July 13, 2001

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Dockets Management Branch (HFA-305)
Food and Drug Administration
12420 Parklawn Dr., rm 1-23
Rockville, MD 20857

Dear Sirs:

Re Docket No. 01D-0194: "Guidance for Industry. Statistical Aspects of the Design, Analysis, and Interpretation of Chronic Rodent Carcinogenicity Studies of Pharmaceuticals"

1. Use of the "fatal" category.

The Peto (1980) statistical analysis uses a category of "fatal" for neoplasms that lead to death. This mathematical model assumes that these neoplasms are rapidly fatal and, hence, the time of death is a surrogate for the time of their onset. However, the proposed draft guidelines appear to designate the usage of "fatal" for all neoplasms that cause death or lead to the moribund sacrifice of an animal. A more appropriate application of the Peto assay would be to use "rapidly fatal" and designate as "incidental" those neoplasms that were slowly fatal. A further complication of this approach is that the pathologist can seldom determine that a neoplasm is "rapidly fatal".

A possible solution to the problem of the use of "fatal" would be to instead employ the Poly K test that NTP uses.

2. The format for electronic submission of tumor data.

This new draft Guidance (page 23 and its reference to the publication to Lin, 1998) gives a format for electronic submissions of neoplasm data which was used in the past but has not, in our experience, been accepted by FDA statisticians for about the last year. Since January, 1999, electronic submissions of neoplasm data from rodent carcinogenicity studies needed to be in the form of SAS transport files according to the CDER's publication "Guidance for Industry. Providing Regulatory Submissions in Electronic Format – NDAs". What will be the new format?

Sincerely,

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