ADVANCED PROCESS MODELLING FORUM 2017
London 25–26 April

Formulated Products update

Efficient and robust workflows combining models and experiments

Sean Bermingham – Head of PSE Formulated Products

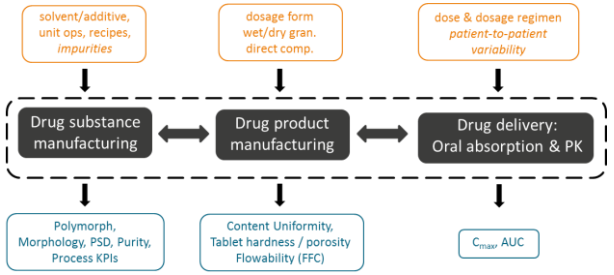
gPROMS

Understanding workflow requirements

How do we get beyond those who intuitively apply mechanistic models (and increase value from existing and future model-based solutions)?

Interactions with a wide range of stakeholders to understand and address workflow requirements

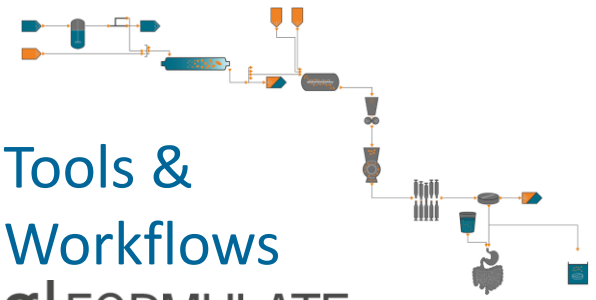
SbP: Vision



SbPA: coordination, industry adoption & regulatory acceptance

gsk Lilly Pfizer Roche

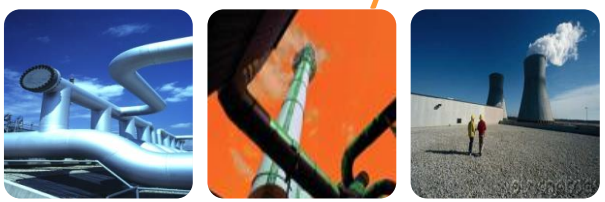
Tools & Workflows



g|FORMULATE

gPROMS gSAFT

PSE experience in, and developments for, other industry sectors



Collaborative R&D

ADDOPT

D3P

ReMediES

Systems-based Pharmaceutics Alliance

- Pre-competitive alliance founded by Eli Lilly, Pfizer and PSE in 2013
  - Accelerating development, adoption and regulatory acceptance of SbP tools
  - Phase I completed Oct '15; Phase II kicked off Dec '15; GSK and Roche Dec '16
  - Close interaction between scientific liaisons from each pharma company in a pre-competitive environment, incl. two 1-week in-person meetings per year
    - requirements and feedback from 30-40 SMEs regarding both tools and workflows
  - FDA has e November meeting
- Key deliver
  - *reactor and fluid separation*, PFC, wet mill, dry mill, *FL*
    in-vitro dissolution and precipitation, in-vivo absorption, *product stability*
- Key deliverables – p
  - PMA selector for est ation
  - *S/L/V properties package and interface*
  - Data import tool
  - *External model validation*

Flavien Susanne (GSK)
Today 12:00

Garry O'Connor (Pfizer)
Parenteral formulations
Tomorrow 14:25

Rob Taylor (Sirius)
Tomorrow 14:00

Edd Close (PSE)
Solid formulations
Tomorrow 14:50

ADDoPT

- Advanced Digital Design of Pharmaceutical Therapeutics
  - A 4-year £20.4m project with £12m government funding led by PSE
  - Multi-scale modelling, Solubility, Sensor models, Big data, Process control
  - AZ, BMS, GSK, Pfizer, Britest, PEL, CCDC, STFC, Leeds, Strathclyde, Cambridge
- Relevant deliverables to date
  - development of gPROMS FormulatedProducts framework
  - initial reactor and solvent recovery models in gFP 1.0 (starting point SbPA-2)
  - initial
  - access
  - prototype
  - enhancing the gSAFT databank

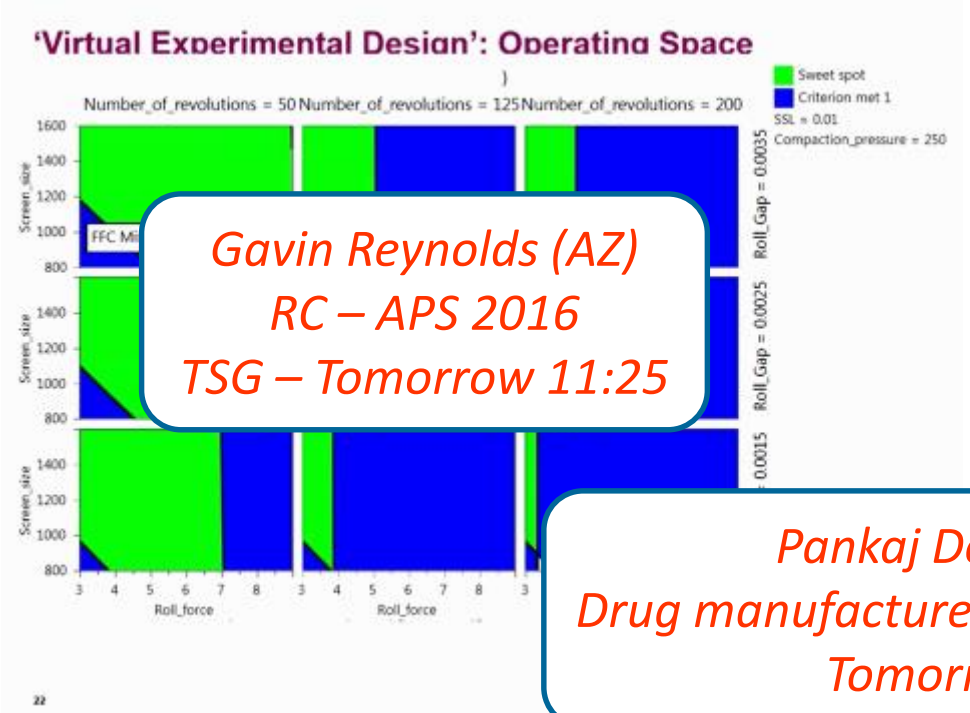
Flavien Susanne (GSK)

