

Academic Perspectives and Opportunities in PAT

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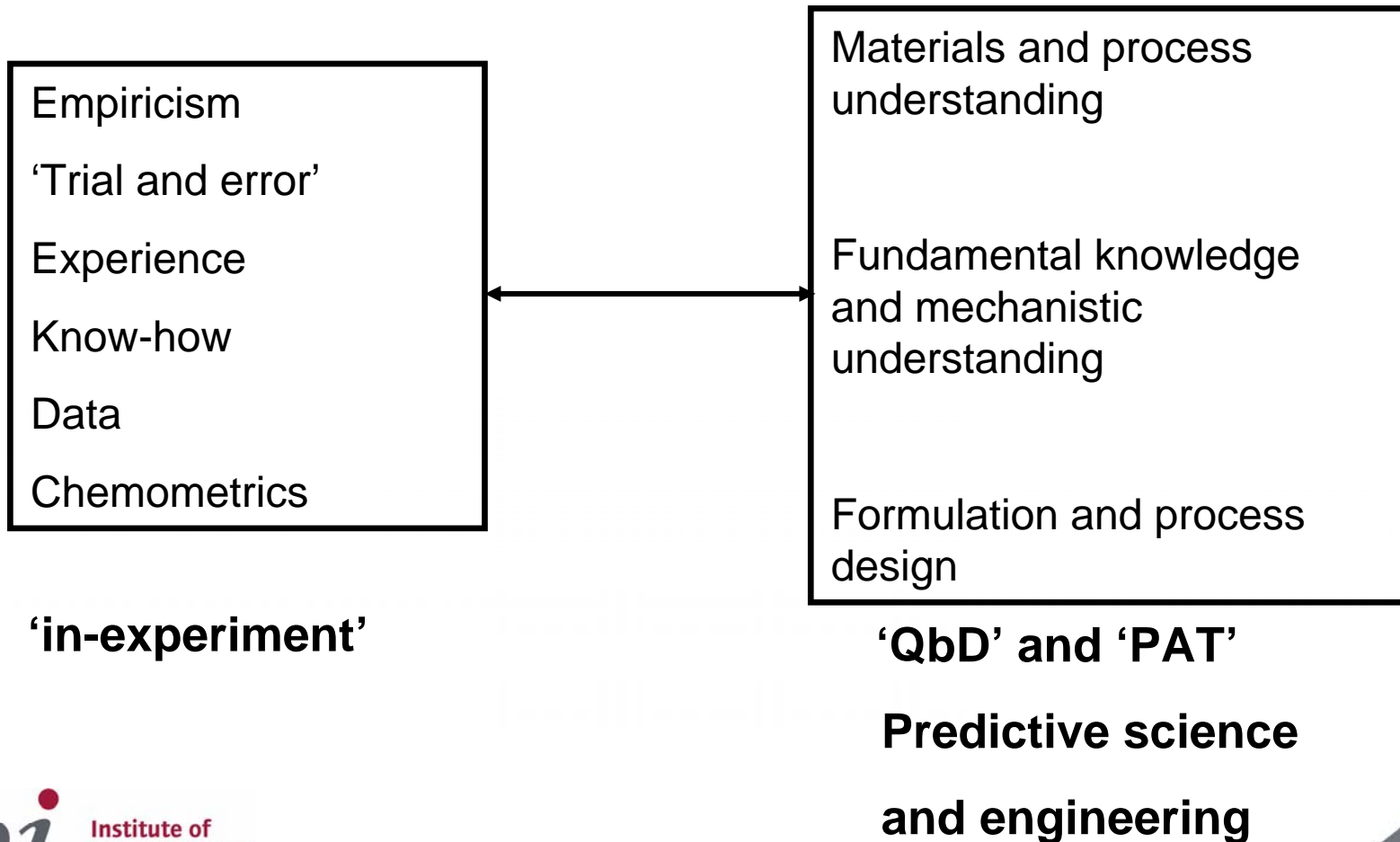
Institute of Pharmaceutical Innovation

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BRADFORD, UK

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Traditional Methods – New Approaches



What will PAT provide?

