EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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European Medicines Agency

Mandatory use of ISO ICSR/ICH E2B(R3) and EDQM terminology for Dosage Forms (DF) and Routes of Administration (RoA)

Change management plan

* Note: Revision 1 contains the following:

- Updated guidance on EDQM dosage form term selection and term description displayed in EV.

1. Introduction

The new EudraVigilance system launched in November 2017 supports the submission and analysis of reports of suspected adverse reactions in the pre- and post-authorisation phase based on the International Organization for Standardization (ISO) Individual Case Safety Report (ICSR) standard – ISO 27953-2[1].

The use of the ISO Individual Case Safety Report (ICSR) format is set out in Article 26(2)(a) of the Commission Implementing Regulation (EU) No 520/2012[2] and the modalities on how to implement and apply the ISO ICSR standard are defined in the ICH E2B(R3) documentation[3],[4].

Additionally, ICH E2B has agreed[5] to use the ISO standard terminology on pharmaceutical dose forms and routes of administration[6] as set out in Article 25(f)(1) of Commission Implementing Regulation (EU) No 520/2012.

Following a transitional period and consultation with the relevant stakeholders, the EMA Management Board announced in December 2019 that ISO ICSR standard and the Individual Case Safety Report standard and the ISO terminology on pharmaceutical dose forms and routes of administration maintained by EDQM should be implemented by all the stakeholders by **30th June 2022[7]** in relation to reporting obligations to EudraVigilance (pre-and post-authorisation).

This change management document describes the activities performed by the EMA to support the stakeholders during the implementation of the above-mentioned standards.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

2. Individual Case Safety Report (ICSR) standard (ISO 27953-2:2011)

As a consequence of the mandatory use of the ISO ICSR standard (ISO 27953-2:2011), ICSRs submitted to EudraVigilance from 30th June 2022 00h:00m:00s CES time in ICH-E2B(R2) format will be rejected. This is applicable to all submissions including initial, follow-ups and nullifications that need to be submitted in the ISO ICSR format even for cases previously submitted in E2B(R2) format.

2.1. Documentation

The Individual Case Safety Report (ICSR) standard (ISO 27953-2:2011) and the modalities on how to implement this standard, are defined in the ICH E2B(R3).

Additionally the EU Individual Case Safety Report (ICSR) Implementation Guide was updated in 2021 with additional technical details and new business rules for implementation.

The EudraVigilance stakeholder change management plan prepared for the launch on the new EudraVigilance system in November 2017, provides further guidance on the ISO ICSR implementation and this is accompanied by the creation of the change management section on the EudraVigilance website where guidance and documents are available including activities for testing.

During 2016 and 2017 the EMA held virtual webinars to support stakeholders on the launch of the new EudraVigilance system and created the launch of the new EudraVigilance System Questions and answers (Q&A) from stakeholders where questions related to the use of ICH-E2B(R3) were addressed.

2.2. Training

The EudraVigilance training and support webpage contains all training materials available for the different processes related to the system.

The face-to-face training courses on electronic reporting of ICSRs in the ICH E2B(R3) format were cancelled due to the COVID-19 pandemic but they were successfully replaced by virtual training coursed that took place monthly during 2021. The information provided in this training will be updated accordingly to reflect the mandatory use. The new calendar for the 2022 training is already available.

The e-learning module PhV-M2a ISO ICSR/ICH-E2B(R3): Impact on adverse reaction reporting outlines the key principles of the ISO/ICH E2B(R3) ICSR standard and guideline and the impact on the collection, reporting and processing of adverse reactions reports. It further highlights the specific EU requirements and the business rules to be adhered to when reports are submitted to EudraVigilance.

The following training modules are aimed for IT developers:

IT-M1 – ISO ICSR Standard implementation for IT developers details the key points that IT system developers should be conscious of when implementing the ISO ICSR standard, and highlights documentation that can be used to assist in this process.

IT-M2 – Testing the electronic reporting of ICSRs /SUSARs submitted to EudraVigilance

On 4 March 2016, the Agency held a workshop on the implementation of ISO ICSR 27953-2:2011 (ICH E2B(R3)) with representatives from software vendors, service providers and pharmacovigilance system implementers. A video recording of the workshop is also available on the EudraVigilance training page with the presentations of the 4 sessions held during the workshop.

Other materials and manuals on EVWEB and EVDAS are also available on the EudraVigilance training page.

