EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Feedback on EudraVigilance & new functionalities

14th industry stakeholder platform – operation of EU pharmacovigilance

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Overview

- EudraVigilance: Processing of ICSRs & Note for Clarification
- EudraVigilance Operational Planning – some highlights

EudraVigilance – Processing of ICSRs

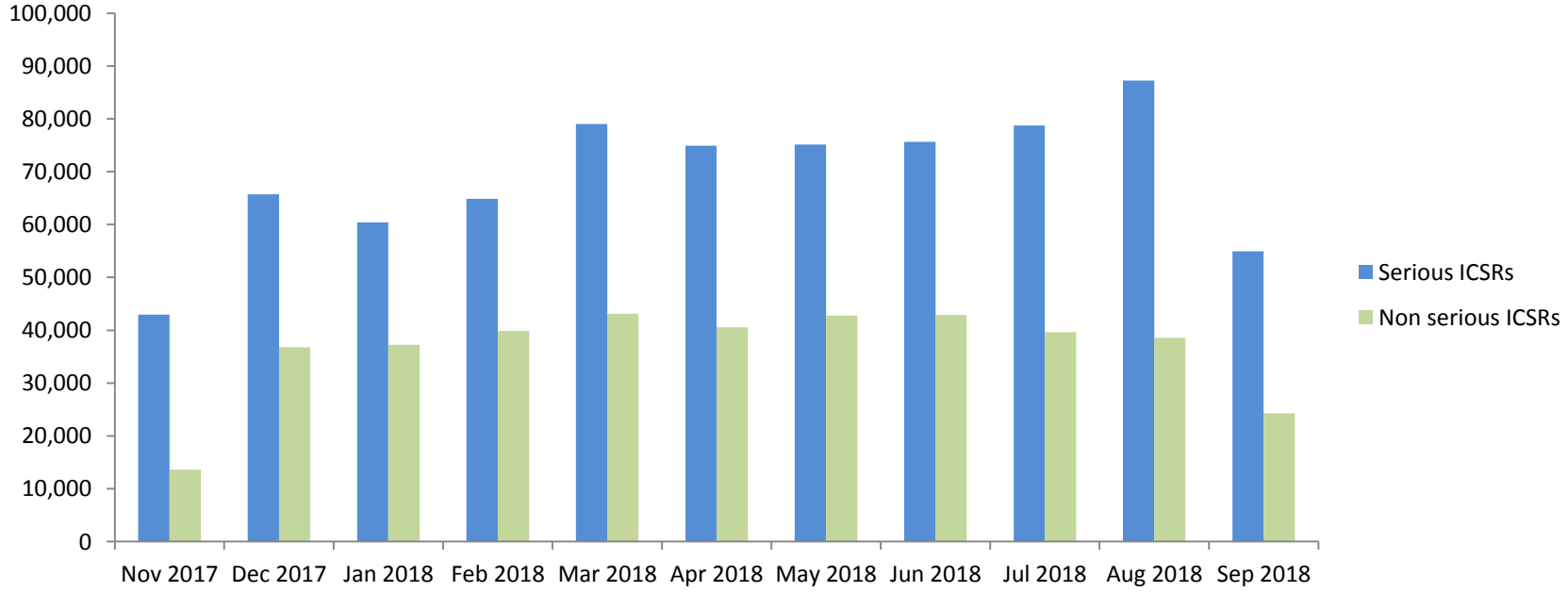
Number of ICSRs received and processed: 22 Nov 2017 – 18 Sept 2018

ICSRs	Total	EEA	Non-EEA
Serious	760,836	229,834	531,002
Non-serious	399,659	389,053	*10,606**

