EMA
EUROPEAN MEDICINES AGENCY

ICH E2D and ICH E2B updates

EMA/HMA Multi-Stakeholder Forum on EudraVigilance and Signal Detection

05 November 2025

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Outline

- Introduction
- Update on E2D(R1)
- Update on E2B(R3)
- Next steps at EU level

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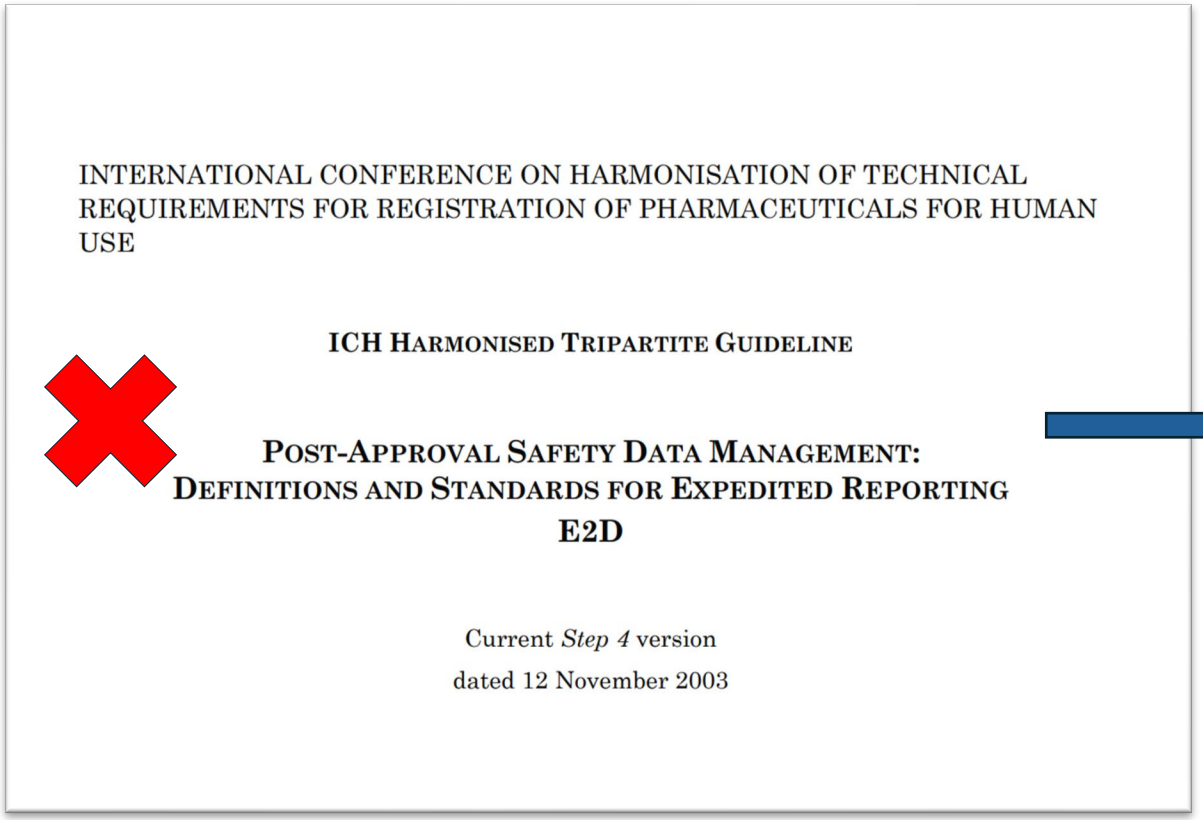
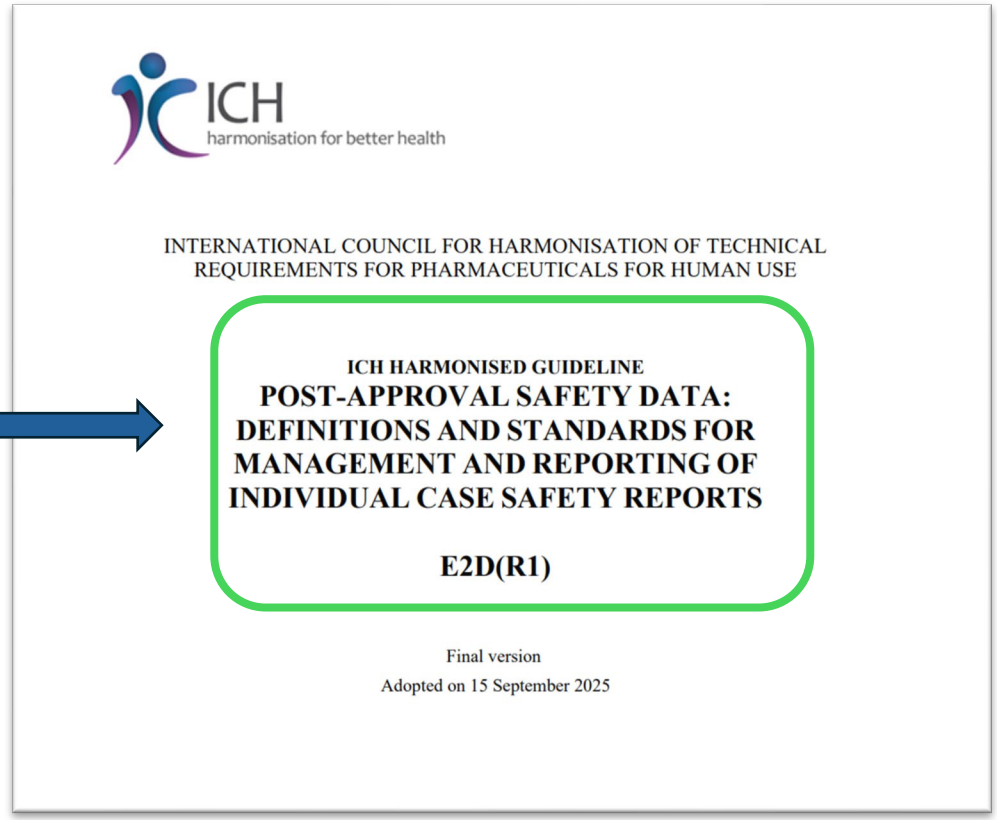
From E2D to E2D(R1)





