

# Q & A's

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**C B G**  
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# Receiving Lareb cases

# Will Lareb stop sending ICSRs to MAHs?

- On 7 Nov 2017 last Lareb export to MAHs
- From 22 Nov 2017 Lareb cases will be available via EV in ICH E2B(R3) format
- Acces granted at active substance level, based on Article 57 database

# Are non-serious Lareb cases available for download from EV?

- Yes, MAHs will have standard access in EV to both serious as well as non-serious reports, including the Lareb reports.

# Which E2B message format will Lareb use for submissions to EV?

- This is important to assess the impact on data when loading ICSR into the system with a Backwards Forwards Compatibility tool.
- From 22 November 2017:  
ICH E2B(R3) message format.
- EV will make ICSRs available for download in E2B(R3) format
  - Lareb cases submitted to EV before 22 Nov 2017 are converted to R3

# How many Lareb cases can we expect ?

- It is not possible to give estimates of how many cases would be relevant for each individual MAHs product portfolio.

	Serious	Non-serious
# Lareb cases 2016	7,6 % (± 150 cases)	92,4 % (± 1850 cases)
	13,6 % (± 1350 cases)	86,4 % (± 8650 cases)

# Which language is used in Lareb reports?

- E2B(R3) message format allows information in different languages.
- All data-elements in English, with exception:
  - Name of medical product as reported by primary source (G.k.2.2.)
  - Indication as reported by primary source (G.k.7.r.1)
  - Reaction as reported by primary source in native language (E.i.1.1a)
  - Case summary reporter's comments (H.5.r.1a)

# What is the process for requesting follow-up for Lareb cases?

- Routine request for follow-up by the MAH is not foreseen.
  - GVP Module VI (Rev 2)
- If follow-up of an ICSR is necessary for a specific situation, a justification should be provided with the request, which should be addressed to Lareb ([info@lareb.nl](mailto:info@lareb.nl)).



# Follow up request

- For each case, the Lareb assessor determines if a follow up request is useful.
- You will be informed if (a part of) the follow up information will be requested within a month. Received follow up will be added to the report and sent to EV.

# Cases in which no follow up is requested to the reporter (1)

- Information which is already asked in the initial reporting form (<https://www.lareb.nl/nl/report-form/>)
  - E.g. medical history, risk factors, concomitant medication
  - If possible, Lareb will provide null flavors through which becomes clear that the information is not received (e.g. batchnumber).

# Cases in which no follow up is requested to the reporter (2)

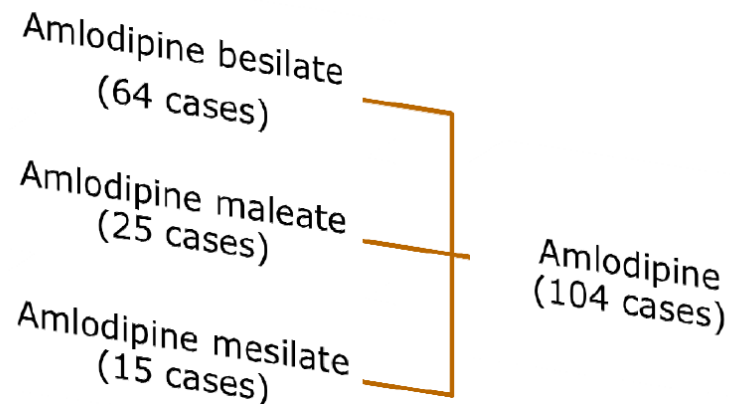
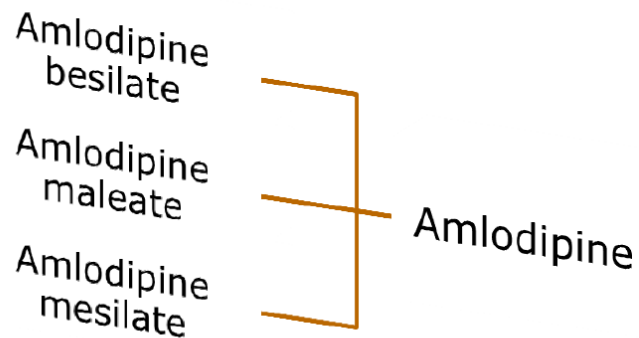
- Medical confirmation for consumer reports
- A consent form for consumer reports to bring his/ her HCP directly in contact with the MAH
- Information which it is not likely the reporter has that type of information, e.g. an ECG and a pharmacist as reporter.

