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Information Management

E2B(R3)/E2B(R2) XML Testing

Instructions guide to support the e-learning training module IT-M2 'Testing the electronic reporting of ICSR/SUSAR to EudraVigilance'.

Version 1.0

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1. Introduction

1.1. Legal background

Regulation (EC) No 726/2004, Directive 2001/83/EC as amended and Directive 2001/20/EC outline the electronic reporting requirements to EudraVigilance (EV), the data processing network and management system for reporting and evaluating suspected adverse reactions during the development and following the marketing authorisation of medicinal products in the European Economic Area (EEA).

1.2. Testing of the electronic reporting to EudraVigilance

This guidance specifies the instructions on how to test the electronic reporting of Individual Case Safety Reports (ICSRs) and Suspected Unexpected Serious Adverse Reactions (SUSARs) to EudraVigilance.

It is intended for EudraVigilance stakeholders who have to test the E2B(R3) or E2B(R2) compliance of their database in order to use it in production with EudraVigilance.

Organisations (Pharmaceutical companies, Sponsors and NCAs) which want to register as Gateway or EVPOST user in EudraVigilance or are making a major upgrade to their existing database should perform the E2B(R3) or E2B(R2) XML testing. E2B XML testing is not required for EVWEB users.

2. Registration with EudraVigilance

Registration in the EV test environment, also known as the external compliance testing environment (XCOMP), is open to all relevant parties as follows:

- National Competent Authorities (NCAs), Marketing Authorisation Holders (MAHs), Marketing Authorisation Applicants (MAAs) and Sponsors are able to register individually for both test and production;

    - Registration in production at the same time as test is possible, but the production profile will not be activated until the E2B XML testing has been completed,

    - Registering for both environments at the same time is strongly advised to minimise any post-testing delays;

- Pharmacovigilance (PV) database developers and PV service providers will also be able to register for E2B XML testing; this will be possible via the EudraVigilance Gateway only, no access to EVWEB will be provided;

    - Once registered, Clinical Research Organisations (CROs) and PV database providers, wishing to perform official testing to confirm technical compliance should send an email to qattesting@ema.europa.eu and include the subject line "***Service provider testing request***". Emails do not need to be sent for permission to send test files during development and configuration checking work;

There are different types of electronic exchange solution that an organisation can opt to use:

- 'Gateway' or 'EV Post' function: new organisations need to register separately to use the external compliance testing environment (XCOMP) and the production environment;

- 'EV WEB application (EVWEB)' users (also known as WEB traders) will be registered in the production environment only, unless they also request to use the XCOMP environment.

XCOMP mirrors the EudraVigilance production environment and allows organisations to test the submission of ICSRs and SUSARs to EudraVigilance.

The testing process is mandatory for organisations submitting safety reports using a gateway solution or the EV Post function, it is not required for organisations using EVWEB.

2.1. Disclaimer – Use of EudraVigilance test system (XCOMP)

The European Medicines Agency provides the possibility for regulators, pharmaceutical industry, non-commercial sponsors, and third party service providers (further referred to as 'electronic data interchange partners') to register and connect to the EudraVigilance test system (XCOMP) in order to analyse whether their software is compatible with the new EudraVigilance system.

However, the Agency accepts no responsibility or liability whatsoever (including, but not limited to, any direct or consequential loss or damage that might occur to you and/or any other third party) arising out of, or in connection, with the EudraVigilance test system (XCOMP).

It is the Agency's goal to minimise disruption caused by technical errors. However, the Agency cannot guarantee that the EudraVigilance test system (XCOMP) will not be interrupted or otherwise affected by such problems. The Agency accepts no responsibility whatsoever with regard to such problems incurred as a result of using the system.

This disclaimer is not intended to limit the liability of the Agency in contravention of any requirements laid down in applicable legislation nor to exclude its liability for matters which may not be excluded under that law.

3. Booking a testing slot

From June 2017, it will be possible to book a testing slot after registering in the test environment.

You should book your testing slot by sending an e-mail to qattesting@ema.europa.eu with your organisation name and sender identifier in the EV test environment.

The number of testing slots will be limited per month and allocated on a first come, first served basis; all testing will be performed in the allocated window.

You may subscribe to EMA [RSS]/[Twitter] feeds to ensure you are informed the moment it is published.

You can book a testing slot at any time before the E2B XML testing starts, but if you delay then your desired timeslot may no longer be available.

4. Gateway Certification

Organisations wanting to use the EudraVigilance Gateway need to confirm that the system they intend to use for reporting ICSRs/SUSARs is compatible with the EudraVigilance Gateway.

The European Medicines Agency (EMA) does not mandate any particular software for the e-reporting of ICSRs/SUSARs. However, the software needs to adhere to the standards outlined in the applicable EU Implementation guide.

5. Testing prior to E2B XML testing

5.1. Communication test

The process of establishing the connection requires several steps:

- Document Transport Choice;

- Exchange of Profile Information;

- Exchange of Public keys for encryption;

- Testing the Connection;

  - Testing is accomplished by sending an encrypted Safety Message to the EudraVigilance Gateway, where it is unencrypted, checked for basic accuracy, then re-encrypted and sent to EudraVigilance.

5.2. Development and validation testing

Once connected, organisations have full access to send data to the EudraVigilance test environment.

Since EV test (XCOMP) is a copy of EV production, including the parser and the Medical Literature Monitoring (MLM) environment for downloading, you can use this system to validate that your cases meet the EV business rules.