Final adopted ICH E2D(R1) Guideline

Step 4 adoption by ICH Assembly: 15 September 2025

Step 5 adoption by CHMP: 18 September 2025

- **Date for coming into force in EU:**

  18 March 2026

Links to final adopted Guidance documents:

- ICH Official web site: ICH
  - ICH E2D(R1) Guideline (Step 4)
  - ICH E2D(R1) Step 4 presentation
- ICH E2D Post-approval safety data management – Scientific guideline | European Medicines Agency (EMA)
  - ICH E2D(R1) Guideline (Step 5)

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- Update on E2B(R3)
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Background E2D(R1)

- The original ICH E2D guideline was adopted in 2003
- New sources of post-market safety information have emerged (or are used more often), which vary in characteristics and contribution to post-market safety surveillance (e.g., patient support programs (PSPs) and social media)
- The definitions and regulatory guidance in the original ICH E2D document are no longer sufficient to provide guidance on current pharmacovigilance practices and needs
- ICH E2D(R1) EWG (Expert Working Group) was established in 2019 to revise ICH E2D to support appropriate post-market safety surveillance
  - Step 2 public consultation early 2024-July 2024 resulting in ≈450 comments
  - Step 4 in September 2025 and subsequent CHMP endorsement

Background E2D(R1) [continued]

- ICH E2D(R1) establishes a framework for current best practices of post-approval safety data management in a dynamic environment
- The guideline has been expanded and modernised to better reflect current practices and sources of safety data
- This updated Guideline provides recommendations that are harmonized to the extent possible, given differences in ICSR reporting requirements among ICH regions
  - Where applicable, this guideline notes where local and regional requirements may vary and, as such, Marketing Authorisation Holders (MAHs) should refer to the relevant regional and local regulatory authority's requirements

Table of Contents

Post-Approval Safety Data: Definitions And Standards for Management and Reporting of Individual Case Safety Reports

Definition Organised Data Collection System (ODCS)

2.8. Organised Data Collection System (ODCS)

For the purposes of this document, an organised data collection system (ODCS) is an activity that gathers data relevant to an MAH's medicinal product or a medical disease area, in a planned manner, thereby enabling review to be performed.

