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November 17, 2000

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

**Subject: Docket 00D-1424; Draft Guidance for Industry on Analytical Procedures and Methods Validation**

Below are comments and questions we have regarding the draft Guidance for Industry on Analytical Procedures and Methods Validation. Please consider them and, if possible, provide answers before finalizing the guidance document.

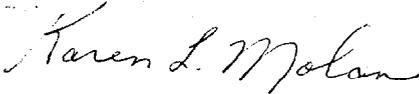
The paragraph beginning on *Line 89* suggests that in-process analytical procedures must be validated. Does this refer to drug product processes only or does this include bulk drug substance manufacturing processes as well? Is there a distinction in the amount of validation necessary for steps early in the manufacturing process vs. later steps? We propose that in-process methods for bulk drug substance manufacturing should not require ICH or GMP validation and that there be a distinction in the amount of validation needed depending on whether the method is used early or late in the manufacturing process.

The sentence beginning on *Line 157* states that "...analytical procedures used to characterize a reference standard are expected to be different from and more extensive than those used..." for drug substance or product. We usually develop HPLC and GC methods that will be used for both analytical standards and drug substance and product because these methods often look for all potential impurities in the materials. However, we agree that additional tests and more extensive tests be used to characterize a reference standard. We propose that the words, "different from", be removed from the sentence.

We propose that the paragraph beginning on *Line 583* regarding validation of Compendial analytical procedures be removed. It would be too burdensome for a company to go back to all of the USP/NF procedures that may have been in place for many years to perform validation that was not previously required.

In the paragraph beginning on *Line 623*, statistical references are discussed. Are the references listed on *Lines 1233 to 1237* the only acceptable references or are other statistical reference books also acceptable?

Best Regards,



Karen L. Molan  
Manager, Analytical Resources  
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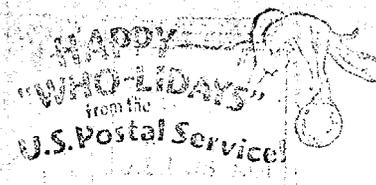
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