EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

To the
Qualified Person Responsible for Pharmacovigilance (QPPV)
Marketing Authorisation Holders in the European Economic Area

12 April 2023
EMA/50808/2023

Dear Madam/Sir,

Subject: Follow-up on the international transfer of personal (health) data in ICSRs originating from EudraVigilance (reference EMA/869259/2022, 8 December 2022)

In response to the letter of the European Medicines Agency (EMA) of 8th December 2022 relating to the international transfer of personal (health) data in Individual Case Safety Reports (ICSRs) originating from EudraVigilance, EMA received questions from marketing authorisation holders (MAHs), which were further discussed at the EudraVigilance Expert Working Group on 7 March 2023.

In this regard, EMA would like to explain that the instructions provided in December 2022 were in direct response to the transmission of ICSRs by MAHs to their US affiliates and onward to the US health authorities which resulted in the publication of personal data including data concerning health.[1] These instructions were provided with a view to mitigate risks to the patients and healthcare professionals concerned, particularly the risk of re-identification of data subjects.

At the request of EMA, the Centers for Disease Control and Prevention[2] and the Center for Biologics Evaluation and Research (CBER) - FDA[3] implemented a process to remove certain data fields (country codes; reported symptom case narrative free text; diagnostic laboratory data free text; illness at time of vaccination free text; chronic conditions free text medical history; allergies free text) from VAERS reports originating from the European Economic Area (EEEA) and which may not comply with European Union data protection legislation.[4] As a result, the instructions provided by EMA set out under points 3, 4 and Annex 1 of its letter of 8th December 2022 no longer apply.

The scope of this letter relates to the processing of personal data performed in the context of your pharmacovigilance obligations as set out in the European Union pharmacovigilance legislation and the applicable use of EudraVigilance. More specifically, EMA would like to reiterate and remind about the following core principles when MAHs access and download Individual Case Safety Reports (ICSRs) from EudraVigilance and further process such information:

[1] In accordance with Article 4(15) of the GDPR 'data concerning health' means personal data related to the physical or mental health of a natural person, including the provision of healthcare services, which reveal information about his or her health status.
[2] Centers for Disease Control and Prevention (cdc.gov)
[3] Center for Biologics Evaluation and Research (CBER) | FDA
[4] VAERS - Data Sets (hhs.gov)

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1. Application of the GDPR

Regulation (EU) 2016/679, the General Data Protection Regulation (GDPR)[5] applies since 25 May 2018. Adaptations to pharmacovigilance systems necessary to comply with the provisions set out in the GDPR are subject to the MAH's own data protection assessment regarding the risks to the rights and freedoms of natural persons. This includes the implementation of the necessary technical and organisational measures based on the principle of data protection by design and default and the security of personal data.[6] As clarified by the European Data Protection Supervisor (EDPS), MAHs are controllers for the personal data processing activities carried out pursuant to the pharmacovigilance legislation[7] including the access and further processing of ICSR data originating from EudraVigilance. This includes accessing and onward transfers of ICSRs originating from EudraVigilance independently of the origin (previous sender) and the level or mode of access granted (EVWEB, EVDAS).

MAHs are therefore accountable to comply with the rules set out in Union data protection legislation i.e., the GDPR and national data protection laws where applicable. This includes adherence to the transfer requirements of personal data to third countries as set out in Chapter V of the GDPR and the confidentiality undertaking of the EudraVigilance Access Policy (as per point 2 below).

More specifically, with reference to transfers of personal data subject to appropriate safeguards[8] and the use of Standard Contractual Clauses (SCC)[9] or Standard Data Protection Clauses (SDPC), we would like to raise your awareness that the use of these clauses is not sufficient to guarantee compliance with the data protection rules under Chapter V of the GDPR as recently emphasised by the EDPS. In line with the Schrems II judgment (C-311/18) and confirmed by the European Commission (EC) in its Questions and Answers[10], the parties are required, prior to concluding the SCC, to assess - namely by carrying out a transfer impact assessment[11] - whether the laws and practices of the third country of destination applicable to the processing of the personal data by the data importer could prevent the latter from complying with the SCC, considering the specific circumstances of the transfer. Should the assessment be negative, the parties may only transfer data based on the SDPCs if they put in place additional ("supplementary") safeguards (e.g., technical measures to ensure data security, such as e.g., end-to-end encryption) that address the situation and thus ensure compliance with the SCC.

