EMA Management Board
EMA/561671/2019

Announcement of the EMA Management Board

Confirmation of the mandatory use of the ISO Individual Case Report standard based on ICH E2B(R3) modalities and related ISO standard terminology

Basis for announcement

The new EudraVigilance system[1] was launched in November 2017 based on an independent audit and the announcement[2] of the EMA Management Board that the database has achieved full functionality and the system meets the functional specifications.

EudraVigilance 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[3]. The use of the ISO ICSR format is set out in Article 26(2)(a) of the Commission Implementing Regulation (EU) No 520/2012[4], and the modalities on how to implement and apply the ISO ICSR standard are defined in the ICH E2B(R3) documentation[5, 6].

Based on the operational experience gained, the need to define a date for the mandatory use of the ISO ICSR format has been recognised. Currently, ICSRs are also accepted in the previous ICH E2B(R2) ICSR format and are converted to the ISO ICSR format upon receipt in EudraVigilance. However, as part of this process, important information is often not available in dedicated data fields and may only be found in case narratives. This reduces data quality as well as search and data analysis capabilities for National Competent Authorities and the European Medicines Agency. It further impacts marketing authorisation holders and the WHO Uppsala Monitoring Centre, which have restricted access[7] to case narratives due to data protection.

Additionally, ICH E2B has agreed[8] to use the ISO standard terminology on pharmaceutical dose forms and routes of administration[9] as set out in Article 25(f)(1) of Commission Implementing Regulation (EU) No 520/2012[4]. This also requires agreement on a date for the use of the ISO terminology for adverse reaction reporting in the EU.

Based on a readiness survey directed to Member States and pharmaceutical industry associations and following consultation of the pharmacovigilance, clinical trials and IT governance of the EU Medicines Regulatory Network, the Pharmacovigilance Risk Assessment Committee (PRAC) considered the matter.

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Pursuant to Article 24(2) third subparagraph of Regulation (EC) No 726/2004, PRAC recommended on 2 October 2019 that the use of the ISO ICSR standard based on the ICH E2B(R3) modalities and the related ISO standard terminology is to become mandatory as of 30 June 2022 as regards reporting obligations to EudraVigilance.

Announcement

Having considered the PRAC recommendation, the EMA Management Board announces that the use of:

- the ISO Individual Case Safety Report standard[3] as referred to in Article 26(2)(a) of the Commission Implementing Regulation (EU) No 520/2012[4] and the modalities on how to use this ISO ICSR standard defined in the ICH E2B(R3) documentation[5, 6], and
- the ISO terminology on pharmaceutical dose forms and routes of administration[9] referred to in Article 25(1)(f) of Commission Implementing Regulation (EU) No 520/2012[4],

shall become mandatory as of 30 June 2022 in relation to reporting obligations to EudraVigilance.

This applies to the reporting obligations:

- laid down in Article 28 of Regulation (EC) No 726/2004[10]: obligations of marketing authorisation holders and Member States as regards the recording and reporting of suspected adverse reactions for medicinal products for human use authorised in accordance with this Regulation.
- laid down in Articles 107 and 107a of Directive 2001/83/EC[11]: obligations of marketing authorisation holders and Member States as regards the recording and reporting of suspected adverse reactions for medicinal products for human use authorised in accordance with Regulation (EC) No 726/2004 and Directive 2001/83/EC/2001.
- laid down in Article 17(1) of Directive 2001/20/EC[12]: obligations of sponsors of clinical trials and Member States as regards the recording and reporting of suspected unexpected serious adverse reactions for investigational medicinal products studied in clinical trials.
- laid down in Article 42 of Regulation (EU) No 536/2014[13]: obligations of sponsors of clinical trials and Member States as regards the reporting of suspected unexpected serious adverse reactions by the sponsor to the Agency once applicable.

Amsterdam, 19 December 2019

Signature on file

Christa Wirthumer-Hoche, Chair of the EMA Management Board
On behalf of the EMA Management Board

References

[1] EudraVigilance: electronic reporting
https://www.ema.europa.eu/en/human-regulatory/research-development/pharmacovigilance/eudravigilance/eudravigilance-electronic-reporting

[2] Announcement of the EMA Management Board - Confirmation of full functionality of the EudraVigilance database (Doc. Ref. EMA/215105/2017)
https://www.ema.europa.eu/en/documents/other/announcement-ema-management-board-confirmation-full-functionality-eudravigilance-database_en.pdf

[3] 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

[4] 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

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

[6] EU Individual Case Safety Report (ICSR) Implementation Guide (Doc. Ref. EMA/51938/2013 Rev 1*)
https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/european-union-individual-case-safety-report-icsr-implementation-guide_en.pdf

[7] European Medicines Agency policy on access to EudraVigilance data for medicinal products for human use (EudraVigilance Access Policy) (Doc. Ref. EMA/759287/2009)
https://www.ema.europa.eu/en/documents/other/european-medicines-agency-policy-access-eudravigilance-data-medicinal-products-human-use-revision-4_en.pdf

[8] 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

[9] 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

[10] Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for

human and veterinary use and establishing a European Medicines Agency (Consolidated version: 28/01/2019).
https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02004R0726-20190128&from=EN

[11] Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use
https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/dir_2001_83_consol_2012/dir_2001_83_cons_2012_en.pdf

[12] Directive 2001/20/EC OF the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use

https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/dir_2001_20/dir_2001_20_en.pdf

[13] Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC

https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32014R0536&from=EN