

**JERUSSI CONSULTING, INC.**

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August 12, 2002

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

Docket No. 02D-0237

Gentlemen:

I wish to comment on the ICH Draft Guidance on Q1E Evaluation of Stability Data whose availability was announced on Friday, June 14, 2002 in the Federal Register Vol. 67, No. 115, 40949. The closing date for comments was August 1, 2002 but I request that these comments be received and considered due, in part, to the short response period of 47 days.

I have several comments/questions on this draft guidance. They are:

1. In the last paragraph of Section 2.1 General Principles the following sentence appears "In general, certain quantitative chemical attributes (e.g. assay, degradation products, preservative content) for a drug substance or product can be assumed to follow zero-order kinetics during long term storage." This sentence is somewhat confusing. Zero order kinetics for what reaction - oxidation, reaction with an excipient, etc.? What chemical transformation is being followed? Additionally, is it zero order for both the kinetics of solid state reactions and of solution reactions? For reactions that are slow or fast? No reference is given to actual experimental data to support this statement. This statement can be found in a standard pharmaceutical text but the references are to rather old journals.
2. Does a statistical treatment require a review by a statistician at FDA? If it does it will slow the review of applications at the Agency.
3. Section 2.4.1 No Significant Change at Accelerated Conditions states that where the data is amenable to statistical analysis, a firm doing a statistical treatment could get a shelf life exceeding the long term data by 12 months. With the same data, if the firm does not do a statistical analysis, only 6 months may be added to the long term data. In cases where it is obvious that the data are good (e.g. show so little degradation and so little variability which is apparent from looking at the data) firms will be encouraged to perform a statistical treatment in order to get the additional 6 months. This creates more work for the firm and more work for FDA. Where it is obvious that a statistical treatment is not

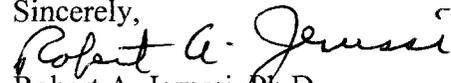
02D-0237

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needed the length of time added to the long term data should be the same whether or not a firm does a statistical treatment.

These comments are respectfully submitted and I am willing to further discuss them with FDA staff either by phone or in person.

Sincerely,

A handwritten signature in black ink that reads "Robert A. Jerussi". The signature is written in a cursive style with a large, prominent initial "R".

Robert A. Jerussi, Ph.D.

President

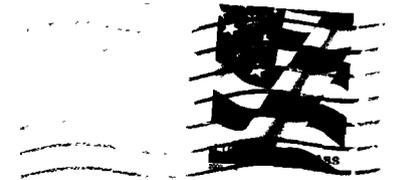
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