Gavin Reynolds (AZ)
Tomorrow 11:25

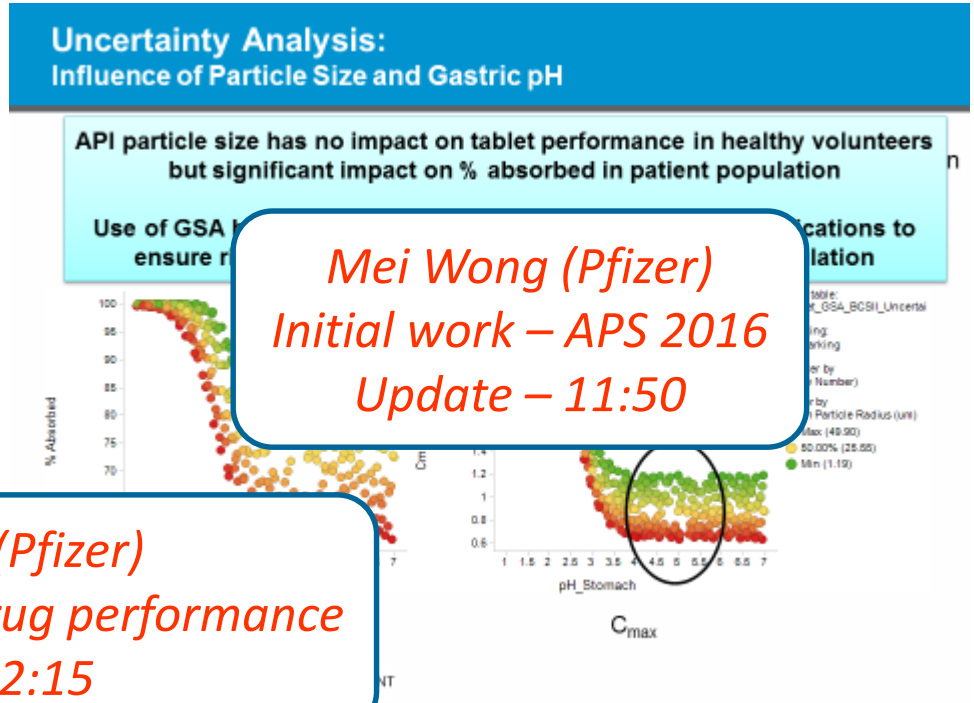
- Deliverables in progress (project ends March 2019)
  - improved mechanistic models for unit operations and product stability
  - interfaces for hybrid mechanistic and statistical models
  - multi-start parameter estimation (and optimisation)

Digital Design of Drug Products (D3P)

- Innovate UK project with AstraZeneca, Britest, GSK and Pfizer
- Funding: £444k funding over 2 years till Jun 2016
- Deliverables
  - Global System Analysis (part of gPROMS 5.0)
  - Industrial case studies presented at conferences and as a webinar



Gavin Reynolds (AZ)
RC – APS 2016
TSG – Tomorrow 11:25



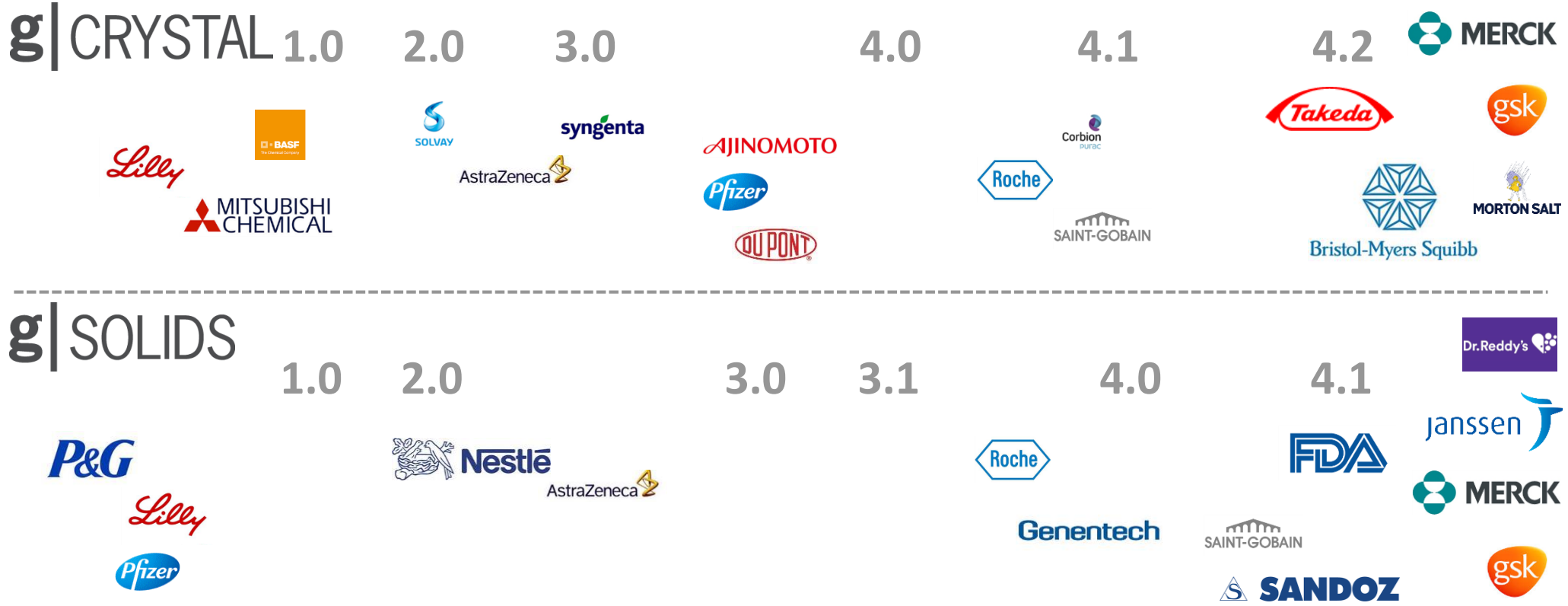
Mei Wong (Pfizer)
Initial work – APS 2016
Update – 11:50

