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The launch of the new EudraVigilance System Questions and Answers (Q&A) from stakeholders

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Glossary

ACK / NACK	Acknowledgment / Negative Acknowledgment
ATU	Autorisation temporaire d'utilisation
BFC	Backward and Forward conversion
CRO	Contract Research Organisation
DEC	Drug event combination
EDI	Electronic Data Interchange
EEA	European Economic Area
EMA	European Medicines Agency
EPITT	European Pharmacovigilance Issues Tracking Tool
eRMRs	Electronic Reaction Monitoring Reports
EU	European Union
EVCTM	EudraVigilance Clinical trial Module
EVDAS	EudraVigilance data analysis system
EV-EWG	EudraVigilance Expert Working Group
EVPM	EudraVigilance Post-Authorisation Module
EVPOST	EudraVigilance post function
EVWEB	EudraVigilance web reporting application
FU	Follow up
GVP	Good pharmacovigilance practice
HQ	Headquarter
ICH	International Conference on Harmonisation
ICSR	Individual case safety report
IG	Implementation Guide
ISO IDMP	International Organization for Standardization for the identification of medicinal products
MAHs	Marketing authorisation holders
MedDRA	Medical Dictionary for Regulatory Activities
MLM	Medical literature monitoring
NCA	National competent authorities
NPhVD	The National Pharmacovigilance Database
PBRER	Periodic benefit-risk evaluation report
PRAC	Pharmacovigilance Risk Assessment Committee
PSMF	Pharmacovigilance system master files
PSUR	Periodic Safety Update Report
PSUR DLP	PSUR Data lock point
QPPV	Qualified Person Responsible for Pharmacovigilance
ROR	Reporting Odds Ratio
RPhV	Responsible of Pharmacovigilance
SD	Signal detection
SDR	Signal of disproportionate reporting
SMQs	Standardized MedDRA Query
WW ID	World Wide ID
XCOMP	EudraVigilance test environment

XEVMPD	Extended EudraVigilance Medicinal Product Dictionary
XML	Extensible Mark-up Language

Introduction

This document addresses questions received from stakeholders in preparation of the launch of the new EudraVigilance System, which is to go-live on 22 November 2017.

The document summarises questions received through the Agency's service desk and as part of the technical and pharmacovigilance/EudraVigilance support webinars organised by the EMA.

The document will be regularly updated and should be consulted as a first reference before contacting the Agency's service desk.

1. EudraVigilance organisation and user registration

Reference	Question	Answer
1.1	Can an individual only be registered under one Organisation Identifier (ID)?	In accordance with the already established process, a user can be registered with several organisations, which are characterised by their organisation ID in EudraVigilance. The user will receive a different user name and password for each organisation and will obtain access to data as determined by the EU Qualified Person Responsible for Pharmacovigilance (QPPV) (or the appointed deputy) of each organisation.
1.2	Can a user be registered both, at headquarter (HQ) level and at affiliate level of the same organisation?	A user can be registered both at headquarter level and at one or more affiliates of this headquarter.
1.3	If a user from a third party is given a user account linked to the headquarters of the organisation, will the third party user have access to all ICSRs of the organisation?	Yes. Taking into account that the "Owner HQ Identifier" of the XEVMPD/Art.57 database is used to determine the access for ICSRs by marketing authorisation holders (MAHs), a user registered at headquarters level will have access to ICSRs for all active substances for which the MAH holds marketing authorisations in the EEA.
1.4	Does the current registration process change for access to XEVMPD and where is the online application for updating the XEVMPD data?	There is no change to the current registration process for submitting information on medicinal products to the Extended EudraVigilance Medicinal Product Dictionary (XEVMPD)/Art.57 database. The XEVMPD is no longer part of the new EVWEB as the current XEVMPD will be replaced at the time of the ISO IDMP implementation 9 See also EMA webpage on ' Implementation of the ISO IDMP standards '). The XEVMPD will be maintained until that time and the URL is: https://eudravigilance.ema.europa.eu/X/?6
1.5	Is there a limit to the number of users who can be registered with EVWEB to ICSR reports/download ICSRs?	EMA has not defined a maximum number of users per organisation that can register with EVWEB. It is recognised that the number of users depends on the size of an organisation and how each organisation defines its business processes in relation to the interaction with EudraVigilance. Performance and scalability testing has been performed by the Agency based on concurrent users of the system. EMA will continuously monitor the usage of the system, which is based on a scalable design.

