H. Lundbeck A/S

9 Ottiliavej DK-2500 Valby
Copenhagen Denmark

Tel +45 36432762
Fax +45 36438297

E-mail lilu@lundbeck.com
www.lundbeck.com

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Food and Drug Administration
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Rockville, MD 20852
USA
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Our ref LILU
Your ref PAT

Comments to "Guidance for Industry PAT - A framework for Innovative Pharmaceutical Manufacturing and quality Assurance" Draft Guidance, docket 2003D-0380

Line # 30:
The level of product quality assurance should be *appropriate*

Line # 77-80:
Clarifying that the PAT application could be for a sub process only.

Line # 80-82:
Clarification that knowledge gained from non-submitted PAT applications could not be used for regulatory or inspection purposes.

Line # 121:
Use the right technology not necessary the latest invented.

Line # 229:
Standards and specifications should be relevant for the product or process too.

Line # 268-269:
Not only differences in the physical but also in the chemical attributes should be managed.

Line # 294-411:
Section 1 PAT Tools should be reduced significantly to clarify the content. Line # 294-358, *a. Multivariate Data Acquisition and Analysis*. Reduced significantly for clarification purposes.

Line # 305-308: We would like the FDA to clarify the content and meaning of the following sentence (highlighted): *"Opportunities need to be identified to improve the usefulness of available relevant product and process knowledge during regulatory decision making — without affecting a manufacturer's development program."*

Line # 360-411, *b. Process Analyzers or Process Analytical Chemistry Tools.* Reduced significantly for clarification purposes.

Line # 440-445:
If PAT is used for monitoring end-point reaction, the conventional time window is not needed/relevant.

Line # 455-456:
Rigorous statistical principles should be combined with chemometrics and chemical knowledge

Line # 466-471:
To be deleted. How PAT data should be presented in the batch record must depend on the application and must be a decision made by the individual company.

Line # 473-480:
Process validation when using PAT seems to be very unclear defined in this draft guidance. We recommend that the process validation as well as the validation of the PAT applications must be defined and evaluated case by case between the applicant and FDA.

Line # 645-646:
Clarifying that FDA **will not** inspect research data collected on an existing product using PAT tools (safe harbour principle).

Line # 662:
Clarifying that an appropriate product quality level is right – not too low neither too high.

Other recommendations:

1. We recommend a **list of definitions** used through out the draft Guidance, including definition of *product and final product*

2. During previous discussions with FDA at different conferences and workshops regarding PAT, **preliminary, temporary or functional specifications** has been identified as a need when submitting a DMF using PAT. Specifications based on three validation batches may not be the right specifications as the process knowledge is still limited. We would recommend FDA to include a section in the

Guidance regarding the possibility of submitting preliminary, temporary or functional specifications to be adjusted by the applicant later in line with the advance of process knowledge.

3. The concept of **Process validation** when using PAT for monitoring the process, real-time analyse or real-time release is not clear to us. We recommend that the issue of process validation should be more specific and to be discussed and evaluated by the applicant and FDA jointly prior to the submission based on the Guidance.

4. **Data maintenance**. From the draft guidance it is not clear to us how to manage and maintain on-line data, data information and data handling systems. To what extend should the Part 11 Guidance be adopted for data not to be used for real-time release?

Best regards

Line Lundsberg-Nielsen
Head of Department
In-Process Analysis
H- Lundbeck A/S

Henrik Schou Sørensen
Head of Department
Quality Assurance
H. Lundbeck A/S