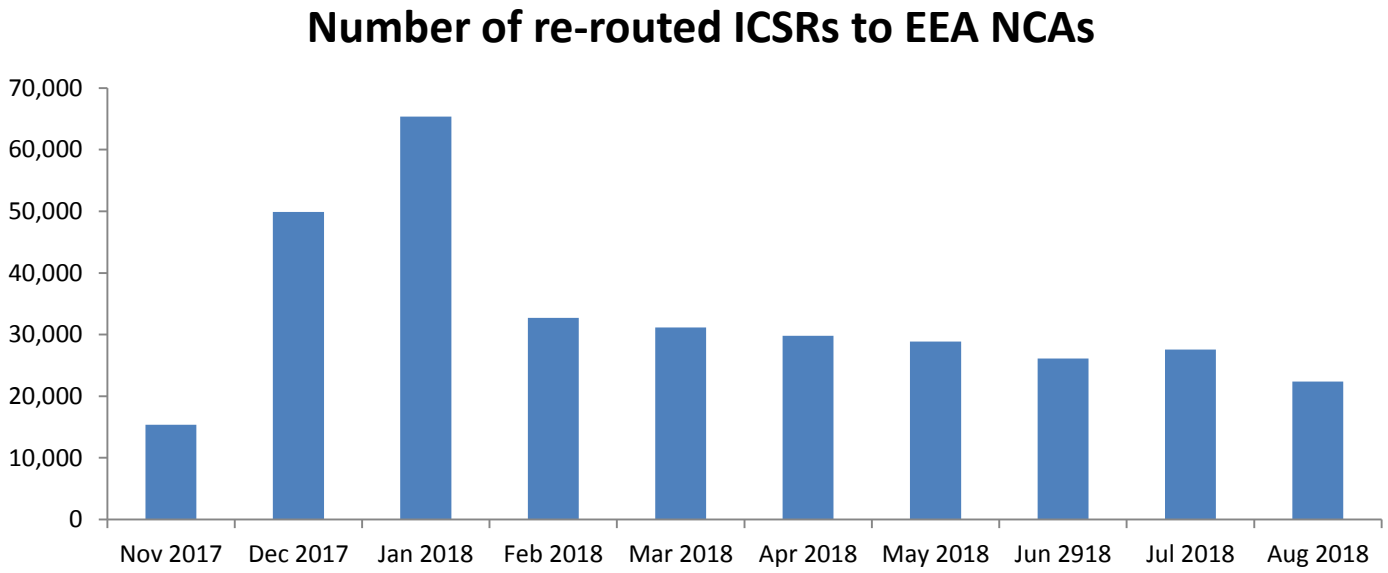
**no routine submission – but may be received due to downgrading of seriousness based on follow-up information*

