EudraVigilance Technical Support Plan for national Competent Authorities in the EEA

In support of the go-live of the enhanced EudraVigilance System

Version 1.1

Agreement by the Pharmacovigilance Business Team	18 May 2017
Agreement by the EudraVigilance Expert Working Group (Members of national Competent Authorities)	18 May 2017
Agreement by the IT Directors of the EU Telematics Governance	23 May 2017
Adoption by Pharmacovigilance Risk Assessment Committee	9 June 2017

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Summary of changes

- Version 1.0 was published in June 2017

- Version 1.1 was amended in September 2017 to reflect changes in the NCAs testing time slot (in section 4.)

1. Scope

Complimentary to the **EudraVigilance Stakeholder Change Management Plan** adopted through the pharmacovigilance governance (EMA/325783/2016, revision 1, August 2016) and published on the dedicated EudraVigilance change management webpage, this document has been prepared for national Competent Authorities (NCAs) in the European Economic Area (EEA) to describe the testing and support activities in preparation of the go-live of the enhanced EudraVigilance (EV) system on 22 November 2017.

In addition, **the ICH E2B(R3) Implementation Guide** and the **EU ICSR Implementation Guide** provide important guidance on how to apply the new ISO Individual Case Safety Report (ICSR) standard and how it should be used for the electronic reporting of suspected adverse reactions related to medicines in the European Economic Area (EEA). These documents can be accessed at EudraVigilance change management webpage: The new EudraVigilance database, where can I find detailed information and guidance?.

Reference is also made to the **training and support offerings,** which are available at the dedicated EudraVigilance training and support webpage, which provides detailed learnings on how to prepare for the changes to come.

2. Declaration of best efforts by the Agency

In the context of this plan, the Agency provides the following declaration of best efforts:

- EMA is fully committed to endeavour to perform testing with all NCAs in the EEA as of 26 June 2017; this refers firstly to the testing of the re-routing of ICSRs to NCAs in E2B(R2) or E2B(R3) format and when applicable, the testing of ICH E2B(R3) ICSRs and acknowledgements (ACKs) generated by local pharmacovigilance databases of NCAs.

- In case of any technical issues at the level of EudraVigilance, EMA shall endeavour to resolve these issues prior to the go-live date.

- To the extent possible, EMA will provide technical assistance to NCAs in the EEA as part of the testing activities.

3. Re-routing testing and testing of ICSRs generated by NCAs

In consultation with the Pharmacovigilance Business Team and the EudraVigilance Expert Working Group members of NCAs, EMA has prepared this test plan, which addresses the following two areas:

- The re-routing of ICSRs to NCAs in the EEA in accordance with Article 24(4) of Regulation 726/2004;

- The testing of ICSRs in ICH E2B(R3) or ICH E2B(R2) format with ACKs generated by local pharmacovigilance databases of NCAs.

The XCOMP (test) environment of the enhanced EudraVigilance System is to be released by the Agency on 26 June 2017 and serves as the basis for the testing with all NCAs in the EEA as well as other stakeholders such as marketing authorisation holders (MAHs) and sponsors of clinical trials (sponsors). The XCOMP environment will be available for testing from 26 June until the go-live of the enhanced system and thereafter.

During the agreed timeframe for the re-routing testing, the EMA project team will be in direct contact with the NCA technical staff to ensure that the necessary technical arrangements are correctly set up for the testing. The preparatory steps are outlined in the [EudraVigilance Checklist for national Competent Authorities in the EEA (Doc. Ref. EMA/172253/2017)](#).

3.1. Testing of the re-routing of ICSRs from EudraVigilance to NCAs in the EEA

EMA will create one or more generic "MAH test accounts" for the purpose of the re-routing testing. EMA will also coordinate further re-routing testing based on test files submitted by MAHs to XCOMP.

