AstraZeneca

7638 '03 OCT 29 18:55

Date: OCT 2 8 2003

Dockets Management Branch
(HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Docket Number 2003D-0380
Response to FDA Call for Comments
Draft Guidance for Industry: Process Analytical Technology – A Framework for Innovative Pharmaceutical Manufacturing and Quality Assurance.

Dear Sir or Madam:

Reference is made to the September 5, 2003 Federal Register notice announcing the request for comments on Draft Guidance for Industry: Process Analytical Technology – A Framework for Innovative Pharmaceutical Manufacturing and Quality Assurance.

AstraZeneca welcomes this guidance and concurs with the key principles outlined:

- The guidance supports a scientific and risk-based approach.
- The guidance embraces both new and marketed products.
- The guidance endorses the safe harbor concept for the exemption of PAT research data from GMP inspection.
- Real Time Release based on process information is accepted as a viable alternative for the release of drug product.

Following review of the guidance, AstraZeneca wishes to seek clarification concerning the following aspects:

Continuous Real Time Quality Assurance

- Line 142: AstraZeneca requests clarification of the term "**continuous**" in the context of "Continuous real time quality assurance."
- Lines 470-474: "In a PAT framework...consist of continuous quality assurance where a process is continually monitored...". AstraZeneca seeks further clarification on the interpretation of "**continuous**" in the context of quality assurance and "**continually**" in the context of monitoring.

US Regulatory Affairs
AstraZeneca Pharmaceuticals LP
1800 Concord Pike PO Box 8355 Wilmington DE 19803-8355

AZ0009 (8/00)

2003D-0380

C3

PAT Framework and PAT Tools

- Lines 185 and 504: AstraZeneca requests clarification of the definition of **environmental variables** in the context of this guidance.

- Line 283: AstraZeneca requests inclusion of **multi-variate tools for design** into the first bullet point: "Multi-variate tools for design, data acquisition and analysis."

Process Monitoring, Control and Endpoints

- Lines 445-455: AstraZeneca seeks clarification of the intention of the Agency with regard to this paragraph. AstraZeneca's interpretation of the paragraph seems to contradict the risk-based approach, which forms the basis of the guidance. AstraZeneca believes that **statistical process control** needs to take into account the level of process understanding and process capability and increased sampling may not be appropriate where it would not add value to the quality decision.

Regulatory Strategies

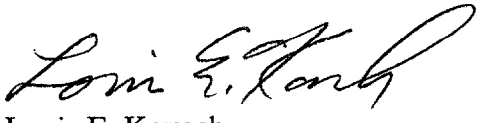
- AstraZeneca seeks clarification on the section of the guidance dealing with regulatory strategies. The **regulatory pathways**, as well as principles on which decisions on appropriate **filing categories** are made, are not clear. For example, lines 722-725 seem to suggest that the principles relating to regulatory pathways for PAT implementation are different to the currently applied principles for CMC changes (e.g., minor, moderate and major potential impact on product quality). This appears to contradict the risk-based approach underlying the guidance.

Terminology

- AstraZeneca recommends that a glossary be added to the guidance. For example, the term "**specification(s)**" is used broadly throughout the guidance, covering a variety of different limits and acceptance criteria employed throughout manufacturing. It would be useful if this term and other significant terms were defined in a glossary.

Please direct any questions or requests for additional information to me.

Sincerely,



Louis E. Kovach
Regulatory Affairs
Telephone: 302-885-4501
Fax: 302-886-2822