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EMEA progress and status – what is needed to document scientific understanding in a PAT application

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EMEA PAT team - who are we?

- **EMEA representatives**
- **Regulatory people from European health authorities**
- **Inspectors from European health authorities**

Group established end of year 2003, and meetings take place at the EMEA, London, UK



EMEA PAT team definition of PAT

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

General objective of Group

A forum for dialogue and understanding between Quality Working Party and ad Hoc Group of GMP Inspection Services to prepare a harmonised approach in Europe on assessment of applications and inspections of systems/ facilities including new approaches to manufacturing and control of actives substance, medicinal product, packaging etc. (PAT)

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Specific objectives of the group

- **Definition of PAT**
- **Review of legal and procedural implications of PAT on EU regulatory system (including new guidelines)**
- **Review and comment on documents produced by other organisations**
- **Review of mock submissions (questions and answers)**
- **Develop a procedure for assessment of PAT related applications (co-ordinated approach by assessors and inspectors)**
- **Avoidance of disharmony with other regions**

Why this rather new PAT concept?

- **New analytical techniques (NIR, Raman etc.) combined with extensive statistical and data-processing instruments**
- **You gain increased process understanding**
- **Reduced number of bat-ches that are not released for sale**
- **Real Time Release**
- **Compliance with cGMP/state of the art technology**

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Expressions/ definitions:

- **Real Time Release (RTR) – test for sterility**
- **At-line, on-line, in-line**
- **Design Of Experiments (DOE)**



Expressions/ definitions - continued

- **Process signature:**
A collection of batch specific information that shows a batch has been produced within the design space for the product (PAT team proposal for comments)
ASTM definition:” a single or multi-dimensional signal indicative of the attributes of the process” is acceptable, however, it might be extended to show an acceptable regulatory process signature
- **Design space:**
The multi-dimensional region within which product of guaranteed quality will be produced



Questions and answers on EMEA home page (example)

**When PAT is implemented will
the manufacturer be allowed
to make changes to the
process without the need for
regulatory approval?**

... acceptable within the design space



Manufacturing - examples

- **Manufacture of tablets/capsules**
- **Biotech manufacture**

**In fact,
all types of manufacturing**

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Important aspects identified in mock applications (1)

- **Overview of PAT approach and strategy (P2 part of CTD)**
- **If quality risk management is used – summary of results (tabulated) and show how conclusions were reached.**
- **Development part important and critical parameters must be identified.**
- **Description of DOE. The results presented should be graphical and/or tabulated and interpreted.**
- **Comparison with approved specifications**
- **Validation of NIR systems should take into account elevated temperatures during processing**

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Important aspects identified in mock applications (2)

- **A description of and justification for the handling of process outliers should be included**
- **Discussions concerning amount of documentation that should be included in the application and amount of documentation that should be available for the inspectors only is on-going**
- **Difficult for regulators to have the statistical expertise needed**

A guidance paper for PAT specific issues in the file (CTD) has been prepared (first draft)

Education of the EMEA PAT team

- **Company visits**
- **Courses**

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EMEA PAT team communication

The Quality Working Party and GMP Inspection Services Group at the EMEA are informed about the outcome of the work in the group and information is provided on the EMEA homepage (www.emea.eu.int)

In addition, the group communicates with the FDA

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Today and the future

- **PAT is used in many other industries today and will probably be used much more in the pharmaceutical industry in the years to come**
- **Applications (variations) are expected to be submitted soon in the EU**
- **The EMEA PAT team will support the industry. The industry is encouraged to approach the group.**
- **Actually, several companies and organisations have approached the group (mock applications, presentations and questions)**
- **My e-mail: cmo@dkma.dk**

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