ADVANCED PROCESS MODELLING FORUM 2017
London 25–26 April

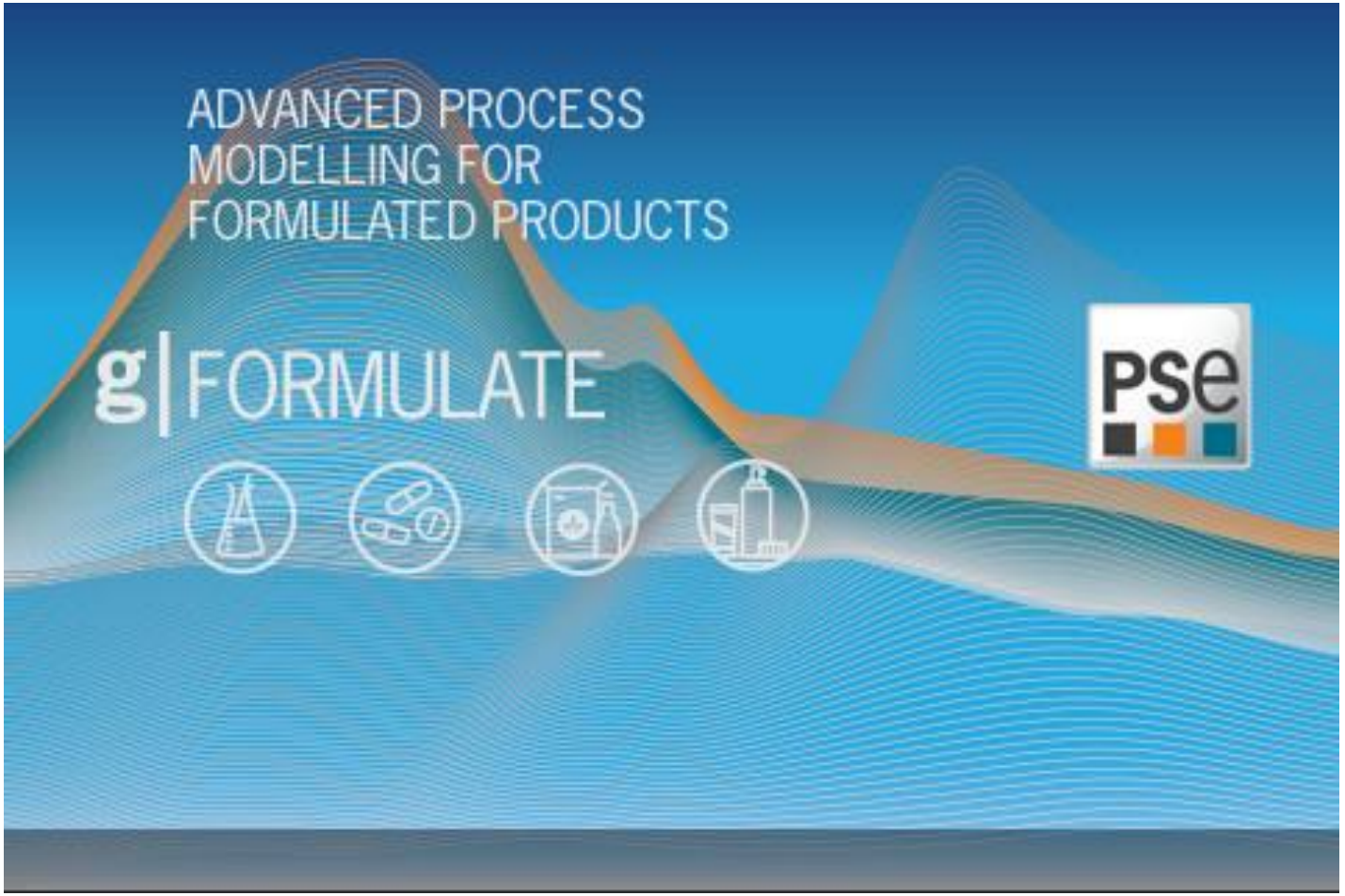
Introducing gPROMS FormulatedProducts

A comprehensive, integrated design tool for formulated products manufacture

Dana Barrasso – Senior Consultant

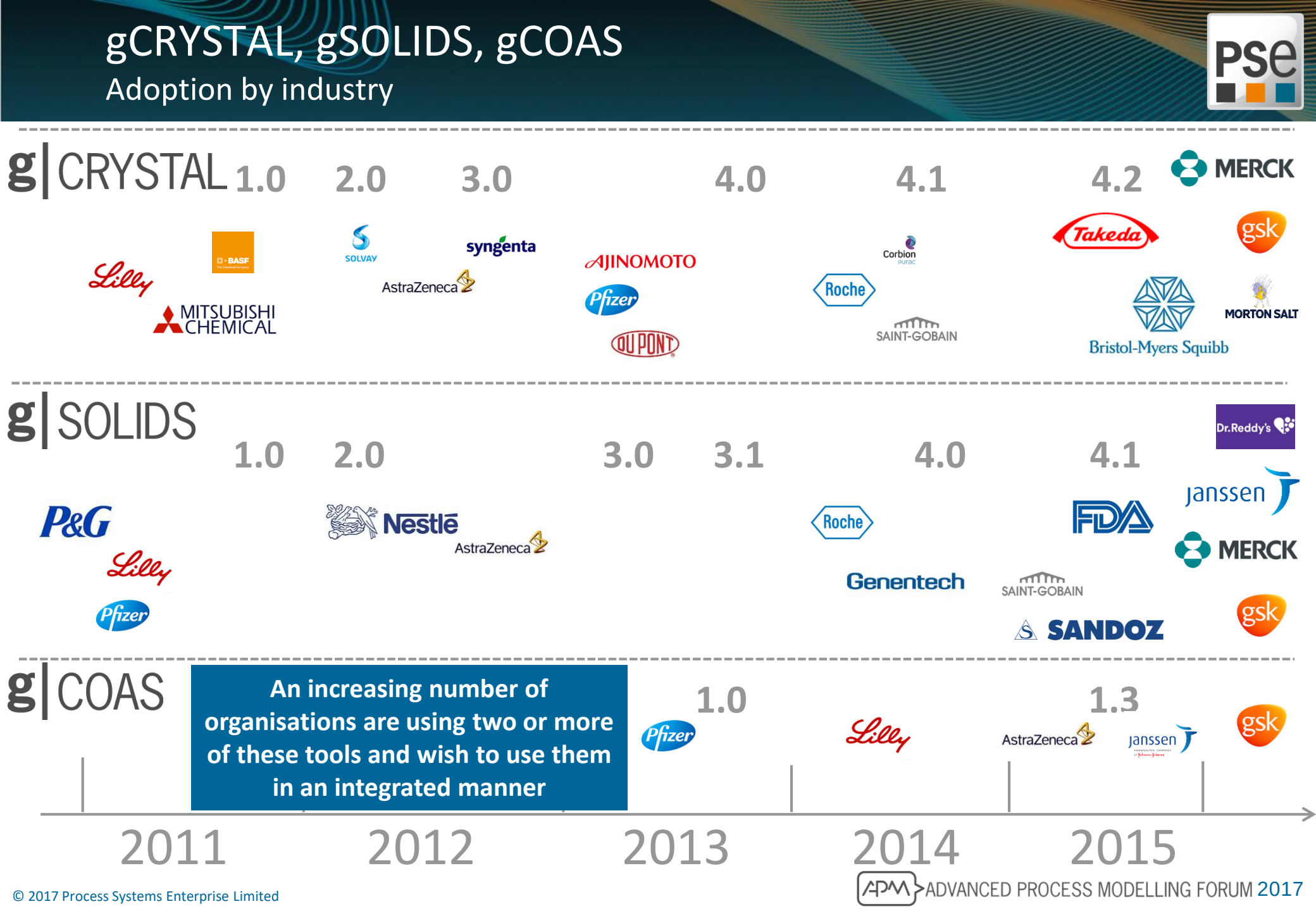
A “new” PSE product

gPROMS FormulatedProducts



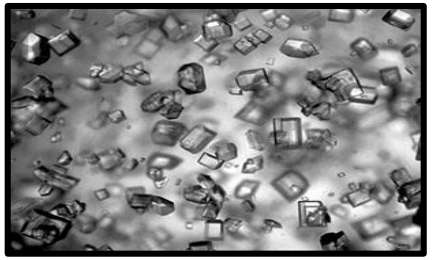
gCRYSTAL, gSOLIDS, gCOAS

Adoption by industry

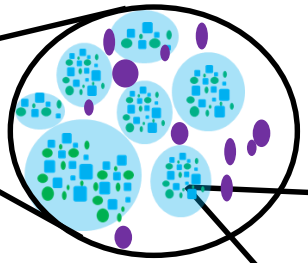


Scope

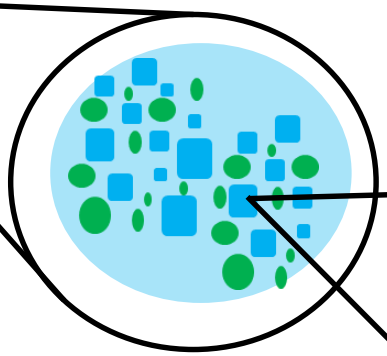
- **Active Ingredients**
  - Process development