Pankaj Doshi, (Pfizer)
Drug manufacture to drug performance
Tomorrow 12:15

Tool developments to improve workflows

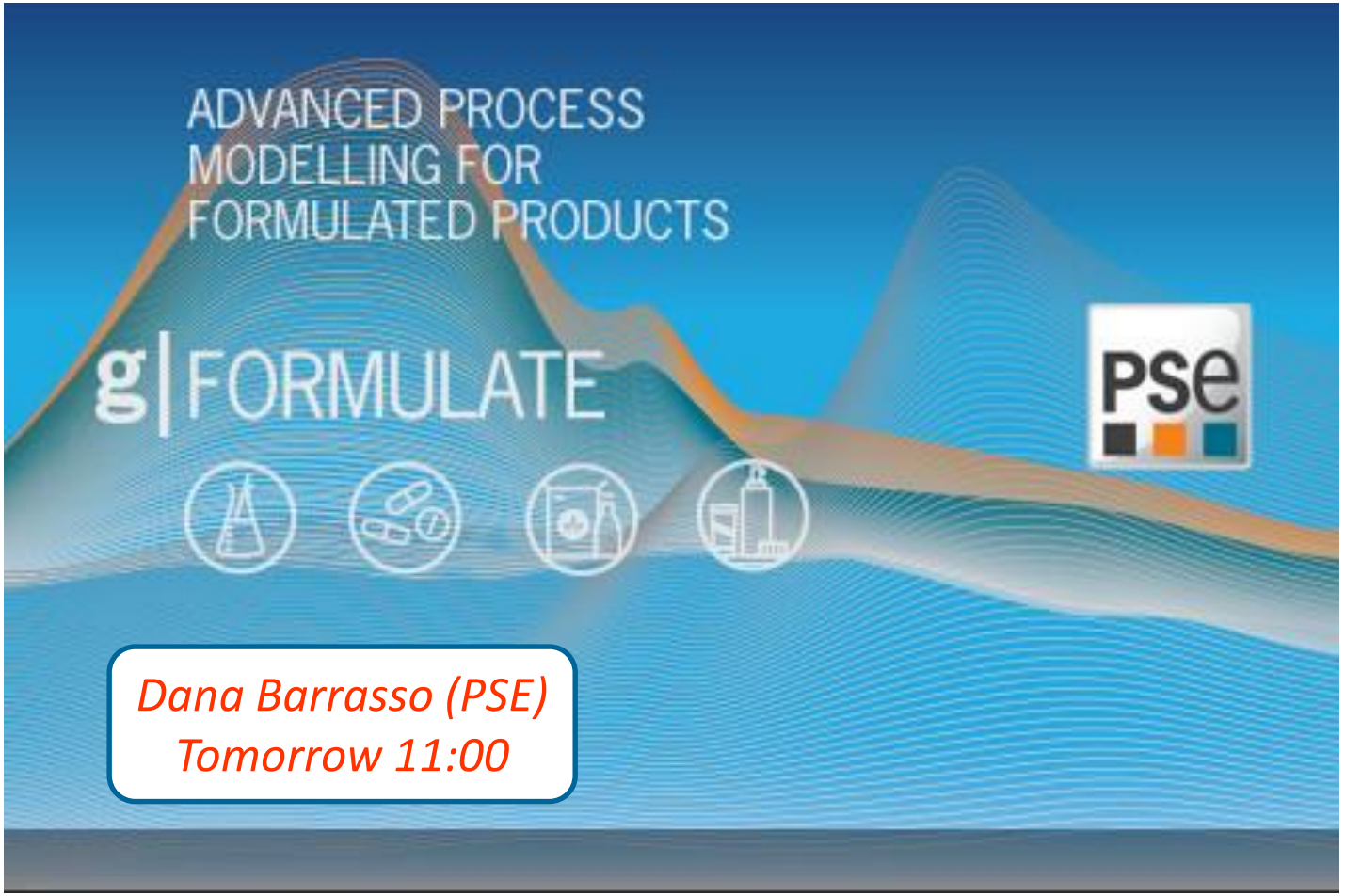
gCRYSTAL, gSOLIDS, gCOAS

Adoption by industry

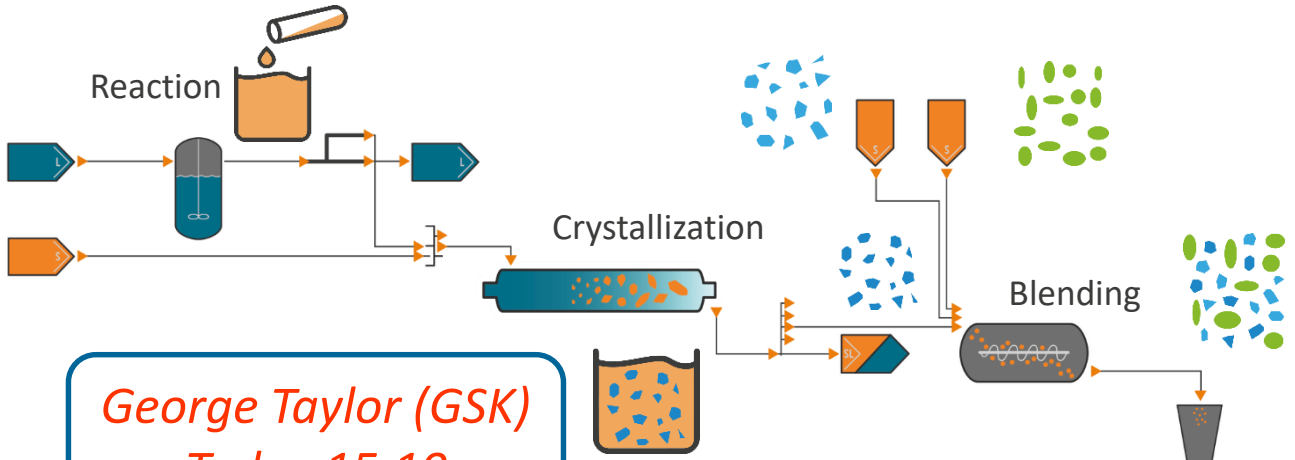