The following scenarios are subject to the testing:

- For **E2B(R2) ICSRs:**
    a. Re-routing of ICSRs related to serious suspected adverse reactions sent by a MAH to the EudraVigilance Post-Authorisation Module (EVPM) by means of the EVPOST function; the ICSRs are re-routed to the NCA (NCA local Gateway/EVWEB inbox) in accordance with the re-routing parameters defined by the NCA in EVWEB; generating and sending of ACKs by the NCA's local pharmacovigilance database/EVWEB (as applicable).

    b. Testing that ICSRs related to serious suspected adverse reactions sent by a MAH to EVPM by means of the EV POST function are not re-routed to the NCA in accordance with the re-routing parameters defined by the NCA in EVWEB; this is to confirm that ICSRs are not re-routed to an NCA (Gateway or EVWEB inbox) where the parameters were set not to receive these type of reports.

    c. Re-routing of ICSRs related to non-serious adverse reactions sent by a MAH to EVPM by means of the EV POST function; to ICSRs are re-routed the NCA (Gateway or EVWEB inbox) in accordance with the re-routing parameters defined by the NCA in EVWEB; generating and sending of ACKs by the NCA's local pharmacovigilance database/EVWEB (as applicable).

    d. Testing that ICSRs related to non-serious adverse reactions sent by a MAH to EVPM by means of the EV POST function are not re-routed to the NCA in accordance with the re-routing parameters defined by the NCA in EVWEB; this is to confirm that ICSRs are not re-routed to an NCA (Gateway or EVWEB inbox) where the parameters were set not to receive these type of reports.

- For **E2B(R3) ICSRs:**
    a. Re-routing of ICSRs related to serious suspected adverse reactions sent by a MAH to EVPM by means of the EVPOST function; the ICSRs are re-routed to the NCA (NCA local Gateway/EVWEB inbox) in accordance with the re-routing parameters defined by the NCA in EVWEB; generating and sending of ACKs by the NCA's local pharmacovigilance database/EVWEB (as applicable).

b. Testing that ICSRs related to serious suspected adverse reactions sent by a MAH to EVPM by means of the EV POST function are not re-routed to the NCA in accordance with the re-routing parameters defined by the NCA in EVWEB; this is to confirm that ICSRs are not re-routed to an NCA (Gateway or EVWEB inbox) where the parameters were set not to receive these type of reports.

c. Re-routing of MASTER ICSR related to serious suspected adverse reactions sent by EMA to EVPM by means of EVWEB; the MASTER ICSR is re-routed to the NCA (NCA local Gateway/EVWEB inbox) in accordance with the re-routing parameters defined by the NCA in EVWEB; generating and sending of ACKs by the NCA's local pharmacovigilance database/EVWEB (as applicable).

d. Testing that MASTER ICSRs related to serious suspected adverse reactions sent by EMA to EVPM by means of EVWEB are not re-routed to the NCA in accordance with the re-routing parameters defined by the NCA in EVWEB; this is to confirm that MASTER ICSRs are not re-routed to an NCA (Gateway or EVWEB inbox) where the parameters were set not to receive these type of reports.

e. Re-routing of ICSRs related to non-serious adverse reactions sent by a MAH to EVPM by means of the EVPOST function; the ICSRs are re-routed to the NCA (NCA local Gateway/EVWEB inbox) in accordance with the re-routing parameters defined by the NCA in EVWEB; generating and sending of ACKs by the NCA's local pharmacovigilance database/EVWEB (as applicable).

f. Testing that ICSRs related to non-serious adverse reactions sent by a MAH to EVPM by means of the EV POST function are not re-routed to the NCA in accordance with the re-routing parameters defined by the NCA in EVWEB; this is to confirm that ICSRs are not re-routed to an NCA (Gateway or EVWEB inbox) where the parameters were set not to receive these type of reports.

g. Re-routing of MASTER ICSR related to non-serious adverse reactions sent by EMA to EVPM by means of EVWEB; the MASTER ICSR is re-routed to the NCA (NCA local Gateway/EVWEB inbox) in accordance with the re-routing parameters defined by the NCA in EVWEB; generating and sending of ACKs by the NCA's local pharmacovigilance database/EVWEB (as applicable).

h. Testing that MASTER ICSRs related to non-serious adverse reactions sent by EMA to EVPM by means of EVWEB are not re-routed to the NCA in accordance with the re-routing parameters defined by the NCA in EVWEB; this is to confirm that MASTER ICSRs are not re-routed to an NCA (Gateway or EVWEB inbox) where the parameters were set not to receive these type of reports.