# How does the download from EV work?

The screenshot displays the 'EV WEB' interface with the 'ICSR Download' tab selected. The 'Criteria (4)' section includes filters for 'Reports: PV obligations reports (L2A)', 'Start Date: 2017/09/07', 'End Date: 2017/09/22', and 'Serious: Yes & No'. A dropdown menu is open for the 'Serious' filter, showing options: 'Yes', 'No', and 'Yes & No'. A 'History' section shows 'Resolved (0)'. A 'More criteria' dropdown menu is also visible, listing options such as 'Active Substance', 'Reporter Country', 'World Wide Case Id', 'Active Substance Group', 'Active Substance Combination', 'Active Substance MLM Group', and 'Active Substance MLM Combination'. A message states: '7 can be downloaded for L2A access from today.'

- Active substances are automatically selected
- Retrieve EEA ICSRs from NCA's & other MAHs

# At what active substance level is access provided?



Access is provided at active substance high level group  
- EMA can provide list of active substance groups associated with a specific MAH's organisation ID (provide Headquarter ID): <https://servicedesk.ema.europa.eu>

# Will the downloaded ICSR have a narrative? (1)

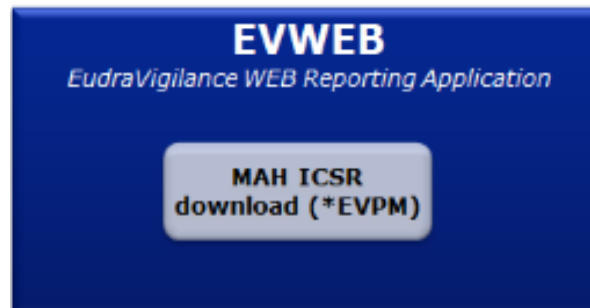
Download Level 2A access does **not** provide case narratives

MAHs can request extended set of ICSR data elements including case narrative ('Level 2B'):

- review of ICSR data is warranted in the context of signal management (GVP Module IX)
- a pharmacovigilance assessment procedure such as the PSUR
- when required by the PRAC in a referral or signal assessment procedure

# Will the downloaded ICSR have a narrative? (2)

- QPPV (or deputy) can grant user rights to staff members who need access to Level 2B.



- Each request requires the confirmation of the confidentiality undertaking.  
(EudraVigilance access policy:  
[http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Other/2016/12/WC500218300.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Other/2016/12/WC500218300.pdf) )

# How does a Level 2B request work in practice? (1)

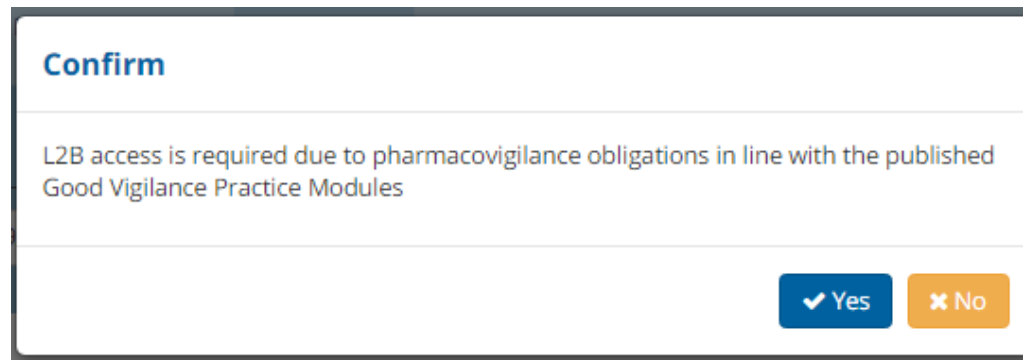
Few simple steps in EVWEB:

- Enter (a list of) worldwide unique case identifier(s)



The screenshot shows the EVWEB interface with a navigation bar containing 'EV WEB', 'Create and send ICSRs', 'WEB Trader', 'ICSRs', 'Post', 'MedDRA', and 'ICSR Download'. Below the navigation bar is a section titled 'Criteria (4)' with three input fields: 'Reports: Case narrative requests (L2B)', 'Start Date: 2017/04/12', and 'End Date: 2017/04/27'. A fourth field contains the text 'World Wide Case Id: IT-NOBEL-QUERYCASE01bisa'.

- Confirm that Level 2B access is required due to PV obligations in line with GVP modules



The screenshot shows a confirmation dialog box with the title 'Confirm'. The main text reads: 'L2B access is required due to pharmacovigilance obligations in line with the published Good Vigilance Practice Modules'. At the bottom right, there are two buttons: a blue button with a checkmark and the text 'Yes', and an orange button with an 'x' and the text 'No'.