- Improved process control and understanding
- Real time information on (and definition of) critical process parameters - rapid intervention; early detection of deviations; reduce risk of batch failure
- Real time continuous monitoring and validation of processes – real-time product release
- Facilitate management of change

Academia and PAT Science and Engineering

QbD - PAT

Innovation and New Thinking

‘Design Science’
‘Manufacturing Science’



Institute of
Pharmaceutical
Innovation

Key Issues

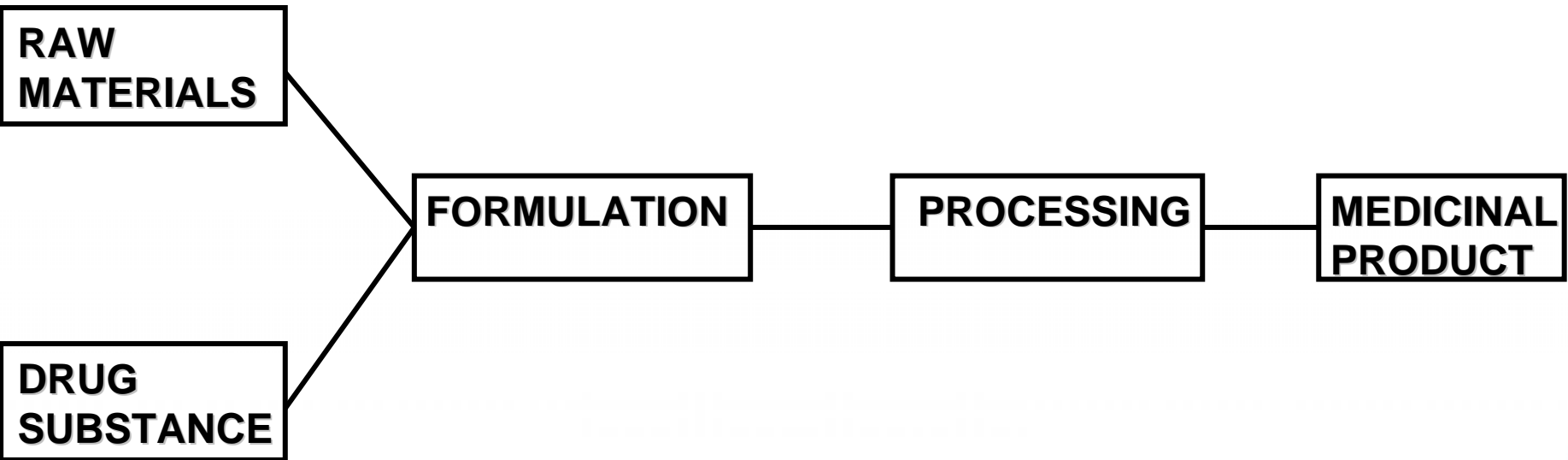
- Need for **new knowledge and innovation** within PAT space to underpin scientific and engineering across the pharmaceutical development/processing landscape
- ‘From molecules to man’ spectrum of activities
- Deliver science into the public domain for benefit of all communities

Product and Product Understanding

- Requires fundamental knowledge of materials, processes and interactions
- Innovation in analytics, materials and characterisation, mechanistic understanding of processes, data management and mining
- Integration of knowledge for broad-based, confident 'product and process design'

PAT Science and Engineering for Bio-Pharma

PAT – Holistic Approach!



PAT Implementation – Underpinned by scientific knowledge

PAT Concepts

**ADVANCED
PROCESS**

**REAL-TIME
QUALITY CONTROL**

PAT Measurements

**MATERIALS
AND PROCESS**

**PROCESS
SCALE-UP**

**PROCESS
VALIDATION**

PAT Science

**MECHANISTIC
UNDERSTANDING**

**MODELLING
AND
SIMULATION**

**PREDICTIVE
SCIENCE**

Process Analytical Technology

‘Process’ and ‘analytical’ encompass an integrated scientific and engineering philosophy accommodating:

chemistry

physics

material science/structures

biotechnology/microbiology

mathematics/computation

risk analysis

engineering (chemical, process, control..)

etc..