Regional or local regulatory authorities may require a protocol for certain types of ODCS (i.e., clinical trials and non-interventional studies). In this context a protocol means a document that describes the objectives, design, methodology, statistical considerations and organisation of a clinical trial or study. The term 'protocol' encompasses successive versions of the protocol and protocol modifications.

For MAH ODCS activities that are not conducted according to a protocol (e.g., a market research program, a patient support program, or accessing data on a digital platform in the context of an ODCS), the MAH should have documentation in place that at least describes the:

1. Objectives of the ODCS activity;
2. Source(s) of the data;
3. Dataset that the MAH will collect or receive and review in order to meet the objectives of the activity detailed under item 1, including the look-back period and/or duration of the data collection;
4. Method the MAH will use to review the dataset to meet the objective of the activity;
5. Process for collection and management of any AEs/ADRs or other observations that may be identified.

For the purposes of this Guideline, ODCS excludes the MAHs' standard procedures for the surveillance, receipt, evaluation, and reporting of spontaneous postmarketing AEs/ADRs and other postmarketing AEs/ADRs managed as spontaneous reports (i.e., the MAHs' routine pharmacovigilance operations for spontaneous reports), see Section 4, Sources of ICSRs.

Documentation requirement

Definition Patient Support Program (PSP)

2.9. Patient Support Program (PSP)

PSPs are ODCSs initiated by an MAH, in which patients enrol for the purpose of supporting their use of the MAH's medicinal product, or the management of their medical condition, and which include a mechanism for two-way communication between the MAH (or third party acting on the MAH's behalf) and patients or healthcare professionals. Examples of PSPs include adherence support, disease management, and certain reimbursement and educational programs. See Section 4.5 Sources of ICSRs, PSPs, for further details.

Programs meet the definition of a PSP if 1) they solicit medical information about the patient's use of a medicinal product and/or 2) the design of the program is such that the MAH (or a third party acting on the MAH's behalf) would foreseeably receive medical information about the patient's use of a medicinal product (e.g., when a program involves HCP interaction with a patient to administer medication or provide medical advice).

MAH-initiated programs that do not meet the criteria above (e.g., delivery of a product to a patient's home, provision of vouchers or coupons) are not considered to be PSPs, as long as the MAH does not request medical information about the patient's use of a medicinal product. PSPs exclude: clinical trials; non-interventional studies, such as post-authorisation safety studies which have a scientific intent or are testing a hypothesis; all forms of compassionate use; and named patient supply.

Excludes certain programmes that are currently considered to be PSP
(e.g. stand-alone medication delivery services)

Chapter 4.5 - Patient Support Programs (PSPs)

- PSPs are considered ODCSs
- PSPs include collection of medical information; or program design is such that the program will likely receive medical information
- For the setup and conduct of PSPs, MAHs should have documentation in place as detailed in Section 2.8, ODCS
- Manage AEs/ADRs as solicited (i.e., study) reports
- Refers to new value in ICH E2B(R3) to identify cases from PSPs

Market Research Programs (MRPs)

2.10. Market Research Program (MRP)

MRPs are ODCSs which are used for planned collection of healthcare professional and/or consumer insights by an MAH (or a third party acting on the MAH's behalf), on medicinal products and/or a disease area, for the purpose of marketing and business development.