Furthermore, the EC has the power to determine, on the basis of Article 45 of the GDPR whether a country outside the EU offers an adequate level of data protection. The effect of such an adequacy decision is that personal data can flow from the EEA to that third country without any further safeguard being necessary. The list of countries currently providing adequate protection is accessible here.

For questions on data protection, the main contact point is the Data Protection Authority (DPA)[12] in the EU Member State where your company is based. If your company processes personal data in different EU Member States or is part of a group of companies established in different EU Member States, that main contact point may be a DPA in another EU Member State. In the case of cross-border processing

[5] Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation)
[6] see Article 25 of the GDPR
[7] EudraLex - Volume 1 (europa.eu)
[8] Article 46 of the GDPR
[9] Standard contractual clauses for international transfers | European Commission (europa.eu)
[10] questions_answers_on_sccs_en.pdf (europa.eu)
[11] Recommendations 01/2020 on measures that supplement transfer tools to ensure compliance with the EU level of protection of personal data
[12] To find the national data protection authorities please see Our Members | European Data Protection Board (europa.eu)

of personal data, please refer to the Article 29 Working party Guidelines for identifying a controller or processor's lead supervisory authority.[13] Before contacting the DPA, you may wish to seek first advice from the Data Protection Officer appointed by your company.

2. Reporting of suspected adverse reactions to EudraVigilance

The requirements for the reporting of suspected adverse reactions to EudraVigilance is set out in Regulation (EC) No 726/2004[14] and Directive 2001/83/EC[15] with the format and content of ICSRs further defined by the Commission Implementing Regulation (EU) No 520/2012[16] and the applicable good pharmacovigilance practices.[17] These rules should be adhered to for reporting of ICSRs to EudraVigilance.

3. Adherence to the principles set out in the EudraVigilance Access Policy[18]

The EudraVigilance Access Policy provides two access levels for MAHs:

a. *Level 2A* – set of data elements to *fulfil the MAHs' pharmacovigilance obligations*;

b. *Level 2B* – Level 2A data elements plus case narratives to validate signals and to *support the review of ICSR data warranted in the context of a pharmacovigilance assessment procedure (GVP Modules VII[19] and IX[20]) in the EEA.*
Access to case narratives is subject to a confidentiality undertaking (*Annex C of the Access Policy*), which sets out the data protection and confidentiality obligations of registered users of MAHs. Whilst it is recognised that MAHs may be subject to adverse reaction reporting obligations outside the EEA, the confidentiality undertaking requires MAHs to "*ensure that personal data reported can no longer be attributed to a specific data subject*".

The confidentiality undertaking as set out in Annex C of the EudraVigilance Access Policy is applicable to all registered users since November 2017 and must be adhered to accordingly. In addition, chapter 5.2.5.3.4. "Personal data protection requirements" of the same Policy sets out that stakeholder group III (i.e., MAHs) is responsible, amongst others, for ensuring that confidentiality of records and the personal data of the data subjects remain protected in accordance with the applicable law on personal data protection.

4. Personal data concerning health and pseudonymisation

Data concerning health originating from EudraVigilance (L2B access), which contain case identifiers (including a country reference), age, gender, medical history, clinical relevant and other personal data (e.g. health history of family members) is considered pseudonymised. In accordance with Recital 26

[13] ARTICLE29 - Guidelines on the Lead Supervisory Authority (wp244rev.01) (europa.eu)
[14] 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
[15] 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
[16] 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
[17] Good pharmacovigilance practices | European Medicines Agency (europa.eu)
[18] European Medicines Agency policy on access to EudraVigilance data for medicinal products for human use (europa.eu)
[19] Guideline on good pharmacovigilance practices (GVP): Module VII – Periodic safety update report
[20] Guideline on good pharmacovigilance practices (GVP) - Module IX – Signal management (Rev 1) (europa.eu)

GDPR, "[*p*]*ersonal data which have undergone pseudonymisation, which could be attributed to a natural person by the use of additional information should be considered to be information on an identifiable natural person*." Consequently, pseudonymised data is considered personal data, as detailed in Article 4(1) of GDPR and is under the scope of the GDPR.

