PDA
Parenteral Drug Association

PDA Global Headquarters
3 Bethesda Metro Center
Suite 1500
Bethesda, MD 20814 USA
Tel: +1 (301) 656-5900
Fax: +1 (301) 986-0296
www.pda.org

March 17, 2006

U.S. Food and Drug Administration
Division of Dockets Management (HFA-305)
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Ref.: [Docket Number: **2005D-0286**]

Draft Guidance for Industry: *INDs – Approaches to Complying with cGMP during Phase I*

Dear Sir/Madam:

The Parenteral Drug Association (PDA) is pleased to provide these comments on the draft *Guidance for Industry, INDs – Approaches to Complying with cGMP during Phase I*. PDA is an international professional association consisting of more than 10,000 individual member scientists having an interest in the fields of pharmaceutical manufacturing and quality. These comments were generated by a PDA Working Group that consisted of industry professionals from 10 different pharmaceutical and consulting firms, and included international representation.

Overall, we consider this document to be helpful guidance. We agree that required manufacturing controls vary with the stage of development; and that the industry has a responsibility to implement appropriate controls that consider the specific product and production situation and current process and product knowledge; in accordance with good scientific principles.

Attached, please find specific detailed suggestions regarding this draft guidance. In addition, our general suggestions are summarized below:

- The scope of Phase 1 studies should be more succinctly described. It should also be clarified that use of this guidance is appropriate for the manufacture of material to use for phase 1 studies, even if the development of the new product itself has progressed into later phases (e.g., repeating a Phase 1 study due to a dosage form change).
- The 1991 FDA Guideline on the *Preparation of Investigational New Drug Products (Human and Animal)* should remain in effect until a new Phase 2/3 guidance document is written.
- The concept of the implementation of appropriate quality control needs clarification. We suggest utilizing the concept of a quality system including suitable use of the terms Quality Unit, Quality Control and Quality Assurance.
- Although the same personnel may perform production and testing in smaller operations, we would suggest that separate personnel perform production and release operations.
- The expectation that this guidance applies to contract manufacturers and other "specialized facilities" such as academic institutions needs to be strengthened.

- We appreciate the difficulty in clearly describing GMP requirements for all various types of production scenarios. To further ensure patient safety, however, we suggest that the guidance recommend that the need for additional controls for the manufacture of products under aseptic conditions be considered when more traditional filling lines are used to manufacture phase 1 materials.

- Requiring an "internal performance review" for bioprocesses is not appropriate for phase 1 materials given the fact that few lots are produced, frequent process changes are made, and each lot needs to be examined on a real-time basis to compare it to previous lots.

We would like to encourage the FDA to develop further guidance for phases 2 and 3 prior to the withdrawal of the 1991 FDA Guideline on the *Preparation of Investigational New Drug Products (Human and Animal)* in view of the fact that 21 CFR Parts 210 and 211, as written, are not appropriate requirements for phase 2 and 3. We also would encourage that concepts given in this guidance be incorporated into other related regulatory guidance documents to achieve worldwide harmonization on this topic (e.g., Annex 13 to Volume 4, Good Manufacturing Practices, ICH Q7A Section 19 – APIs for use in clinical trials). This is particularly important since many pharmaceutical companies are international companies producing materials for clinical trials throughout the world.

We appreciate the opportunity to comment on this guidance document as we both strive to develop guidance that facilitates the production of investigational new drugs while ensuring patient safety. Please contact us if we can be of any further assistance with the development of this important Guidance for Industry.

Sincerely,

Richard V. Levy, PhD
Vice President, Scientific and Regulatory Affairs
PDA