



# **PROCESS ANALYTICAL TECHNOLOGY (PAT)**

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# PROCESS ANALYTICAL TECHNOLOGY

## WHAT IS PAT?

FDA's vision:

A system for **designing, analyzing, and controlling** manufacturing through **timely** measurements (during processing) of critical quality and performance attributes of raw, and in-process materials and processes with the goal of ensuring final product quality for a significant number of **products on the market or in development**





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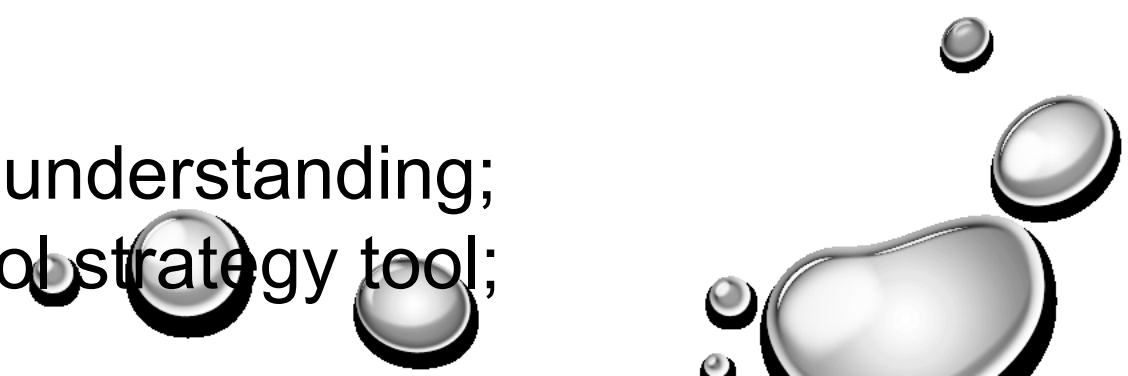
## WHAT IS PAT?

Any *in-situ* measurement that participate in control or gathering data for understanding of the process;

E.g. FTIR, Raman, ATR-UV, NIR probes, MS, HPLC, FBRM, PVM, NMR;

PAT probe can measure either chemical or physical aspects (flow, temperature, pressure, pH value);

PAT role in development is process understanding;  
PAT role in manufacturing is a control strategy tool;






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## WHY USE PAT?



- The use of PAT can improve R&D efficiency and minimize personnel hazard;
  - Speeds up processes → sampling, analyses
  - Reliable, rapid analyses of a process
  - Significant data for developing process chemistry understanding (detection of reaction intermediates, mechanisms, relationship between process variables);
  - Reduction of the number of critical parameters;
  - Results in set of controls (off-line or in-line);
  - Fully supported by authorities;
  - More frequent data collection;
  - Automated measurement;
  - Real time process control;
  - Eliminates difficult and hazardous sampling
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## WHEN TO USE PAT?

Depends on many factors throughout the product life cycle:

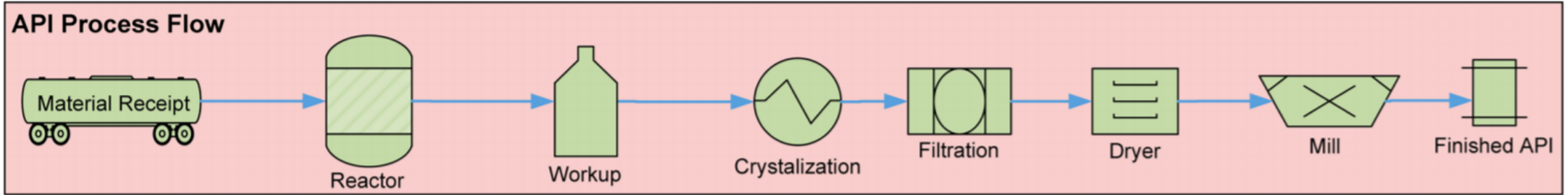
- Development
- Manufacturing (e.g. heterogeneous reaction sampling)
- Troubleshooting
- Capacity of PAT tools
- Sensitivity of a PAT tool

Especially useful during **continuous** processes



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## WHEN TO USE PAT?



