

**Alice E. Till, Ph.D.**  
VICE PRESIDENT  
SCIENCE POLICY AND TECHNICAL AFFAIRS



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July 30, 2002

Dockets Management Branch (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, Maryland 20852

Re: International Conference on Harmonisation; Draft guidance on Q1E Evaluation of Stability Data [Docket No. 02D-0237, 67 *Federal Register*, 40949, June 14, 2002]

Dear Sir/Madam:

The Pharmaceutical Research and Manufacturers of America (PhRMA) represents the country's leading research-based pharmaceutical and biotechnology companies, which are devoted to inventing medicines that allow patients to lead longer, happier and more productive lives. Investing more than \$30 billion in 2001 in discovering and developing new medicines, PhRMA companies are leading the way in the search for cures.

PhRMA, therefore, appreciates the opportunity to provide the attached comments on the Draft Guidance on Q1E.

We hope that you will give careful consideration to the attached comments as you work to finalize the guidance. Please contact me if there are any questions.

Sincerely,

Alice E. Till, Ph.D.

CC Chi-wan Chen

Att.

02D-0237

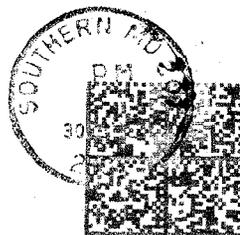
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*Pharmaceutical Research and Manufacturers of America*

**PhRMA Statistics Working Group Comments on Q1E Step 3 02Feb2002**

<b>Section</b>	<b>Paragraph #</b>	<b>Sentence #</b>	<b>Comments</b>
Appendix B, Section B.1	3	first	The use of confidence limits for the regression line involves inference on the means, not individual values. We suggest that this sentence should be changed to read "If the above approach is used, the mean value of the quantitative attribute (e.g., assay, degradation products) can be expected to remain within acceptance criteria through the end of the retest period or shelf life at a confidence level of 95 percent."
Appendix B, Section B.1	3	last	It is not clear as to which products or attributes this sentence refers to. Although one ensures that content uniformity is met at shelf life, content uniformity is not routinely tested during stability studies. In most cases, where the acceptance criterion calls for individual values, the tests are multi-stage in nature. The multi-stage nature of the tests calls for a more complicated analysis, possibly with no closed forms for computing limits on individual values. Unless more clarification and guidance is given on the implementation of this sentence, this sentence should be deleted.
Appendix B, Section B.2.1.2			Some of the statistical procedures described in this section require one to specify a desired level of power. Some guidance is needed on what would be considered an acceptable level of power.

**FDA**



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