PharmaSys
Compliance & Validation

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January 12, 2009

Division of Dockets Management (HFA-305)
Food and Drug Administration,
5630 Fishers Lane, rm. 1061
Rockville, MD 20852
Ref: Docket No. FDA-2008-D-0559

Dear Sir,

This letter represents comments by PharmaSys on "Guidance for Industry, Process Validation: General Principles and Practices, DRAFT GUIDANCE", published in the Federal Register: November 18, 2008 (Volume 73, Number 223), Docket No. FDA-2008-D-0559, and open to comments until January 20, 2009.

PharmaSys has provided contract compliance and validation services to the Pharmaceutical industry since 1998 and as such, is an interested party to this guidance

In general, PharmaSys strongly agrees with the principles and methodologies stated with the following comments:

1. Lines 27-29 "The lifecycle concept links product and process development, qualification of the commercial manufacturing process, and maintenance of the process in a state of control during routine commercial production."

   PharmaSys believes that the guidance document should define what is meant by "commercial manufacturing process" and "commercial production". Without definition, the term, "commercial", leaves too much room for interpretation.

2. Line 44 excludes Dietary Supplements from this guidance

   PharmaSys strongly believes that process validation guidelines should be applicable to Dietary Supplements as well as pharmaceuticals.

3. Lines 377-381 – "Success at this stage signals an important milestone in the product lifecycle and needs to be completed before a manufacturer commences commercial distribution of the

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drug product. The decision to begin commercial distribution should be supported by data from commercial batches. Data from laboratory and pilot studies can provide additional assurance."

PharmaSys believes that this process validation guideline should state whether or not the process for manufacturing Phase 2 or Phase 3 clinical study material should be validated/qualified.

4. Lines 438-439 implies that acceptance criteria should use "statistical metrics defining both intra-batch and inter-batch variability"

   It has long been customary that three consecutive batches within specifications constitute a successful Process Qualification. Does this statement imply a departure from traditional methodology?

   PharmaSys believes that this statement could also be interpreted that Process Qualification does not necessarily have to meet process specifications in order to pass Process Qualification. Perhaps the guideline should specify that process specifications should be met for successful Process Qualification.

   PharmaSys believes that the FDA should provide additional guidance on how much intra-batch and inter-batch variability is acceptable for successful Process Qualification.

   PharmaSys believes this guideline should also elaborate upon the FDA's position of the number of consecutive batches needed to qualify a process.

5. Lines 456-457 "Protocol execution should not begin until the protocol has been reviewed and approved 457 by all appropriate departments, including the quality unit. "

   PharmaSys strongly agrees that the quality unit should review the Process Qualification protocol(s) before execution starts.

6. Lines 539-541 " Variation can also be detected by the timely assessment of defect complaints, out-of-specification findings, process deviation reports, process yield variations, batch records, incoming raw material records, and adverse event reports."

   PharmaSys believes that guidelines on the period between the event and the assessment that is considered "timely" vs. delinquent should be provided.

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Yours truly,

Charles Lankford,

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