
Guidance for Industry

Q & A

Content and Format of INDs for Phase 1 Studies
of Drugs, Including
Well-Characterized, Therapeutic,
Biotechnology-Derived Products

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biological Evaluation and Research (CBER)**

**October 2000
Pharmacology/Toxicology**

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I. INTRODUCTION

This guidance is intended to clarify when sponsors should submit final, quality-assured toxicology reports and/or update the Agency on any changes in findings since submission of non-quality-assured reports or reports based on non-quality-assured data.

In November 1995, FDA published a guidance for industry entitled *Content and Format of Investigational New Drug Applications (INDs) for Phase 1 Studies of Drugs, Including Well-Characterized, Therapeutic, Biotechnology-Derived Products*. The guidance states that

If final, fully quality-assured individual study reports are not available at the time of IND submission, an integrated summary report of toxicologic findings based on the unaudited draft toxicologic reports of completed animal studies may be submitted.... [...] full toxicology department individual study reports should be available to FDA, upon request, and individual study reports should be available to FDA, upon request, as final, fully quality-assured documents ***within 120 days*** of the start of the human study... [emphasis added].

If the integrated summary is based upon unaudited draft reports, sponsors should submit an update to their integrated summary 120 days after the start of the human study(ies)....²

¹ This guidance has been prepared by the Pharmacology and Toxicology staff, Office of Review Management (ORM), Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) in the Food and Drug Administration.

There has been some confusion over when the 120-day clock starts, specifically, whether it means 120 days after the start of the clinical trial, or 120 days after the submission of the toxicology information.

Q: How does FDA measure the start of the 120-day period within which sponsors should submit updates to their integrated summaries?

A: The Agency measures the 120-day period based on the Agency's receipt (date of receipt stamped on the IND submission) of the *integrated summary report* including the toxicology information. If the sponsor does not submit the final, quality-assured report and update at this time, the sponsor should make the final, quality-assured report available upon the request of the Agency and update the Agency on any changes in the findings. In any case, the final, quality-assured report should be submitted with the NDA.

The Agency believes that 120 days from submission of an integrated toxicology summary should provide sponsors with adequate time to complete a final, quality-assured document. Because the Agency assumes that clinical studies will generally be initiated immediately following the initial 30-day clock (or upon submission of the protocol for an existing IND), the intention of the 120-day allowance is to encourage the initiation of clinical studies by, in effect, allowing earlier submissions of clinical protocols based on unaudited reports.

² See guidance, section III(G)(2), Toxicology: Integrated Summary.