1st EMA/HMA Multi-Stakeholder Forum on EudraVigilance and Signal Detection

5 November 2025 (09:00 – 17:00 CET)

Summary report

1st EMA/HMA Multi-Stakeholder Forum on EudraVigilance and Signal Detection

Welcome and Opening remarks

EudraVigilance, the centralised system for managing and analysing information on suspected adverse reactions to medicines in the EEA, was launched in December 2001. The electronic reporting of individual case safety reports (ICSRs) to EudraVigilance became mandatory in November 2005. To mark the 20th anniversary of this milestone, the first Multi-Stakeholder Forum on EudraVigilance and Signal Detection took place on 5 November 2025.

The main objective of the Forum was to inform stakeholders on ongoing and forthcoming developments in international guidance, adverse drug reaction case processing and data analysis in EudraVigilance, with a focus on data quality and its importance for signal detection and management.

Peter Arlett (EMA, Head of Data Analytics and Methods Task Force) welcomed the participants, and Alexis Nolte (EMA, Head of Human Medicines Division) provided the opening remarks.

The Forum was attended in person by 25 NCA experts and almost 600 stakeholders and partners attended online, with several hundred more joining via the online broadcast of the event.

Session 1: Updates to EU legislation, guidance and international standards

Chair: Anja van Haren (EV-EWG Co-chair, CBG-MEB, NL)

Key topics

- Main changes introduced by the amendment of the Implementing Regulation (IR) EU 520/2012 and implications for Marketing Authorisation Holders.
- Updates on ICH guidelines - E2D(R1) and E2B(R3).
- ADR chapter of the EU Data Quality Framework guideline: aims to guide stakeholders in improving ADR processes with a focus on data quality. It is expected to be released for public consultation in early 2026.

New Commission Implementing Regulation (EU) No 2025/1466 amending IR (EU) No 520/2012, and update of GVP Module IX

Speakers: Georgy Genov and Eleni Savvaidou (EMA)

This presentation explored the key changes introduced by Commission Implementing Regulation (EU) No 2025/1466 of 22 July 2025 amending IR (EU) No 520/2012 of 19 June 2012. According to this update of EU legislation, Marketing Authorisation Holders (MAHs) shall monitor the data available in the EudraVigilance (EV) database and use it together with data from other available sources. The use of EV should be proportionate to the safety profile and characteristics of the product and should be integrated and coherent within the MAH's established pharmacovigilance procedures and other sources of information. In addition, MAHs are no longer expected to submit validated signals to the EMA & NCAs via the standalone notification form in accordance with the deletion of Article 21, paragraph 2 of the IR (EU) No 520/2012. 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.

With the update of IR (EU) No 520/2012, the pilot phase of signal detection in EudraVigilance by MAHs, that started in 2018 with a focus on a limited number of active substances and combinations ('pilot list'), has come to an end. The corresponding Q&A document was updated accordingly and GVP Module IX (Signal management) will be updated in 2026 to reflect the changes driven by the amended IR.

Presentation available here.

ICH E2D and E2B

Speakers: Gilles Touraille and Tom Paternoster-Howe (EMA), Anja van Haren (EV-EWG Co-chair, CBG-MEB, NL)

As the pharmacovigilance landscape evolves, revisions to the ICH guideline E2B(R3) on the data elements and message specification of electronic transmission of ICSRs, as well as the ICH E2D guideline on definitions and standards in post-approval safety data management, have become necessary. To align with the E2D guideline revision (E2D(R1)) which comes into force in the EU on 18th March 2026, new E2B(R3) values like dosage and strength units are being introduced.

The session emphasised the introduction and definition of new sources of ICSRs, such as digital Platforms (replacing former E2D section "3.1.3. Internet"), non-interventional studies - distinguishing between studies with primary data collection from secondary data use – and Organised Data Collection Systems (ODCS), like Patient Support Programs (PSPs) and Market Research Programs (MRPs). Training materials developed by ICH E2D(R1) expert working group will be provided to support the new concepts in E2D(R1).

The implementation of E2D(R1) will trigger a revision of GVP Module VI (Collection, management and submission of reports of suspected adverse reactions to medicinal products), for which a public consultation is expected to take place at the earliest by the end of 2026.

Presentation available here.