Analysis Needs:  
Identification

Typical Techniques:  
**In Field:**  
MIR, NIR, Raman  
(Hand Held)  
**In Lab:**  
MIR, Chromatography

Analysis Needs:  
Reaction completion,  
impurity profile,  
kinetics, solvent  
composition

Typical Techniques:  
Calorimetry,  
Chromatography  
MIR, NIR, UV,  
Raman, NMR,  
Polarimetry  
pH, Temperature,  
Pressure

Analysis Needs:  
Reaction yield,  
impurity profile,  
solvent  
composition

Typical Techniques:  
Chromatography,  
MIR, NIR

Analysis Needs:  
Particle  
distribution,  
shape, form,  
supersaturation

Typical Techniques:  
Turbidity,  
FBRM, PVM,  
Raman, MIR

Analysis Needs:  
Moisture/solvent  
content, form,  
particle attrition/  
agglomeration

Typical Techniques:  
FAIMS, MIR, NIR,  
MS (Exhaust),  
NIR (direct),  
Raman, FBRM

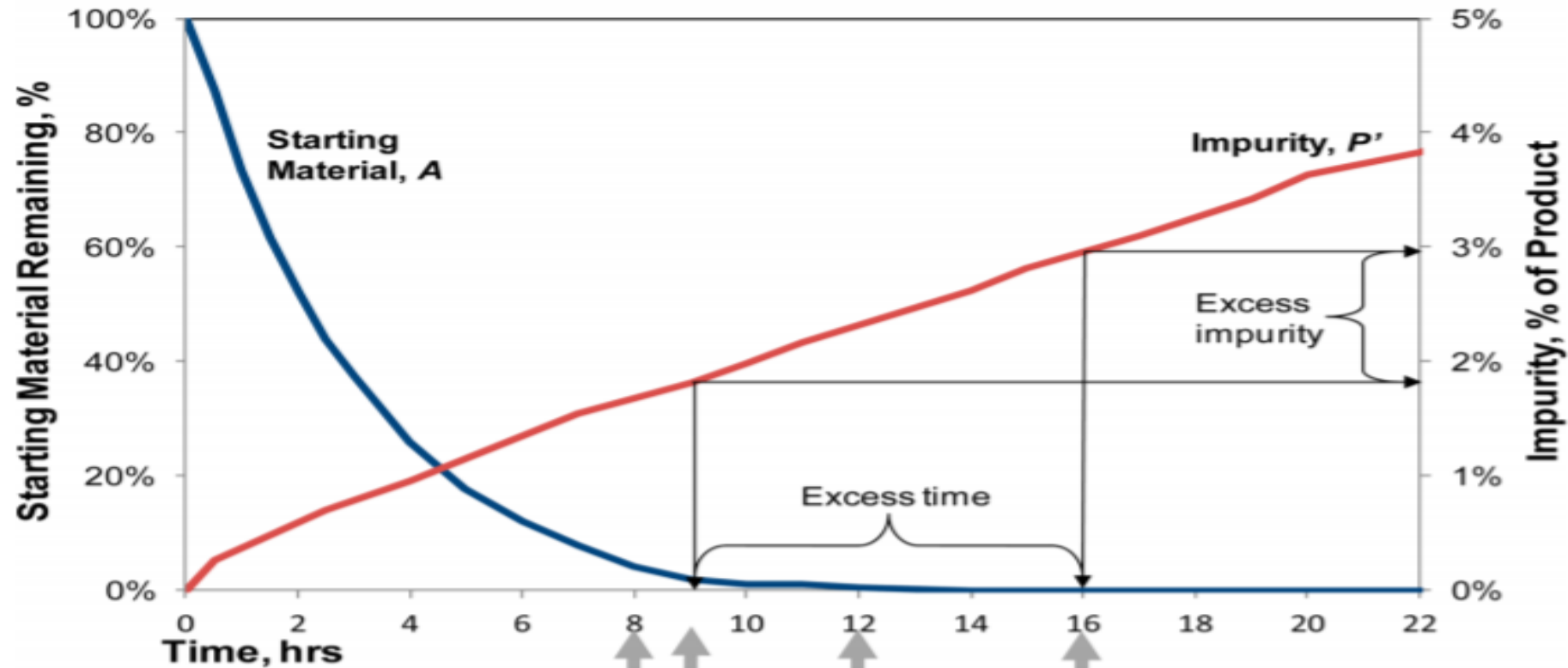
Analysis Needs:  
Particle size

Typical Techniques:  
FBRM

Analysis Needs:  
Identification

Typical Techniques:  
MIR, NIR,  
Raman

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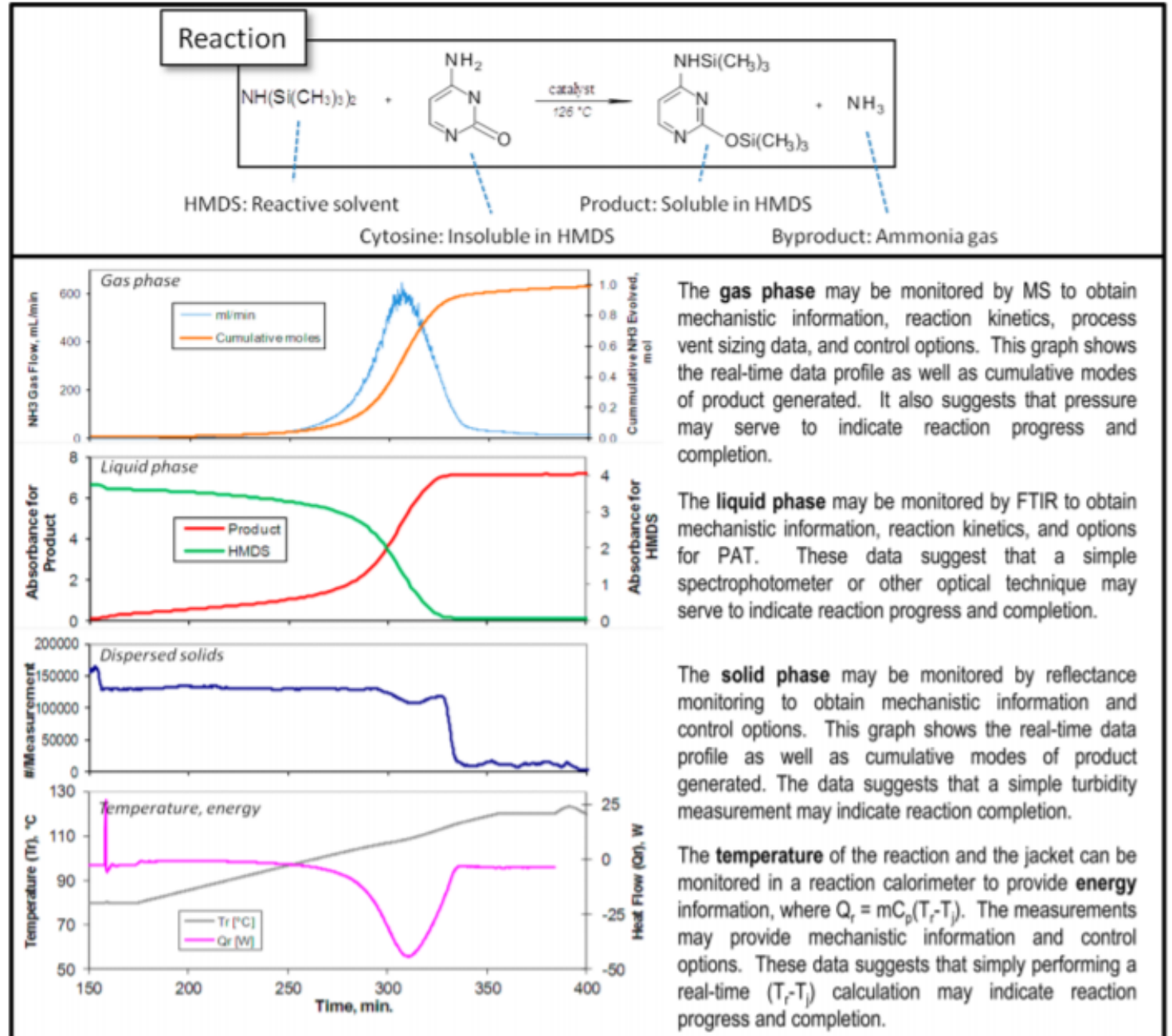
① Reaction sample obtained

② Reaction complete

③ 1<sup>st</sup> HPLC result returned showing incomplete reaction. 2<sup>nd</sup> reaction sample obtained

