

**E2B(M) Implementation Working Group
Questions & Answers
Version 0.2 (including FDA revisions)**

18 July 2003

This Q&A document provides conventions for the harmonized interpretation of the E2B(M) guideline version 4.4.1 and the M2 specification document version 2.3. This will facilitate the implementation of the electronic transmission of Individual Case Safety Reports (ICSRs) in the three ICH regions.

It is not meant as an all-inclusive document, as further questions may be addressed in the future.

Pharmaceutical companies, regulators and vendors were encouraged to submit implementation-related questions to the ICH E2B(M) IWG.

Answers to these questions were developed by the ICH E2B(M) IWG in accordance with the ICH consensus process.

Questions concerning the time frame and specific regional requirements currently not communicated in the E2B(M) guidance are answered in guidance documents published for each region.

Additional questions and comments on this document in English should be addressed to the following e-mail address: "question-to-E2BM-guideline@ich.org".

Additional questions and comments on this document in Japanese should be addressed to the following e-mail address: "iche2b@mhlw.go.jp".

The responses that the ICH Steering Committee approves are posted on the ICH website every 6 months, either for discussion or as a finalized document.

Questions requiring immediate answers should be addressed directly to the appropriate regional regulatory authority(ies).

E2B(M) Questions and Answers		
Date of Approval	Questions	Answers
1 July 2003	<p>During the period of transition, as Health Authorities or pharmaceutical companies migrate from paper to electronic ICSR submissions and exchanges using E2B/M2 standards, certain ICSRs will likely be exchanged in both paper and electronic format.</p> <p>This could occur either because the initial ICSR was on paper and the follow-up is in electronic format or because the two parties are in a pilot program where they are exchanging ICSRs in both paper and electronic format.</p> <p>Two questions arise:</p> <p>Question 1: How can two or more exchanges of the same ICSR be linked together to avoid a duplicate report?</p> <p>Question 2: How can the current paper forms accommodate the full ICH format of the worldwide unique case identifier?</p>	<p>Answer 1:</p> <p>Compliant with the definition of field A.1.0.1, the ICH format of the worldwide unique case identifier (country code-company or regulator name-report number) should always be used, and copied into field A.1.10.1 or A.1.10.2, as appropriate.</p> <p>In the event that the ICSR either has been exchanged by the two parties in the past using a different identifier or that it is exchanged simultaneously with a different identifier, this other identifier should be listed in field A.1.11.2 and the organizations name should be captured in field A.1.11.1, consistent with the definition of the A.1.11 field for the identification of duplicates.</p> <p>This recommendation applies to DTD version 2.0 and DTD version 2.1.</p> <p>Answer 2:</p> <p>In case the ICH conforming worldwide unique case identifier cannot be accommodated on the paper forms, it is recommended that the report number alone (without the country code or the company or regulator name) be used.</p>

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2 July 2003	<p>For fields where only one MedDRA coding level is accommodated, should I use PT or LLT?</p> <p>Section B.2 contains fields B.2.i.0, B.2.i.1 and B.2.i.2 to capture the verbatim term, LLT and PT, respectively. However, sections B.1.7.1a, B.1.8f, B.1.8g, B.1.9.2, B.1.9.4, B.1.10.7.1a, B.1.10.8f, B.1.10.8g, B.4.k.11, B.4.k.17.2, B.4.k.18.1, B.1.10.8g, B.4.k.11, B.4.k.17.2, B.4.k.18.1, B.5.3 contain only one field and do not specify whether the LLT or PT should be used.</p>	<p>For the ICH E2BM fields B.1.7.1a, B.1.8f, B.1.8g, B.1.9.2, B.1.9.4, B.1.10.7.1a, B.1.10.8f, B.1.10.8g, B.4.k.11, B.4.k.17.2, B.4.k.18.1, B.5.3 the following should be used:</p> <p>for EU regulators: LLTs ; for FDA: PTs ; for MHLW: PTs.</p>
3 July 2003	<p>What is the process to maintain, add, modify, or delete entries in the code lists in attachments 1 and 2 of E2BM?</p>	<p>Currently these lists cannot be modified.</p>
4 July 2003	<p>The current definition of B.4.k.7 calls for the use of free text until a controlled vocabulary is available. Is a harmonized vocabulary for pharmaceutical dosage forms available?</p>	<p>There is currently no harmonised vocabulary for pharmaceutical dosage forms.</p> <p>Until an ICH vocabulary is available, the following should be used:</p> <p>for EU Regulators: the European Pharmacopoeia standard list; for FDA: Free text; for MHLW: The list of pharmaceutical forms as made available by MHLW.</p>