  - Manufacture
- **Formulations**
  - Product & process development
  - Manufacture
- **Product performance**
  - Oral absorption
  - *Product stability*
  - *Dermal absorption*
  - *Food digestion*
  - *Agrochemical take-up by plants*
  - . . . . . .



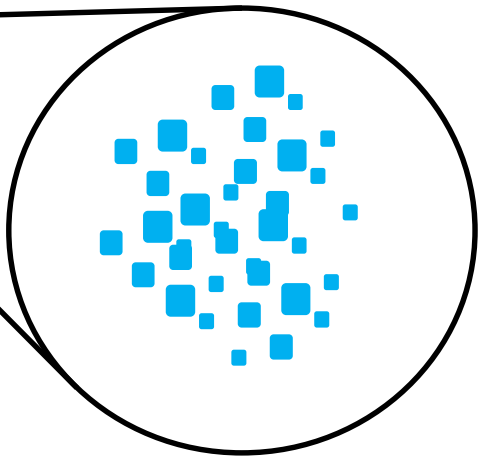
Description of complex material structures



Tablet structure, e.g.
- Granule PSD
- Extra granular excipient
- Ungranulated API / excipient

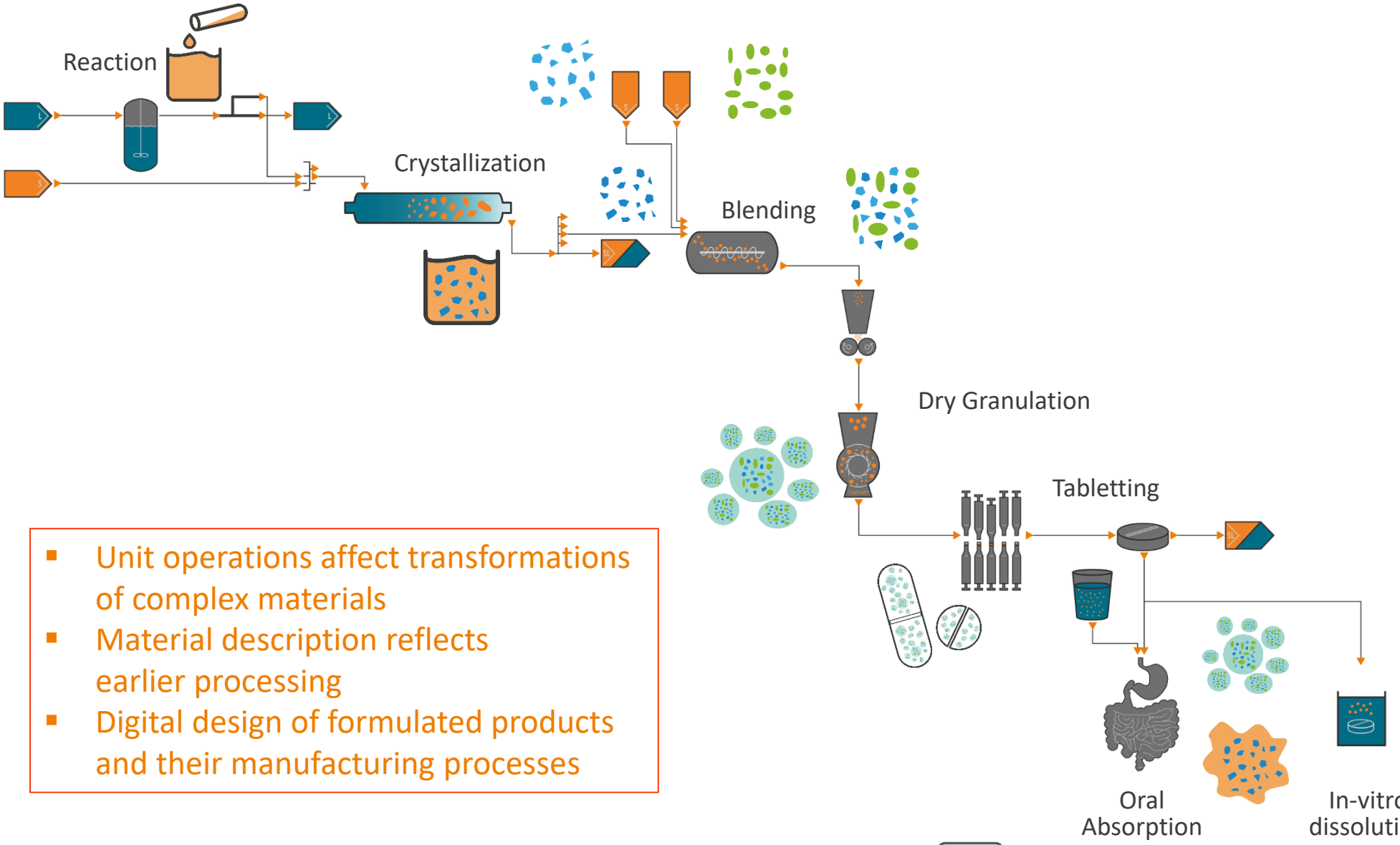


Granule structure, e.g.
- PSD of primary particles (API & excipient)
- Porosity or liquid content