EudraVigilance – Processing of ICSRs

Number of ICSRs received and processed: 22 Nov 2017 – 18 Sept 2018



EudraVigilance – Processing of ICSRs



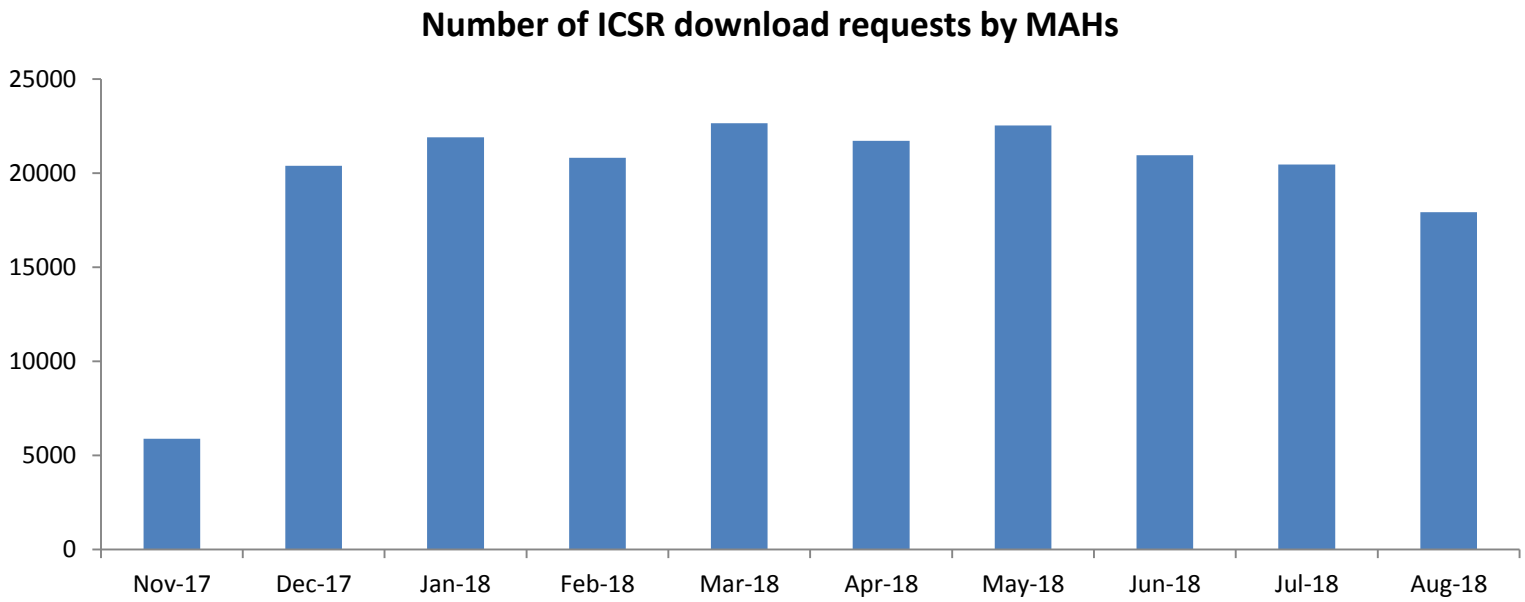
EudraVigilance –Processing of ICSRs

Number of ICSRs downloaded by MAHs: 22 Nov 2017 – 18 Sept 2018

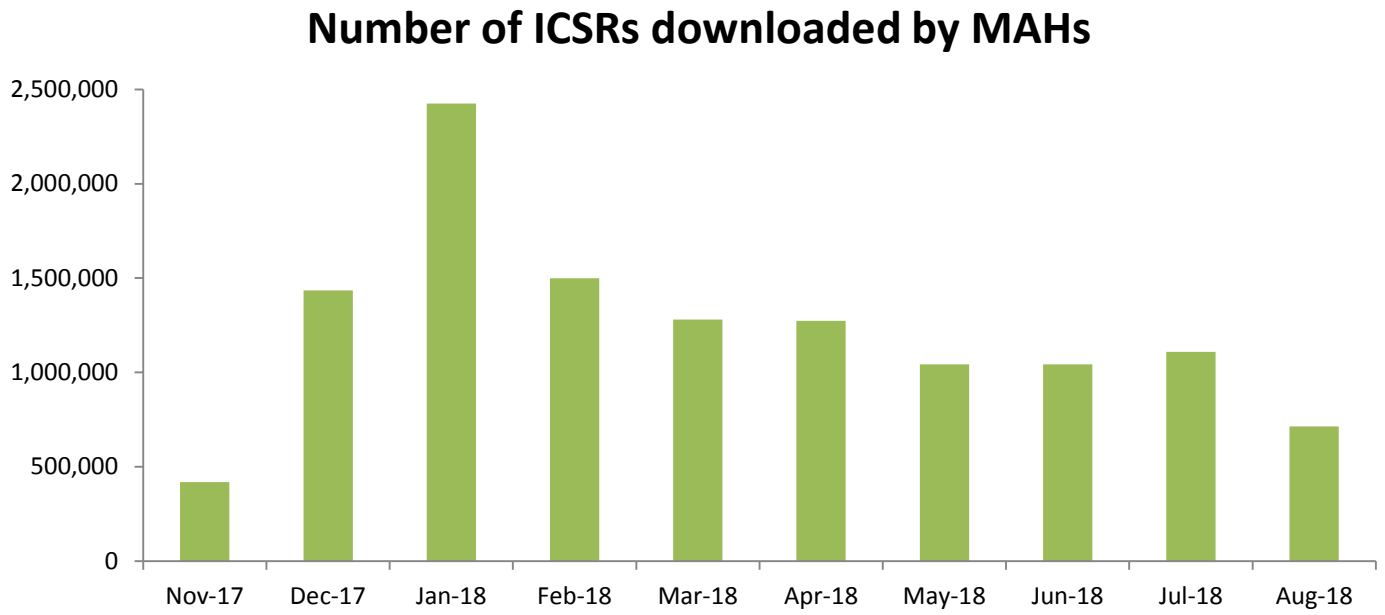
- 1,480 MAHs submitted download request to EV
- 204,119 download requests successfully executed

