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July 2, 2001

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 01D-0185

Dear Sir or Madam:

The Renal, Fenwal and Medication Delivery Divisions of Baxter Healthcare Corporation appreciate the opportunity to submit comments regarding the draft document- *Guidance for Industry-Providing Regulatory Submissions in Electronic Format-Postmarketing Expedited Safety Reports.*

Baxter Healthcare Corporation, as a manufacturer of medical devices and drugs, adheres to all appropriate regulatory requirements for the reporting of adverse events [21 CFR 310, 314, 803]. Global regulatory agencies along with industry have worked together to promote international harmonization of regulatory requirements. The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Humans Use (ICH) has coordinated the effort for drugs. The Global Harmonization Task Force, Study Group 2, has championed the effort for devices.

After review of this draft guidance document, Baxter agrees in theory with the need for global adverse event information exchange between industry and regulators. However, Baxter objects to the proposed mechanism, which is perceived to be overly burdensome and complex. The proposed mechanism to submit adverse events in electronic format consists of the following:

- To submit data electronically, the individual case safety reports (ICSR) contains data elements as defined for industry in a guidance document entitled *E2B Data Elements for Transmission of Individual Case Safety Reports.*
- The electronic format to be used with the E2B elements is defined in the ICH document entitled *M2 Electronic Transmission of Individual Case Safety Report Message Specifications*. Standard Generalized Markup Language (SGML) is used. Information for electronic submission in SGML is prepared by inserting data appropriately between the start and end tags so information maintains the relationship specified by the DTD (Document Type Definition.) This allows for structured data sets of all types of individual case safety reports to be transported from database to database

To comply with the guidance in the draft document, manufacturers will need to modify, create or purchase new database systems to submit ICSR's electronically. The life cycle development process and validation of a new system or modification of an existing system is resource intense and presents a significant cost to industry. It is unclear how significantly changing the format of required information being provided to regulatory agencies would add value to the pharmacovigilance process.

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As an alternative to the above, industry should be allowed to submit domestic ICSR electronically on the MedWatch Form 3500A, as currently mandated in the United States for both drug and device adverse events. ICSR of foreign adverse event experiences can be submitted on either a FDA Form 3500A or on a Council for International Organization for Medical Sciences Form (CIOMS). In an effort to move toward global standardization, a compromise may be to combine data elements from the MedWatch Form 3500A and the CIOMS form and create an electronic submission. This endeavor would be less labor intensive than following the E2B format using SGML.

This draft document only addresses electronic adverse event reporting for drugs and not devices. No standardization effort has been made to incorporate medical devices in the electronic submission process. There needs to be an effort to standardize and promote international harmonization of regulatory requirements for both drugs and devices. Electronic submission standards should be simultaneously developed for drugs and devices. If industry and global regulators are serious about global standardization and harmonization, now is the time to link reporting processes, methods, formats and nomenclature. The entire process must be harmonized in order to be efficient and effective. The creation and use of two different systems will pose multiple challenges for industry.

Per the draft guidance, if an ICSR contains attachments (published articles, hospital discharge summaries, autopsy reports, etc.) these must be submitted electronically. Submission of these attachments for adverse events can be viewed as being redundant, as relevant information from these documents is summarized and included in the appropriate boxes on the FDA Form 3500A. Why is the agency requesting paper attachments when it appears industry and the regulators are moving towards a paperless electronic environment?

Based on the complexity of the information contained within this guidance document, would the agency/ICH consider developing a program integrating the MedWatch 3500A, CIOMS and other presently utilized forms into one tool that everyone would be required to use for electronic submission of ICSR's? Implementation of this program, with all required parameters and elements, would ease the burden for industry.

Baxter Healthcare Corporation appreciates the opportunity to comment on this draft document – *Guidance for Industry-Providing Regulatory Submissions in Electronic Format - Postmarketing Expedited Safety Reports*. If you have any questions, I may be contacted at (847) 948-3514. We look forward to the future revision of this draft guidance document.

Sincerely,

Margaret Brown

Margaret Brown
Director, Quality Systems
Baxter Healthcare

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