Chapter 4.6 Market Research Programs (MRPs)

- MRPs are considered ODCSs
- For the setup and conduct of MRPs, MAHs should have documentation in place as detailed in Section 2.8, ODCS
- Manage AEs/ADRs as solicited (i.e., study) reports
- Refers to new value in ICH E2B(R3) to identify cases from MRPs

Chapter 4.3 - Digital Platforms

- Replaces original E2D Section 3.1.3 Internet
- Defines what is meant by digital platforms as data source
- Provides description of MAH responsibilities depending on digital platform ownership
- No obligation for MAHs to screen external digital platforms
- Clarifies the start of the time clock for reporting

4.3.1 Digital Platforms under the MAH's responsibility

- MAHs should regularly screen digital platforms under their responsibility
- Provides guidance on process for post-approval safety data management depending on nature of activity (i.e., spontaneous or solicited)

Chapter 4.3 - Digital Platforms

4.3.2 Digital platforms not under MAH's responsibility

- Provides guidance when accessing data on digital platforms in context of Organized Data Collection System (ODCS)
  - Supports limiting the scope of screening for AEs/ADRs
  - Refers to a new value in E2B(R3) to identify cases from ODCS with source data from Digital Platforms
  - Provides guidance for managing AEs/ADRs identified on a digital platform outside the context of an ODCS

Chapter 4.4 - Non-interventional Studies

- Defines what is meant by non-interventional studies and describes primary data collection and secondary use of data
- Describes MAH responsibilities for review and reporting of AEs/ADRs depending on the type of data used (primary data collection versus secondary use of data)

Alignment E2D(R1) and E2B(R3)

- To align the ICH E2D(R1) guideline with the ICH E2B(R3) reporting specifications, and to support stratification of cases by their source during signal detection and signal analysis, 3 new values will be added to ICH E2B(R3) data element, C.5.4 'Study Type Where Reaction(s)/Event(s) Were Observed'
- Step 2 Public consultation was accompanied by explanatory note on proposal for additional E2B(R3) values to already existing data element 'study type'
  - To be applied for cases from
    - Patient Support Programs (PSP)
    - Market Research Programs (MRP)
    - Organized Data Collection Systems (ODCS) with source data from a digital platform

Information Paper E2B(R3)

- ICH E2B(R3) EWG/IWG will publish the updates (as shown in red) initially via an Information Paper (information will be incorporated in an update of the E2B(R3) Package)

Type of Report ICH E2B(R3) C.1.3	**Study Type Where Reaction(s) / Event(s) Were Observed** ICH E2B(R3) C.5.4 (only populated if Type of Report = 2, (ICH E2B(R3) C.1.3)) *
1 = Spontaneous report 2 = Report from study * 3 = Other 4 = Not available to sender (unknown)	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 Programme* *5 = Market Research Programme* *6 = Organised Data Collection System with source data from a digital platform*

* Value '2=report from study' and the data element 'study type where reaction(s)/event(s) were observed' is used for studies as well as other Organised Data Collection Systems

Training material E2D(R1)

- Practical implementation of the E2D(R1) guideline will be supported by training material illustrating:
  - Concepts used in E2D(R1)
  - E2B(R3) coding examples on how to use the 3 new values in E2B(R3) C.5.4 “Study Type Where Reaction(s)/ Event(s) Were Observed”
- Material to be published Q4 2025 (ICH and EMA website, see links slide 5)