A “new” PSE product

gPROMS FormulatedProducts

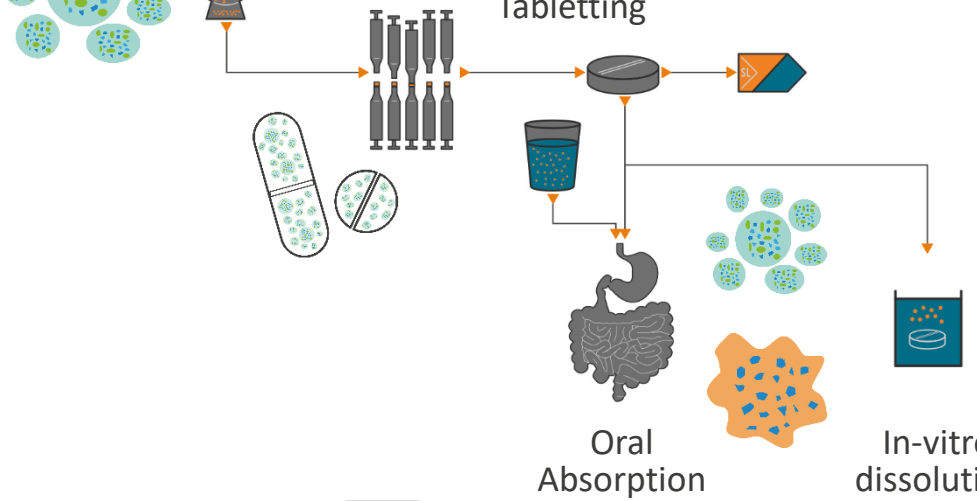


Linking manufacture directly to product performance



George Taylor (GSK)
Today 15:10

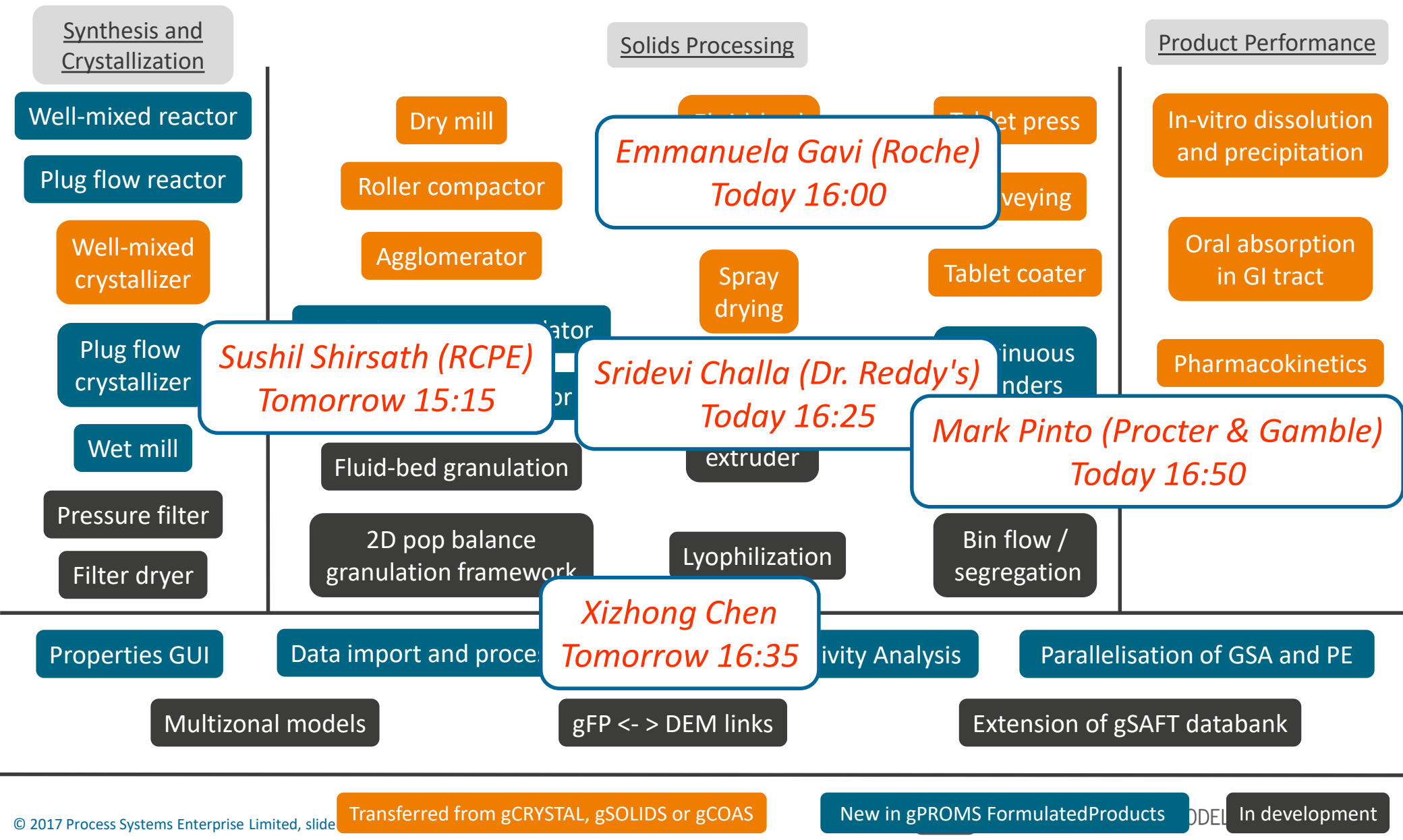
Frantisek Stepanek (U. Prague)
Tomorrow 16:10