# How does a Level 2B request work in practice? (2)

- Select the reason for the request
- Agree with the terms related to protection of personal data

The screenshot shows the 'L2B request' form in the EV WEB system. The 'Reason' dropdown menu is open, showing several options: 'Signal management following completion of initial validation steps in accordance with GVP Module IX Signal Management', 'Review of ICSR data in the context of a PSUR pharmacovigilance assessment procedure', 'Review of ICSR data in the context of a pharmacovigilance assessment procedure required by the PRAC', 'Review of ICSR data in the context of a pharmacovigilance referral assessment procedure', and 'Review of ICSR data in the context of a pharmacovigilance signal assessment procedure'. The 'I agree' checkbox is checked, and the 'Submit' button is visible at the bottom of the form.

- ICSRs with narratives will be provided within minutes



# Submitting ICSRs to EudraVigilance

# What to do in case of system failure? (1)

- Please follow the instructions provided by the EMA:  
[http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general\\_content\\_000686.jsp&mid=WC0b01ac0580a69261#What to do in case of system failure](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000686.jsp&mid=WC0b01ac0580a69261#What to do in case of system failure)
- From 22 Nov submission of CIOMS forms is no longer supported
- There is no need to inform the MEB separately

# What to do in case of system failure? (2)

If EVWEB/gateway are not available:

- Submit your ICSRs when EV becomes available again
- Reports submitted within 2 EMA business days of EV being made available again will have their reporting compliance calculated against the first day of system failure

# Is there a requirement to use Dutch language when submitting ICSRs to EV?

- No, there is no such requirement. Both English and Dutch language are acceptable.

# For literature cases: is there a national requirement to submit the published article?

- No, there is no such requirement. The published article only needs to be submitted upon request.

# What to do when a downloaded Lareb case is a duplicate of a MAH case submitted to EV?

Send email to EMA with information on which cases are suspected to be duplicates ([duplicates@ema.europa.eu](mailto:duplicates@ema.europa.eu))

- If EMA confirms that the cases are indeed duplicates, a master case will be created and this will also be made available for download

See GVP Module VI Addendum I – ‘Duplicate management of suspected adverse reaction reports’

[http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Regulatory\\_and\\_procedural\\_guideline/2017/08/WC500232765.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2017/08/WC500232765.pdf)