④ 2<sup>nd</sup> HPLC result returned showing complete reaction

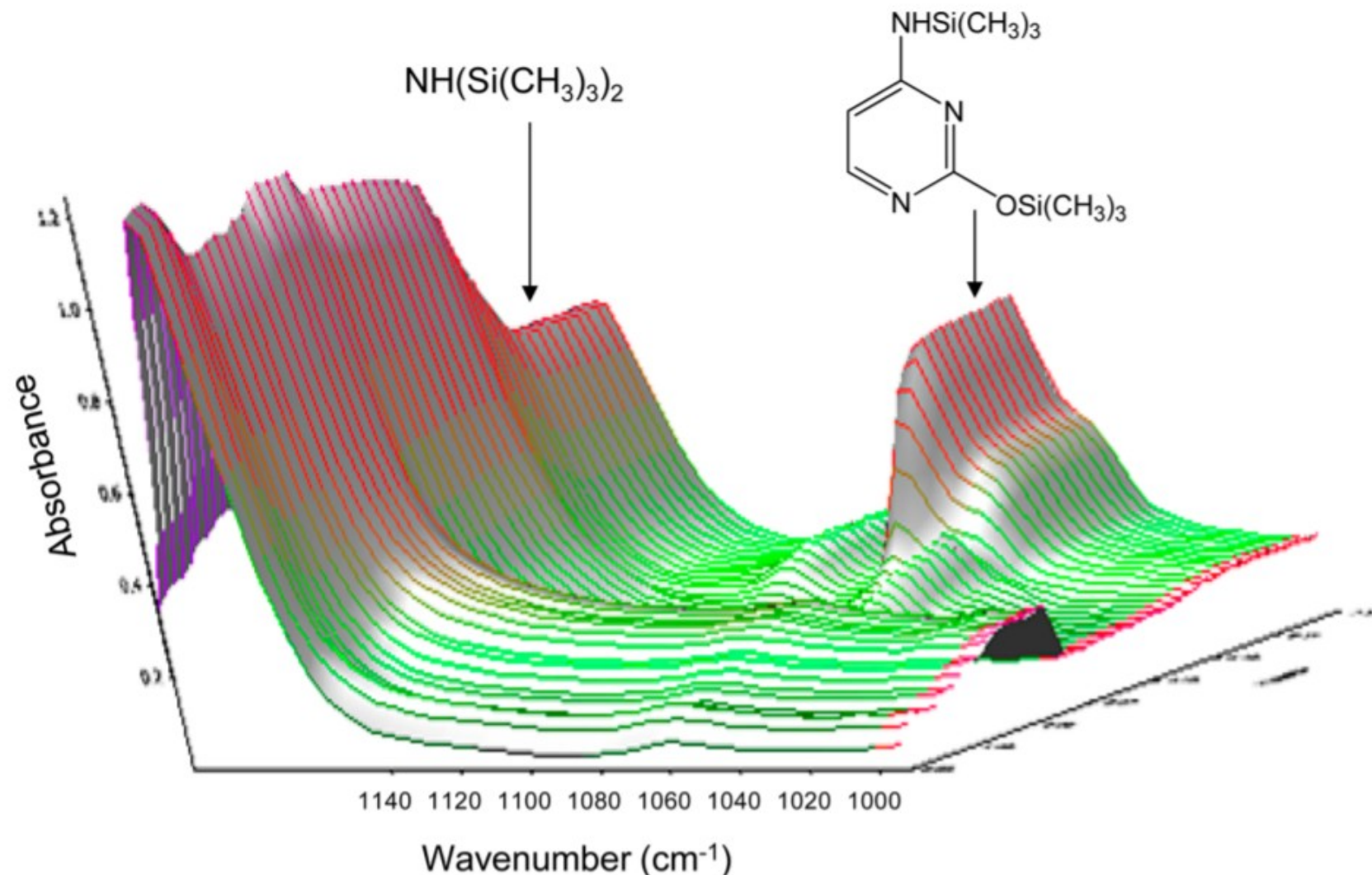
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Chanda, A. *et al*  
*Org.Process Res.Dev.* 19,  
 63 (2015)



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Chanda, A. *et al* *Org.Process Res.Dev.* 19, 63 (2015)