Reference	Question	Answer
1.6	<p>What is the Agency’s position on MAH personnel who reside outside of the EEA accessing data from EudraVigilance for the purposes of signal evaluation/signal detection activities? Are there any “data privacy” constraints that have been considered here?</p>	<p>The EudraVigilance database is made accessible to the EU QPPV as the regulatory representative of the MAH. The QPPV, as a representative of the MAH, shall be established in the EU territory, and therefore it must be subject to EU data protection law.</p> <p>This implies that it is the MAH, as a data controller under the applicable legislation that should ensure that the access to the data via its organisation is in compliance with EU data protection law, i.e. that the transfer of data within the MAH are in line with the applicable rules. There are therefore no geographic restrictions from the EMA perspective to non-EEA users as the responsibility for these users rest solely with the authorised representative of the MAH.</p>
1.7	<p>What happens if a MAH misses the allocated EVDAS registration timeslot? If we as MAH don’t get access we might face challenges in being compliant by November in accessing EVDAS. What are the implications and contingency provisions?</p> <p>Are there any rules for allowing changes to registered EVDAS users given that for many MAHs, the final business process may not be in place by November 2017?</p>	<p>The list of allocated timeslots for MAHs to register EVDAS users has been published by the Agency in May. As of 1 June the EVDAS user registration has been initiated and the MAH has a window of one month to perform their EVDAS user registration.</p> <p>If an MAH misses the allocated registration timeslot, registration requests will be processed as soon as possible following receipt of the delayed request However, EMA cannot guarantee a specific timeframe.</p> <p>Where changes to registered EVDAS users are required, the EU QPPV should inform the EudraVigilance Team and the request will be processed as soon as possible.</p>

Reference	Question	Answer
1.8	<p>What is the difference in the administrative and scientific profile of EVDAS users?</p> <p>Can a MAH have five registered users for each profile?</p> <p>What is the rationale for the limitation in users?</p> <p>We'd like to suggest considering that the number of registrations should instead be proportionate to the number of marketing authorisations that a company holds in the EU/EEA.</p>	<p>The number of EVDAS users for each MAH has been defined with five users for both the administrator and scientific profile. The EVDAS scientific profile allows users generating electronic Reaction Monitoring Reports (eRMRs), line listings and downloading individual cases. The EVDAS administrator role allows generating eRMRs and line listings but excludes the download of individual cases e.g. an administrator can generate eRMRs and line listings for all substances for which an MAH holds a marketing authorisation in the EEA.</p> <p>Users with an administrator profile can distribute the eRMRs and associated line listings to the signal management teams within the organisation. The signal management experts can access the individual cases of interest via EVWEB.</p> <p>EMA has defined a maximum number of users per organisation to ensure optimal performance of EVDAS. It is recognised that the number of users is linked to the size of an organisation and how each organisation defines its business processes in relation to the interaction with EudraVigilance. Performance and scalability testing has been carried out by the Agency based on concurrent users of the system. EMA will continuously monitor the usage of the system, which is based on a scalable design and taking into account initial experience gained may revisit the number of EVDAS users for MAHs with a large product portfolio.</p>
1.9	<p>Can the QPPV access be delegated? Given there are complex arrangements for medicinal products licenced across multiple MAHs, can the Company A QPPV access be delegated to someone in Company B?</p>	<p>From a registration perspective the EU QPPV (company A) can delegate the functions related to EudraVigilance registration to a trusted deputy (e.g. a trusted deputy of company B). The trusted deputy can then perform the registration of new users, affiliates and any other changes on behalf of the EU QPPV (company A).</p> <p>The overall responsibility for EudraVigilance access and user registration remains with the EU QPPV (company A).</p>

Reference	Question	Answer
1.10	If a EU QPPV registers users with a scientific profile, does the EU QPPV also need to register these users with EVWEB so they can access individual cases from the individual case line listing?	<p>If an EU QPPV registers EVDAS users with a scientific profile, the EU QPPV does not need to register these users with EVWEB so they can access individual cases via the individual case line listing. The EVDAS Scientific profile in itself provides access to individual cases via the ICSR form directly from the individual case line listing. EVDAS users with the scientific profile do not need to be registered in addition with EVWEB.</p> <p>Note that the EVWEB and EVDAS registration processes are separate processes and are not linked. Registering a user with an EVDAS scientific profile does not add the EVWEB profile to create/send ICSRs.</p> <p>To register users for EVDAS, the EU QPPV has to register the user via the secure area of the EudraVigilance web page. The EVWEB Profile to create/send ICSRs can then be chosen in addition to the EVDAS scientific role if the user also performs these activities.</p>
1.11 (new)	Which username and password have to be used to enter into EVDAS for MAH? The same as to enter into Eudralink or to EMA Service Desk?	To access EVDAS (via the BI tool) users need to use the same password that they use for Eudralink or for the Service Desk. Within EVDAS, if users require access to the ICSR forms, they need to use their EudraVigilance login details.
1.12 (new)	How long it will take since EVDAS access is requested by a MAH user and EMA provide access?	EVDAS access is provided within 25 working days. Please note that access to EVDAS is not live until 22 November 2017 but the initial EV password must be used and changed within 30 days of receipt.