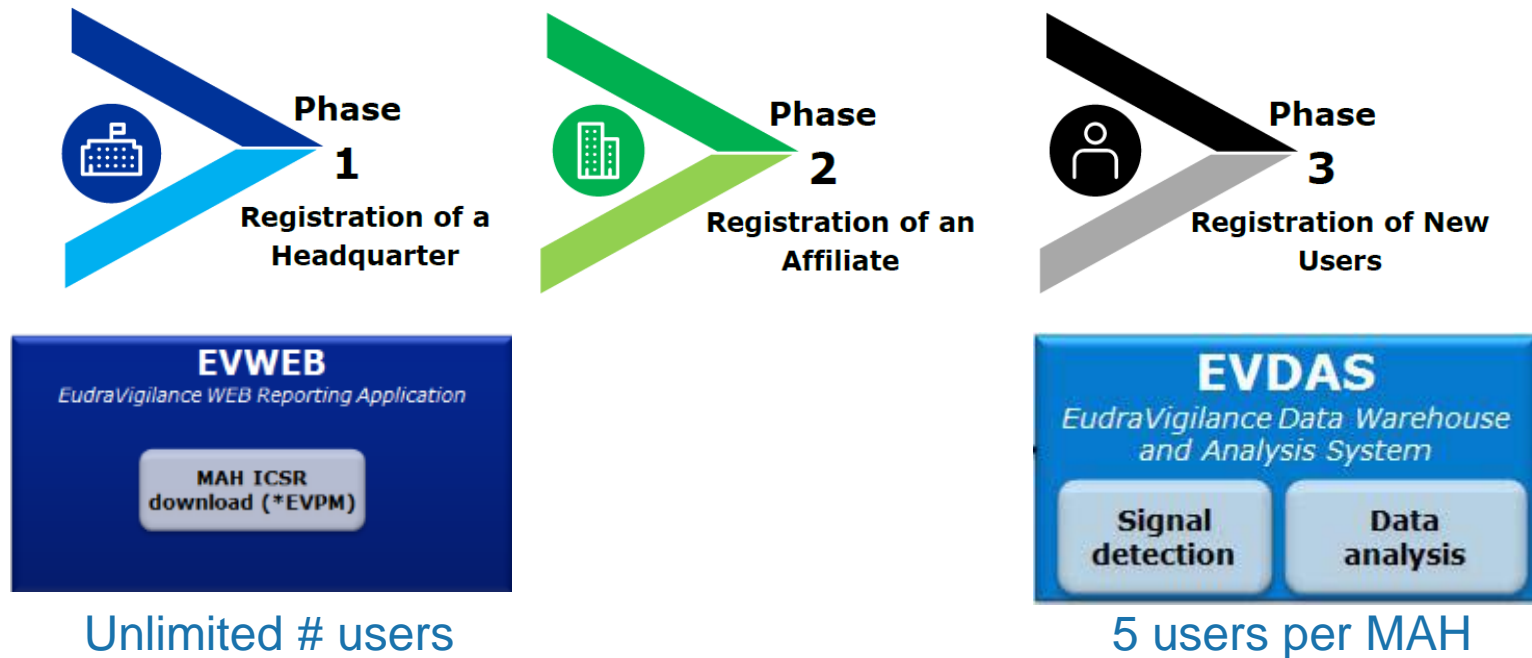


# How to prepare for 22nd Nov?



# 1: Review EV User Registration

- Grant appropriate EV access to users
- Check that passwords are still working



# 2: Ensure Art57 data is up to date

The screenshot shows the European Medicines Agency (EMA) website. The header includes the EMA logo and name, a site-wide search bar, and a navigation menu with options like Home, Find medicine, Human regulatory (selected), Veterinary regulatory, Committees, News & events, Partners & networks, and About us. The main content area is titled 'Data submission on authorised medicines (Article 57)' and includes a breadcrumb trail: Home > Human regulatory > Post-authorisation > Data on medicines (ISO IDMP standards) > Data submission on authorised medicines. The page contains a bolded key message, a paragraph about the aim of data submission, a list of purposes, and sections for related documents and EU legislation. A left-hand navigation menu lists various topics such as Overview, Research and development, Marketing authorisation, Post-authorisation (selected), Advanced therapies, Compliance, Data on medicines, Data submission on authorised medicines, Reporting requirements, Registration, Training, Medicine shortages, Orphan medicines, and Improving quality of.

**EUROPEAN MEDICINES AGENCY**  
SCIENCE MEDICINES HEALTH

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Overview  
Research and development  
Marketing authorisation  
▼ Post-authorisation  
Advanced therapies  
Compliance  
▼ Data on medicines (ISO IDMP standards)  
▶ Data submission on authorised medicines  
Reporting requirements for authorised medicines  
Registration  
Training  
Medicine shortages  
Orphan medicines  
Improving quality of

▶ Home ▶ Human regulatory ▶ Post-authorisation ▶ Data on medicines (ISO IDMP standards) ▶ Data submission on authorised medicines

## Data submission on authorised medicines (Article 57)

Email Print Help Share

**All holders of marketing authorisations for medicines in the European Union (EU) and the European Economic Area (EEA) must submit information to the European Medicines Agency (EMA) on authorised medicines and keep this information up-to-date. This is a legally binding requirement from the EU pharmaceutical legislation. The Agency uses this information to support the analysis of data, regulatory activities and communication.**

The aim of the submission of data is to establish a complete inventory of all medicines authorised for use in the EU and EEA, including medicines authorised centrally via the EMA and those authorised at national level.

The Agency uses this information for a range of purposes. These include:

- ▶ performing data analysis, including:
  - ▶ analysis of data in [EudraVigilance](#) and [signal management](#);
  - ▶ reporting and coding of [individual case safety reports](#);
  - ▶ data analytics and business intelligence;
- ▶ facilitating medicines regulation and fulfilling regulatory actions and legal obligations, such as:
  - ▶ coordination of regulatory actions to safeguard public health, including [referral procedures](#), establishment of a repository of [periodic safety update reports \(PSURs\)](#) and literature monitoring;
  - ▶ supporting the calculation of fees for [pharmacovigilance](#);

**Related documents**

- ▶ [Transition plan from Article 57 and XEVMPD data submission to SPOR \(01/12/2016\)](#)
- ▶ [Data submission of authorised medicines in the European Union: Outlines on Article 57\(2\) of Regulation \(EC\) No 726/2004 \(23/02/2015\)](#)