Note: There will be no changes to the reporting of suspected unexpected serious adverse reactions during clinical trials 1 until the application of the [Clinical Trial Regulation]. Therefore, the re-routing testing of the suspected unexpected serious adverse reactions related to clinical trials will take place at a later stage.

3.2. Testing of ICSRs and ACKs in ICH E2B(R3) or ICH E2B(R2) format as generated by local pharmacovigilance databases of NCAs

The following *is applicate to NCAs using the EudraVigilance Gateway for th*e electronic transmission of ICSRs:

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[1] 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 (OJ L 311, 28.11.2001, p. 67).

- NCAs should use the sample ICSRs as described on the dedicated webpage: EudraVigilance: electronic reporting "Preparing for the electronic exchange of safety reports". This will allow for checking if the XML files (safety and acknowledgement messages) are correct and comply with the required specifications: syntax, field lengths, minimum information and data coding against the ICH E2B(R2)/M2 and ICH E2B(R3) formats and ICH M1 terminology.

- NCAs will also be able to test the application of the business rules when sending ICSRs as part of the simplified adverse reaction reporting process.

- If NCAs continue to use E2B(R2) pharmacovigilance databases, they are encouraged to use the E2B(R3) test files for the testing of the loading of these files using a Backwards/Forwards Conversion (BFC) tool. If NCAs encounter any issues as part of the BFC process, NCAs should report these to EMA IT Service Desk. For the specific E2B(R2) testing with EudraVigilance supported by the EMA, only the E2B(R2) test files provided should be used.

3.2.1. Sample files and scripts for E2B(R2) ICSRs/ACKs

The sample files and scripts for E2B(R2) ICSRs/ACKs, testing includes the following scenarios:

1. Fatal report with cause of death and autopsy sections filled in

2. A follow up report (sent in after the initial report)

3. A report including patient medical and drug history

4. A parent child report

5. A nullification report

6. A report where the worldwide unique safety report number (A.1.10) is either a Regulatory authority's case report number (A.1.10.1) or a Other sender's case report number (A.1.10.2) that is different from the sender's safety report unique identifier (A.1.0.1)

7. A non-intervention study (observational) report sent to EVPM (Receiver ID EVTEST)

8. If applicable to the organisation an interventional study (Clinical Trial phase I-IV) report sent to EVCTM (Receiver ID EVCTMTEST)

9. A case reported in the literature

10. A report with the section report duplicate (A.1.11.1) completed

Test files are published on the dedicated webpage EudraVigilance: electronic reporting (Step 5a: XML test phase for organisations using the E2B(R2) format).

3.2.2. Sample files and scripts for E2B(R3) ICSRs/ACKs

The sample files and scripts for E2B(R3) ICSRs/ACKs, testing includes the following scenarios as outlined in the EU ICSR Implementation Guide:

1. Initial and follow-up

2. Patient death

3. Parent/child

4. Past drug / past medical history / Test results

5. Advanced therapies (device component)

6. Product name parts

7. Clinical trial SUSAR

8. Observational studies

9. Literature report with article attached

Test files are published on the dedicated webpage [EudraVigilance: electronic reporting](#) (Step 5b: XML test phase for organisations using the E2B(R3) format).

If an NCA does not report certain types of ICSRs (e.g. Clinical Trial SUSAR) they are not required to test such types of reports. However, if the situation changes in the future and they will send these types of reports to EudraVigilance, they will need to complete the testing for the applicable test scenarios.

3.2.3. Testing steps

The testing steps are summarised as follows:

- **Step 1:**
  - Load the XML files into the local NCA pharmacovigilance database.
  - Note: it may be necessary to manually set a receiving organisation identifier within the XML files.
  - The messages need to be loaded into the NCA's pharmacovigilance database and then sent back to EVTEST or EVCTMTEST as applicable.
  - In every test scenario a suspect medicine called 'Spare drug' has been included, enabling the NCA to import and process test ICSR for its own medicine. It has 'Spare MAH' as the marketing authorisation holder and 'Spare substance' as the substance. It is optional to amend any of the fields, which are populated in this section, but none of the other drug sections may be changed and no other fields may be added to this medicine. The medicine is not referenced in the narrative.
  - For **cases 1-6**, **9 and 10** changes in no more than these sections should be necessary, R2 and R3 files should be submitted in the same format as the original file:
- safety report ID: A.1.0.1 for R2 and C.1.1 for R3

- receive date: A.1.6b for R2 and C.1.4 for R3

- receipt date A.1.7b for R2 and C.1.5 for R3

- suspect medicine 'Spare drug' and the populated fields within that section.

