

FDA Stakeholder's Meeting: Safety Assurance in Clinical Trials

James Nickas, PharmD

Director Drug Safety, Genentech, Inc.

Revised Version

On behalf of Genentech, I would like to thank the Food and Drug Administration (FDA) and Stanford Law School for organizing this important forum for drug development stakeholders to share ideas. Active collaboration and communication between the FDA; academic and medical communities; industry and consumer groups will result in great benefits for patients. P1:55

My topic is "Safety Assurance in Clinical Trials."

Introduction

Recent publicity surrounding the safety of gene therapy trials and the recent withdrawal of the insulin drug, Rezulin, have caused a breach in public confidence and stimulated a re-evaluation of the systems used to assure safety in clinical drug trials.

Acknowledging there may be breaches in current safety monitoring systems, the reality is that much needed therapies are getting to patients faster than ever, and the relative number of product withdrawals due to safety problems has not increased, and may in fact be on the decline. So, the question being posed to development stakeholders should be, Could current clinical safety monitoring systems that have worked remarkably well be improved upon? I think the answer is yes and will propose a few leveraging ideas for consideration.

Leveraging Ideas

In probing ways to improve current systems, it is important to note that safety assurance in clinical trials requires informed risk-benefit decision making by development stakeholders, the FDA and the patient, which in turn depends upon good data.

Considering these dependencies,

- Breakthroughs in the way we collect and review safety data could add value to current systems.

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- Development of benefit-risk metrics so that newly identified adverse drug reactions can be put into proper perspective.

These are two areas worthy of further FDA resource investment and guidance (streamlined data collection and benefit-risk metrics).

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How else can the FDA leverage its limited resources to build upon already effective safety monitoring systems and to get all stakeholders moving in the same direction?

1. Promote and negotiate product life cycle safety monitoring plans. This will require that we acknowledge and communicate (to the public) limitations of clinical trials, and effectively utilize the entire spectrum of safety monitoring modalities where applicable.
2. Co-sponsor with nationally recognized groups (eg. IOM, NCI, NHLI) programs on developing hypothesis-driven, science-based safety monitoring plans during clinical trials.
3. Create guidance documents that identify and promote practical data quality standards so that only information critical to safety evaluations is gathered. This will facilitate more rapid collection and review of potentially relevant information.
4. Develop guidelines for dividing "safety data" into logical buckets to facilitate easier capture and ongoing review during clinical trials.
 - Partner w/FDA advisory committees, research centers such as the NCI and other specialist groups to develop standardized lists of important clinical outcomes and disease-symptom endpoints to be monitored during clinical trials, and that can be compared across trials.
 - Partner w/clinical pharmacology and safety monitoring experts to develop guidelines for recognition and accurate recording of "treatment emergent adverse events" during clinical trials.
 - Issue general guidance on use of Independent Data Monitoring Committees.
5. Finalize, publicize and promote Draft Guidance issued in November 1996: "Conducting a Clinical Safety Review of a New Product Application and Preparing a Report on the Review."
 - The draft document contained valuable insights into what data is important, analyses strategies, and desired safety data displays.

The common theme throughout these suggestions is more education and standardization, not more regulation.

Thank you for the opportunity to present this evening and we look forward to further participation in the process.

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