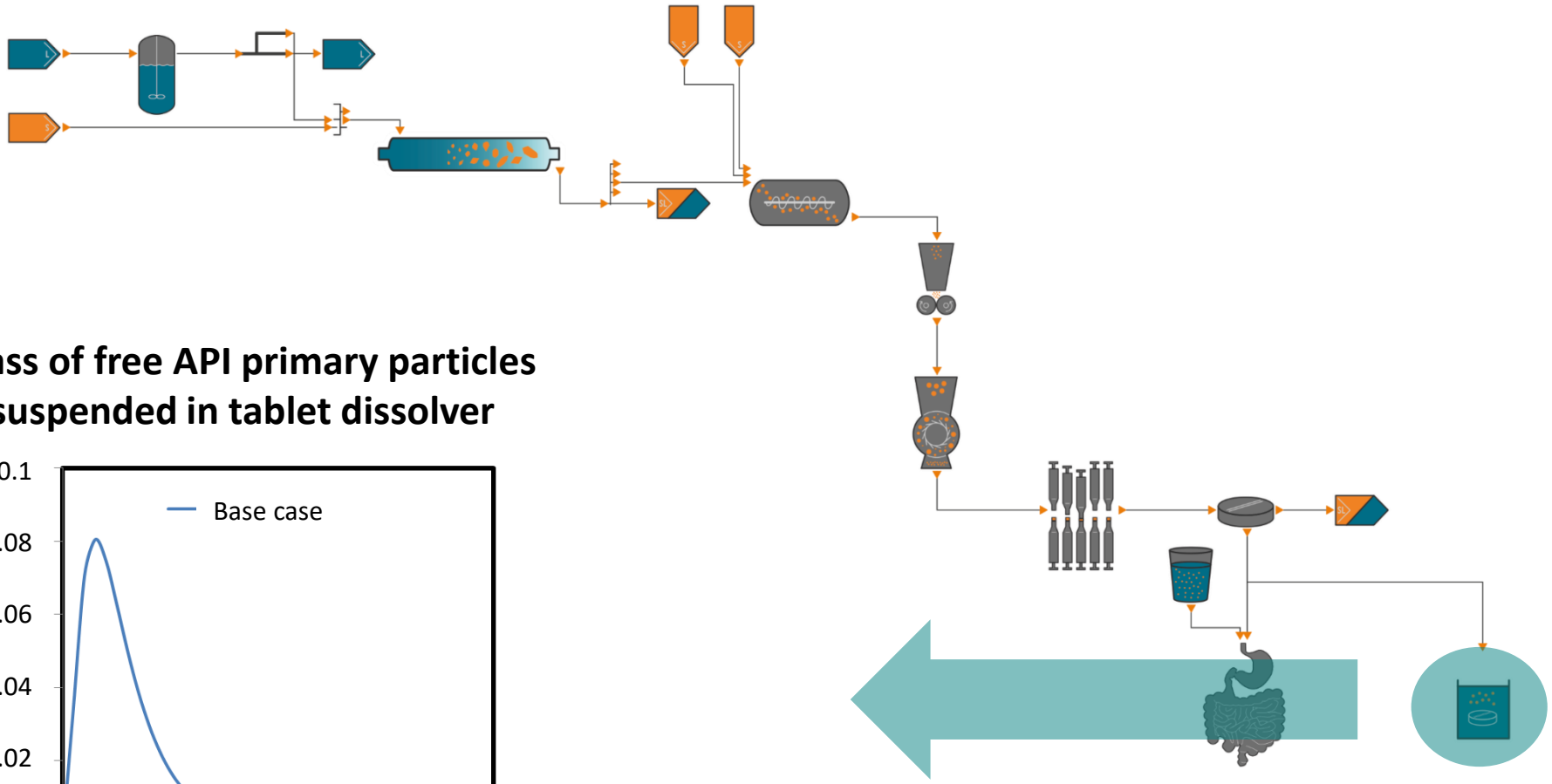
Primary particles, e.g.
- Impurities
- Shape