Illustrative Examples of Emerging PAT Science

- Polymer heat extrusion
- High shear wet granulation

Polymer Heat Extrusion Study - At-process Analysis

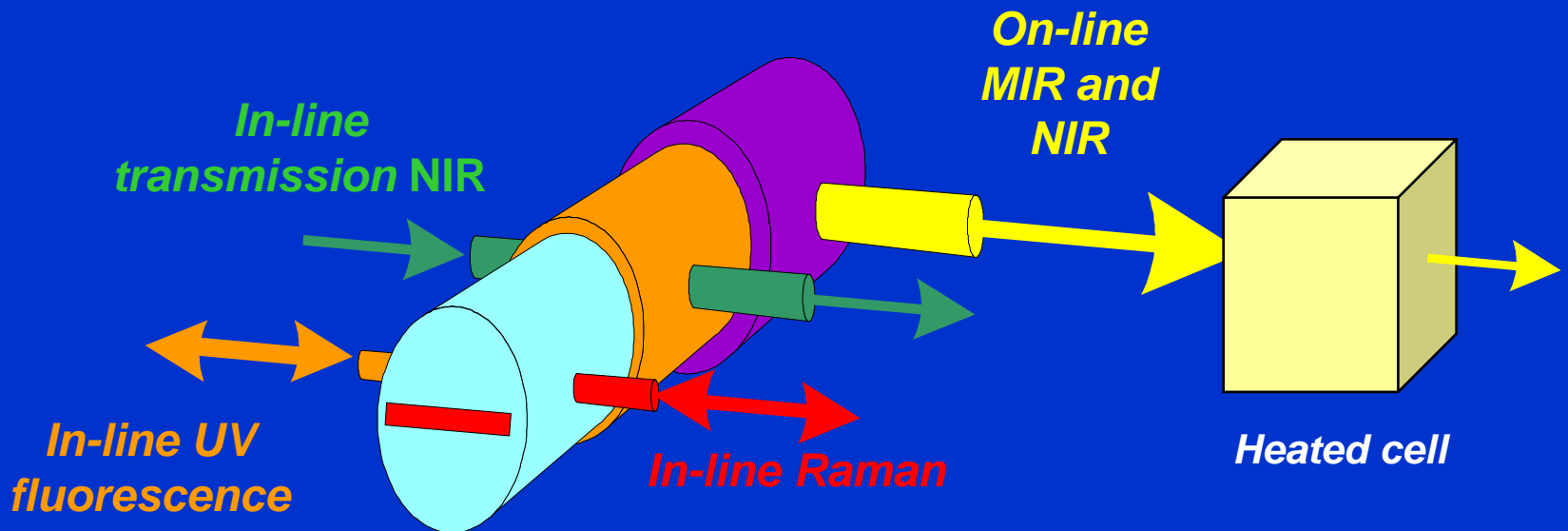
- Polymer blend with additives
- Quality monitoring, and control
- Process monitoring, and control
- Data capture from several spectroscopic probes
- Polymer IRC/IPI research programme, collaborative programme led by team at Bradford University

