

PHARMACIA

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Dockets Management Branch (HFA-305)
Food and Drug Administration
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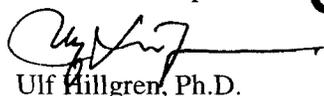
Re: Docket No. 02D-0337; Draft Guidance for industry on Liposome Drug Products: Chemistry, Manufacturing, and Controls; Human Pharmacokinetics and Bioavailability; and Labeling Documentation

Dear Sir or Madam:

We have reviewed the draft **Guidance for Industry, Liposome Drug Products - Chemistry, Manufacturing, and Controls; Human Pharmacokinetics and Bioavailability; and Labeling Documentation** and would like to offer the following comments:

- 1) *II E, Control of Drug Product: Specification, line 213-214, and III D, In Vitro Stability, line 343-344*: it is not clear what is meant by "release characteristics of product over time". We suggest the following wording in stead (line 343): "in-vitro release characteristics of the product over time during storage". Further, we believe that the intent with this test is no to simulate in-vivo release and hence does not require using simulated biofluids. This should be clarified.
- 2) *III B, In Vivo Integrity (Stability) Considerations, line 310-317*: We propose to change the wording to the following: "For the purpose of determining the pharmacokinetics and bioavailability, the total drug substance concentration can be measured, either
 - a. if the ratio between the unencapsulated to encapsulated drug substance remains constant, or
 - b. if the liposome is stable, since in this case the drug substance remains substantially in the encapsulated form in the circulation.However, for an unstable..." etc. until the end of line 319.
- 3) *III C, Protein Binding, line 333-335*: Please consider changing the sentence beginning with "The protein..." to "The protein binding of the drug substance given as liposome and nonliposome drug products should be determined."

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