Linking manufacture directly to product performance



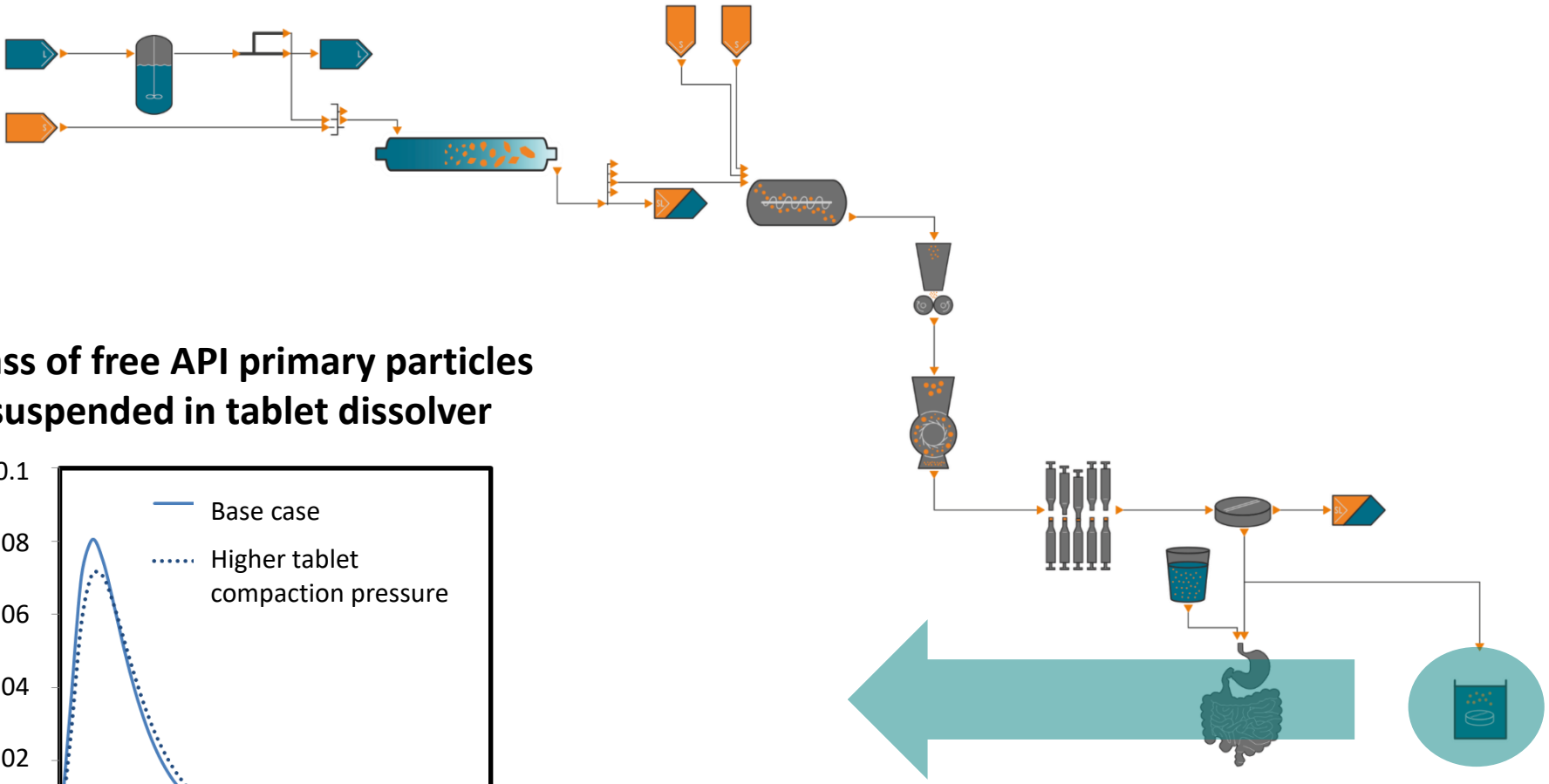
- Unit operations affect transformations of complex materials
- Material description reflects earlier processing
- Digital design of formulated products and their manufacturing processes

Linking manufacture directly to product performance



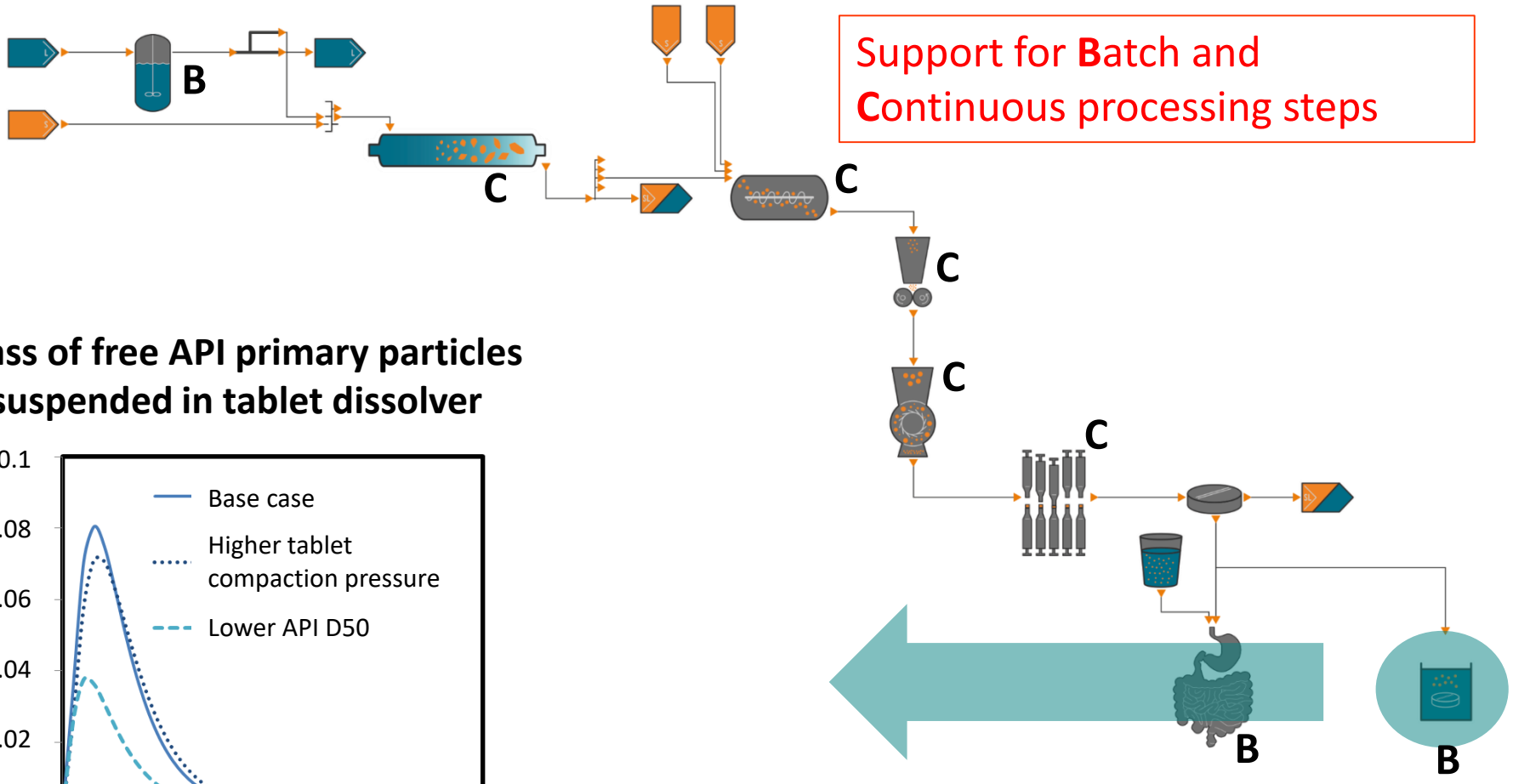
Mass of free API primary particles suspended in tablet dissolver

Linking manufacture directly to product performance



Mass of free API primary particles suspended in tablet dissolver

Linking manufacture directly to product performance



Support for **B**atch and
Continuous processing steps

Mass of free API primary particles suspended in tablet dissolver

gPROMS FormulatedProducts

Model libraries and features

Synthesis and Crystallization

- Well-mixed reactor
- Plug flow reactor
- Well-mixed crystallizer
- Plug flow crystallizer
- Wet mill
- Pressure filter
- Filter dryer

Solids Processing

- Dry mill
- Roller compactor
- Agglomerator
- High shear wet granulator
- Twin screw granulator
- Fluid-bed granulation
- 2D pop balance granulation framework
- Fluid-bed drying
- Spray drying
- Hot melt extruder
- Lyophilization
- Tablet press
- Conveying
- Tablet coater
- Continuous blenders
- Film coater
- Bin flow / segregation