  - For **cases 7 and 8**, there are specific instructions in the sender's comment field on what follow-up to do. Testers need to send the first versions of these two ICSRs along with the other ICSRs (making the same changes as in cases 1-6), then make the required additional changes and send them again.

- Send the XML files to EMA via the EudraVigilance system

- Receive back ACK for XML files from the EudraVigilance system

- Store ACK into NCA local system

- **Step 2:**

  - EMA confirms the successful completion of the testing via email to the NCA local contact point.

Note: *There will be no changes to the reporting of suspected unexpected serious adverse reactions during clinical trials2 until the application of the [Clinical Trial Regulation](#).*

3.3. Testing of the new nullification process for nullifications sent by MAHs for ICSRs that were previously forwarded to EudraVigilance by NCAs

For this testing the following steps should be followed:

- Send a valid EEA ICSR from the NCA local test system;

- Receive back an acknowledgement from the EudraVigilance system;

- Using the same ICSR sent by the NCA account, create a follow-up nullification using a MAH test account;

- Send the MAH nullification to the EudraVigilance system.

- Receive back a positive acknowledgement from EudraVigilance that nullification request received.

4. Testing schedule – planned testing between EMA and NCAs

The following testing plan has been agreed:

- 3 July 17:

  - Austria (re-routing & R3 testing)

  - Romania (re-routing testing)

- 10 July 2017:

  - Netherlands (re-routing & R3 testing)

  - Czech Republic (re-routing & R3 testing)

- 17 July 2107:

  - Lithuania (re-routing & R3 testing)

- 24 July 2017:

  - Germany – Bfarm (R3 testing)

  - Portugal (re-routing testing)

- 31 July 2017:

  - Ireland (re-routing testing)

  - Hungary (re-routing testing)

- 14 August 2017:

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[2] 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 (OJ L 311, 28.11.2001, p. 67).

- – Latvia (re-routing testing)

- 04 September 2017

  - – Slovenia (re-routing testing)

  - – Germany – PEI (re-routing & R3 testing)

- 11 September 2017

  - – Spain (re-routing & R3 testing)

  - – Denmark (re-routing testing)

- 21 September 2017

  - – Germany – Bfarm (re-routing testing)

  - – United Kingdom (re-routing testing)

  - – Norway (re-routing & R3 testing)

  - – Ireland (R3 testing)

- 25 September 2017

  - – France (re-routing testing)

  - – Finland (re-routing testing)

- 02 October 2017

  - – Sweden (re-routing testing)

  - – Bulgaria (re-routing & R3 testing)

  - – Greece (re-routing testing)

- 09 October 2017

  - – Romania (R3 testing)

  - – Slovakia (re-routing testing)

  - – Italy (re-routing testing)

- 16 October 2017

  - – Croatia (re-routing & R3 testing)

- 06 November 2017

  - – Finland (R3 testing)

- 27 November 2017

  - – Greece (R3 testing)

- January 2018

  - – Italy (R3 testing)

  - – Sweden (R3 testing)

5. Other NCA testing activities

As per the agreed implementation roadmap (chapter 5.1 of the [EudraVigilance Stakeholder Change Management Plan](#)), the release of the new XCOMP (test) environment will take place on 26 June 2017.

From this date onward, the EV XCOMP system can be used by NCAs for any testing they wish to perform.

Existing registered users with valid log-in credentials will be automatically migrated to the new EudraVigilance XCOMP (as of 26 June 2017) and production environment (as of 22 November 2017).

For new users that would like to access the XCOMP environment for testing as of 26 June 2017, please initiate the registration as outlined at the dedicated webpage [EudraVigilance: how to register](#).

6. NCA technical support webinar

Following the feedback received from PRAC and IT Directors in March 2017, EMA is organising technical support webinars as of June 2017 for IT staff from NCAs, which are responsible for adaptations of their local NCA pharmacovigilance system.