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5 July 2003	How can I send product-specific registration or other regulatory administrative information to multiple receivers in a single transmission?	<p>A single transmission for administrative information of an ICSR to multiple receivers in the ICH regions is currently not possible.</p> <p>Various Health Authorities have engaged in production or pilot programs to implement E2BM.</p> <p>A need to capture in more detail registration-related information (similar to the existing paper submission process using fax cover sheets or regulatory forms) became evident. As a consequence, local guidance has been introduced to transmit additional information accompanying each ICSR:</p> <p>For EU Regulators: see E2B section B.4.k.4.</p> <p>For FDA: Field B.4.k.4.1. should contain the NDA, BLA or STN number in the appropriate format.</p> <p>For MHLW: Each ICSR should be accompanied by a corresponding J-file, as detailed in the relevant MHLW guidance documents.</p>

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6 July 2003	What language should I use for an ICSR transmission?	<p>For EU Regulators: ICSRs in English are generally accepted. However, there can be local requirements for a translation of the case narrative in the official local language.</p> <p>For FDA: English</p> <p>For MHLW: Japanese</p>
7 July 2003	How can I submit a causality or scientific assessment in either an algorithmic or text representation in the current E2BM format?	<p>The current structure of E2BM includes fields B.4.k.18.1-4, which allow the sender to indicate such assessments for each drug-event combination.</p> <p>Additionally, field B.5.4 can be used to further elaborate the sender's position or assessment. Local regulatory requirements regarding expedited and periodic reporting determine whether inclusion of sponsor assessments are necessary.</p>
8 July 2003	How can I identify the primary source and the reporter qualification when an ICSR is forwarded by Health Authorities with minimal or no information on the primary source?	<p>If no information on the primary source is available, section A.2.1 should identify the Health Authority as the primary source.</p> <p>Field A.2.1.4 'Qualification' should be populated with a code of "3" (Other health professional).</p> <p>Additionally, field A.1.4 'Type of report' should be populated with a code of "4" (Not available to sender (unknown), if appropriate).</p>

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9 July 2003	How can I identify the study name, study number, the patient, and the drug in clinical trials to be reported to the EU regulators and MHLW in the E2BM format?	<p>The code list of 'Study type' in field A.2.3.3. is very short, so the type of study should be characterised more clearly in the study name. For a more explicit description of the study beyond 100 characters, the full study name should be given in the case narrative. In addition, some regulatory authorities request the additional submission of a regulatory study number (e.g. EUDRACT number). For this situation, the study name in element A.2.3.1 should be a concatenation of the EUDRACT number and the 'Study name', i.e., EUDRACT number-Study name.</p> <p>The 'Study number' in field A.2.3.2 should be the sponsor study number.</p> <p>The patient identification in a clinical trial can be transmitted in field B.1.1.1d 'Patient investigation number'. Note that multiple elements from the source database, like Center- Patient and random number, should be concatenated in this element to assure a unique patient identification.</p> <p>The trial drug identification is possible through the usual elements for the description of the suspected drug B.4.k.2.1 and B.4.k.2.2. For some countries, the project-related regulatory drug identification number can be submitted in field B.4.k.4.</p> <p>The present version of E2BM allows for the distinction of unblinded vs. blinded information.</p>

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10 July 2003	<p>There may be cases where for one drug, one or more formulation/dosage, lot number and indication are provided. How should this information be presented in the electronic transmission?</p>	<p>The drug section B.4 is a repeatable block. If for one drug there is information on multiple dosages/formulations or indications, the entire section should be repeated to capture all the information. For lot numbers, the guidance allows for multiple batch/lot numbers in the same field B.4.k.3. However, it is recommended that the drug section B.4 be repeated.</p>
11 July 2003	<p>Field B.1.2.1 'Patient birth date' provides for population with a full date format including day, month, year. If incomplete dates are reported, how should these be presented?</p>	<p>If an incomplete date of birth is reported, then the field B.1.2.2. 'Age at the time of onset of reaction/event' should be used, as indicated in the user guidance. Alternatively, field B.1.2.3 'Patient age group (as per reporter)' can be used to indicate the age of the patient.</p>