Product Performance

- In-vitro dissolution and precipitation
- Oral absorption in GI tract
- Pharmacokinetics
- Stability

- Properties GUI
- Data import and processing
- Global Sensitivity Analysis
- Parallelisation of GSA and PE
- Multizonal models
- gFP <- > DEM links
- Extension of gSAFT databank

Transferred from gCRYSTAL, gSOLIDS or gCOAS

New in gPROMS FormulatedProducts

In development

Database capabilities

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

Materials

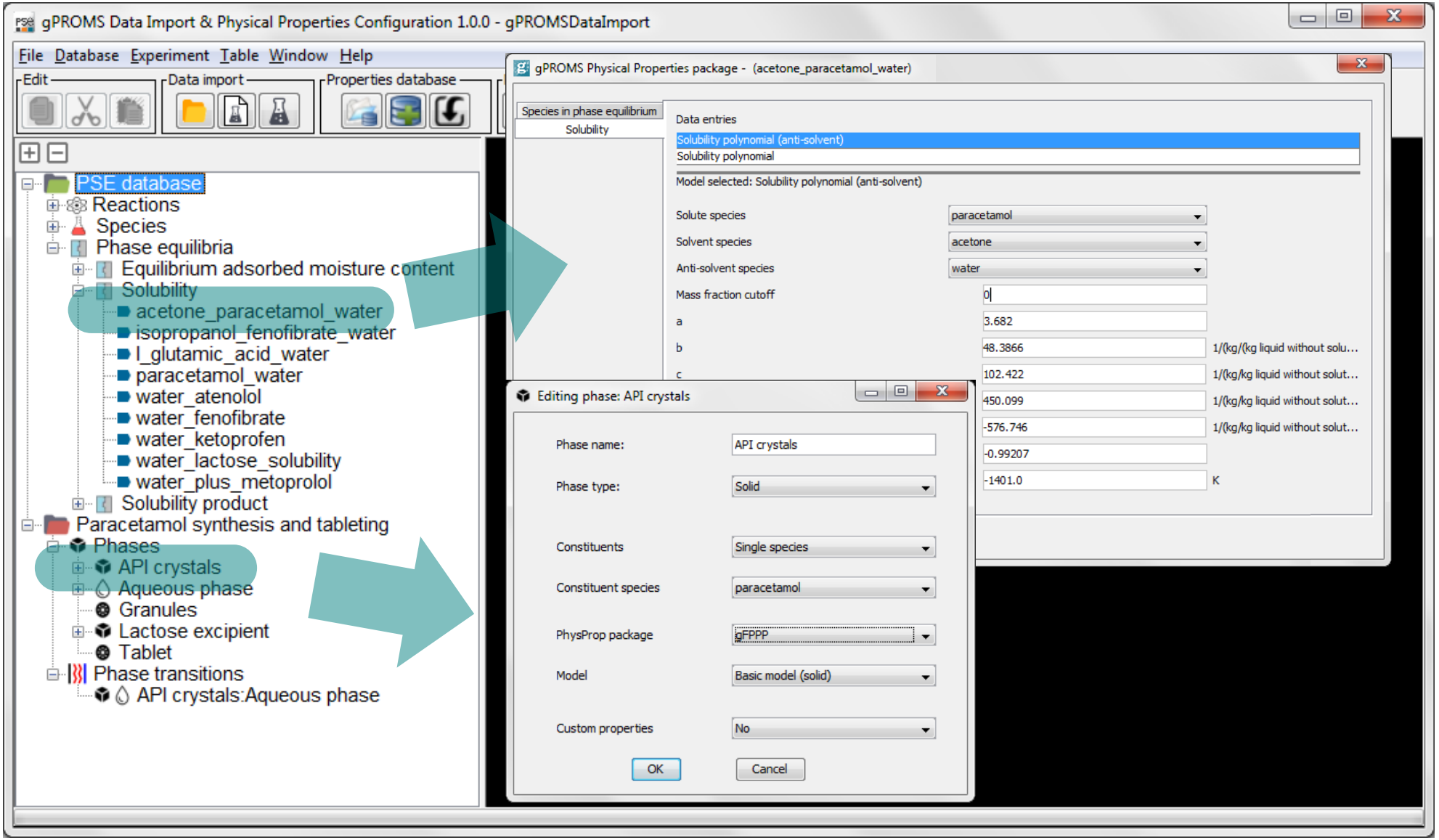
Dosage forms

Equipment

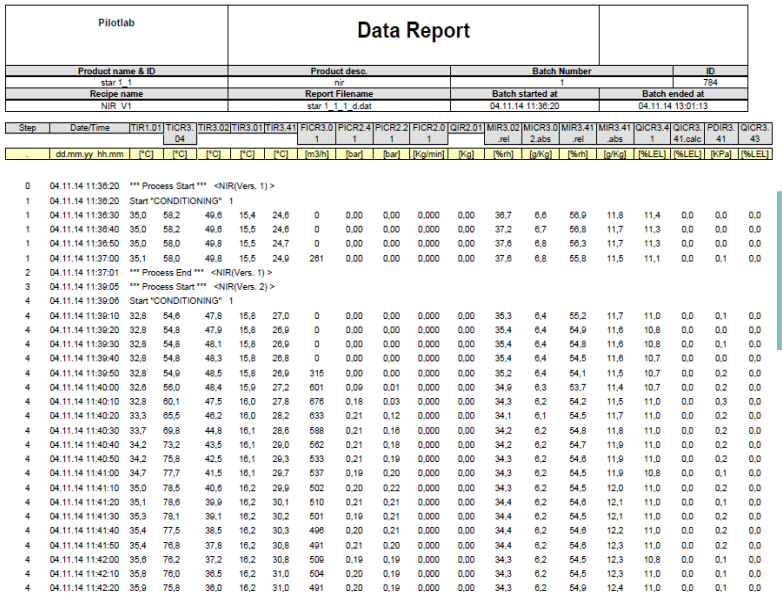
Physiology

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

Database management



Data import and processing – **previously**

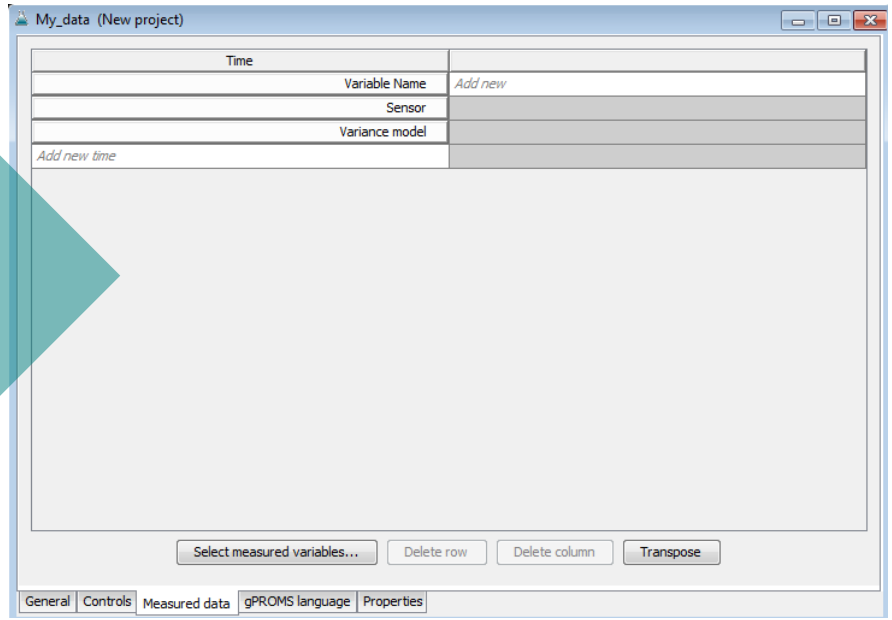


Pilotlab

Data Report

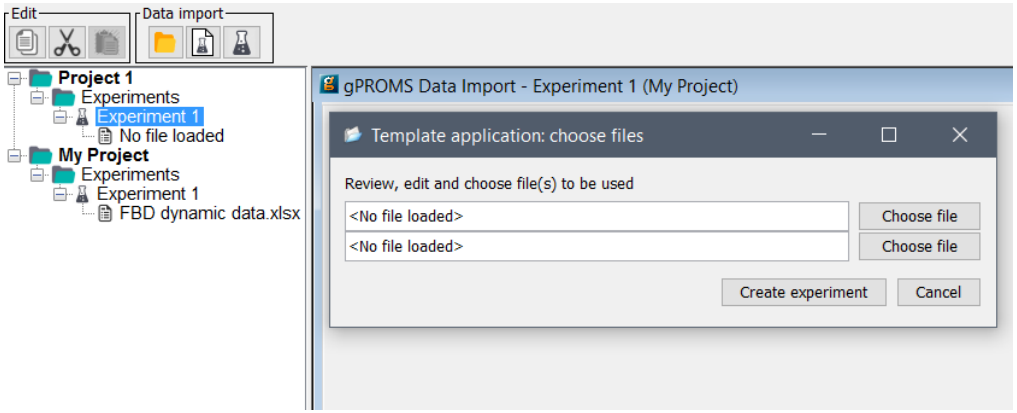
Product name & ID	Product desc.	Batch Number	ID
star 1_1	nir	1	784
Recipe name	**Report Filename**	**Batch started at**	**Batch ended at**
NIR_V1	star 1_1_1_d.dat	04.11.14 11:36:20	04.11.14 13:01:13

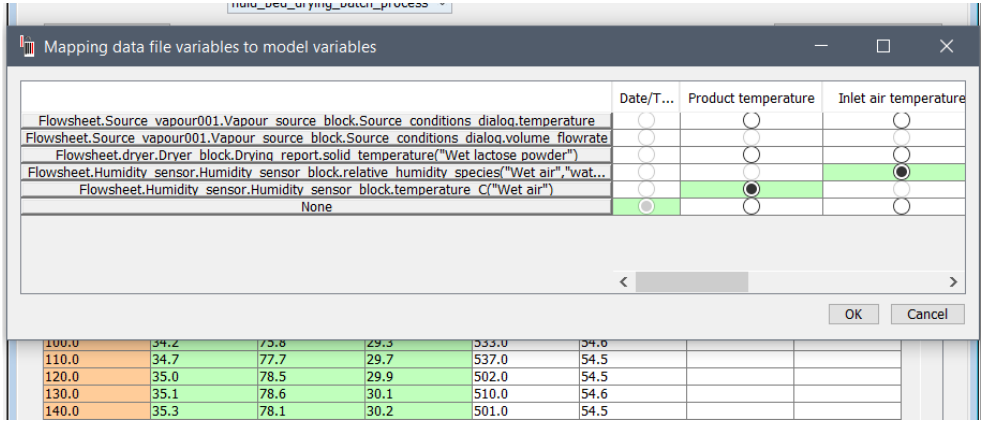
Step	Date/Time	TIR1.01	TICR3.04	TIR3.02	TIR3.01	TIR3.41	FICR3.01	FICR2.41	FICR2.21	FICR2.01	QIR2.01	MIR3.02.rel	MICR3.02.abs	MIR3.41.rel	MIR3.41.abs	QICR3.41	QICR3.41.calc	PDIR3.41	QICR3.43
-	dd.mm.yy hh.mm	[°C]	[°C]	[°C]	[°C]	[°C]	[m3/h]	[bar]	[bar]	[Kg/min]	[Kg]	[%rh]	[g/Kg]	[%rh]	[g/Kg]	[%LEL]	[%LEL]	[KPa]	[%LEL]
0	04.11.14 11:36:20	*** Process Start *** <NIR(Vers. 1) >																	
1	04.11.14 11:36:20	Start "CONDITIONING" 1																	
1	04.11.14 11:36:30	35,0	58,2	49,6	15,4	24,6	0	0,00	0,00	0,000	0,00	36,7	6,6	56,9	11,8	11,4	0,0	0,0	0,0
1	04.11.14 11:36:40	35,0	58,2	49,6	15,5	24,6	0	0,00	0,00	0,000	0,00	37,2	6,7	56,8	11,7	11,3	0,0	0,0	0,0
1	04.11.14 11:36:50	35,0	58,0	49,8	15,5	24,7	0	0,00	0,00	0,000	0,00	37,6	6,8	56,3	11,7	11,3	0,0	0,0	0,0
1	04.11.14 11:37:00	35,1	58,0	49,8	15,5	24,9	261	0,00	0,00	0,000	0,00	37,6	6,8	55,8	11,5	11,1	0,0	0,1	0,0
2	04.11.14 11:37:01	*** Process End *** <NIR(Vers. 1) >																	
3	04.11.14 11:39:05	*** Process Start *** <NIR(Vers. 2) >																	
4	04.11.14 11:39:06	Start "CONDITIONING" 1																	