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

gPROMS FormulatedProducts

Model libraries and features



Database capabilities

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

Materials

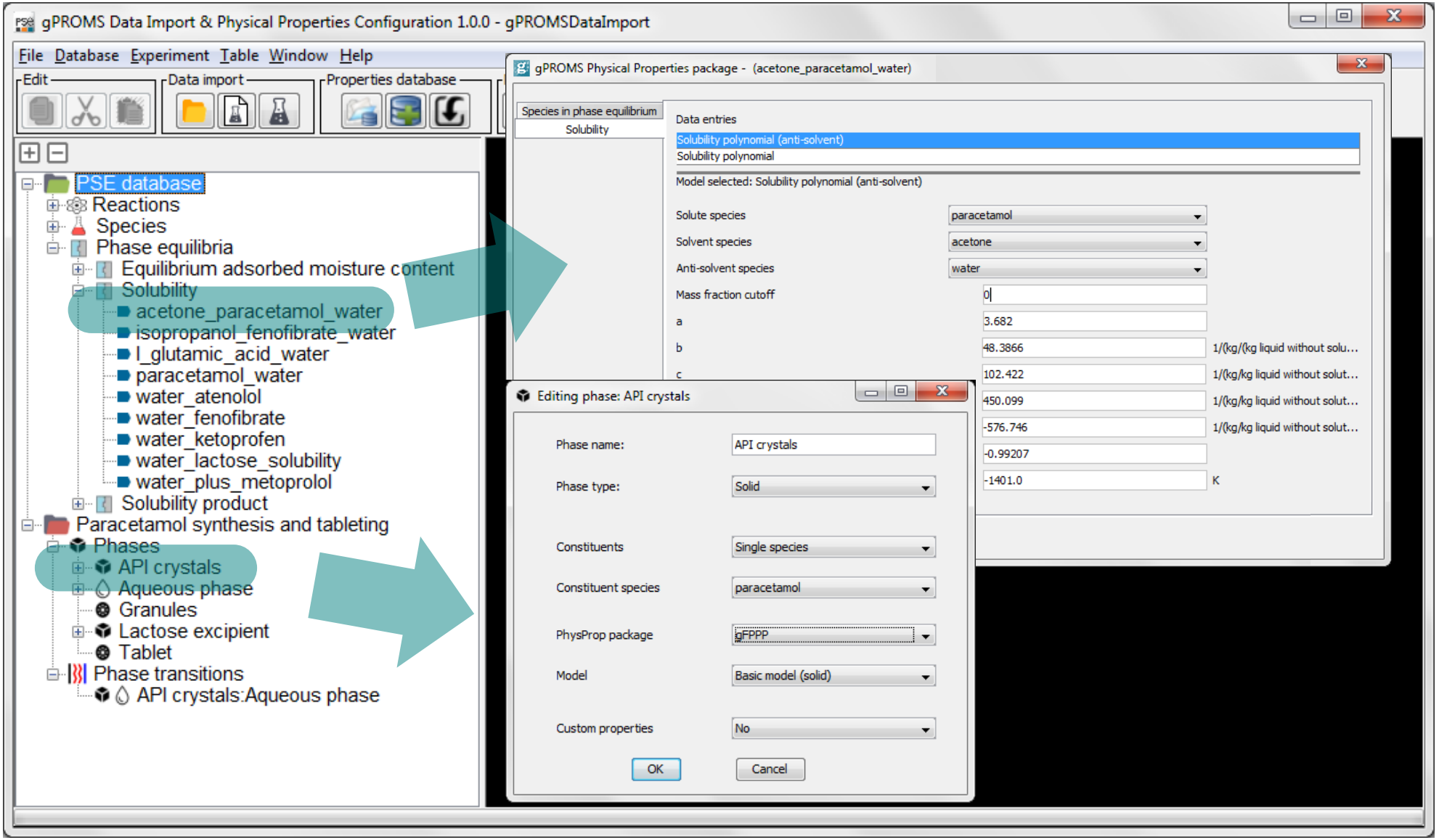
Dosage forms

Equipment

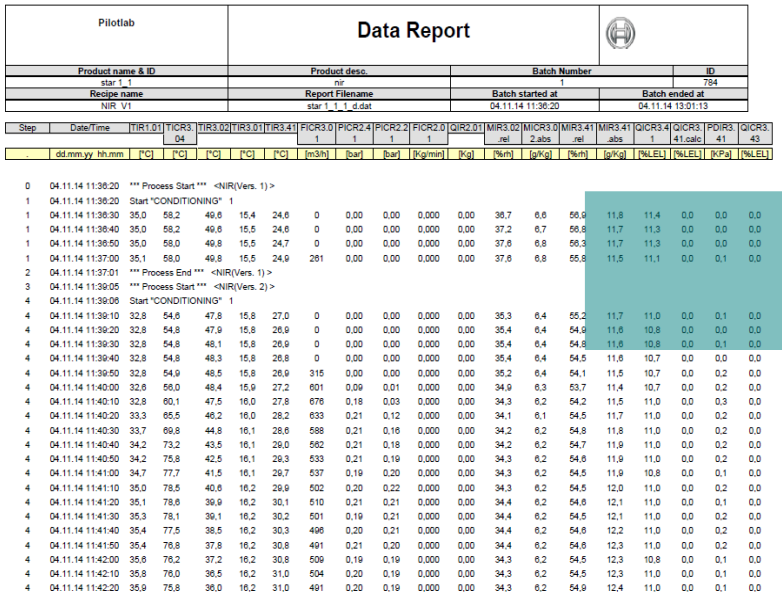
Physiology

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

Database management



Data import and processing – **previously**

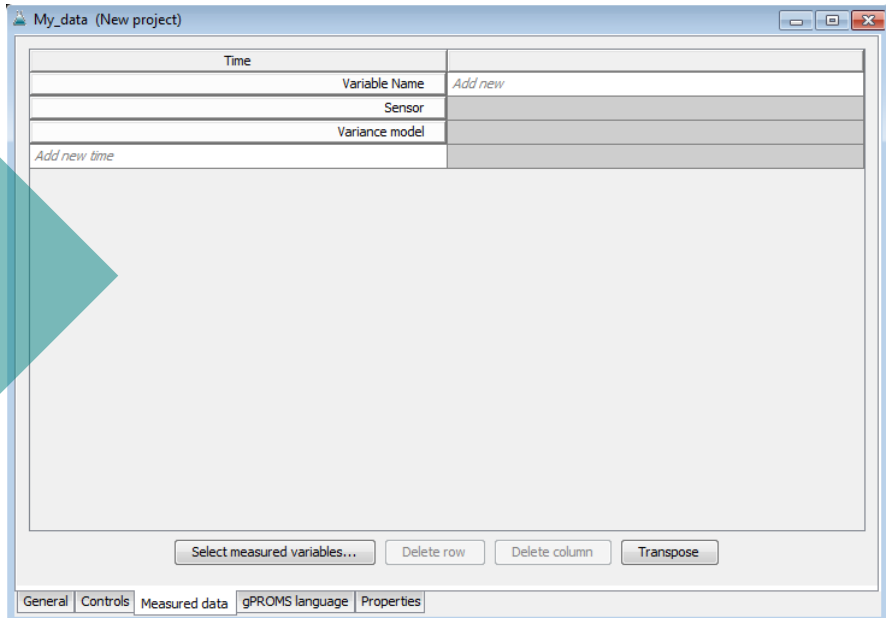


Pilotlab

Data Report

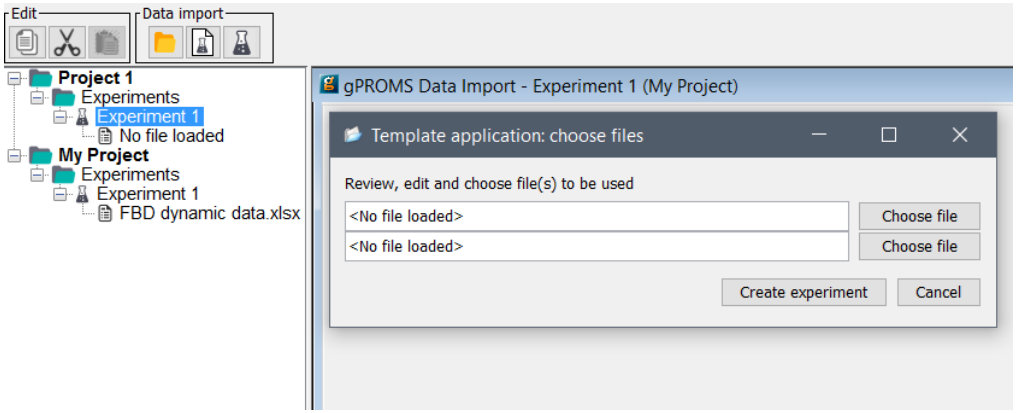
Product name & ID	Product desc.	Batch Number	ID
star 1_1	nir	1	784
Recipe name	**Report Filename**	**Batch started at**	**Batch ended at**
NIR_V1	star 1_1_1_d.dat	04.11.14 11:36:20	04.11.14 13:01:13