12,2 million ICSRs downloaded

EudraVigilance –Processing of ICSRs



EudraVigilance –Processing of ICSRs



EudraVigilance – Processing of ICSRs

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

12 July 2018
EMA/396720/2018
Inspections, Human Medicines, Pharmacovigilance and Committees Division

Recording by marketing authorisation holders of information on suspected adverse reactions held in EudraVigilance

Note for clarification

Guidance issued in July 2018 to address questions from MAHs on the prospective and retrospective processing of ICSRs accessed through EudraVigilance

EudraVigilance Operational Planning

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

8 June 2018
EMA/100194/2018
Inspections, Human Medicines, Pharmacovigilance and Committees Division

EudraVigilance Operational Plan
Milestones 2018 to 2020

EudraVigilance
Monitoring the
Safety of Medicines

Pharmacovigilance Business Team (agreement)	15 March 2018
Pharmacovigilance Risk Assessment Committee (PRAC) (agreement)	22 March 2018
EU Pharmacovigilance Oversight Group (agreement)	26 March 2018
IT Directors Executive Committee (for information)	12 April 2018
Telematics Forum (for information)	27 April 2018

- Objective is to:
  - Outline technical as well as operational activities with anticipated timelines and to highlight how EudraVigilance and the stakeholders that interact with the system will be affected.
  - Facilitate planning by the Agency, which is operating EudraVigilance on behalf of the network and ensure timely preparedness of NCAs, MAHs, commercial and non-commercial sponsors of clinical trials and the WHO Uppsala Monitoring Centre.

EudraVigilance Operational Planning (OP) – 15 priority areas

1. EudraVigilance hypercare and maintenance
2. Integration with identity and access management
3. UK withdrawal from the Union
4. Mandatory use of E2B(R3)
5. Use of IDMP standards
6. Signal management
7. Data Quality Review
8. GDPR – implication on ICSR reporting
9. SUSAR reporting and Clinical Trial Regulation
10. Medical literature monitoring
11. GVP Module VI – revision 3
12. EudraVigilance Benefits Realisation
13. EudraVigilance and operation of pharmacovigilance
14. Training and support
15. Stakeholder communication and engagement

EudraVigilance OP – 1. Hypercare and Maintenance

- ✓ Hypercare period ended in May 2018
- ✓ EV is now subject to routine maintenance – for 2018 & 2019
- ✓ Priority is given to relocation preparedness
- ✓ Maintenance releases are scheduled based on technical updates and improved functionalities in collaboration with the Telematics Change Management Board on the basis of prioritised change requests

EudraVigilance OP – 1. Hypercare and Maintenance

- **Electronic Reaction Monitoring Report (eRMR)**
  - ✓ Updated configuration so that ad-hoc & fixed eRMR are available with a "3-day delay" e.g. data received on 28 AUG is available on 31 AUG; line listings reflect the latest data up to the previous day i.e. 6 p.m
- **Line listings and E2B(R3) dose units**
  - ✓ Dose unit is now displayed in the drug columns of the line listing for ICSRs submitted in E2B(R3) format

EudraVigilance OP – 1. Hypercare and Maintenance

Under development - planned for Q4 2018 & Q1 2019

- **Threshold for 'Signal of disproportionate reporting (SDR)' flag**
  - Threshold on the number of cases to take into account all the substances classified under additional monitoring
- **Ad-hoc eRMR**
  - When the end date of the reference period is set in the past, the duplicate cases should not be included in the 'New EVMP' field (Total count is not affected)

