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Dockets Management Branch (HFA-305)
Food & Drug Administration
5630 Fisher's Lane, Room 1061
Rockville, MD 20852

RE: Docket #00N-1484, CDER199665 Safety Reporting Requirements for Human Drug and Biologic Products

From: Safety Surveillance Group
Duke Clinical Research Institute (an academic contract research organization)

Dear Sirs,

We appreciate the opportunity to provide comment on the proposed safety reporting requirements for human drug and biologic products made public this past March. The extension of the comment to October has allowed our thoughtful review and discussion with our many investigators. We represent the safety surveillance group at the DCRI managing expedited adverse event reporting across all therapeutic areas for drug device and biologic agents. Over the last year we have managed this activity for over 30 clinical trials, and have experience with a great number of sponsors as well as IRB's. We believe our position as an academic contract research organization provides a unique prospective of the implications of full implementation of the proposed rule. We appreciate in advance your time and consideration of our attached comments.

Sincerely,

Michael S. Cuffe, MD, FACC
Medical Directior of Safety Surveillance
Duke Clinical Research Institute

Cynthia Gordon, RN
Clinical Trials Manager
Duke Clinical Research Institute

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Duke Clinical Research Institute
P.O. Box 17969 • Durham, NC 27715

Express Mail and Deliveries:
2400 Pratt Street • Room 0311 Terrace Level • Durham, NC 27705

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Comments from:

Safety Surveillance
Duke Clinical Research Institute
Duke University
2400 Pratt Street
Durham, NC 27715

Regarding:
FDA Proposed Rule for Safety Reporting Requirements for Human Drug and Biological Products "The Tome" [Docket No. 00N-1484]

Section III.A. 1. Suspected Adverse Drug Reaction (SADR)

- While we agree with the benefits of consistent definitions within the ICH E2B framework we would similarly encourage the use of standard terminology. The new acronym (SADR) is not consistent with ICH terminology "adverse drug reaction" and "adverse drug event". The ICH E2B guidelines were published in 1995 and are widely recognized in clinical research. We would encourage FDA to use definitions and acronyms consistent with the established ICH E2B guidelines, or provide clear rationale for ignoring these international standards.

- DCRI Safety Surveillance is gravely concerned about the expanded reportable causality definition to include (serious, unexpected) AEs with a relationship that "can not be ruled out". It is certain this will cause significant increase in cost, and potentially drown out important signals; many previously non-expedited events will fall under this new causality definition. In clinical research, we believe Investigators provide an important and informed medical review of causality, especially in the presence of complex disease states where many adverse events occur as a result of the underlying disease process. Clear guidance and careful medical judgment is needed in these situations where the impact on Ethics Committees (IRBs), investigators (workload), study subjects (informed consent) and regulators will be great. The proposed reporting rule will create a larger volume of challenging data for IRBs and industry to review and evaluate for significant safety signals. We would suggest rather that FDA to provide clear guidance on reportable causality. We would also propose that excess resources (industry and FDA, if such are assumed to exist) that may otherwise be used to manage the increased creation and submission of IND Safety reports be instead shifted to process improvement and implementation of prompt identification of important safety signals.

- It is our experience that local IRBs are presently overwhelmed with the volume of IND Safety Reports received for review, and that the utility of this review is uncertain. DCRI Safety Surveillance would suggest that industry provide IRBs with routine timely aggregated reports of listings of adverse events instead of

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individual AE reports. This approach will allow IRBs to make better informed decisions that protect patient safety at their institutions.

- DCRI Safety Surveillance encourages the agency to continue open discussions regarding the collection and reporting of safety data during the early phase of clinical trial development process. We recognize that each clinical trial is unique. Disease under study, concomitant medications, AE labeling, clinical trial design, must be considered in the context of regulation for the optimal design of the safety data collection and reporting process. The agency's continued support and flexibility will assist in reporting schemes that meet the needs of the clinical trial, regulation, and patient safety. This includes the possibility of submitting IND Safety Reports in a blinded manner when appropriate.

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