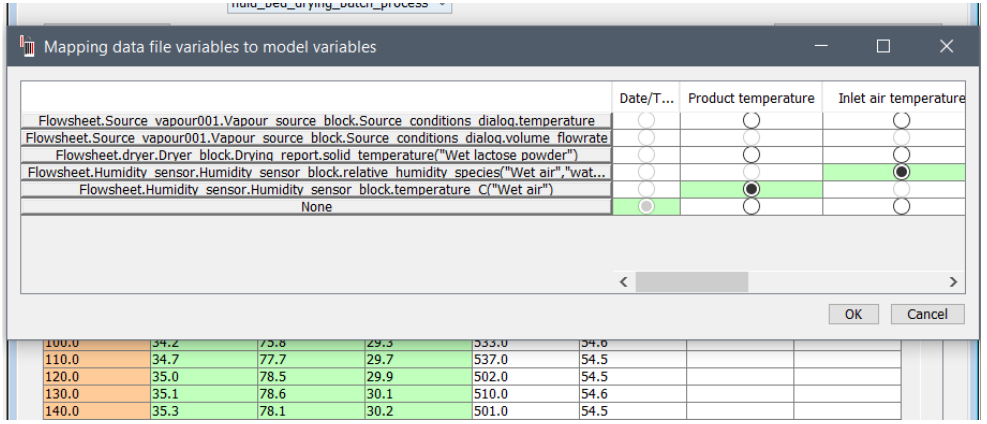
Step	Date/Time	TIR1.01	TICR3.04	TIR3.02	TIR3.01	TIR3.41	FICR3.01	FICR2.41	FICR2.21	FICR2.01	QIR2.01	MIR3.02.rel	MICR3.02.abs	MIR3.41.rel	MIR3.41.abs	QICR3.41	QICR3.41.calc	PDIR3.41	QICR3.43
-	dd.mm.yy hh.mm	[°C]	[°C]	[°C]	[°C]	[°C]	[m3/h]	[bar]	[bar]	[Kg/min]	[Kg]	[%rh]	[g/Kg]	[%rh]	[g/Kg]	[%LEL]	[%LEL]	[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



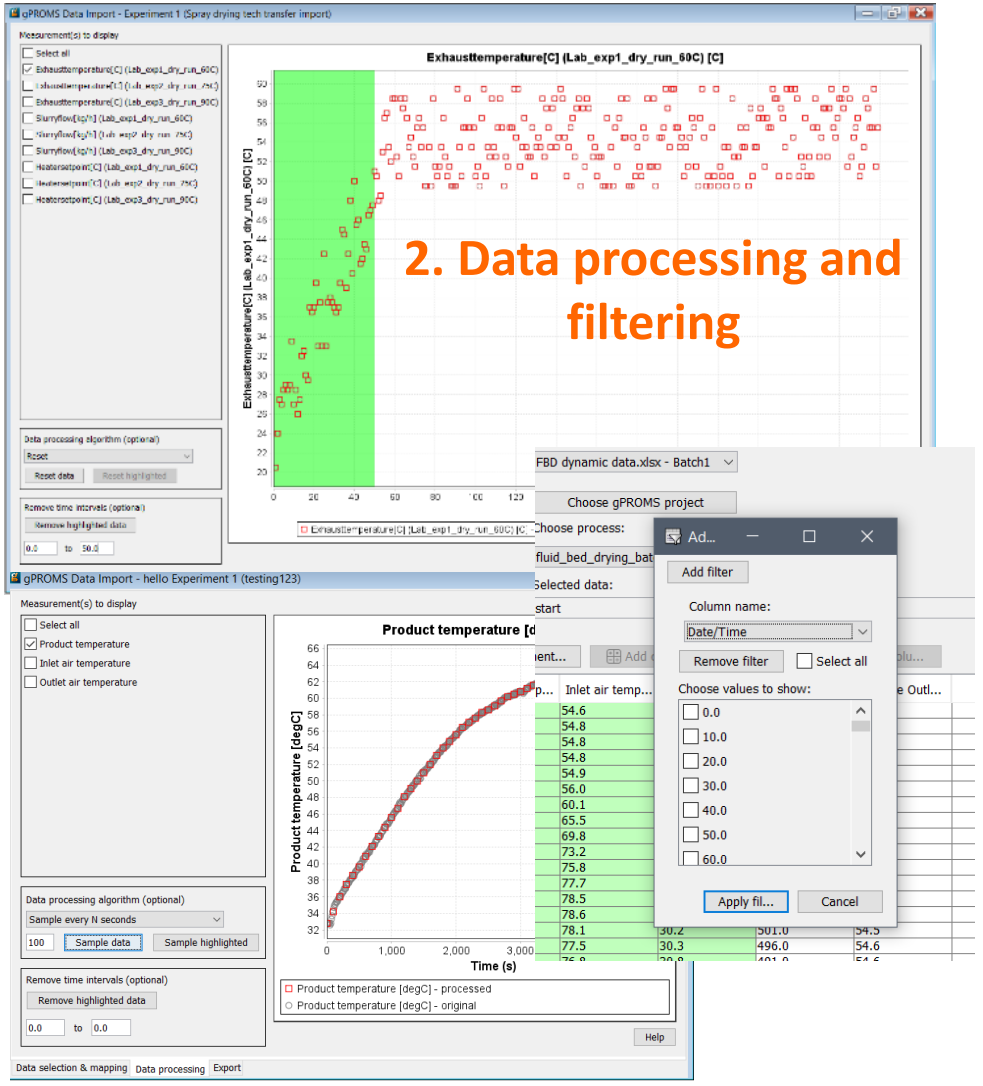
- Creating performed experiment entities is a key step in the model validation workflow.
  - Significant manual effort has been required.
  - Often there are many experiments, and manual steps are repeated.
  - Data may not be in the right format, right units, same place.