PAT Science

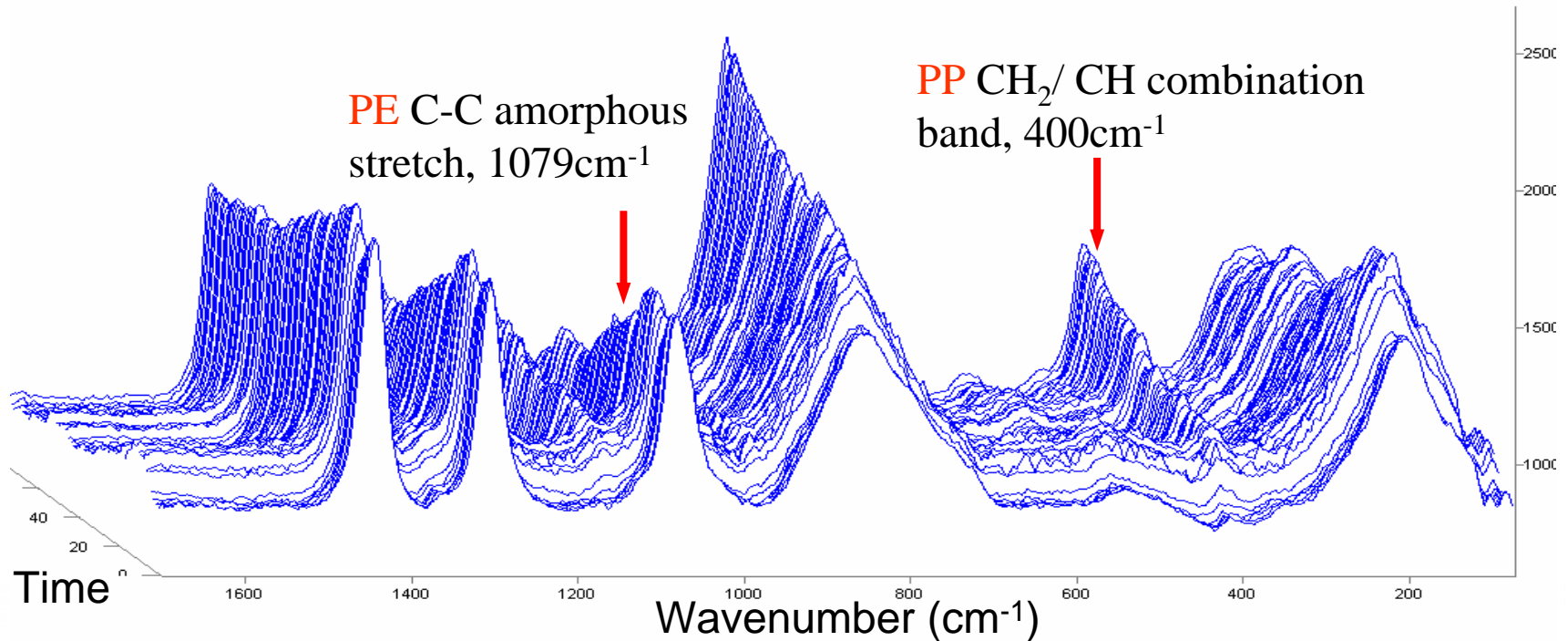
- Polymer Heat Extrusion Study

- Fundamental chemical and structural information on material interactions and reaction kinetics
- Opportunity to model material behaviour and process
- Identify key material and critical process parameters
- Feedback control loops via pattern recognition tools