Reference	Question	Answer
1.13 (new)	<p>With the release of EVDAS functionality in November 2017, we would like to ask about registration for service providers / CROs.</p> <p>May MAHs outsource their signal detection activities; therefore it is important that these service providers / CROs have adequate access to the EVDAS system in November.</p> <p>Will a service provider be able to gain access to the system independently to perform signal screening for multiple MAHs?</p> <p>If this is not possible and an MAH would like to register a service provider /CRO to perform the screening on their behalf, how can this be done? For example when MAHs do not wish to register a CRO user at headquarters level, or require more than 5 users?</p>	<p>The obligation related to the monitoring of EudraVigilance is placed on the marketing authorisation holder as follows: "MAHs shall monitor the data available in the EudraVigilance database to the extent that they have access to that database". [Commission Implementing Regulation 520/2012 Art 18(2)]</p> <p>The legislation does not foresee access to EudraVigilance data by service providers or CROs.</p> <p>However, CROs and IT vendors may be registered by a marketing authorisation holder, applicant, commercial or non-commercial sponsor as a third party service provider acting on behalf of these organisations by providing services related to EudraVigilance.</p> <p>It is for the MAH to define how they organise the monitoring of the data available in the EudraVigilance database. EVDAS registrations are to be managed by the EU QPPV or the appointed deputy and access to EVDAS data for the purpose of signal management is only granted at headquarter level.</p>

2. Use of EVWEB and the ICSR download manager

Reference	Question	Answer
2.1	<p>The ICSR download eLearning video states that there is no need to specify the active substance or medicinal product name in the filter as the download will include all ICSRs for medicinal products registered by the MAH in the EVXMPD.</p> <p>Based on this, is it correct that MAHs won't be getting cases where another MAHs medicinal product name is reported.</p>	<p>The download function is based on the EudraVigilance Access Policy L2A. <i>Access is based on the active substance</i> for medicinal products, for which a MAH holds a marketing authorisation. Therefore the download algorithm does not exclude ICSRs where the medicinal product of another MAH is reported in the ICSR.</p> <p>Downloaded ICSRs contain information on the medicinal product (trade) name as reported by the primary source, which allow an MAH to determine ownership of the medicinal product.</p> <p>Please refer to slide 62 onwards of the EudraVigilance Access Policy eLearning material (http://www.ema.europa.eu/docs/en_GB/document_library/Presentation/2016/06/WC500209351.pdf)</p> <p>and 36:55 of the eLearning video on EudraVigilance Access Policy: https://www.youtube.com/watch?v=WfuogTpCFWM&feature=youtu.be</p>
2.2	<p>Will only valid ICSRs be available for download?</p>	<p>The EudraVigilance Access Policy states that ICSRs classified as 'Error Reports' are excluded from access as they refer to incomplete or erroneous reports. If an ICSR is classified as 'Error Report', the sender is required to correct the ICSR and retransmit it before it will be further processed in EudraVigilance.</p> <p>Please refer to slide 22 of the EudraVigilance Access Policy presentation (http://www.ema.europa.eu/docs/en_GB/document_library/Presentation/2016/06/WC500209351.pdf)</p> <p>and 10:35 of the eLearning video on EudraVigilance Access Policy: (https://www.youtube.com/watch?v=WfuogTpCFWM&feature=youtu.be)</p>

Reference	Question	Answer
2.3	<p>What clock start date should an MAH use (e.g. for onward sending outside the EEA)?</p> <p>Will this be defined by the EMA or left to MAHs to decide i.e. based on download date as per MLM?</p>	<p>The pharmacovigilance legislation does not define a “day zero” for ICSRs accessed via EudraVigilance by MAHs.</p> <p>For ICSRs to be included in PSURs, the MAH should define what the cut-off date is for ICSRs downloaded from EVWEB as part of the PSUR data lock point.</p> <p>For reporting obligations outside the EEA, MAHs need to consult with the respective regulatory authorities and their requirements.</p> <p>For MLM ICSRs, the following was agreed:</p> <p>The clock starts (day zero) with awareness of a publication containing the minimum information for reporting. In practice this means that for records of confirmed ICSRs, the clock starts for the MLM Service at the time of performing the search; whereas for marketing authorisation holders the clock starts when the information on which substances are suspected to have caused a reaction is made available to marketing authorisation holders. This information is first made available when the ICSR is transmitted to EudraVigilance; therefore the date of transmission of an ICSR by the MLM Service to EudraVigilance is day zero for marketing authorisation holders in the EEA. MAHs should ensure that they download cases regularly.</p>
2.4	<p>Will ICSR messages retrieved from EVWEB contain local language content?</p>	<p>ICSRs will be made available in the language as they were reported to EudraVigilance. If for example an NCA submits ICSRs that contain local language in free text data elements, access to these data elements is provided in accordance with the EudraVigilance Access Policy (revision 3). For language requirements, refer to Article 28(4) of the Commission Implementing Regulation (EU) 520/2012.</p>