Data import and processing – **now**





1. Data file import and link to gPROMS variables



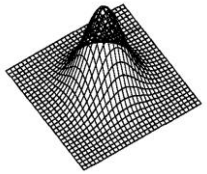
2. Data processing and filtering

3. Export to gPROMS

Manage risk by quantifying impact of uncertainty

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



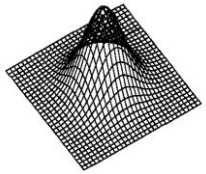
Variability

Decisions
- Design
- Operational

System

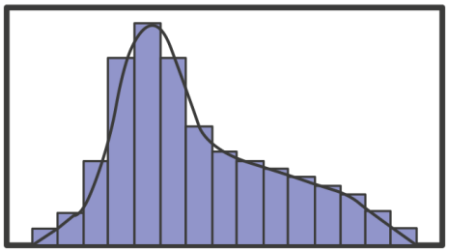
Model

Model parameters



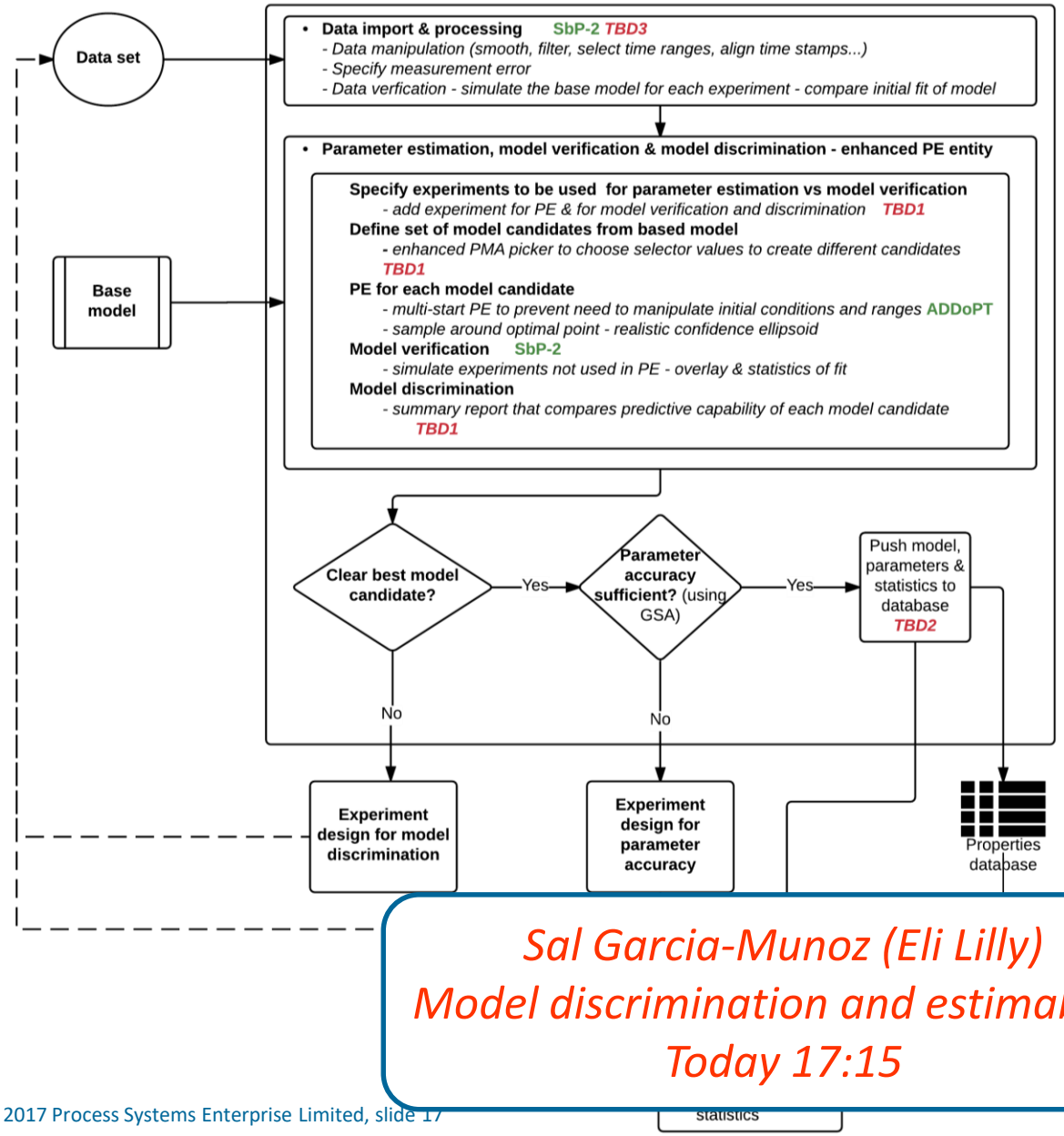
Uncertainty

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



Risk associated with model-based decisions

Automation and improvement of model validation



- Recently completed
  - data import tool
- Ongoing
  - external model validation
  - multi-start parameter estimation
  - experiment design for parameter precision
- Future
  - pushing parameters and metadata to databases
  - automated model discrimination
  - experiment design for model discrimination

Sal Garcia-Munoz (Eli Lilly)
Model discrimination and estimability
Today 17:15

Streamlining workflows involving models and experiments

Development of documentation / video tutorials for specific workflows

- *Have recently recruited one person and are recruiting another one*

  Close interaction with SMEs in industry is clearly key (via SbPA, ADDoPT, FP Advisory Board)

- Need to develop specific workflows
  - not one per unit operation
  - one per question you wish to answer with models calibrated / validated using experimental data
  - include advice on experiments to conduct, measurements to perform

1 Establish material properties

2 Collect experimental data

3 Build system flowsheet

4 Run parameter estimation

Tech transfer

5 Build new system flowsheet

6 Run simulation

7 Conduct validation experiment(s)

8 [OPTIONAL] Run parameter estimation

Developing workflow tutorials may not be sufficient to increase adoption of digital design

Many organisations do not have the facilities and/or expertise to characterise materials and/or equipment

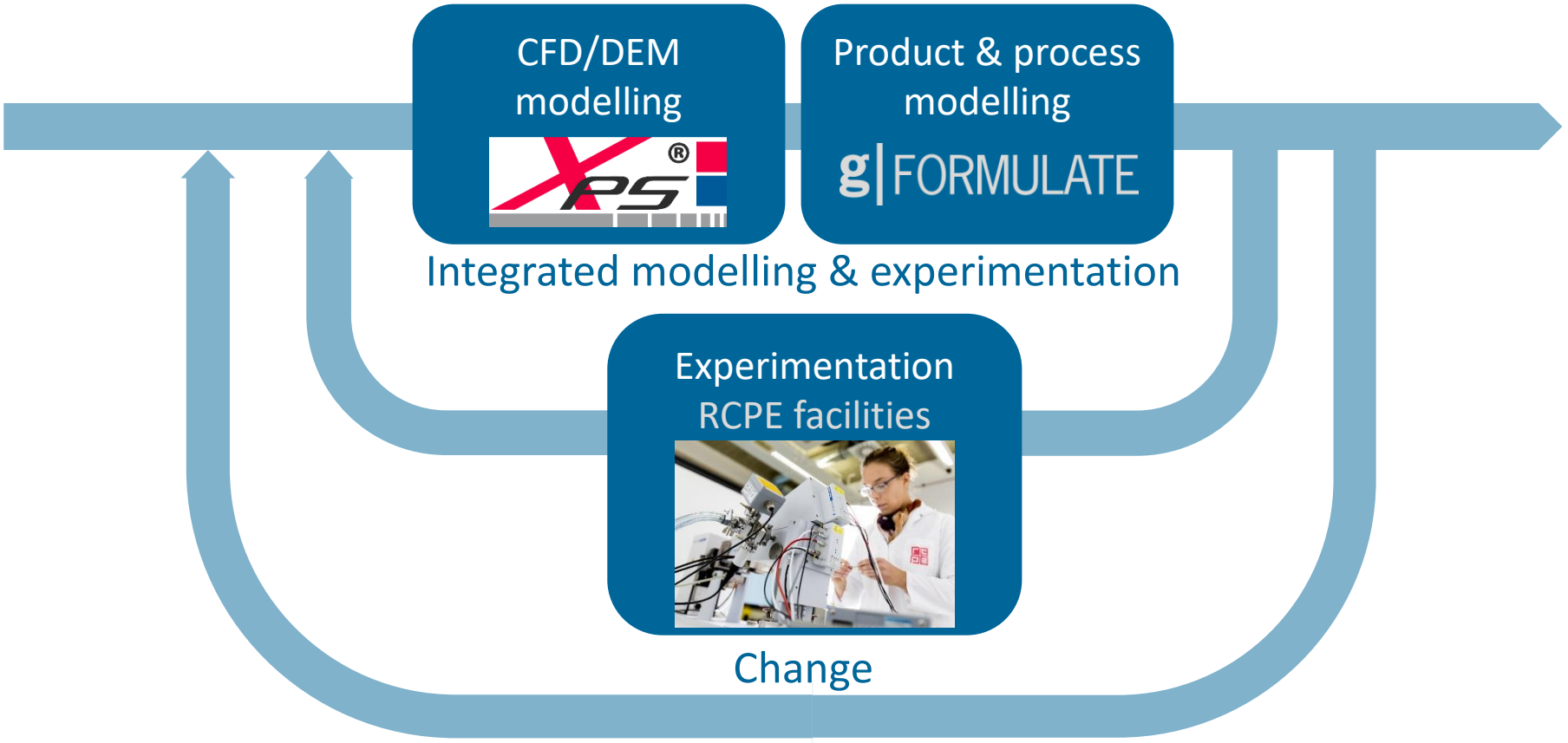
Addressing needs of **pharma** industry: modelling and experimentation