4	04.11.14 11:39:10	32,8	54,6	47,8	15,8	27,0	0	0,00	0,00	0,000	0,00	35,3	6,4	55,2	11,7	11,0	0,0	0,1	0,0
4	04.11.14 11:39:20	32,8	54,8	47,9	15,8	26,9	0	0,00	0,00	0,000	0,00	35,4	6,4	54,9	11,6	10,8	0,0	0,0	0,0
4	04.11.14 11:39:30	32,8	54,8	48,1	15,8	26,9	0	0,00	0,00	0,000	0,00	35,4	6,4	54,8	11,6	10,8	0,0	0,1	0,0
4	04.11.14 11:39:40	32,8	54,8	48,3	15,8	26,8	0	0,00	0,00	0,000	0,00	35,4	6,4	54,5	11,6	10,7	0,0	0,0	0,0
4	04.11.14 11:39:50	32,8	54,9	48,5	15,8	26,9	315	0,00	0,00	0,000	0,00	35,2	6,4	54,1	11,5	10,7	0,0	0,2	0,0
4	04.11.14 11:40:00	32,6	56,0	48,4	15,9	27,2	601	0,09	0,01	0,000	0,00	34,9	6,3	53,7	11,4	10,7	0,0	0,2	0,0
4	04.11.14 11:40:10	32,8	60,1	47,5	16,0	27,8	676	0,18	0,03	0,000	0,00	34,3	6,2	54,2	11,5	11,0	0,0	0,3	0,0
4	04.11.14 11:40:20	33,3	65,5	46,2	16,0	28,2	633	0,21	0,12	0,000	0,00	34,1	6,1	54,5	11,7	11,0	0,0	0,2	0,0
4	04.11.14 11:40:30	33,7	69,8	44,8	16,1	28,6	588	0,21	0,16	0,000	0,00	34,2	6,2	54,8	11,8	11,0	0,0	0,2	0,0
4	04.11.14 11:40:40	34,2	73,2	43,5	16,1	29,0	562	0,21	0,18	0,000	0,00	34,2	6,2	54,7	11,9	11,0	0,0	0,2	0,0
4	04.11.14 11:40:50	34,2	75,8	42,5	16,1	29,3	533	0,21	0,19	0,000	0,00	34,3	6,2	54,6	11,9	11,0	0,0	0,2	0,0
4	04.11.14 11:41:00	34,7	77,7	41,5	16,1	29,7	537	0,19	0,20	0,000	0,00	34,3	6,2	54,5	11,9	10,8	0,0	0,1	0,0
4	04.11.14 11:41:10	35,0	78,5	40,6	16,2	29,9	502	0,20	0,22	0,000	0,00	34,3	6,2	54,5	12,0	11,0	0,0	0,2	0,0
4	04.11.14 11:41:20	35,1	78,6	39,9	16,2	30,1	510	0,21	0,21	0,000	0,00	34,4	6,2	54,6	12,1	11,0	0,0	0,1	0,0
4	04.11.14 11:41:30	35,3	78,1	39,1	16,2	30,2	501	0,19	0,21	0,000	0,00	34,4	6,2	54,5	12,1	11,0	0,0	0,2	0,0
4	04.11.14 11:41:40	35,4	77,5	38,5	16,2	30,3	496	0,20	0,21	0,000	0,00	34,4	6,2	54,6	12,2	11,0	0,0	0,2	0,0
4	04.11.14 11:41:50	35,4	76,8	37,8	16,2	30,8	491	0,21	0,20	0,000	0,00	34,4	6,2	54,6	12,3	11,0	0,0	0,2	0,0
4	04.11.14 11:42:00	35,6	76,2	37,2	16,2	30,8	509	0,19	0,19	0,000	0,00	34,3	6,2	54,5	12,3	10,8	0,0	0,1	0,0
4	04.11.14 11:42:10	35,8	76,0	36,5	16,2	31,0	504	0,20	0,19	0,000	0,00	34,3	6,2	54,5	12,3	11,0	0,0	0,1	0,0
4	04.11.14 11:42:20	35,9	75,8	36,0	16,2	31,0	491	0,20	0,19	0,000	0,00	34,3	6,2	54,9	12,4	11,0	0,0	0,1	0,0