EudraVigilance OP – 1. Hypercare and Maintenance

Under development - planned for Q4 2018 & Q1 2019

- **Drug treatment duration**
  - When the duration is reported in any other unit than days, the unit should not be displayed as days in the line listings

EudraVigilance OP – 1. Hypercare and Maintenance

EVDAS release management

- **MedDRA version management (vs 21.5) NOV 2018**
  - EVDAS remains available although the data will not be refreshed during the upgrade
  - eRMR reports will be unavailable during the upgrade (eRMR rebuilt necessary using the latest MedDRA version, covering the last 105 days)
  - Detailed communication (via email) close to the maintenance period will follow

EudraVigilance OP – 4. Mandatory use of E2B(R3)

- **Organisations sending E2B(R3) ICSRs**
  - 30 MAHs and 1 non-commercial sponsor report in R3 format since March 2018
- **Current Total:**
  - 79 MAHs with gateway profile (including affiliates), corresponding to ~30% of all gateway profile MAHs.
  - 3 commercial and 1 non-commercial sponsors with gateway profile
  - 9 NCAs with gateway profile
- Other organisations continue to send E2B(R2) ICSR files via gateway or are using the new EVWEB

EudraVigilance OP – 4. Mandatory use of E2B(R3)

- Timeframe for mandatory use of E2B(R3) ICSR format to be established in the EU
- E2B(R3) readiness survey of NCAs launched in August 2018
- Proposal to launch E2B(R3) readiness survey of MAHs with support from European Industry Associations

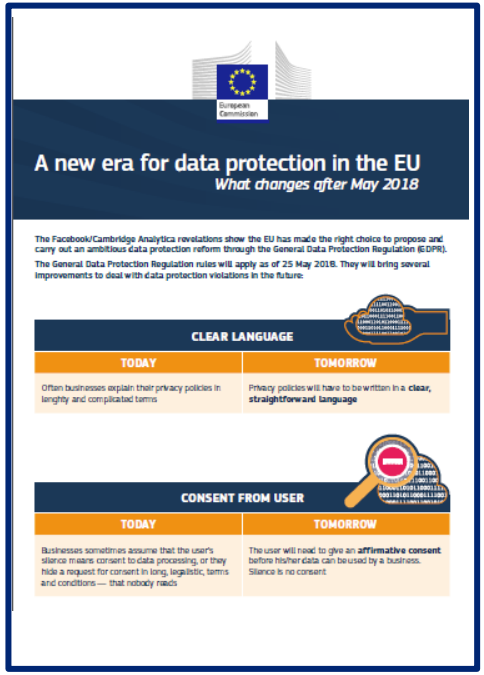
EudraVigilance OP – 7. Data quality review

- Routine quality review activities ongoing

Data Quality Processes	Activities Performed	2015	2016	2017	2018 (up to end Q2)
Identifying and managing duplicates	Duplicate couples assessed	31,797	72,655	212,062	102,960
	Master reports generated	40,022	48,111	133,635	63,729, including FU masters
Manual classification of reported medicines and active substances	ADR reports classified (ICSRs)	54,535	64,686	41,124	25,342

- PhV Business Team is:
  - Preparing quality criteria for ICSR review process
  - Reviewing submission process of reports with no adverse reaction

EudraVigilance OP – 8. GDPR



- PhV Business Team/EV-EWG have collected input from NCAs and MAHs based on the new GDPR with main focus on adverse reaction reporting and EudraVigilance.
- A Q&A document is under preparation.