3. Use of terms for dose forms and routes of administration as specified in the ISO standard 11239 for use in the electronic exchange of ICSRs

ICH published supplementary information on the use of terms for dose forms and routes of administration as specified in the ISO standard 11239 for use in the electronic exchange of ICSRs according to the ICH E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). It specifies the use of terminology for pharmaceutical dose forms and routes of administration as published in the EDQM Standard Terms.

Use of EDQM terms for Dosage forms and Routes of administration shall become mandatory as of 30 June 2022 in relation to reporting obligations to EudraVigilance.

EDQM publishes updates as soon as terms are approved and SPOR RMS loads these updates once they are published.

A code-list mapping the EU ICH-E2B(R2) Dosage forms to EDQM terms is also available.

The Pharmacovigilance business team and the EudraVigilance Expert Working Group were consulted on the need for a dynamic implementation of the new EDQM terms or a minimum period should be agreed for the time between publication by EDQM and implementation of those new terms in pharmacovigilance databases.

EudraVigilance will synchronise weekly, on Sundays, with SPOR RMS. Organisations should also aim to regularly update their systems with EDQM changes to ensure that they are exchanging up-to-date terms so they are able to process ICSRs downloaded/rerouted from EudraVigilance correctly and to avoid rejections of submissions of ICSRs if terms are marked as non-current by EDQM.

Specific guidance documentation for using the SPOR RMS system for obtaining the EDQM terms is published on the EMA change management section.

The EU Individual Case Safety Report (ICSR) Implementation Guide contains specific technical information on using EDQM terms in ICSRs submitted in E2B(R3) format.

The table below provides additional information to help with the correct term selection for few specific EDQM dosage form terms. In addition, these specific terms will be displayed in EudraVigilance along with a clarifying description in brackets:

EDQM code	EDQM term	EV description	Comment
BDF-0069	Tablet	Tablet *(unspecified)*	Basic dose form for a tablet where it is not known if it is coated, has a release type, nor if the site of administration is known. For example, when the information provided is "tablet taken orally".
PDF-10219000	Tablet	Tablet *(uncoated, oral)*	Pharmaceutical dose form of tablet, which is known to be uncoated, conventional re-lease and for oral use
BDF-0096	Unknown	Unknown *(other/unspecified)*	This term is used when the dosage form is reported, but it doesn't match with any of the available terms, for example, "living tissue equivalent". Note that null flag "UNK" is available in ICSR to reflect a truly unknown dosage form.

Please note that when obtain these specific terms from SPOR RMS or EDQM, only the original EDQM description will be available.

This additional information will be also included in the next revision of the EU ICSR Implementation guide.

During Q1 2022, EMA made available the new business rules in the EudraVigilance test environment (XCOMP) to enable stakeholders to test changes to their own systems. This new XCOMP system do not accept ICH E2B(R2) messages and the EDQM terms available for testing will not be periodically updated.

References

[1] ISO 27953-2: 2011 Health informatics - Individual case safety reports (ICSRs) in pharmacovigilance -- Part 2: Human pharmaceutical reporting requirements for ICSR
https://www.iso.org/standard/53825.html

[2] COMMISSION IMPLEMENTING REGULATION (EU) No 520/2012 of 19 June 2012 on the performance of pharmacovigilance activities provided for in Regulation (EC) No 726/2004 of the European Parliament and of the Council and Directive 2001/83/EC of the European Parliament and of the Council
https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2012:159:0005:0025:EN:PDF

[3] ICH E2B(R3) Individual Case Safety Report (ICSR) Specification and Related Files
http://estri.ich.org/e2br3/index.htm

[4] EU Individual Case Safety Report (ICSR) Implementation Guide (Doc. Ref. EMA/51938/2013 Rev 2)
https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/european-union-individual-case-safety-report-icsr-implementation-guide_en.pdf

[5] Explanatory Memorandum EDQM Terminologies for Dose Forms and Routes of Administration as Part of ISO/IDMP Standards for ICH Use in Individual Case Safety Reports Created in E2B(R3) Format
http://estri.ich.org/e2br3/E2B-R3_ExplanatoryMemorandumEDQM_SignOff_2018_0306.pdf

[6] ISO 11239:2012 Health Informatics, Identification of Medicinal Products (IDMP) standard, 'Data elements and structures for unique identification and exchange of regulated information on pharmaceutical dose forms, units of presentation and routes of administration'
https://www.iso.org/standard/55032.html

[7] Management Board announcement of mandatory use of ISO ICSR format
https://www.ema.europa.eu/en/documents/other/announcement-ema-management-board-confirmation-mandatory-use-iso-individual-case-report-standard_en.pdf