1. Type of Harmonisation Action Proposed

The type of harmonization action proposed by the ICH E2B(M) IWG is referring to an update of the existing E2B(M) guideline on Clinical Safety Data Management of the ICH E2B(M) EWG with the title ‘Data Elements For Transmission Of Individual Case Safety Reports’ version 4.4.1 dated 9 November 2000 including the editorial changes dated 5 February 2001. The update of this guideline may consequently also require an update of the guideline of the ICH M2 EWG referring to the ‘Electronic Transmission of Individual Case Safety Reports Message Specification (ICH ICSR DTD Version 2.1)’ version 2.3 dated 1 February 2001.

2. Statement of the Perceived Problem

Implementation of electronic reporting of Individual Case Safety Reports (ICSR's) based on the ICH E2B(M), M1 (MedDRA), and M2 standards is progressing quite rapidly across the ICH regions. However, a number of implementation and maintenance concerns have emerged as a result of the experience gained in the Pilot and Implementation Projects that have been conducted by Regulators and Industry in the three ICH regions. In addition, certain implementation aspects have been identified that require guidance at ICH level to maintain harmonization in the future.

Although the remit of the current E2B(M) IWG is to answer questions concerning the implementation issues, there is currently no mechanism in place that allows to respond in a fast and efficient way to address maintenance issues that have been identified in the frame of the implementation processes in the three ICH regions or that have emerged as new business requirements or advancements in technology.

In addition, regional requirements led to differences in the implementation requirements with regard to the electronic reporting of ICSRs. An increasing disharmony in the E2B(M) data elements and the specifications (M2) related to their electronic transmission is observed jeopardizing the huge effort made in the three regions during the last 6 years to reach a consensus on these aspects. Lack of harmonisation is felt by the partners as a major threat on the progress being made and might discourage sustained activities in this area.

Most of the identified issues can currently not be resolved through the recently established Q&A process handled by the ICH E2B(M) IWG, which is limited in its activities to the interpretation of the existing guideline without any possible changes.

As such, the goal of a single transmission to multiple receivers in the three regions has not been achieved requiring pharmaceutical industry and regulators to invest substantial human and financial resources to comply with and handle different regional requirements.
3. Issues to be Resolved

The following issues need to be urgently resolved and harmonized:
- Errors, omissions and inconsistencies between the E2B(M) and M2 documents e.g.
  i. Specific code lists are inconsistently applied in the E2B(M) and M2 documents;
  ii. Missing code list for units in M2 specifications contrary to E2B(M) requirements have been identified.
- Remaining issues from San Diego (2000) meeting need to be addressed i.e.
  i. The use of MedDRA is not consistently applied for all E2B(M) data elements including different coding levels (PT or LLT);
  ii. Time zones need to be introduced to cover international transmissions;
  iii. Repeatable indications in the drug section;
  iv. Seriousness criteria need to be addressed at each event level.
- MedDRA qualifiers (e.g. worsening) need to be accommodated requiring a significant change of the current E2B(M) data elements;
- Some data elements urgently require an agreement on reporting standards (i.e. test names, pharmaceutical/dosage forms);
- Several free text fields need further structuring;
- A maintenance process needs to be put in place for all code lists;
- New fields are required e.g. to capture additional regulatory and administrative information to ensure a single transmission in all three ICH regions (J-file requirements need to be accommodated) or to allow for the reporting of classes of drugs;
- Adaptation of the data elements to accommodate further specific requirements for adverse event and reaction reporting in clinical trials;
- Provision of specific data elements for reporting of biologic products including blood products and vaccines;
- Specific sections need to be further structured to accommodate repeatable subsections (e.g. repeatable active substances for multiple ingredients in the drug section or repeatable lot numbers);
- Corresponding field lengths in the M2 specifications need to be adjusted;
- Language requirements in the free text fields need to be resolved;
- A standardized mechanism for linking attachments, such as autopsy reports and publications, to ICSRs should be established;
- Adjustments need to be made to facilitate the reporting of potential medication error reports that do not meet the minimum dataset requirements.
- Handling of duplicates taking into account the international dimension of pharmacovigilance;
- Add new date format for lab tests to distinguish tests performed on the same day.