ADR data quality framework

Speaker: Tom Paternoster-Howe (EMA)

Significant progress has been made in developing the EU Adverse Drug Reaction (ADR) chapter of the Data Quality Framework (DQF). The EU DQF describes concepts and metrics applicable to all data sources used in medicine regulation across the EU regulatory network. It defines the terminology around data quality, providing the regulator with a framework to measure and describe the data quality of a given data source. Its ADR chapter aims to guide stakeholders in improving ADR processes with a focus on data quality.

Input has been gathered from a broad range of stakeholders involved in ADR reporting (e.g., regulatory authorities, pharmacovigilance inspectors, commercial and non-commercial sponsors, industry representatives, veterinary experts and investigators) to identify the key topics which should be covered in the EU DQF ADR chapter. A draft is being prepared for public consultation before submission to PRAC and approval by the Network Data Steering Group (NDSG).

Presentation available here.

Session 2: Signal management

Chair: Liana Martirosyan (PRAC Vice-chair, CBG-MEB, NL)

Key topics

- A tier-based approach in signal management, i.e., a risk-proportionate strategy where products are grouped into categories (tiers) based on their safety profile, is advocated by industry to focus resources on higher-risk products and ensure timely identification of safety concerns.
- MAHs use EudraVigilance data alongside other available sources of medicines' safety data.
- Description of the workflow of the signal management process by regulators, highlighting the do's and don'ts when additional information is needed from MAHs.

Industry perspective on signal management

Speakers: Raphael Van Eemeren (EFPIA), Jelena Zanetic and Amit Kubavat (Medicines for Europe)

Industry representatives shared their approaches and perspectives on signal management. A tier-based approach was advocated to optimise resource allocation and ensure timely detection of high-risk events. Tier levels may be assigned based on factors such as time on market, statistical limitations, additional monitoring requirements, number of signals, therapeutic area complexity, periodic report frequency, and drug pharmacology.

The importance of the EVDAS tool for signal validation and assessment was discussed, acknowledging that the volume and complexity of data require a pragmatic review and resource prioritisation. The risk-based approach in signal management, being data-driven, offers flexibility being adaptable to different product types (generic/biosimilar, innovative), supports proportionate analysis, and is fit for purpose.

Presentation available here.

Best practice for signal assessment

Speaker: Bianca Mulder (CBG-MEB, NL)

This presentation described the workflow of the EU signal management process overseen by the Pharmacovigilance Risk Assessment Committee (PRAC) as outlined in GVP Module IX. In this presentation, practical guidance and examples of do's and don'ts were provided to support MAHs when a signal for their product undergoes PRAC evaluation.

Presentation available here.

Session 3: EudraVigilance data quality and medical literature

Chair: Paolo Alcini (EMA)

Key topics

- Details on the monthly automated compliance monitoring reports that, since September 2025, are sent to QPPVs/RPs of all sender organisations, covering submissions made to EV in the previous month.
- Main points to consider when preparing for an EV inspection, and some of the most common findings.
- 10th anniversary of the MLM service of EMA – the work developed on behalf of MAHs has saved industry from preparing and submitting over 140,000 EEA ICSRs.

Automated compliance monitoring

Speaker: Richeal Nic An Rí (EMA)

In September 2025, automated compliance monitoring was introduced to help ensure MAHs and NCAs comply with the legal basis for ICSR reporting timelines and to complement internal quality management systems. It provides MAHs/NCAs with a clear overview of compliance reporting statistics for their ICSR submissions to EV (presented in tables and bar charts). These monthly automated reports are generated by EVDAS and sent via email to the applicable sender organisations. The incorporated Batch Sender Identifier offers a unique identifier for each sender, allowing parent companies to manage and divide responsibilities among affiliates.

There are three ICSR compliance reports in total to capture compliance with the 7, 15 and 90-day submission timelines to EVPM and EVCTM. Within each of these, there are three sub-reports which include a listing of non-compliant cases, an overview of submissions within and outside the timelines and an overview of Submission Timelines of ICSRs.

Error reports, nullification reports, and amendment reports are excluded from compliance notifications. Time zones must be carefully considered when meeting submission deadlines; however, a 12-hour grace period beyond the CE(S)T time zone is allowed for submissions from other regions.

Presentation available here.

