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

Re: Docket No. 2004D-0117, CDER 2003189. International Conference on Harmonisation (ICH); Draft Guidance on E2E Pharmacovigilance Planning.

Abbott Laboratories (Abbott) is very pleased to have the opportunity to comment on the Draft Guidance on ICH-E2E Pharmacovigilance Planning, published in the Federal Register on March 30, 2004.

We thank the Agency for their consideration of our attached comments. Should you have any questions, please contact Ivone Takenaka, Ph.D. at (847)-935-9011 or by FAX at (847) 938-3346.

Sincerely,

Douglas L. Sporn / jms
Douglas L. Sporn

2004D-0117

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**Comments on
ICH E2E: Pharmacovigilance Planning (PvP)
Draft Version 4.1 dated on 11th November 2003**

Docket No. 2004D-0117

The following comments on the International Conference on Harmonisation; Draft Guidance on E2E Pharmacovigilance Planning are provided on behalf of Abbott Laboratories (Abbott).

GENERAL COMMENTS

Abbott applauds and supports FDA's efforts towards global harmonization, and their participation on ICH and WHO development of guidelines. Many of the recommendations provided in the ICH-E2E guidelines overlap those of the FDA's Risk Management draft guidances, recently released for public consultation. However, the later guidelines also contain specific requirements that may diverge from the harmonization process. This will require industry to prepare different documents specific to each region. Compliance with regional regulatory requirements for a complex process such as Pharmacovigilance creates an enormous burden to industry and potential confounding reporting timelines, mechanisms and procedures in place. We recommend that the ICH regulatory agencies assess the emerging and established guidances and regulatory requirements, including those by the CIOMS and WHO, for the purposes of eliminating inconsistencies. Global consistency in submission and reporting of adverse events will help improve signal detection, evaluation and communication.

Greater clarity with respect to how this guideline should be interpreted and implemented in all 3 regions is needed. It is unclear as to whether the Pharmacovigilance Specification, Pharmacovigilance Plan and study protocols submitted and accepted by one of the ICH region regulatory agency will automatically be accepted by others. On the contrary to the CTD format submission that has only been harmonized in its format and not on content, we recommend that the Pharmacovigilance Specification and Plan submissions be fully harmonized in regards to format, content, reporting timeline and submission requirements in all the ICH regions.

SPECIFIC COMMENTS

1.3 Scope

1st and 3rd paragraphs

Abbott appreciates the FDA's disclaimer for guidances in the title page of this guidance. However, the soft and broad language used in this ICH guidance leaves industry unclear as to whether these recommendations must be followed. We recommend that the underlined language such as "[T]he guideline 'could be most useful' for new chemical

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entities and biotechnology-derived products”; “... established products that are to be introduced to new populations or in ‘significant’ new indications”; “[T]he main focus of this guideline is on a Pharmacovigilance Specification and Pharmacovigilance Plan that ‘might’ be submitted at the time of license application” be revised for clarity. These guidelines apply to new submissions, thus, companies would not wish for the application to be declared “incomplete” or “deficient” because of the absence of these documents.

5th paragraph

The guidance mentions that “*important emerging risk information*” should be used to revise the plan. However, further information is neither given with respect to a need to regularly update the plan nor the expected frequency of any such updates. For example, there is no discussion concerning whether updates to the plan or outcomes from the plan should be addressed in Periodic Safety Update Reports (PSUR), which might be appropriate in order to avoid duplication of effort in maintaining both a plan and a PSUR. Neither is there any discussion as to whether the timing of any updates can be harmonised with the PSUR or other periodic reports, such as Annual Safety Reports. Further clarification on these issues should be provided.

2.1.2 Clinical

b. Populations not studied in the pre-approval phase

The guidance recommends that the Pharmacovigilance Specification discuss the populations that have not been studied or have only been studied to a limited degree in the pre-approval phase. It lists “*sub-populations with genetic polymorphism*” and “*patients of different ethnic origins.*” There is a need for the language to be more specific. We recommend changing to the following wording “sub-populations carrying known relevant genetic polymorphism”. Furthermore, we recommend changing the word “*ethnic*” to race, as ethnic groups can be very broad and unclear. There is also a need to clarify what would be a reasonable number of patients of different ethnic/(race rather) groups to be exposed to the drug during clinical trials.

e. Epidemiology of the indication(s) and important adverse events

We appreciate that the guidance is primarily written for the 3 ICH regions. However, pharmacovigilance activities may encompass countries outside the ICH region, as it is stated under the Introduction section that the guidance takes into consideration ongoing work in the three regions and *beyond*.... In this section, the guidance recommends that the discussion on epidemiology “*should include incidence, prevalence, and mortality, and should take into account whenever possible stratification by age, sex, and ethnic origin. Differences in the ‘epidemiology in the different regions’ should be discussed,*

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where this information is available.” Despite the global nature of the Pharmacovigilance activities, for the purposes of the above recommendations and other proposals throughout this guideline, we assume from the Scope (section 1.3) that these recommendations are to be assessed in the three ICH regions (EU, USA and Japan) only, and not in other individual countries or in regions within countries.

ANNEX – Pharmacovigilance Methods

It is unclear as to whether there is a need to include in the Pharmacovigilance Plan, the drafts, prototypes or final versions of questionnaires, and/or materials to be distributed to audience other than the regulatory agencies, such as patients and physicians. There should also be greater clarity about the intended audience for the Pharmacovigilance Specification and Pharmacovigilance Plan, so that they can be written appropriately.

3. Active Surveillance

Sentinel sites

A clear definition of “sentinel sites” should be provided, as the term may be interpreted in a number of ways. For example, are these simply sites that the marketing authorisation holder believes can provide a suitable cohort of patients, or are they sites that act to collate information from a wider selection of sites?