PSE and RCPE announce pharma Centre of Excellence

Combination of mechanistic modelling and experimentation boosts drug development and manufacturing

LONDON, 6 December 2016 — Process Systems Enterprise (PSE), the Advanced Process Modelling company, and the Research Center for Pharmaceutical Engineering GmbH (RCPE), an independent R&D Centre specialised in Advanced Manufacturing Science and Pharmaceutical Engineering, today announced the formation of a Centre of Excellence (CoE) aimed at bringing combined model-based analytical technology and services to pharmaceuticals manufacturers.

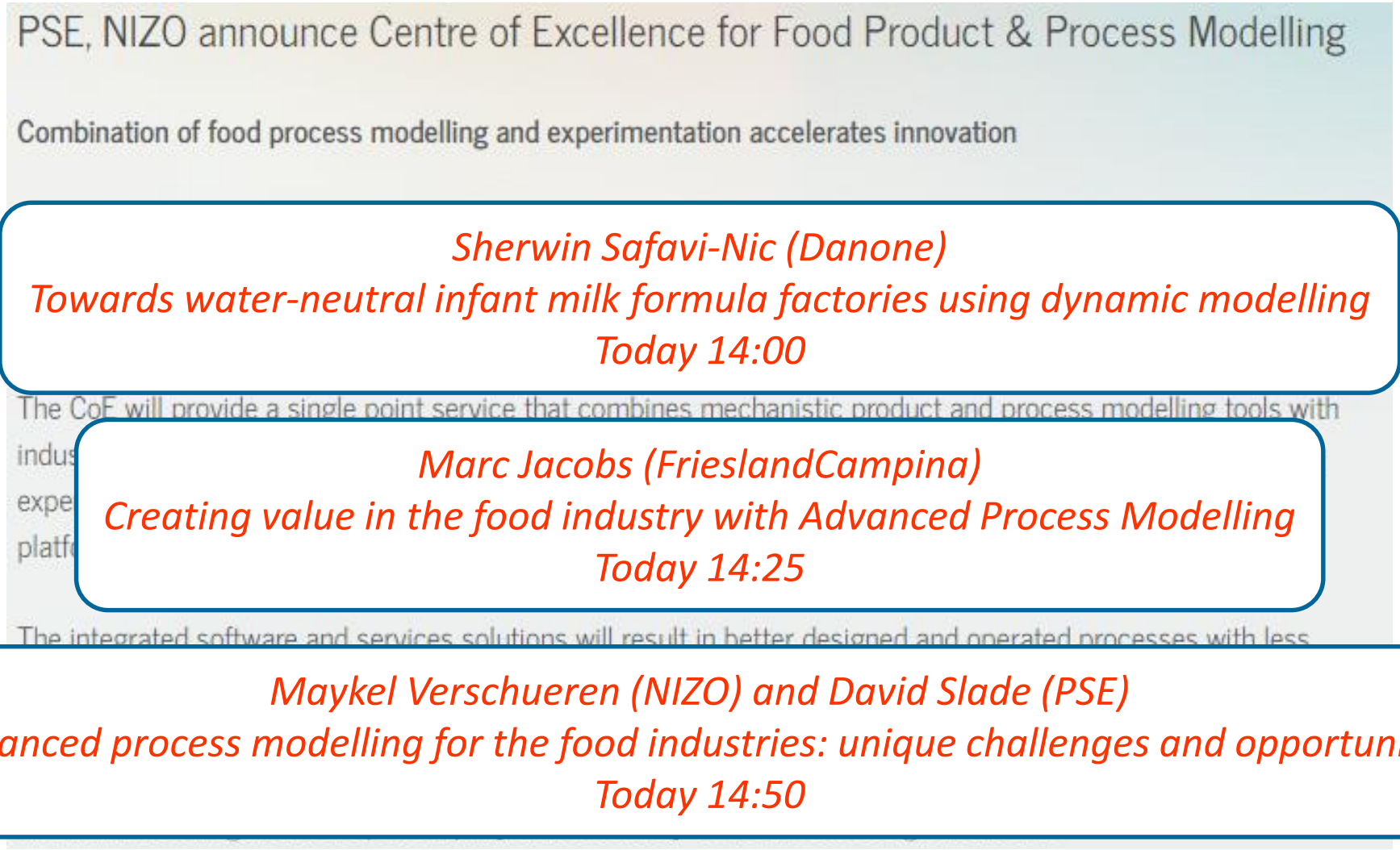
Integration



Combining mechanistic models and targeted experimentation

Provided in the form of software and/or services

Addressing needs of **food** industry: modelling and experimentation


PSE, NIZO announce Centre of Excellence for Food Product & Process Modelling

Combination of food process modelling and experimentation accelerates innovation

The CoE will provide a single point service that combines mechanistic product and process modelling tools with

The integrated software and services solutions will result in better designed and operated processes with less

Sherwin Safavi-Nic (Danone)
Towards water-neutral infant milk formula factories using dynamic modelling
Today 14:00

Marc Jacobs (FrieslandCampina)
Creating value in the food industry with Advanced Process Modelling
Today 14:25

Maykel Verschueren (NIZO) and David Slade (PSE)
Advanced process modelling for the food industries: unique challenges and opportunities
Today 14:50

To find out more

speak to our industrial and academic partners present today and …

… to members of the Formulated Products team

Business development



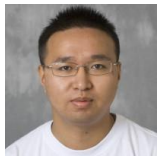
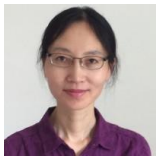

Applications engineering (formerly technical sales)





Andrew Salmon

Product development

Sarah Fadda

Project management


Product management & strategic business development






Technical architecture

BU management & strategic business development

Focus on development of efficient and robust workflows that combine fit-for-purpose models and fewer, targeted experiments

To increase adoption of digital design beyond those who intuitively apply mechanistic models to design robust formulated products and their manufacturing processes, and hence

to increase value from existing and future model-based solutions

Thank you for your attention

gPROMS