In-line / on-line techniques



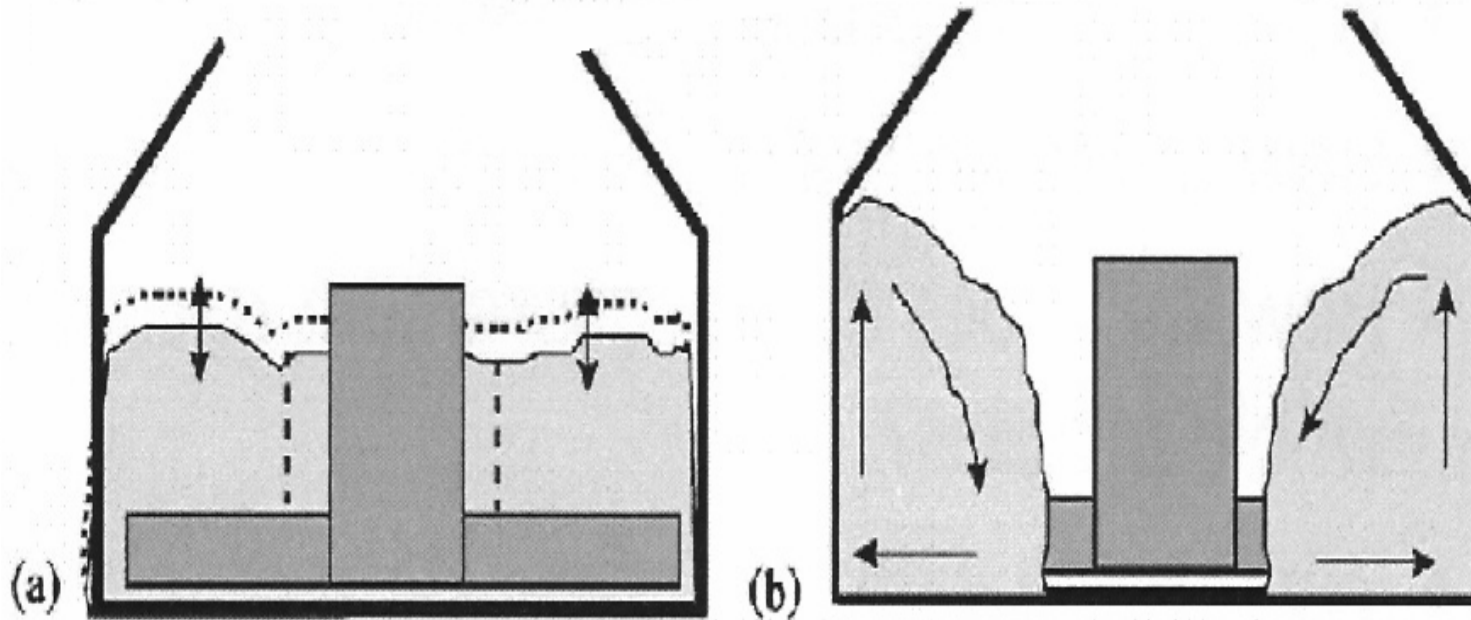
In-line Raman Results



3D plot of Raman spectra taken every minute during sequential blend extrusion (1600-100cm⁻¹) 100%PE - 100%PP, 15rpm, 200C

- This region of the spectrum showed the most change during blend extrusion
used for multivariate analysis
- Intensity of the two most isolated peaks monitored for calibration
used for univariate analysis

Studies of High Shear Granulation



Studies of High Shear Granulation

Empirical
↓
Mechanistic

Multivariate process modelling
Relative swept volume/trip speed
Dimensionless numbers
Normalised impeller work
Integrated power over time
Population balance modelling
DEM models – flow patterns

What is Academia Doing?

- Comments from US and European perspective
- FDA initiatives triggered 'action'
- Number of 'networks' starting up 'design science' activities in USA – eg C-SOPS, NIPTE
- In Europe, number of initiatives by various agencies – eg EUFEPS PAT Steering Group

Center for Organic Particulate Systems (C-SOPS)

- SOPS (Structured Organic Particulate Systems) systems where performance depends on microstructure
- Research into critical material and processing science and development of predictive models
- Provision of educational and training programmes
- Cross-disciplinary team of engineers and scientists, and industry leaders

Center for Organic Particulate Systems (C-SOPS)

- Three Universities –Rutgers, New Jersey Institute of Technology, Puerto Rico
- National Science Foundation (NSF) funding of \$15m in 2006
- Over 25 industrial members (at different levels of funding)
- For pharmaceutical, nutraceutical and agrochemical industries

National Institute for Pharmaceutical Technology and Education (NIPTE)

- Research and educational programmes in pharmaceutical technology related to QbD and PAT
- Currently defining study areas to provide 'road maps'
- Network of 11 Universities in USA providing multidisciplinary in science and engineering (coordinated at Purdue University)

National Institute for Pharmaceutical Technology and Education (NIPTE)

- Senate bill being introduced to Congress to give boost to a multi-University consortium (NIPTE) created 'to develop pharmaceutical products faster, more safely and at lower costs to consumer'
- FDA and NIPTE have signed a Memorandum of Agreement
- Major funding sought - \$10m - \$25m per annum for 5 years