The EMA will not assess the cases you use for validation; you can use this environment as you wish for any development or validation activities. It is at your discretion if you wish to perform any such validation, but it is strongly recommended to ensure that the final XML testing runs smoothly.

Please note that any misuse of the *EudraVigilance test system (XCOMP)* (e.g. by sending large volume of data, preventing others from testing), would result in the withdrawal of access to the system.

6. E2B(R3) and E2B(R2) XML testing

From June 2017:

- Database testing:

  - vendors and CROs can perform testing for a specific version and build of their database,

  - EMA will confirm if that a precise version and configuration of the database has completed testing,

  - significant changes to the database will require re-testing with the EMA,

  - During the testing you will be requested to inform the EMA of the precise version and build of your database. This information will be held by the EMA and will be made available to pharmacovigilance inspectors upon request.

6.1. Testing process

You should download the test cases available on the EMA website, import them into your database, make the appropriate changes and transmit the cases to EV test environment (XCOMP).

Please follow the instructions on the EMA website in order to obtain either the E2B(R2) or E2B(R3) XMLs needed for your testing.

EMA webpage for testing:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000686.jsp&mid=WC0b01ac0580a69261

6.2. Testing instructions

- Change the receive & receipt dates for all cases to the day you downloaded them;

- Change the safety report IDs;

- If necessary change the drug called "Spare drug" to one of your company's drugs;

- You can change any of the populated fields, but please do not add data in any other fields;

- For the cases with "followmeup" or "nullifyme" in the case number, make the same changes as above & send an initial version, then follow the instructions in the senders comment field (before sending the follow-up versions);

- Send the cases to EVTEST or EVCTMTEST as applicable;

- Receive and check the Acknowledgment (ACK);

- Email qattesting@ema.europa.eu to inform them of the Safety Report IDs of the test cases and your sender identifier/organisation name;

- EV QA testing team will validate test cases were transmitted successfully and inform you if there are any errors to be corrected or any issues to be fixed.

6.3. Testing confirmation

Once you have completed the testing, you will receive confirmation from the EMA that the specific version and build of your PV database has completed testing and can be used in production.

If you are a MAH, MAA, Sponsor or NCA then you must include this when you contact the EV registration team to activate your production profile.

If you are a CRO or a PV database provider you should provide a copy of the relevant tested version to your clients for their registration with EudraVigilance. However, it should be noted that if changes to tested version and configuration have been made for the client this may require the installation to go through the normal testing process.

The confirmation provided upon completion of the testing process through the *EudraVigilance test system (XCOMP)* is for information purpose only, and does not entail any implicit or explicit recommendation or endorsement by EMA. The *electronic data interchange partner* is restricted from using this confirmation as an endorsement by EMA.

By confirming the completion of the testing process EMA makes no warranty of any kind, implicit or explicit, including, without limitation, the implied warranty of merchantability, fitness for a particular purpose, non-infringement and data accuracy of the software. EMA neither represents nor warrants that the operation of the software will be uninterrupted or error-free, or that any defects will be corrected. EMA does not warrant or make any representations regarding the use of the software or results thereof including but not limited to the correctness accuracy, reliability, or usefulness of the software.

7. E2B(R3) and E2B(R2) XML testing for accepted database

If you are purchasing and installing, without customisation, a database that has already passed testing, then there are 5 steps to reporting to EudraVigilance:

1. Register with EudraVigilance;

2. Obtain EudraVigilance Gateway certification (for internet communication);

3. Perform communication test (to ensure successful Gateway to Gateway communication);

4. Send a single case test;

5. Activate the production profile (after successful testing is confirmed by the EV QA testing team).

Please note that if there is customisation to a purchased database, then full re-testing will be required.

7.1. Single case test

- Send a single case to EV test environment (EVTEST or EVCTMTEST as applicable);

- Receive and check ACK;

- Email qattesting@ema.europa.eu informing them of the single test case's safety report ID and your sender identifier/organisation name;

- EV QA testing team will validate the case was transmitted successfully with correct sender ID & case numbers and confirm that the tested PV database can be used in production;

- If you are an MAH, MAA, Sponsor or NCA then you must include this along with the email you received from your CRO or database provider when you contact the EV registration team to activate your production profile.

8. Related guidance and documents

EU Individual Case Safety Report (ICSR) Implementation Guide (for R3 XML)

Note for guidance – EudraVigilance Human – Processing of safety messages and individual case safety reports (ICSRs) (for R2 XML)

GVP Module VI – Management and reporting of adverse reactions to medicinal products

E2B(R3) ICSR Specification and Related Files

EudraVigilance support guide (EV Helpdesk)

9. List of Abbreviations/Acronyms used in this document

Abbreviations/Acronyms	Description
ACK	Acknowledgment message
CRO	Contract Research Organisation
EMA	European Medicines Agency
EVCTMTEST	EudraVigilance Clinical Trial test module
EVPOST	EudraVigilance Post function
EVTEST	EudraVigilance Post-Authorisation test module
EVWEB	EudraVigilance Web Application
ICSR	Individual Case Safety Report
MAA	Marketing Authorisation Applicant
MAH	Marketing Authorisation Holder
MLM	Medical Literature Monitoring
NCA	National Competent Authority
PV	Pharmacovigilance
SUSAR	Suspected Unexpected Serious Adverse Reaction