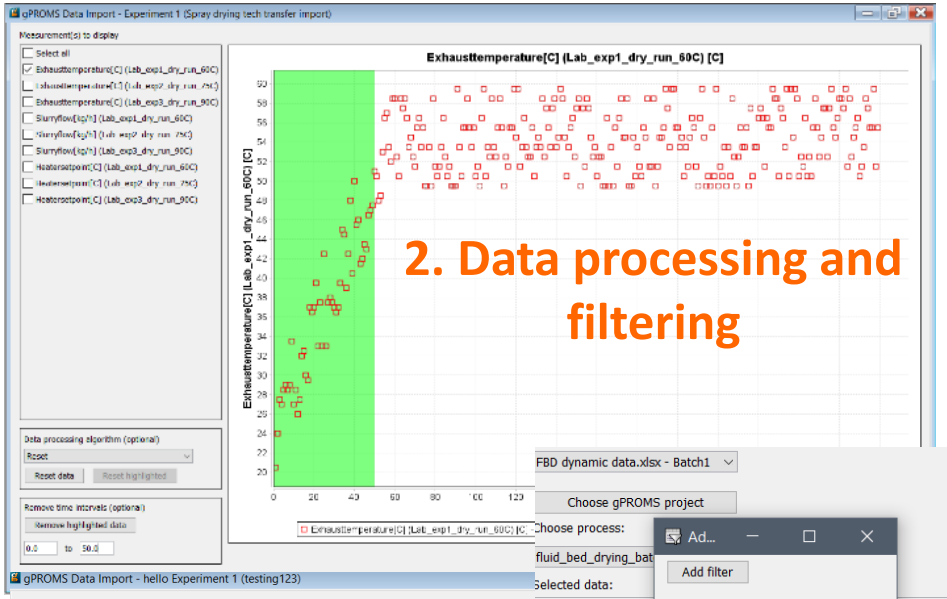
- Creating performed experiment entities is a key step in the model validation workflow.
  - Significant manual effort has been required.
  - Often there are many experiments, and manual steps are repeated.
  - Data may not be in the right format, right units, same place.

