The FDA and the others: European and ROW PAT regulatory status

Starting Comments for Discussion Group

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for Pharmaceutical Process Analytics Roundtable
San Francisco October 2004

Merck Manufacturing Division Process Analytics Group

Regulatory Issues around PAT

- Regulatory guidance isn't the sole ***driver*** for use of PAT in pharmaceutical industry
- …but it is a key ***issue*** when trying to use PAT in the pharmaceutical industry
- Large pharma companies operate globally
  - Harmonization of world-wide regulatory situation in other technical areas is far from ideal…
  - …but in the case of PAT there is a high degree of non-harmonization
  - This can present a significant internal and external challenge, especially in manufacturing PAT installations

US Situation

- FDA showed initiative for and sought input into their strategy
  - Very vocal about PAT topic from the start - A. Hussain “road show”
  - Very approachable - several contacts
  - Organized several forums for input (2002 to 2003)
    - Industry and Academia
    - Technical, strategic and regulatory topics
    - Without immediate context to particular process/product
  - Established draft guidance
    - Asked for feedback before finalizing
    - Finalized (?) guidance based on ensuing discussion (?)

US Situation cont.

- FDA looked for technical training of their PAT team
  - industry/academia responded
- FDA could be approached throughout the whole process on any topic
  - From general technical discussions to specific regulatory filings
  - Was open to any flavor of PAT and any “comfort zone” for pharma companies
- Pharmaceutical Industry PAT community
  - Showed promising amount of common effort to make FDA regulation scientifically sound and practically relevant

European Situation

- EMEA formed *"Joint Team of QWP/Ad Hoc GMP Inspectors Group for PAT"* in Feb 2004
  - Objectives:
    - Agree on Definition of PAT
    - Review implications on EU regulatory system
    - Review and comment on outside documents (EDQM, FDA,..)
    - Review related international procedures and approaches
    - Perform review of "mock" submissions
    - Develop PAT assessment procedure
- EMEA and national regulatory agency members started appearing at PAT conferences
  - Presentations/statements very general
  - At times mixed messages
- EMEA appears to seek alignment with ICH
  - *Benefits of larger alignment vs. cost of perceived slow progress*

European Situation –difference to US

- EMEA has not widely sought input from pharma industry/academia
- EMEA has not (at least not publicly) encouraged informal PAT interaction with industry
  - "Mock submission" as the only departure point?
  - Such submission are high-effort situations that are mostly not preferred as first interaction

- Concerted effort by pharma industry to communicate with EMEA to date
  - EFPIA draft paper on real-time release (2002)
    - Status ?
  - Other? Individual companies? Individual sites?

Rest of World

- Other regions?
  - Canada
  - Australia
  - Japan