INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH E2B(R3) Expert Working Group / Implementation Working Group

Information Paper Regarding Alignment with ICH E2D(R1) Guideline

Final version
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Document History

Version	History	Date
1.0	Approved by the Regulatory and Industry Members of the E2B(R3) EWG/IWG	14 October 2025
1.0	Endorsement by the members of the ICH Management Committee	16 December 2025

Table of Contents

1 Introduction

This Information Paper explains the alignment of ICH E2B(R3) specifications with the revised ICH E2D guideline (referred to as ICH E2D(R1)) which was agreed in September 2025. This will require clarification and updates to two existing ICH E2B(R3) data-elements: **"C.1.3 Type of Report"** and **"C.5.4 Study Type Where Reaction(s) / Event(s) Were Observed"**.

Addition of new value options to an existing data element can be accommodated as per the established ICH E2B(R3) maintenance process. This Information Paper will be available until the update has been incorporated into the E2B(R3) Implementation Guide package and ICH E2B(R3) Questions and Answers document.

2 Background

The revision of the ICH E2D guideline aims to clarify the management of safety data derived from solicited sources, such as social media, market research programs, patient support programs and others, which vary in characteristics and contribution to the quality of post-approval safety information.

The User Guidance for data-element **"C.1.3 Type of Report"** has been updated to clarify that the value *'2 = Report from study'* is used for studies as well as for other **solicited sources.**

The ICH E2D(R1) guideline also refers to several ICH E2B values used in data element **"C.5.4 Study Type Where reaction(s) / event(s) Were Observed"** to reflect the origin of the solicited report.

Accordingly, the User Guidance for data element **"C.5.4 Study Type Where Reaction(s) / Event(s) Were Observed"** has been updated to align with definitions in ICH E2D(R1). It includes new values to classify solicited reports originating from patient support programs (see ICH E2D(R1) section 4.5), market research programs (see ICH E2D(R1) section 4.6) and organized data collection systems with source data from digital platforms (see ICH E2D(R1) section 4.3.2). This update will allow Marketing Authorization Holders (MAHs) and regulators to separate the analyses of case reports from these sources and provide a clearer understanding of their contribution to safety signal identification.

3 Alignment of E2B(R3) with E2D(R1)

The changes to the ICH E2B(R3) data elements are highlighted in **bold underlined** text. ICH Code List 8 (CL8) has been updated to accommodate the new values.

C.1.3 Type of Report

User Guidance	This data element captures the type of report independently of its source; a separate element for the designation of the source is covered in item C.4 and is not duplicated in this section. For example, if a case in the literature arises from spontaneous observations, "type of report" should be *Spontaneous report*. If a case in the literature arises from a study, "type of report" should be *Report from study* and the differentiation between types of studies (e.g., clinical trials or others) should be given in Section C.5.4 (See the user guidance for C.5.4). If it is unclear from the literature report whether or not the case(s) cited are spontaneous observations or whether they arise from a study, then this item should be *Other*. **The value '2' (*Report from study)* is used for studies as well as for other solicited sources, as described in E2D(R1).** The *Not available to sender* option allows for the transmission of information by a secondary sender (e.g., regulatory authority) where the initial sender did not specify the type of report; it differs from *Other,* which indicates that the sender knows the type of report but cannot fit it into the categories provided.
Conformance	Required
Data Type	1N
OID	2.16.840.1.113883.3.989.2.1.1.2
Value Allowed	1 = Spontaneous report 2 = Report from study 3 = Other 4 = Not available to sender (unknown)
Business Rule(s)	

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C.5.4 Study Type Where Reaction(s) / Event(s) Were Observed

User Guidance	This information should be provided if the "Type of Report" (C.1.3) has been populated with *"Report from study"*. **Definitions provided in ICH E2D(R1) for Patient Support Program, Market Research Program, Organised Data Collection System and Digital Platform should be taken into account.** **The value *'6 = Organised Data Collection System with source data from a digital platform'* should only be used if the Individual Case Safety Reports (ICSR) originated from a digital platform and none of the other study types (1-5) apply.** **For example, value *'6 = Organised Data Collection System with source data from a digital platform'* should be selected if the ICSR originated from a digital platform in the context of "social listening" activity on a digital platform that is not under the responsibility of the MAH.** **If the ICSR originated from a digital platform in the context of a Patient Support Program, then the value *'4 = Patient Support Program'* should be selected, instead of the value *'6 = Organised Data Collection System with source data from a digital platform'*.**
Conformance	Optional, but required if C.1.3 = 2 (Report from study).
Data Type	1N
OID	2.16.840.1.113883.3.989.2.1.1.8
Value Allowed	1 = Clinical trials 2 = Individual patient use *(*e.g., "*compassionate use" or "named patient basis")* 3 = Other studies *(*e.g., *pharmacoepidemiology, pharmacoeconomics, intensive monitoring)* **4 = Patient Support Program** **5 = Market Research Program** **6 = Organised Data Collection System with source data from a digital platform**
Business Rule(s)	

4 Transition

The new values for data-element **"C.5.4 Study Type Where Reaction(s) / Event(s) Were Observed**" should be used prospectively:

- ICSRs that have already been submitted to regulatory authorities do not need to be re-submitted with a new value.
- However, when submitting a follow-up ICSR or an amendment report, the new values should be used as appropriate. For example, submitting a follow-up ICSR for a case from a market research program that was previously submitted to the regulatory

authorities, the new value *'5 = Market Research Program'* should be used in data element **"C.5.4 Study Type Where Reaction(s) / Event(s) Were Observed"**.

- The new values should be used as appropriate for newly submitted ICSRs, not just for newly introduced solicited data sources. For example, ICSR submissions arising from a patient support program that has been running for years should use the new value *'4 = Patient Support Program'* in data-element **"C.5.4 Study Type Where Reaction(s) / Event(s) Were Observed**" for all new and follow-up ICSRs submitted from this program.

It is acknowledged that the ICH E2D(R1) definition for a Patient Support Program (PSP) **(**see ICH E2D(R1) sections 2.9 and 4.5) excludes certain types of programs which historically may have been considered to be PSPs (e.g., MAH activities that only allow one-way interactions such as delivery of a product to a patient's home, or provision of vouchers or coupons). ICSRs that have already been submitted to regulatory authorities for programs no longer considered PSPs do **not** need to be re-submitted with a new value. When submitting a follow-up or an amendment report for a previously submitted ICSR originating from these types of programs, the data-element **"C.1.3 Type of Report"** should be updated with the value *'1 = Spontaneous report'* and the data-element **"C.5.4 Study Type Where Reaction(s) / Event(s) Were Observed**" should be left empty. The case narrative of the follow-up ICSR should also clarify that the ICSR originates from a one-way interactions service program and not from a patient support program.

5 Regional implementation

See websites of regional regulators for the implementation timelines for accepting the new values for data-element **"C.5.4 Study Type Where Reaction(s) / Event(s) Were Observed"** and additional regional considerations, as appropriate.

When a region has not yet implemented the new values for data-element **"C.5.4 Study Type Where Reaction(s) / Event(s) Were Observed",** the value *'3 = Other studies (e.g., pharmacoepidemiology, pharmacoeconomics, intensive monitoring)'* should be used for ICSRs originating from patient support programs, market research programs or from organized data collection systems with source data from digital platforms.