Data import and processing – **now**

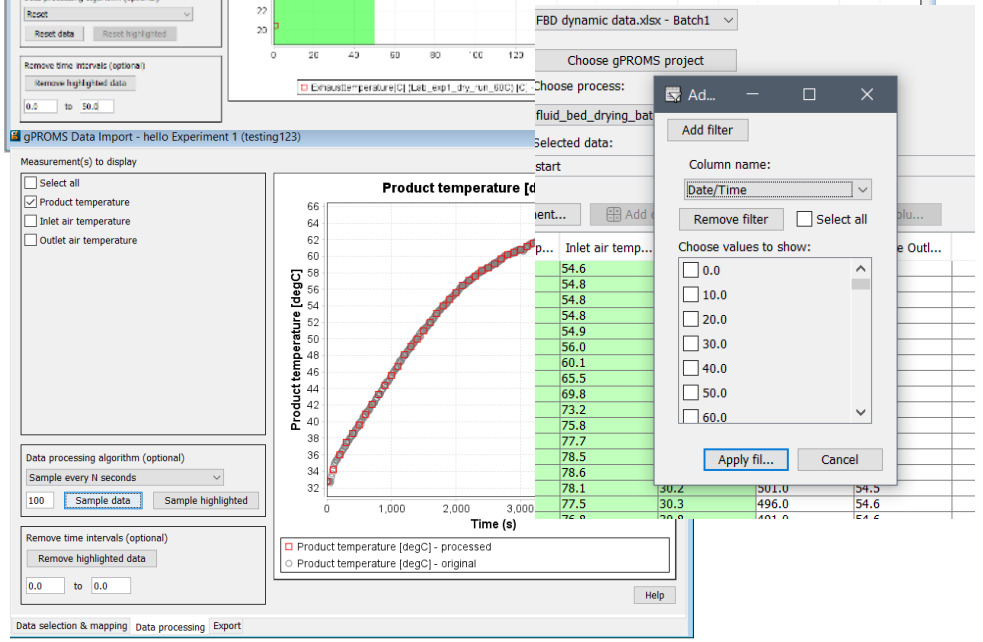




1. Data file import and link to gPROMS variables



2. Data processing and filtering

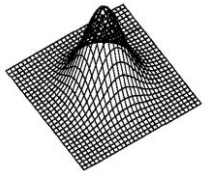


3. Export to gPROMS

Manage risk by quantifying impact of uncertainty

Environmental inputs
- External disturbances
- Commercial environment

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



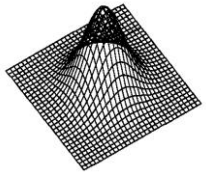
Variability

Decisions
- Design
- Operational

System

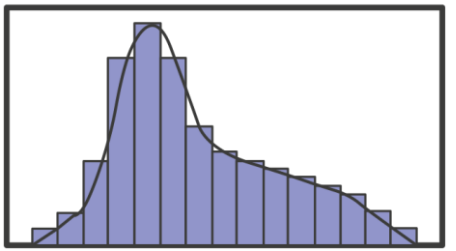
Model

Model parameters



Uncertainty

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



Risk associated with model-based decisions

Transitioning to gPROMS FormulatedProducts

Backward compatibility

Is gPROMS FormulatedProducts 1.0 backward compatible with respect to gCRYSTAL 4.2, gSOLIDS 4.1, and gCOAS 1.3?

- User specifications
  - We currently only guarantee backward compatibility with respect to **physical properties** entered in via the global specifications objects.
  - We are aiming for a future release to provide back compatibility with respect to specifications entered in **unit operations**.
- Model results
  - **Yes**
  - PSE has performed extensive testing to ensure that the results obtained in gPROMS FormulatedProducts match those obtained in gCRYSTAL, gSOLIDS, and gCOAS.

Upgrading your work

When should I start using gPROMS FormulatedProducts?

- When creating a new flowsheet model
- When you'd like to use new functionality with an old flowsheet model
  - Adding a new unit operation that wasn't previously available or interfacing with the properties database.
  - Some manual conversion will be necessary.
  - Note that you will be able to use **Global System Analysis** and the **Data Import Tool** without migrating to the new libraries.

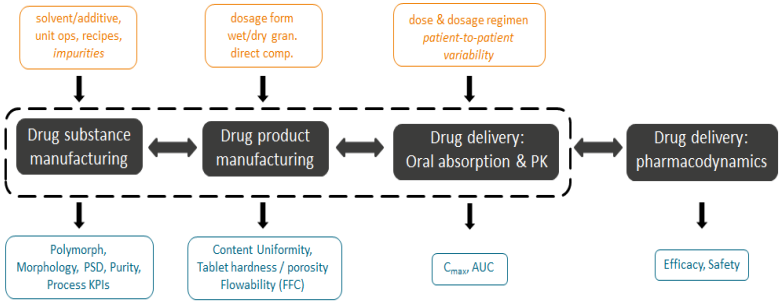
Licensing considerations

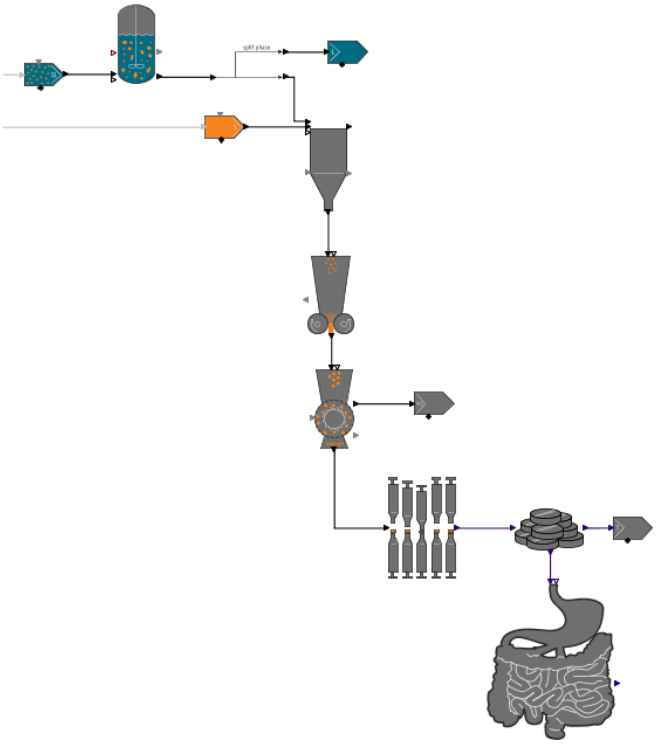
Will my licenses support gPROMS FormulatedProducts?

- **Yes** – Licenses for gCRYSTAL, gSOLIDS, and gCOAS will allow you to launch gPROMS FormulatedProducts and open and use the new versions of the libraries you previously could access.
- gPROMS FormulatedProducts will contain libraries for which you do not have licenses:
  - Libraries corresponding to previous products for which you did not have licenses.
  - New libraries containing models not existing in any previous product (reactor models, plug flow crystallizer, wet mill, continuous blenders, high shear and twin screw granulators)
- For the libraries which are new in gPROMS FormulatedProducts 1.0, PSE is happy to offer free 3-month evaluation licences to start no later than 1 June 2017.

In summary, gPROMS FormulatedProducts …

- … is PSE's new tool to deliver integrated design of formulated products and their manufacturing processes
- … merges and builds on gCRYSTAL, gSOLIDS and gCOAS
- … has been developed with input from
  - SbP Alliance: Pfizer, Lilly, PSE
  - Collaborative R&D projects, partially funded by UK government
    - D3P (Digital Design for Drug Products)
    - REMEDIES
    - ADDoPT





Acknowledgments

- Formulated Products team
- Software Technology Group
- Many others at PSE
- Formulated Products Advisory Board
- Collaborators across industry and academia
  - SbP Alliance
  - ADDoPT
  - REMEDIES
  - D3P

Thank you