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European Medicines Agency

Questions and Answers on Implementing Regulation (EU) 2025/1466: Amendment of Regulation (EU) No 520/2012 and Conclusion of the Signal Detection in EudraVigilance Pilot by MAHs

This document provides clarification on key topics of interest to Marketing Authorisation Holders (MAHs) regarding the termination of the signal detection pilot in EudraVigilance by MAHs. These changes follow the revision of Implementing Regulation (EU) No 520/2012.

***Note:** This revision includes

- Clarification to Question 4 in alignment with the applicable regulatory framework.

- Amendment to Question 5: The update to the (GVP) IX is scheduled to be implemented in Q2 2026 and other updates to the Implementing Regulation that take effect as of February 2026.

- Amendment to Question 3: This section has been updated to include an additional paragraph offering further clarification on key concepts that required greater explanation. The revision enhances transparency and supports a clearer understanding of the intended requirements.

- Editorial changes

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1. What is the impact of the revision of Article 18, paragraph 2 of the Implementing Regulation (EU) No 520/2012 regarding the pilot phase of signal detection in EudraVigilance by MAHs?

With the update of the IR 520/2012 (as amended by Commission Implementing Regulation (EU) 2025/1466), the pilot phase – launched on 22 February 2018 and focused on a limited number of active substances and combinations ('pilot list') - has terminated. The update clarifies that all MAHs with medicinal products authorised in the EEA shall monitor the data available in the EudraVigilance database and use it as an additional source of safety information to support their processes and enhance signals detected through other sources [IR Art 18, 2].

2. What is the impact of the deletion of Article 21 paragraph 2 of the Implementing Regulation (EU) No 520/2012?

With the deletion of Article 21, paragraph 2,, which took effect in August 2025, MAHs are no longer expected to submit validated signals to the EMA and NCAs via the standalone signal notification form. Signals detected through all sources, including the EudraVigilance database, should be handled according to the marketing authorisation holder's own signal management process, considering the guidance in GVP IX.B.

Actions triggered by signal assessments should be performed using existing legal framework in the EU as appropriate, taking into account the general obligations of the MAHs to keep their product information up-to-date throughout the product's lifecycle by variation applications and to present the signal evaluation in the PSURs (see GVP Module VII) for the MAHs with obligation to submit PSURs.

3. What are the expectations for MAHs regarding the implementation of Article 18, paragraph 2 of Implementing Regulation (EU) No 520/2012?

MAHs should describe the changes driven by the updated IR 520/2012 in their signal management and pharmacovigilance procedures. In relation to Art 18, paragraph 2, MAHs should describe how the data in EudraVigilance will be monitored and how those data will be used in conjunction with other available sources.

During the signal management activities, MAHs shall monitor the data available in EudraVigilance in conjunction with those from other available data sources within their established processes with a frequency proportionate to the risk, the known safety profile of the product and the characteristics of the product.

MAHs should determine at which step in the signal-management process EudraVigilance data will be used. MAHs may decide to screen the database for signal-detection purposes as a primary source with an established frequency. The use of EudraVigilance should be proportionate to the safety profile and characteristics of the product and should be integrated and coherent within the MAH's established high quality pharmacovigilance procedures and other sources of information. It is expected that MAHs use EudraVigilance data during the validation and evaluation stages of signal management.

During the assessment of signals led by the PRAC, and in response to PRAC requests for cumulative reviews, analyses, and proposed actions, MAHs are expected to consider and include all relevant data available also in EudraVigilance. This should be done in accordance with the specific context of the

substance on the market (e.g. different indications, formulations, or routes of administration) and the scope of the signal.

4. Do MAHs with products authorised in Northern Ireland (NI) need to monitor the data in EudraVigilance?

MAHs with EU products authorised in NI should monitor EudraVigilance, even if they are not authorised in an EU/EEA Member State. For further information on safety information reporting into EudraVigilance and access to EudraVigilance data please refer to Q&A 9.1 of the EMA's Q&A to stakeholders on the implications of Regulation EU 2023-1182 for centrally authorised medicinal products for human use

5. What MAHs need to do from the moment the IR is published until GVP IX is updated?

The changes to Article 18 and 21 of Commission Implementing Regulation (EC) 520/2012 took effect as of August 2025, the MAHs are therefore expected to implement the changes related to Article 18, paragraphs 2 and 3, and Article 21, deletion of paragraph 2 of the Implementing Regulation (EU) 2025/1466. An update to the Good Pharmacovigilance Practices (GVP) IX is scheduled to be implemented in Q2 2026, in alignment with these requirements and other updates to the Implementing Regulation that take effect as of February 2026.