European Perspective for PAT

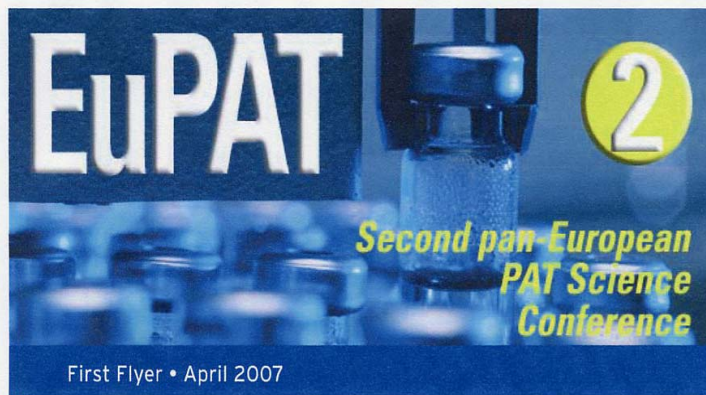
- Brussels 2000, EUFEPS Workshop for New Safe Medicines Faster
- Session considered how to move ‘hurdles in drug development’ to wider audience and action!
- Nothing moved – importance of PAT Science not generally acknowledged.....until FDA initiative ...’innovation or stagnation...’
- EUFEPS 2004 Congress Brussels – establishment of a PAT Science Network; attempts to deliver a report on European needs via a Workshop forum

EUFEPS PAT Science Steering Group

- Encourage, stimulate and initiate PAT scientific approaches and interactions in pharmaceutical sciences
- Initiate educational/ training programmes in the field
- Act as a resource and 'neutral' debating forum to stimulate and promote fundamental scientific and engineering research and innovative approaches in PAT
- Approach these issues from a multidisciplinary perspective; aid in establishing networks
- Communicate and establish dialogue with other stakeholders in PAT in the EU, and beyond (eg ISPE PAT Group)

European PAT Science Forum

- EuPAT Conferences (EuPAT2, November 2007), cosponsored by ISPE
- Engage all stakeholders – researchers (academic, industry), industrialists, regulators
- Establish interdisciplinary network and define way forward
- Neutral forum to nurture and catalyse research, innovation and debate
- Link ‘new thinking’ to ‘design and manufacturing science, and PAT implementation



Scientific Progress Underpinning Process Analytical Technology (PAT)

November 13-14 • 2007 • Copenhagen • Denmark

Aim and Alert for Papers

This is to invite you to plan for the EuPAT2, the second pan-European Science Conference on Process Analytical Technology (PAT), building on the success of EuPAT1 in 2006, to be held in Copenhagen, Denmark, on November 13-14, 2007. At EuPAT2, bioprocessing will be in focus.

The new EuPAT Conference Series is a unique forum for scientists and engineers, encouraging and promoting progress in the science behind PAT and strengthening the interdisciplinary scientific discussion that bridge between the various fields underpinning PAT. Common denominators of these fields, that also constitute the corner stones of PAT:

- Information-Rich Process Sensors
- Advanced Process and In-Process Material Characterisation
- Process Modelling, Simulation and Control
- Real-Time Process and Quality Informatics

The EuPAT2 programme will comprise both invited presentations and oral and poster presentations selected from submitted abstracts.

The EuPAT2 is co-organised by the European PAT Science Network of the European Federation of Pharmaceutical Sciences (EUFEPS) and the Nordic Affiliate of the International Society of Pharmaceutical Engineering (ISPE), supported by the ISPE Community of Practices (CoP) of PAT.

The ISPE CoP for PAT provides a network of active PAT practitioners from industry, academia, the regulatory agencies and suppliers which promotes understanding, open communication and exchange of useful and relevant information about PAT and process understanding between all parties.

www.eufeps.org and www.ispe.org/nordic



PAT Science and Engineering in Academia

Concluding remarks

PAT Science and Engineering in Academia

- High quality and efficiency is not tested into products – it has to be built in by design
- Shift from empirical to science based principles
- Requirement for multidisciplinary, fundamental scientific and engineering research – academic dimensions

PAT Science and Engineering in Academia

- Continue to strengthen the research base and the core competencies in individual subject areas
- Achieve multidisciplinary required by establishing collaborative networks
- Innovation and new thinking, feeding from fundamental and mechanistic understanding/knowledge
- Informed by close interaction with 'end-users'

‘Why does this magnificent applied science which saves work and makes life easier bring us so little happiness? The simple answer runs: because we have not yet learned to make sensible use of it.’

Albert Einstein (in 1931)

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