**Related content**

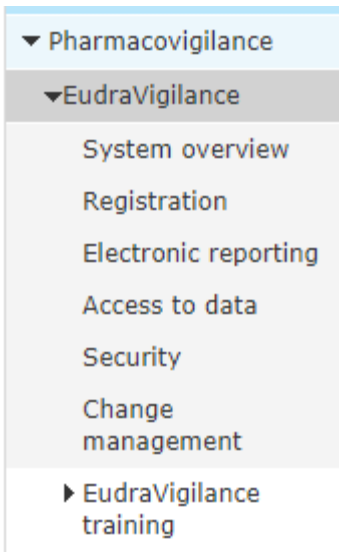
- ▶ [Pharmacovigilance](#)
- ▶ [EudraVigilance](#)
- ▶ [Data on medicines \(ISO IDMP standards\)](#)
- ▶ [Substance, product, organisation and referential \(SPOR\) master data](#)
- ▶ [Information management](#)

**Related EU legislation**

- ▶ [Regulation \(EC\) No 726/2004](#)

# 3: Familiarise yourself with the changes

## EMA EudraVigilance training webpage



## 3: Familiarise yourself with the changes

- Testing with the EMA may be required depending on the IT changes to your system
- If you are intending to use E2B(R3) conversions tool you should start testing it to see how it will work with your existing systems

## 4. Prepare for the go-live (1)

Launch of the new EV system requires a downtime period of 10 business days:

start: 8 Nov 2017 (00:00 a.m. UK time)

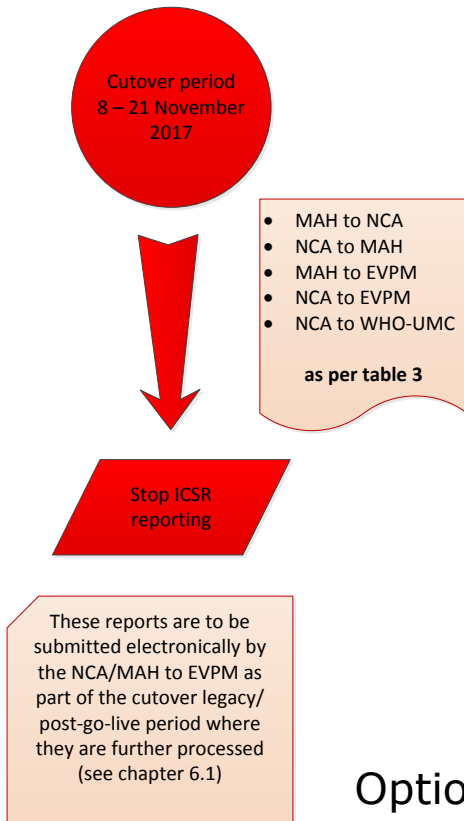
end: 22 Nov 2017 (9:00 a.m. UK time)

Key components of EV will not be available or only partially available

EV go-live plan will be published 1st week Oct

# 4. Prepare for the go-live (2)

## ADR Reporting Option 1 Cutover period Pharmacovigilance



- Submission of ICSR stops
  - last Lareb export on 7 Nov
- No need for alternative arrangements for submission
- Start submissions to EV when system goes live on 22 Nov
  - Lareb cases available for download via EV

Option 1 applies to: AT, BE, BG, CY, EE, ES, FI, FR, HR, IE, LI\*, LU\*, LT, LV, MT\*, NL, NO, PL, PT, SE, SI, SK (\* to be confirmed)

# 4. Prepare for the go-live (3)

SUSAR reporting Option 1  
Cutover period  
Clinical Trials

Cutover period  
8 – 21 November  
2017

- Sponsor to Member State
- Sponsor to EVCTM

As per table 6

Stop ICSR reporting

These reports are to be submitted electronically by the sponsor to the Member State/EVCTM as applicable as part of the cutover legacy/post-go-live period where they are further processed (see chapter 6.2)

NL has taken same approach for SUSARs:

- Stop submitting to EV
- No need for alternative arrangements for submission
- Start submissions to EV when system goes live on 22 Nov

**note:**  
continue submissions to METCs  
via Toetsing Online !

## 4. Prepare for the go-live (4)

- Reports requiring submission from 8 to 21 Nov should be sent within 2 EMA business days following the go-live of EV
- Compliance calculations will be corrected for the downtime period + the 2 business days
- Events/observations which may affect the risk-benefit balance of a medicinal product, should be notified as ESI



## 5. From 22th Nov onwards



Submit and receive  
ICSRs only via EV



Any other questions?