

Comments on the FDA "Guidance for Industry PAT – A Framework for Innovative
Pharmaceutical Manufacturing and Quality Assurance"

Docket # 2003D-0380

Comments From:

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- 1) Line 309-313: *“To achieve this benefit, some manufacturers use multivariate mathematical approaches, such as statistical design of experiments, response surface methodologies, process simulation, and pattern recognition tools, in conjunction with knowledge management systems.”*
 - a. We request that the definition of multivariate mathematical approaches include “chemometrics” as an option as well. Use of the word of chemometrics conveys the utilization of PCA (Principle Components Analysis) and PLS (Partial Least Squares) as well as other techniques and algorithms. Though we do not see the need to do into the fine detail of listing the specific algorithms themselves, we are missing a field of analysis if “chemometrics” is excluded from this document.
- 2) In the document there is a distinction between the use of PAT for new products (ie: as part of the regulatory approval process) and the use of PAT for existing approved products. We feel that the emphasis of the current version of the document is placed on new products.

Just as there is an emphasis on the new product lines, there seems to be a treatment of existing lines as being a footnote to the entire document – see Line 626-7 *“We also encourage the use of PAT strategies for the manufacture of currently approved products.”*

We feel that at the beginning of the document there should be a definition of PAT that includes a note stating that PAT can be equally applied to both new and existing product lines.

Why is this a concern? Currently, many of the “expensive” product lines for manufacturers (ie: costly to produce product, regulatory fines/concerns, large scrapped product, recycled product, pipe-line delays, etc.) are on existing production lines. Therefore, it makes sense to encourage the use of these techniques to help these lines. These production lines are often “black box” lines – ie: they are many years old and the process is not well understood or well analyzed. There is a natural fit for PAT related technology to help augment these production lines to help reduce the production costs.

- 3) To help aid this adoption of PAT technology to both new and old production lines, the exact definition of what is meant by “research data” (see Line 632-3) should be clarified. In particular, a step by step outline of how a manufacturer site should take research data to validated system would be beneficial.

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