5. Location data

Location data (e.g., country, city, postcode, name or place of hospitals) are personal data in accordance with the definition of personal data as set out in Article 4(1) of the GDPR. In certain instances, such location data together with details of a patient's adverse reaction experience, medical condition, laboratory findings and medical history can allow for the reidentification of the individual concerned. In particular, where location data including information in narratives may be subject to publication or other forms of disclosure by the receiving party, it is essential to minimise the risk of reidentification of patients or healthcare professionals.

The use of "EU" is an exceptionally reserved code of the ISO 3166 country codes list. In accordance with the ICH E2B(R3) specification[21], "EU" can be used for the following E2B(R3) data elements: E2B(R3) C.1.1 Sender's (case) Safety Report Unique Identifier, E2B(R3) C.2.r.3 Reporter's Country Code, E2B(R3) C.5.1.r.2 Study Registration Country, E2B(R3) E.i.9 Identification of the Country Where the Reaction/Event Occurred, E2B(R3) G.k.2.4 Identification of the Country Where the Drug Was Obtained and G.k.3.2 Country of Authorisation/Application. More specifically, the following should be considered:

- The Sender's (case) Safety Report Unique Identifier, data element E2B(R3) C.1.1, is based on a concatenation of three segments consisting of the country code, the organisation's name and the report number. In accordance with the ICH E2B(R3) rules, the Sender's (case) Safety Report Unique Identifier should be updated upon retransmission by the sender. This is also to avoid identification of the country of origin of the individual case e.g., for EudraVigilance access level 2A, the Sender's (case) Safety Report Unique Identifier of a regulatory authority case in the EEA should be replaced by the identifier of the MAH when submitting the case to a regulatory authority in a third country. It should be noted, that for certain non-EEA regulatory authorities, the country code as part of Sender's (case) Safety Report Unique Identifier is published and is also used to remove certain data elements as part of their publication process.
- The medicinal product name (data element ICH E2B(R3) D.10.8.r.1 Name of the Drug as Reported, and data element ICH E2B(R3) G.k.2.2 Medicinal Product Name as Reported by the Primary source) may contribute to the identification of a patient or healthcare professional i.e., by indirectly disclosing country information. The likelihood of such information leading to the identification of the individual concerned should be assessed and the medicinal product information redacted as needed e.g., for medicinal products indicated for the treatment of rare diseases which relate to small patient populations. Similar may also apply to the data element ICH E2B(R3) D.7.3. Concomitant Therapies. When this data element is set to 'true', it indicates that at the time of the reaction there were concomitant therapies such as radiotherapy, drug class, dietary supplements

[21] ICH Official web site : ICH

or other products not otherwise describable in the ICH E2B(R3) section G, and for which further details may be provided in the narrative section H.1.

6. Narrative sections in ICSRs

With reference to ICSR free text sections (data element ICH E2B(R3) D.7.1.r.5 Comments, data element ICH E2B(R3) D.7.2 Text for relevant medical history and concurrent conditions, data element ICH E2B(R3) D.10.7.1.r.5 Comments, data element ICH E2B(R3) F.r.6 Comments (free text), data element ICH E2B(R3) G.k.11 Additional Information on Drug (free text), data element ICH E2B(R3) H.1 Case narrative including clinical course, therapeutic measures, outcome and additional relevant information, data element ICH E2B(R3) H.2 Reporter's Comments and data element ICH E2B(R3) H.4 Sender's Comments), it is advised to perform a risk assessment taking into account the principles set out above including the need to comply with the rules set out in the GDPR and the principle of data minimisation as set out in Article 5(1)(c) "*adequate, relevant and limited to what is necessary in relation to the purposes for which they are processed*".

Finally, we would like to inform you that as advised by the EDPS, in October last year EMA initiated a consultation on the ICSR reporting to third countries based on the requirements set out in chapter V of the GDPR with the DPA in one EU Member State. Once available, the outcome of that consultation may be further instructive on current reporting practices of which we will keep you informed.
We do hope the above further clarifies the principles of safeguarding personal data of patients and healthcare professionals in the context of the performance of your pharmacovigilance activities in the context of EudraVigilance and compliance with Union data protection legislation.

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CC: Members of the Pharmacovigilance Risk Assessment Committee (PRAC), Pharmacovigilance Inspectors Working Party, Data Protection contact points for EudraVigilance