As such changes, corrections and updates to the E2B(M) and M2 documents are urgently needed. In addition, the process to address implementation questions needs to be maintained.

4. Background to the Proposal

The ICH Steering Committee, during its meeting in July 2003, gave permission to the ICH E2B(M) IWG to prepare a concept paper that addresses the resolution of the maintenance issues and new business requirements that were identified in the frame of the implementation activities in the three ICH regions. The ICH E2B(M) IWG unanimously agreed upon the following position:
The E2B(M) Implementation Projects in the European Union, Japan and the United States have shown that electronic reporting of ICSRs has matured to a point where the routine electronic (paperless) transmission of ICSRs is feasible. Indeed, implementation programs are being completed and regulators and companies are shifting to a full E2B(M) production mode.

In the course of implementation in the three ICH regions, however, a number of practical implementation issues arose, which show the need for urgent resolution.

The group consensus is that this resolution cannot be achieved using the current E2B(M) step 4 document.

To achieve the goal of a fully harmonized implementation of E2B(M) in all regions requires the reopening of the E2B(M) guideline to accommodate the resolution of all issues as identified in Chapter 3. This can only be achieved through the establishment of an E2B(M) Expert Working Group.

5. Type of Expert Working Group

To build upon the successes of the Implementation Programs in the three regions and to ensure continuation of harmonization activities in identified aspects of electronic data management for pharmacovigilance, the E2B(M) IWG proposes the establishment of an E2B(M) Expert Working Group with the following remit:

- To address the identified business issues and maintenance aspects with the intention of a stepwise resolution by amending the current E2B(M) step 4 document and adjusting the current M2 standards;

- To develop harmonized solutions for implementation issues that become apparent in the ICH regions and which cannot be solved by the ICH E2B(M) IWG;

- To develop user guidance in the frame of the guideline addressing the needs that have arisen from changes in technology, processes, and procedures as electronic management of pharmacovigilance data becomes more and more operational;

- To work in close collaboration with the MedDRA Management Board, the Points to Consider Working Group and the MedDRA Maintenance and Support Services Organisation (MSSO);

- To work in close collaboration with other relevant ICH Working Groups towards meeting the rapidly evolving needs of Pharmacovigilance;

- Technical issues will be addressed through the M2 EWG.

Members of the proposed EWG should be recruited from the same parties represented in the current E2B(M) IWG including a representative appointed by M2 EWG. These experts are already familiar with the matter from first-hand implementation experience. In addition, observers representing MedDRA, Canada, EFTA and WHO should participate.

The meetings should be organized as follows:

- Tele/ Videoconference on a quarterly basis;
- Ad hoc experts invited when necessary;
- Agenda to be prepared by the Rapporteur;
- Minutes and brief report to the Steering Committee;
- At least two face-to-face meetings (4 days each) per year at the time of ICH Steering Committee meetings or special workshops organized by a third party;
- Meeting with other ICH EWGs if needed.

The ICH E2B(M) EWG working process will be as follows:

- Develop a 2-year work plan for use by the EWG (Nov. 03 - Nov. 05)

For each identified issue/need:
- The current implementation status in each region;
- Option analysis of possible solutions;
- Stakeholder consultation and testing in the three regions;
- Progress report to the Steering Committee every 6 months.

The deliverables of the E2B(M) EWG should be as follows:

- Revised E2B(M) guidelines with new and updated code lists;
- In collaboration with the M2 EWG, revised M2 specifications according to changes in E2B(M);
- Procedure to resolve the upcoming issues arisen from the introduction of the revised E2B(M) guideline and the related M2 specification.