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

Ref.: [Docket Number **2005N-0285**]

Direct Final and Proposed Final Rules: *Current Good Manufacturing Practice Regulation and Investigational New Drugs*

Dear Sir/Madam:

The Parenteral Drug Association (PDA) is pleased to provide these comments on the Direct Final and Proposed Final Rules *Current Good Manufacturing Practice Regulation and Investigational New Drugs*. 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 welcome the proposed change in regulatory requirements associated with the manufacture of Phase 1 investigational new drugs, however, we would like to offer the following suggestions:

1. If the 1991 FDA Guideline for the Preparation of Investigational New Drug Products is eliminated when the draft *Guidance for Industry, INDs – Approaches to Complying with cGMP during Phase I* document is finalized, all portions of 210 and 211 could be considered applicable to phases 2 and 3. This would place undue burden on the industry since all parts of 21 CFR Parts 210 and 211, as written, are not appropriate for phase 2 and 3. Therefore, we suggest that it be made clear that the 1991 guideline will remain in effect for phase 2 and 3 materials until the new phase 2 and 3 guidance document is available.
2. It should be made clear that the direct final rule applies to investigational new drug products, and not to API.
3. Section V, "Analysis of Impacts" states "For drug manufacturers that produce Phase 1 drug products in-house and also produce approved drug products, this direct final rule is expected to reduce the amount of documentation they produce and maintain when they manufacture a Phase 1 drug." In our opinion, this statement regarding savings is questionable because we do not know at the time of phase 1 manufacture if a drug will move into phase 2. For this reason, manufacturers may elect to take a more conservative approach by manufacturing to Phase 2 requirements.

4. Suggest changing the wording of the proposed/new regulation at § 210.2 (c) from:

“However, this exemption does not apply to an investigational drug for use in a Phase 1 study once the investigational drug has been made available for use by or for the sponsor in a Phase 2 or Phase 3 study, as defined in 312.21(b) and (c) of this chapter, or the drug has been lawfully marketed. If the investigational drug has been made available in a phase 2 or phase 3 study or the drug has been lawfully marketed, the drug for use in the phase 1 study must comply with part 211.”

to:

“However, this exemption does not apply to an investigational drug for use in a Phase 2 or Phase 3 study, as defined in 312.21(b) and (c) of this chapter, or if the drug has been lawfully marketed. If the investigational drug has been made available in a phase 2 or 3 study or the drug has been lawfully marketed, yet further phase 1 studies need to be conducted to generate data to support the registration of the clinical indication being developed, the drug used in the phase 1 study need not comply with part 211.”

We appreciate the opportunity to comment on the Direct Final and Proposed rules. Please contact us if we can be of any further assistance.

Sincerely,



Robert B. Myers,
President, PDA