The dates of the webinars are be published on the [EudraVigilance Training and Support](#) webpage.

Technical support webinars	
Target Audience	National Competent Authorities in the EEA • IT experts responsible for adaptations of national pharmacovigilance/safety system.
Duration	1 hour Webinars will be run regularly from June to December 2017.
Learning Outcomes	EMA staff will be available to answer technical questions raised by webinar participants. These webinars will focus on IT system implementation/upgrade questions related to pharmacovigilance/safety databases as well as enquiries related to testing performed with the new EudraVigilance test environment (XCOMP). Questions should be submitted to **EV-Webinar-support-technical-NCA@ema.europa.eu** 4 days in advance of the webinars. Enquiries can also be raised during the webinars. Places are restricted to 100 participants for each webinar and will be available on a first come first served basis.
Webinars	**NCAs- technical support webinars**

dates 2017:

        27 June 2017 13:00 -14:00

        18 July 2017 13:00 -14:00

        1 August 2017 14:00 -15:00

        5 September 2017 14:00 -15:00

        21 September 2017 14:00-15:00

        11 October 2017 14:00 -15:00

        7 November 2017 14:00 -15:00

        21 November 2017 14:00 -15:00

7. NCA operational support webinar

EMA is organising pharmacovigilance and EudraVigilance operational support webinars on a monthly basis.

The dates of the webinars are be published on the [EudraVigilance Training and Support](#) webpage.

Operational pharmacovigilance and EudraVigilance support webinars	
Target Audience	National Competent Authorities in the EEA • Experts in charge of pharmacovigilance and drug safety with obligations to report suspected adverse reactions related to medicines and to perform signal management • Users of EudraVigilance (EVWEB and EVDAS)
Duration	2 hours During 2017, webinars will be run regularly from June to December 2017: NCAs webinars will be run monthly
Learning Outcomes	EMA staff will be available to address operational pharmacovigilance questions as well as procedural and operational inquiries related to EudraVigilance raised by webinar participants. The webinars will focus on: • Operation of pharmacovigilance with main focus on the latest revision of GVP Module VI " Management and reporting of adverse reactions to medicinal products" and GVP Module IX "Signal management" • Procedural and implementation planning related questions related to the launch of the new EudraVigilance System including the use of the new ICH E2B(R3) Individual Case Safety Report (ICSR) format and the use of EVDAS for signal detection. Organisation and user registration questions and EudraVigilance Access Policy related points will be also addressed.

	Questions should be submitted to **EV-Webinar-support-MAH-NCA@ema.europa.eu** 4 days in advance of the webinars. Questions can also be raised during the webinars. Places are restricted to 100 participants for each webinar and will be available on a first come first served basis.
Webinars dates 2017:	**NCAs operational pharmacovigilance and EudraVigilance support webinars** 30 June 2017 12:00-14:00 27 July 2017 13:00-15:00 31 August 2017 13:00-15:00 28 September 2017 13:00-15:00 26 October 2017 13:00-15:00 30 November 2017 13:00-15:00 14 December 2017 13:00-15:00

8. Checklist for national Competent Authorities in the EEA

In consultation with the Pharmacovigilance Business Team and the EudraVigilance Expert Working group members, a checklist (EMA/172253/2017) is also made available to provide a summary of easy to follow steps to assist NCAs in preparing for the go-live of the new EudraVigilance System in November 2017.

9. Increased EMA technical support to stakeholders

From June 2017 and the release of the new system into the XCOMP environment, EMA will increase its technical support to address additional queries from NCAs.

Once the new EudraVigilance functionalities are released in production to all stakeholders in November 2017, EMA will further strengthen its technical support to stakeholders by triggering a 'Hypercare' period for a duration of 3 months following the go-live.

During this period the following critical activities will be executed:

- Technical user support making sure that unforeseen events or incidents are managed and addressed in the most agile manner.
- Helpdesk for incidents triage.

10. EMA service desk support

- If you have pharmacovigilance questions and other general enquiries: Send a question to the European Medicines Agency
- If you require technical support using EudraVigilance and the gateway/web client contact the: EMA IT Service Desk (Tel. +44 (0)20 3660 7523).