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October 27, 2003

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, room 1061
Rockville, MD 20852

Reference: Docket No. 2003D-0380: *Guidance for Industry: (PAT) Process Analytical Technology – A Framework for Innovative Pharmaceutical Manufacturing and Quality Assurance*

Dear Madam or Sir:

On behalf of Purdue Pharma L. P. and associated companies, comments are being submitted on your DRAFT *Guidance for Industry: (PAT) Process Analytical Technology – A Framework for Innovative Pharmaceutical Manufacturing and Quality Assurance.* We appreciate the opportunity to provide the attached comments for your consideration.

Purdue Pharma L.P. is an independent company known for its commitment to helping to alleviate suffering that arises from a wide range of human conditions. Headquartered in Stamford, Connecticut, Purdue is part of an international group of independent associated companies – including Mundipharma in Germany and Napp Pharmaceutical Group in the United Kingdom – employing people in pharmaceutical research, manufacturing, and marketing worldwide.

Sincerely,
Suzett L. Perry

Sr. Regulatory CMC Associate
Regulatory Affairs

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Purdue Comments and Questions

Line Number(s)	Comment or Question
72	Please provide clarification on whether this guidance is applicable to products supplied for clinical studies.
100	Should "U.S." be replaced by a global term to reflect the wider audience impacted by exported/imported products?
233-246	Please provide an example of the additional information that can be obtained using the new technologies, or provide an alternative way of emphasizing the ability to measure attributes other than the distribution or release of active ingredient. An example might involve the ability to look at the uniformity of distribution of lubricant and disintegrant as a predictor of dissolution.
509-520	Please provide a specific case where a direct comparison of new and conventional analytical techniques would not be needed and one where it would be needed.
512-518	Please clarify the amount of validation that would be required to introduce on- or in-line process analyzer to replace a conventional laboratory test. Please also clarify the level of validation required to introduce an on- or in-line process analyzer that generates data to produce a "process signature". Such an analyzer may not generate absolute values but monitor change and provide additional information not obtained from conventional laboratory tests.
611-615	How will a PAT inspection differ from a cGMP inspection?
611-615	How will PAT compliance be measured by the FDA PAT review, inspection, and compliance staff?
Regulatory Strategies	There is limited guidance in the regulatory strategy section on which filing mechanism should be used for various post approval changes to move manufacturing and control of a product to or toward PAT principles. Reference is made to "current regulations" as being sufficiently broad to accommodate these new strategies, but will these regulations (e.g., *Guidance for Industry: Changes to an Approved NDA/ANDA*) be updated to include PAT specific examples and recommended filing types/categories?

Line Number(s)	Comment or Question
General	We realize there have been entire meetings and an issue of the *The Gold Sheet* devoted to the relationship between 21CFR Part 11 and PAT, and this guideline hints at the attitude the FDA will have. We recommend a single section clearly describing the relationship between PAT and Part 11 in each of the situations where an innovative on-line measurement system could be used (e.g., early research, research where the data will be used to conclude information on process parameters, clinical supplies, routine production).
General	On a similar, general theme, the issue of how companies would be expected to handle data would be worth a section. For example, you can currently determine if the content uniformity of a batch of tablets is acceptable based on a sample of 10. There are limits for number of outliers and the RSD of the sample. Using an on-line technique, the technology is available to test thousands of dosage units. How does the FDA expect the data to be interpreted? Batches within the current USP limits for content uniformity, but with a relatively high RSD and a mean not centered on 100%, could be found to contain a many dosage units lower than 85% or higher than 115%. How do we determine if the batch is acceptable?
General	At what phase of product development will companies be encouraged to perform process capability?
General	From this guidance, it is clear that better process understanding would lead to a decrease in post-approval changes and traditional validation activities. If a company successfully implements PAT initiatives, please specify reduction in validation work and regulatory submissions that will be possible.