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# **PAT Applications Regulatory and Inspection Perspective**

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# Definitions

- **Definition of PAT**

A system for designing, analysing and controlling manufacturing through timely measurements (i.e. during processing) of critical quality and performance attributes of raw and in-process materials and processes with the goal of ensuring final product quality



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# Definition of PAT

**PAT is a useful tool to achieve the desired state.**

PAT tools

- Multivariate tools for design, data acquisition and analysis
- Process analyzers
- Process control tools
- Continuous improvement and knowledge management tools



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# IMB Participation in PAT Initiatives

- Membership of EMEA PAT Team
- IMB PAT Team – Senior Scientific Advisor, 4 assessors and 2 inspectors.
- ISPE Community of Practice (COP) Irish meetings
- EMEA-EFPIA Meeting 31st March -2<sup>nd</sup> April
- Participation in EMEA Work Sharing Initiative



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# EMEA PAT Team

- **EMEA PAT team**
- *www.emea.europa.eu/Inspections/PAT*
- **General objective:**
- Prepare a harmonised approach within EU on assessment of :

applications and performing GMP inspections of systems/facilities for Process Analytical Technology, including quality by design principles and manufacturing science in the context of PAT for Human and Veterinary products.



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# EMEA PAT Team

- **Composition:**
- Assessors and GMP inspectors and BWP members
- EDQM-observer
- Support from EMEA secretariat



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# EMEA PAT Team Objectives

- Forum for dialogue with applicants on QbD/PAT aspects
- Review “mock” submissions of PAT related applications
- When requested, to provide specialist input into dossier assessment and scientific advice
- Communicate the outcomes to the relevant EMEA WPs
- Identify training needs of assessors and inspectors and organise Training



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# Role of EMEA and IMB PAT Teams

The role of the EMEA and the IMB PAT team is to give advice to companies to help to provide consistency of interpretation to communicate this to all concerned assessors and to provide leadership and training where possible to ensure that such applications are critically evaluated and smoothly introduced when there are good grounds for so doing.



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# Role of EMEA and IMP PAT Teams

Regulators and assessors from the authorities need to work closely together in regard to quality by design, design space, PAT and real time release applications.



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# PAT Installation and Operation

- As a general principle, where PAT techniques are being used to generate information, there is no particular expectation on the Qualified Person because the measurements do not have any direct impact on the product quality.



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# PAT Installation and Operation

- However, where measurements do have direct impact and when PAT is being used for monitoring or control purposes, the QP should ensure that PAT equipment is properly qualified, analytical methods are validated and that measures are in place to investigate OOS results.



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# MISCONCEPTIONS REGARDING PAT APPLICATIONS

PAT application **must be registered** before installation.

PAT applications **need not be registered** if Quality system aspects are met. e.g. PAT Equipment Qualification.

Information generated from PAT monitoring **can be used** to invalidate out of specification results.



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# PAT Applications in Practice

- Very few examples seen during inspections even with those companies pioneering the technology.
- Companies are proactively including PAT Application Installations into new equipment even though they have not installed them yet
- Types of Equipment observed during inspections in development or (in a few cases) in operation.



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# PAT Applications in Practice

- NIR
- Applications
  - Identification
  - Reaction monitoring
  - Monitoring drying operations
  - On line Assay of unit doses



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- Applications Continued
  - FBRM (Focused Beam Reflection Measurement)
  - Crystallisation
  - Milling operations



- Applications Continued
  - GC (Gas chromatography)
  - Solvent Recovery



# PAT Applications in Practice

- TOC- on line measurement of TOC  
Is it a form of PAT?
- Checkmaster systems on tablet presses

Weights

Hardness

Dimensions



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# Inspections

- Inspection Experiences

One specific inspection carried out in Ireland for a PAT application.

No deficiencies with respect to the PAT application.

Increased number of sightings of PAT initiatives in manufacturing sites



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# PAT and Quality By Design

- Link between PAT and QBD
- PAT possible applications without QBD approach
- Difficult to envisage a QBD application without PAT



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# Installation issues

- Equipment installation
- Optimum installation location.
- Retrospective Installation-  
Convenient or available port.



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# Quality by Design Applications

- Knowledge of QBD aspects from an inspectors perspective.
- Likelihood of joint inspections between inspectors and assessors.



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