EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Inspections and Human Medicines Pharmacovigilance Division

Reporting requirements of Individual Case Safety Reports (ICSRs) applicable to marketing authorisation holders during the interim period

1. General reporting requirements of ICSRs

During the interim period, in accordance with the transitional provisions set out in Article 2(4) and Article 2(5) of Directive 2010/84/EU, the reporting requirements detailed in Table 1 shall apply to valid ICSRs reported by healthcare professionals and non-healthcare professionals. This is irrespective of the conditions of use of the suspected medicinal products and of the expectedness of the adverse reactions.

Table 1. Reporting requirements applicable to marketing authorisation holders - Interim period

Marketing authorisation procedure	Origin	Adverse reaction type	Destination	Time frame
• Centralised • Mutual recognition, decentralised or subject to referral • Purely national	EU	All serious	• Member State where suspected adverse reaction occurred (a)	15 days
		All non-serious	• Member State where suspected adverse reaction occurred, if required (b)	90 days
	Non-EU	All serious	• EudraVigilance database • Member States where suspected medicinal product is authorised, if required (b)	15 days

(a) Member States may request marketing authorisation holders to report serious EU ICSRs originating in their territory to them and/or to EudraVigilance. Those requirements are detailed in Table 2.

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(b) Member States' reporting requirements during the interim period for non-serious EU ICSRs and for serious non-EU ICSRs are presented respectively in Table 3 and 4.

Table 2. Reporting requirements applicable to marketing authorisation holders – Interim period – Serious ICSRs originating in the territory of a Member State

Marketing authorisation procedure	Origin	Adverse reaction type	Destination
• Centralised • Mutual recognition, decentralised or subject to referral • Purely national	EU	All serious	Member State where suspected adverse reaction occurred: AT, CZ, DE, DK, ES, FI, HR, IE, IT, LT, LV, NO, PT, RO, SI, SK, UK.
			EudraVigilance: BE, CY, EE, FR[1], GR, IS, LI, LU, MT, NL, PL, SE.
			Member State where suspected adverse reaction occurred and EudraVigilance: BG, HU.

FR[1]: Marketing authorisation holders already submitting ICSRs directly to France can continue to do so during the interim period (France retransmits these ICSRs to EudraVigilance), or can switch to direct transmission to EudraVigilance.

Table 3. Reporting requirements applicable to marketing authorisation holders – Interim period – Member States' requirements for non-serious EU ICSRs

Marketing authorisation procedure	Member states who wish to receive non-serious ICSRs of suspected adverse reactions occurring in their territory
• Centralised • Mutual recognition, decentralised or subject to referral • Purely national	AT[1], DE[2], DK, HR, IT[3], PL, RO.

AT[1]: Only for non-serious ICSRs related (i) to vaccines or plasma preparations (Verordnung betreffend Identifizierungserfordernisse für bestimmte Arzneispezialitäten), or (ii) to those medicinal products which are included in the list of products subject to additional monitoring pursuant to Art. 23 of Regulation (EC) No 726/2004.

DE[2]: Only for non-serious ICSRs related to vaccines reportable to the Paul-Ehrlich-Institut. Reporting of other non-serious ICSRs related to non-vaccines medicinal products will only be requested individually in case of safety concerns.

IT[3]: Not required for non-serious ICSRs published in the scientific and medical literature.

Table 4. Reporting requirements applicable to marketing authorisation holders – Interim period – Member States' requirements for serious non-EU ICSRs

Marketing authorisation procedure	Member States who wish to receive non-EU serious ICSRs of adverse reactions suspected to be related to a medicinal product authorised in their territory
• Centralised • Mutual recognition, decentralised or subject to referral • Purely national	DE, UK[1].

UK[1]: Only for healthcare professional serious non-EU ICSRs.

2. Reporting requirements of literature reports

Literature reports are defined in GVP Module VI, chapter VI.B.1.1.2.

To enhance the efficiency of reporting and to provide a simplification for pharmaceutical industry, Article 27 of Regulation (EC) No 726/2004 sets out the following:

1. The Agency shall monitor selected medical literature for reports of suspected adverse reactions to medicinal products containing certain active substances. It shall publish a list of active substances being monitored and the medical literature subject to this monitoring.
2. The Agency shall enter into the EudraVigilance database relevant information from the selected medical literature.
3. The Agency shall, in consultation with the Commission, Member States and interested parties, draw up a detailed guide regarding the monitoring of medical literature and the entry of relevant information into the EudraVigilance database.

The Detailed Guide, the list of active substances being monitored and the medical literature subject to the monitoring by the Agency are published at the dedicated Medical Literature Monitoring webpage accessible via the EMA website[1].

During the interim period outlined in Article 2(4) and Article 2(5) of Directive 2010/84/EU and in line with national legislation and guidance where applicable, the following therefore applies to valid ICSRs originating from the literature:

i. For **active substances and literature not subject to the medical literature monitoring conducted by the Agency** pursuant to Article 27 of Regulation (EC) No 726/2004, the reporting modalities as outlined in Chapter 1 of this document apply.

ii. For active **substances subject to the medical literature monitoring conducted by the Agency** pursuant to Article 27 of Regulation (EC) No 726/2004 but when the **publication containing the relevant information is not included in the list of publications monitored by the Agency**, the reporting modalities as outlined in Chapter 1 of this document apply.

[1] http://www.ema.europa.eu/ema/

iii. For **active substances subject to the medical literature monitoring conducted by the Agency and when the publication containing the relevant information is included in the list of publications monitored by the Agency** pursuant to Article 27 of Regulation (EC) No 726/2004, the reporting modalities as outlined in Table 5 apply.

Table 5. Reporting requirements applicable to marketing authorisation holders – Interim period – active substances and journals **subject to the service of the Agency** pursuant to Article 27 of Regulation (EU)

Marketing authorisation procedure – substances subject to the service of the Agency	Origin Based on journals subject to the services of the Agency	Adverse reaction type	Destination	Time frame
• Centralised • Mutual recognition, decentralised or subject to referral • Purely national	EU	All serious[2]	• DE[1] when suspected adverse reaction occurred in this territory	15 days
		All non-serious[2]	• DE[1] when suspected adverse reaction occurred in this territory but only if requested individually in case of safety concerns	90 days
	Non-EU	All serious[2]	• DE[1] when suspected medicinal product is authorised in this territory	15 days

[1] Federal Institute for Drugs and Medical Devices (BfArM)
[2] Valid ICSRs are submitted by the Agency to the applicable Member State in line with chapter 1 of this document and as outlined in the Detailed Guide[2].

[2] Detailed guide regarding the monitoring of medical literature and the entry of relevant information into the EudraVigilance database by the European Medicines Agency" (EMA/161530/2014)