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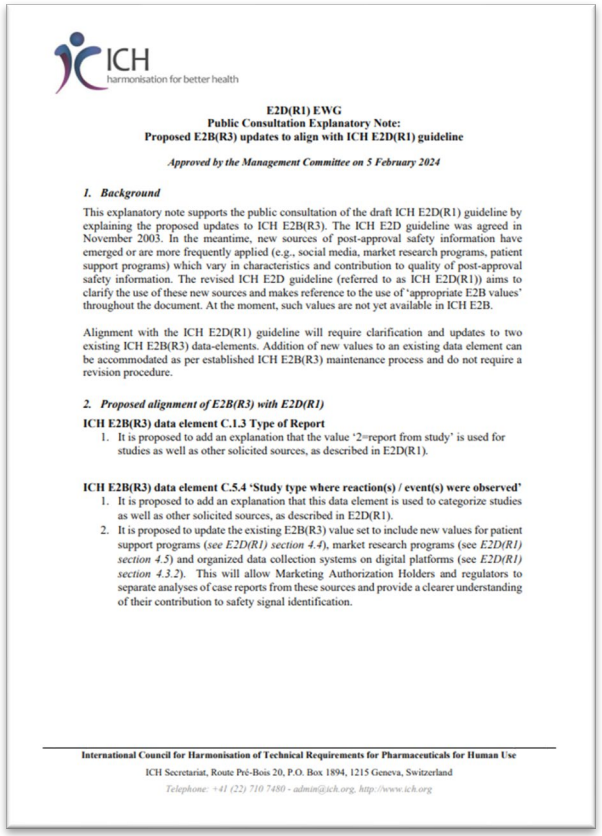
Information Paper E2B(R3)

- ICH E2B(R3) EWG/IWG will publish the updates to align with E2D(R1) via an Information Paper

This is based on the Public Consultation Explanatory Note that accompanied Step 2 public consultation of the E2D(R1) guideline

Information Paper will e.g. explain that new E2B values should be used prospectively



ICH harmonisation for better health

E2D(R1) EWG
Public Consultation Explanatory Note:
Proposed E2B(R3) updates to align with ICH E2D(R1) guideline

Approved by the Management Committee on 5 February 2024

1. Background

This explanatory note supports the public consultation of the draft ICH E2D(R1) guideline by explaining the proposed updates to ICH E2B(R3). The ICH E2D guideline was agreed in November 2003. In the meantime, new sources of post-approval safety information have emerged or are more frequently applied (e.g., social media, market research programs, patient support programs) which vary in characteristics and contribution to quality of post-approval safety information. The revised ICH E2D guideline (referred to as ICH E2D(R1)) aims to clarify the use of these new sources and makes reference to the use of 'appropriate E2B values' throughout the document. At the moment, such values are not yet available in ICH E2B.

Alignment with the ICH E2D(R1) guideline will require clarification and updates to two existing ICH E2B(R3) data-elements. Addition of new values to an existing data element can be accommodated as per established ICH E2B(R3) maintenance process and do not require a revision procedure.

2. Proposed alignment of E2B(R3) with E2D(R1)

ICH E2B(R3) data element C.1.3 Type of Report

1. It is proposed to add an explanation that the value '2=report from study' is used for studies as well as other solicited sources, as described in E2D(R1).

ICH E2B(R3) data element C.5.4 'Study type where reaction(s) / event(s) were observed'

1. It is proposed to add an explanation that this data element is used to categorize studies as well as other solicited sources, as described in E2D(R1).
2. It is proposed to update the existing E2B(R3) value set to include new values for patient support programs (*see E2D(R1) section 4.4*), market research programs (see *E2D(R1) section 4.5*) and organized data collection systems on digital platforms (see *E2D(R1) section 4.3.2*). This will allow Marketing Authorization Holders and regulators to separate analyses of case reports from these sources and provide a clearer understanding of their contribution to safety signal identification.