Pharmacovigilance inspections - common findings and use of EV data

Speaker: Eva-Maria Jahn (PEI, DE)

This presentation highlighted the use of the EVDAS performance indicator dashboard, containing post marketing and clinical trials ICSR numbers and reporting timelines by MAHs, as a valuable information source used when preparing pharmacovigilance inspections. Data can also be collected for a specific substance or substance group. For case transmissions with errors, checks can be performed to investigate if correct follow-up was submitted and, if yes, within which timeframe. Master cases and duplicate reports are also checked for, as they significantly increase the size of the data contained in EV and impact the quality of the data, thereby directly influencing signal detection activities performed in the database.

The most common findings from pharmacovigilance inspections using EV data include incomplete or missing information (including at follow-up), incorrect coding of reported events, overreporting of invalid reports, and incorrect assessments of seriousness or causality.

Presentation available here.

Achievements and impact of the MLM service – a retrospective review of the first 10 years

Speaker: Tom Paternoster-Howe (EMA)

The MLM service celebrates its 10-year anniversary in 2025. It has significantly supported MAHs, received ongoing feedback, improved its functionality, and has been widely used with 1.5 million searches performed to date and almost 6 million articles screened and reviewed. The work the MLM Service performs on behalf of MAHs has saved industry from having to prepare and submit over 140,000 EEA ICSRs (90,000 cases) and has significantly contributed to reduce duplicate reporting to EudraVigilance.

Surveys will soon be sent to stakeholders to gather insights for further improvement of the service. The substance group will be updated in 2026 based on data added to XEVMPD. Downloading ICSRs will be simplified through the introduction of an application programming interface (MLM-API) to reduce the need for human interaction and simplify the process of downloading the ICSRs created by the MLM Service.

Presentation available here.

Session 4: New perspectives on data analysis

Chair: Georgy Genov (EMA)

Key topics

- Current priorities of the SMART WG include automatic screening based on statistical tools, as well as SafetyNet. Future improvements will cover the integration of AI and automation in EMA signal detection process workflow, with various ongoing and upcoming projects.
- Several perspectives, concerns, and areas for improvement on AI in pharmacovigilance were described by industry, highlighting the need to have a regulatory and operational framework on AI.
- The CIOMS Working Group XIV Report on AI in Pharmacovigilance, addressing the use, opportunities, and challenges of AI specifically within the field of pharmacovigilance, will soon be published. Acknowledging that AI has the potential to improve efficiency and consistency increasing data insights, it describes the principles that should guide the use of AI in pharmacovigilance.

SMART Methods Working Group: harnessing collective expertise to strengthen signal detection

Speaker: Cosimo Zaccaria (EMA)

In a collaboration between the Member States and EMA, the Signal Management Review Technical (SMART) Working Group was set up to strengthen and streamline the signal management process across the EU. Two workstreams were created: one focusing on simplifying the workflow of signal management processes, and the other leveraging expertise to review and test novel approaches in signal detection.

The SMART Methods WG engages internationally and plays a central role within the complex ecosystem of pharmacovigilance innovation. The group manages a portfolio of initiatives by prioritising research areas, validating new methods, implementing evidence-based approaches, and ultimately improving and communicating results. Examples of SMART deliverables include the development of tools that support the screening of adverse reactions in EudraVigilance based on safety nets and statistical analyses, including methods that enhance signal detection in vulnerable populations. The COVID-19 pandemic acted as a catalyst for innovation in signal detection and management, driven by the unprecedented volume of data and the need to contextualise findings using additional data sources.

Looking ahead, future improvements will focus on integrating AI and automation into EMA's signal detection workflows with several ongoing and upcoming projects being developed such as automatic literature screening for signals, automatic ADR data extraction, AI-enhanced case adjudication, and knowledge extraction from historical reviews.

Presentation available here.

Artificial intelligence in pharmacovigilance

- **Industry perspective**

  Speakers: Claudia Lehmann (EFPIA), Attila Oláh (Medicines for Europe)

Industry representatives highlighted various use cases, perspectives, concerns, and areas for improvement on AI in pharmacovigilance. One example showcased the use of AI in case processing. Although undoubtedly useful, it was emphasised that two-factor human oversight remains necessary to ensure the accuracy of AI-generated outputs – quality control within the case processing workflow and monitoring of the performance of AI outside of the workflow are needed. AI should be viewed as an assistant to human work in Pharmacovigilance, not a replacement. A key caveat is that AI does not always produce consistent outputs from identical inputs (especially Agentic AI), making reproducibility a challenge. In addition, even if AI consistently produces correct outputs, there may still be occasional errors that human reviewers can overlook.

