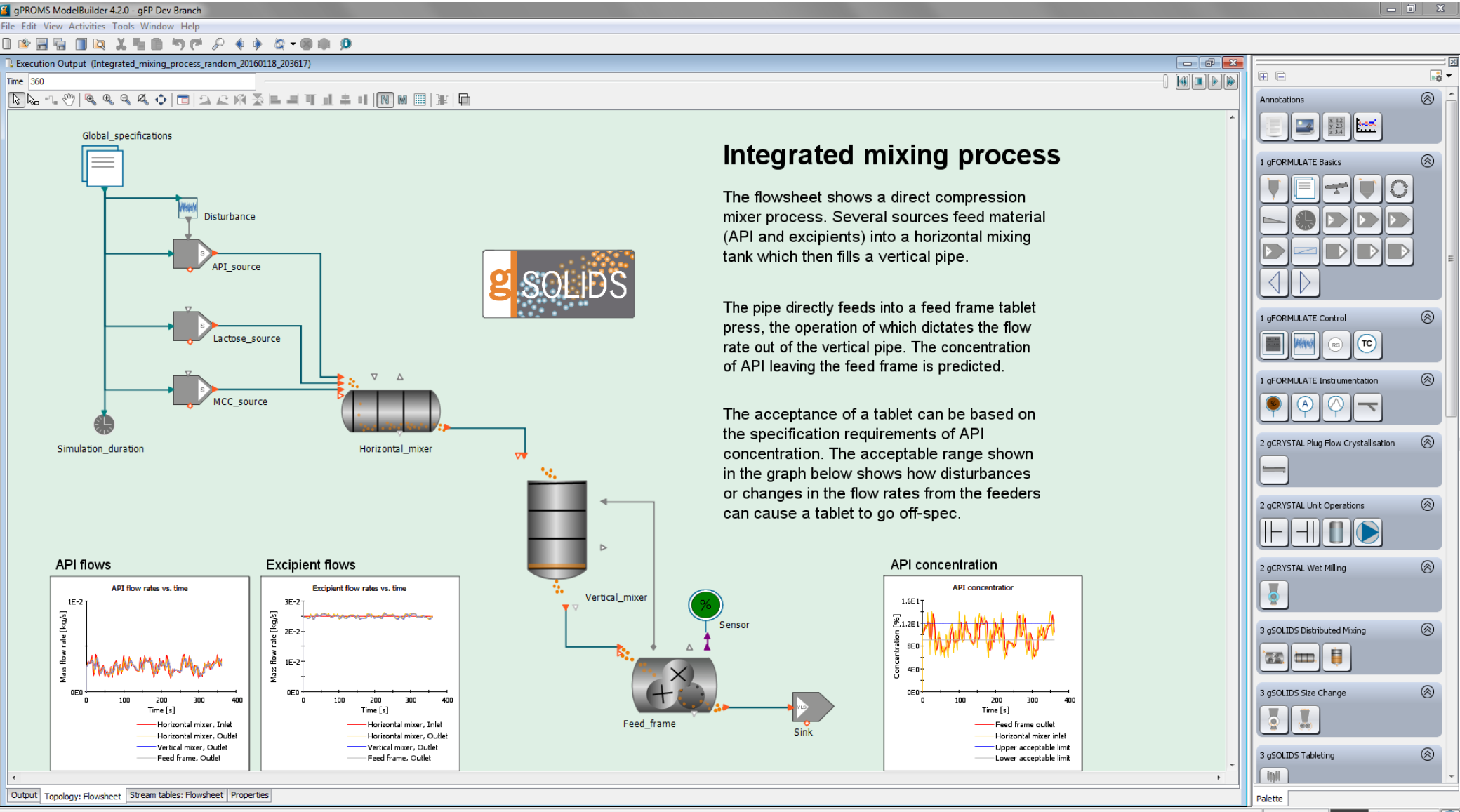
# Plug flow crystallisation



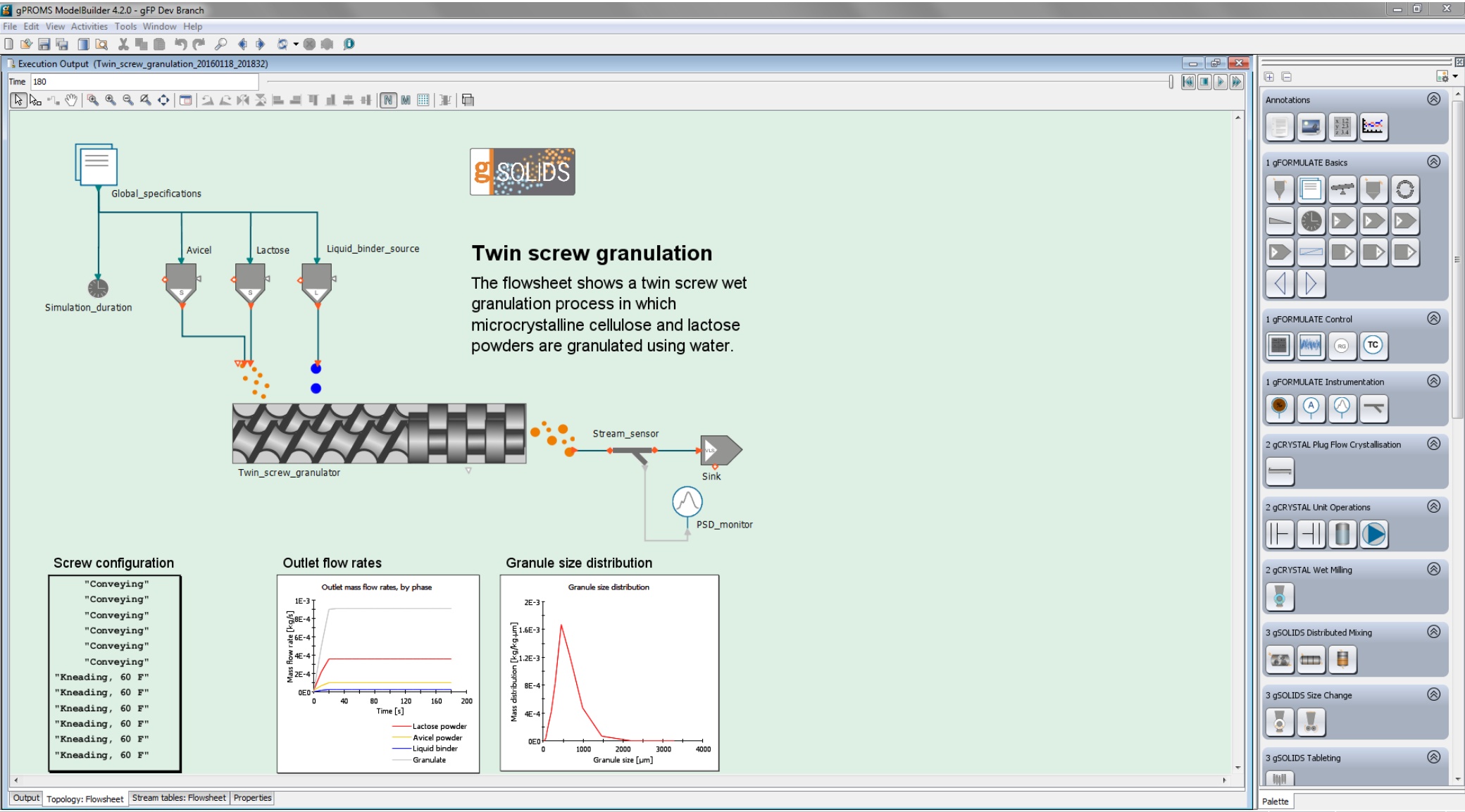
# Wet milling



# Continuous manufacture



# Twin screw granulation



# Tablet disintegration