EudraVigilance OP – 10. Medical Literature Monitoring

PhV Business Team is developing a note for clarification on:

- Management of literature referring to multiple patients presented in summary format & with single identifiers available
- EEA NCAs have been consulted to collect further input on current practices
- Further guidance to be developed to ensure harmonised approach in reporting cases from the literature

EudraVigilance OP – 15. Stakeholder Engagement

EudraVigilance and Signal Management Information Day

- Planned for 7 December 2018 in London (venue TBC)
- Programme will focus on industry experience working and interacting with EV

Thank you for your attention

Further information

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For reference

Note for clarification: ICSRs accessed by MAHs "prospectively" in EV – as of 22 Nov 2017

a. MAHs **should record** all **individual cases of suspected adverse reactions** for substances of medicinal products, for which they hold a marketing authorisation in the EEA and **that are submitted by NCAs in EEA Member States to EudraVigilance (EV)**.

b. MAHs **should decide whether they record individual cases of suspected adverse reactions** for substances of medicinal products for which they hold a marketing authorisation in the EEA and **which were submitted by other MAHs to EV**. The **decision should be based on the processes necessary to comply with their pharmacovigilance obligations** listed in Title IX of Directive 2001/83/EC – this is further detailed in Annex A.

c. This applies to all individual cases where the MAH cannot exclude ownership (based on GVP VI) of the medicinal product reported (suspect or interacting).

Note for clarification: ICSRs accessed by MAHs "prospectively" in EV – as of 22 Nov 2017

Annex A- criteria to determine pharmacovigilance obligations

1. Recording and reporting of suspected adverse reactions

Criterion for recording and reporting of suspected adverse reactions to EudraVigilance
• As part of the pharmacovigilance systems that MAHs operate and for the purpose of reporting of suspected adverse reactions to EudraVigilance, MAHs are not obliged to record individual cases of suspected adverse reactions, which are submitted by other MAHs directly to EudraVigilance. • Article 107 of Directive 2001/83 sets out the process of how MAHs should record and report suspected adverse reactions. In this context EudraVigilance is presented as the 'target' for such reporting, where information on ICSRs should be stored, and not as the source of new case reports to be (again) reported and recorded.

Note for clarification: ICSRs accessed by MAHs "prospectively" in EV – as of 22 Nov 2017

Annex A- criteria to determine pharmacovigilance obligations

2. Periodic Safety Update Reports (PSURs)

Criterion for preparation of PSURs
• As part of the pharmacovigilance systems that MAHs operate and for the purpose of the preparation of PSURs, MAHs are not obliged to record individual cases of suspected adverse reactions, which are submitted by other MAHs directly to EudraVigilance. • MAHs should follow the guidance set out in the Explanatory Note to GVP VII, chapter 9.5 "Use of EudraVigilance data by MAHs during the preparation of PSURs".

Note for clarification: ICSRs accessed by MAHs "prospectively" in EV – as of 22 Nov 2017

Annex A- criteria to determine pharmacovigilance obligations

3. Signal Detection

Criterion for signal detection and management
• As part of the pharmacovigilance system that MAHs operate and for the purpose of signal detection, MAHs are not obliged to record individual cases of suspected adverse reactions, which are submitted by other MAHs directly to EudraVigilance. • The Commission Implementing Regulation (EU) 520/2012 requires MAHs to monitor the data available in EudraVigilance to the extent that they have access to that database. The monitoring of the safety of medicines and the detection of any changes to their risk-benefit balance is therefore provided for.

Note for clarification: ICSRs accessed by MAHs "retrospectively" in EV – ICSRs submitted prior 22 Nov 2017

a. **MAHs are not obliged** to screen EudraVigilance for individual cases that are not yet recorded in their databases **to complement and/or reconcile the respective internal information retrospectively** where appropriate.

b. **MAHs are not obliged to record in their MAH databases individual cases submitted to EudraVigilance prior to 22 November 2017** of which they gained knowledge retrospectively **as part of their signal management or other pharmacovigilance obligations**.

c. This does not preclude a MAH choosing to reconcile and record individual cases identified in EudraVigilance in the context of the assessment of a safety issue e.g. the end-point of the signal management or safety monitoring activities such as the identification of a new risk/adverse drug reaction or change in the status of a risk/adverse drug reaction as part of a validated signal.