



November 19, 2002

Dockets Management Branch (HFA-305)
Docket Number 02D-0337 CDER 19981
Food and Drug Administration
5630 Fishers Lane
Rockville, Maryland
USA 20852

To the Liposome Guidance Working Group,

Please find our comments pertaining to the "Guidance for Industry, Liposome Drug Products." We have included our comments providing the line number of the PDF file and the appropriate comment or rewording suggestion in bold for clarity. We wish to thank the Agency for this opportunity to address this important guidance document.

- Line 45 - Please revise sentence starting at the end of line 45 to read, "Liposome drug products are formed when a liposome is used to incorporate a drug substance within the lipid bilayer or encapsulate a drug substance in the interior aqueous space of the liposome."
- Line 74 - Is the molar ratio and percentage by weight of each lipid or of the total, e.g., "The quantity of **each** lipid," or perhaps, "The quantity of the **total** lipid"
- Line 157 - Please alter the comment, "Procedures to ensure the removal of animal proteins and viruses should be described.." to read, "Procedures to ensure the removal **or inactivation** of animal proteins and **viruses** should be described.."
- Line 194 - Please include hydrogen peroxide in place of oxygen for the stress testing conditions.
- Line 210 - Alter bullet point to read: **assays for unencapsulated (i.e., free), encapsulated and/or total drug substance.**
- Line 228 - Clarify what integrity means in the statement, "The physical stability of liposome drug products is a function of the integrity and the size distribution of the liposomes."
- Line 229 - Please include the word "Some" at the start of the sentence, to provide: "**Some** liposomes are susceptible to fusion,..."

02D-0337

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- Line 234 - Change "developed" to "applied" to provide: "Therefore, tests for physical parameters should be **applied** to assess the integrity and size of the liposomes."
- Line 458 - Type A, B, C is draconian and potentially confusing. The possibility exists for type A to be a slow release liposome for one API and a fast release liposome for another API. This could be very confusing to the prescribing public. Has the Office of Drug Safety concurred with this nomenclature?
- Line 477 - Please remove from the warning "or cannot be substituted for" in the line: "...is not equivalent to ~~or cannot be substituted for~~ other drug products containing the same drug substance."

Yours sincerely,

INEX PHARMACEUTICALS CORPORATION

A handwritten signature in black ink, appearing to read 'K. Swiss Ph.D.', with a long horizontal flourish extending to the right.

Kevin Swiss, Ph.D.
Senior Manager, Regulatory Affairs