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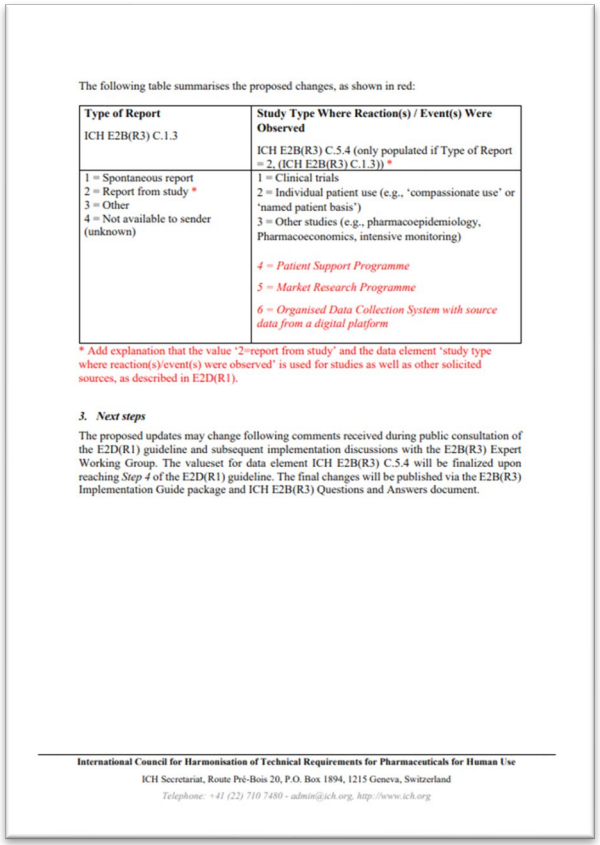

The following table summarises the proposed changes, as shown in red:

Type of Report ICH E2B(R3) C.1.3	**Study Type Where Reaction(s) / Event(s) Were Observed** ICH E2B(R3) C.5.4 (only populated if Type of Report = 2, (ICH E2B(R3) C.1.3)) *
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* Add explanation that the value '2=report from study' and the data element 'study type where reaction(s)/event(s) were observed' is used for studies as well as other solicited sources, as described in E2D(R1).

3. Next steps

The proposed updates may change following comments received during public consultation of the E2D(R1) guideline and subsequent implementation discussions with the E2B(R3) Expert Working Group. The valueset for data element ICH E2B(R3) C.5.4 will be finalized upon reaching *Step 4* of the E2D(R1) guideline. The final changes will be published via the E2B(R3) Implementation Guide package and ICH E2B(R3) Questions and Answers document.

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Other E2B(R3) news

- ICH E2B(R3) recently published several updated documents (July 2025)
- These do not impact the EU implementation of E2B(R3)

Package Version	Publication Date	Notes
1.10	July, 2025	• Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs) – E2B(R3) Data Elements and Message Specification, was updated, **with incorporation of the Q&As.** • ICH Code Lists – has been updated to include **new dosages and strengths** in the **CL25 ich-dosestrength-unit.** • Appendix I (G) to the Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs) Technical Information was updated.

Q&A Document Version	Publication Date	Notes
2.5	July, 2025	Move Q&As to last section which were merged into the Implementation Guide.

- Implementation guide version 5.03 contains editorial corrections and updates based on existing Q&A document
- updated ICH CodeList 25 for dosage and strength units is now in line with EU implementation
- Appendix I(G) typo's and editorial corrections made to "dose Quantity"

Other E2B(R3) news

- Module II published in ICH training library explains general E2B(R3) principles

  (Helpful for 1st-time implementers)

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Next steps at EU level

- Implementation of E2D(R1) triggers a revision of GVP Module VI - Collection, management and submission of reports of suspected adverse reactions to medicinal products
  - Public consultation is aimed for end 2026 (provisional)
- As date for coming into force of E2D(R1) in EU is 18 March 2026 guidance will be developed for the transitional period, in particular:
  - Required documentation for ODCS
  - New PSP definition that excludes certain programmes that are currently considered to be PSP
- Technical implementation of new values in E2B(R3) data element 'Study Type Where Reaction(s)/ Event(s) Were Observed' (E2B(R3) C.5.4)
  - Consult stakeholders on timeframes for implementation of the new values

    (See session 5 on Updates on EudraVigilance)

Key take aways

- PHV is rapidly evolving and its future is being shaped by new trends, driven by advances in technologies, increasing RWE use
- ICH E2D(R1) establishes a framework for current best practices of post-approval safety data management in a dynamic environment
- Revised ICH E2D(R1) Guideline provides updated guidance on post-approval safety data management by better reflecting current practices and sources of safety data
- ICH E2B(R3) evolving in line with ICH E2D(R1) to adapt to stakeholders needs

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Thank you

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