The relevance of having a regulatory and operational framework around AI was stressed. Indeed, it is important that every user is adequately trained on the risks of AI and how these can be addressed, as well as on data confidentiality and the principles laid down in the EU AI Act.

Presentation available here.

- **CIOMS on use of AI in pharmacovigilance**
  Speaker: Julie Durand (EMA)

The CIOMS Working Group XIV is finalizing its report on AI in pharmacovigilance, expected by the end of the year. For clarity, the definition of AI system used in the report is adopted from the Organisation for Economic Co-operation and Development (OECD). The working group aimed to address the use, opportunities, and challenges of AI specifically within the field of pharmacovigilance. AI has the potential to improve efficiency and consistency, and to increase data insights. The COVID-19 pandemic served as a major catalyst in the process of including AI in pharmacovigilance processes, highlighting the need to process and analyse vast amounts of data and to develop scalable solutions.

The report targets professionals and organisations working in pharmacovigilance and/or researching or developing AI systems for the pharmacovigilance space. It is not intended to be a detailed technical guide, as AI technologies evolve rapidly. Instead, it focuses on long-term guiding principles expected to remain relevant despite technological changes: risk-based approach, human oversight, performance, validity and robustness, transparency, data privacy, governance and accountability, fairness and equity.

Presentation available here.

Session 5: Looking at the future

Chair: Paolo Alcini (EMA)

Key topics

- XEVMPD is currently the receiving system for authorised and development product data, and its data will be migrated to PMS, where the ISO IDMP standards will be fully implemented. The transition from XEVMPD to PMS is a multi-year effort.
- The EV data masking guideline, developed to address EDPS recommendations, was published in July 2025 as addendum II to GVP Module VI. It is intended to be complied with by all senders of ICSRs and SUSARs.
- The possibility of developing an ICSR download application programming interface (API) is currently being explored by the Agency to simplify level 2A and MLM data retrieval from EV by MAHs.

Medicinal product reporting / ISO IDMP

Speakers: Ana Cochino (EMA), Anja van Haren (CBG-MEB, NL)

The ISO Identification of Medicinal Products (IDMP) is a set of standards for the unique identification of medicines, to enable global interoperability in medicinal product information across the regulatory and healthcare communities. The International exchange of ICSRs among various stakeholders (e.g., MAHs, NCAs, EMA) was the initial driver for developing the ISO IDMP standards. Currently, drug information is exchanged as free text, requiring reclassification against the drug dictionary implemented in EV (XEVMPD). Replacing free text drug information with ISO IDMP identifiers is expected to improve efficiency of ICSR processing, accuracy of data analysis of ICSRs and international interoperability between safety databases, with the final aim to facilitate earlier and more effective signal detection.

The ISO ICSR standard in ICH E2B(R3) format became mandatory in the EU in June 2022 and, until the ISO IDMP standards are implemented, free text in drug information fields will remain in use. The implementation will require data migration from the current XEVMPD to PMS (Product Management Service), in which, where possible, free text data will be transformed into structured and standardised IDMP product data. PMS implementation (particularly XEVMPD replacement) is a multi-year effort.

Presentation available here.

Updates on EudraVigilance

Speaker: João Caetano (EMA)

Following the audit of the European Medicines Agency's (EMA) processing of personal data in the context of the EudraVigilance database, the European Data Protection Supervisor recommended the Agency, together with joint controllers (EC and NCAs), to adopt a common masking policy for all entities reporting to EV. In response, the Agency, in collaboration with NCAs and MAHs, developed a masking guideline for all senders of ICSRs and SUSARs. The EV data masking guideline was published in July 2025 as addendum II to GVP Module VI and is intended to be complied with by all senders of ICSRs and SUSARs.

Other updates on EudraVigilance include: (1) the possibility of developing an ICSR download application programming interface (API), currently being explored by the Agency to simplify level 2A and MLM data retrieval from EV by MAHs; (2) new values for ICH E2B(R3) field C.5.4 Study Type Where Reaction(s) / Event(s) Were Observed [to align with the ICH E2D(R1)] and (3) a new value reflecting Intersex as a possible regional variation of the code list for ICH E2B(R3) field D.5 "Patient Sex".

Presentation available here.

Closing remarks

The event was closed by Georgy Genov.