Reference	Question	Answer
2.5	Please confirm what dates are used to perform the export of ICSR messages. Are these the dates received by the EudraVigilance (EV) system or the E2B data element "Receive date", or the gateway "Transmission date"?	<p>The ICSR download functionality uses the date that the ICSR's suspect and interacting drugs have been classified against the data held in XEVMPD/Art.57 database. Classification is either performed automatically in the EudraVigilance Database Management System (EDBMS) or, if not automatically classified (e.g. due to data quality issues in the reported ICSR), is performed at a later stage through the manual classification process.</p> <p>The MAH access to data in accordance with the EudraVigilance Access Policy (revision 3), i.e. levels L2A/L2B depends on the completion of the classification process. As the linkage of ICSRs to XEVMPD/Art.57 data can only occur through the classification process (automatic or manual), the date that the suspect or interacting drug(s) have been classified against the data held in XEVMPD/Art.57 database is used by the ICSR download tool rather than the official receipt date of the ICSR.</p>
2.6	Is a user's login ID connected to an Organisation ID (Org Id) to obtain a list of "Active Substances" associated with that Organisation's ID?	<p>A user's login ID is linked to the related organisation, for which the user is registered. The user's organisation ID is also linked to the XEVMPD/Art.57 data, based on the data element "Owner HQ Identifier". The XEVMPD/Art.57 data associated through this linkage determine which ICSRs can be accessed by the MAH in EudraVigilance.</p> <p>Only user's registered at Headquarter level will be able to make L2 access requests.</p>
2.7	Large organisations will have many active substances registered in the XEVMPD/Art.57 database. Is there a way to distinguish between serious and non-serious ICSRs from the file names or using query criteria?	<p>The current ICSR export tool does not distinguish between serious and non-serious ICSRs. Note that seriousness in E2B (R3) format is assigned at reaction level. The download manager allows ICSRs to be downloaded in accordance with L2A\L2B access as outlined in the EudraVigilance Access Policy (revision 3). The downloaded ICSRs will then provide information on the seriousness of the cases.</p>

Reference	Question	Answer
2.8	How can a MAH determine if an E2B (R3) ICSR is serious before loading it into our database?	<p>The following two options might be considered:</p> <p>Option 1: You can use the EU BFC tool and create an E2B (R2) format of the ICSR. The seriousness criteria at case level for the E2B (R2) format will be set automatically. However, a quality control should be put in place to validate the conversion.</p> <p>Option 2: The following XPATH statement can be used to determine if an ICSR in E2B(R3) format is serious. If the resulting value of the count is greater than 0 it means that at least one reaction has one of the seriousness criteria marked as "Yes".</p> <pre>count(/MCCI_IN200100UV01/PORR_IN049016UV/controlActProcess/subject/investigationEvent/component/adverseEventAssessment/subject1/primaryRole/subjectOf2/observation/outboundRelationship2/observation[code[@code='34' or @code='21' or @code='26' or @code='33' or @code='35' or @code='12'][@codeSystem="2.16.840.1.113883.3.989.2.1.1.19"]]/value[@value='true'])</pre>
2.9	Will a MAH have access to reports for the same active substance submitted by a third party company?	Yes. Access is provided in accordance with the EudraVigilance Access Policy (revision 3). MAHs have access to ICSRs based on the active substances for medicinal products (reported as suspect/interacting in the ICSR) for which they hold a marketing authorisation in the EEA. This is to support their pharmacovigilance obligations.

Reference	Question	Answer
2.10	<p>If a patient is in an ATU or compassionate use program with a non-approved medicinal product and adverse reactions are reported (per legislation) directly to the local health authority and not to the company, then it seems we might not be able to download these cases from EudraVigilance because we would not have an entry in XEVMPD (I think) for the product prior to approval, and so cases would not be available to us for download. Currently we would/should (although probably not consistently) receive the cases directly from the local health authority.</p>	<p>For unapproved medicinal products for which there is no record in the XEVMPD, which is used to determine the substance based access in EudraVigilance, it is not possible to establish, which company should have L2A access. The cases are accessible via level 1 access and the MAH would need to screen the line listings to identify cases which might relate to the compassionate use programme.</p> <p>If the company already holds a marketing authorisation in the EEA with the active substance contained in the non-approved medicinal product used for the compassionate use programme, then the ICSRs are included for download from EudraVigilance as long as the MAH has entered their product into the XEVMPD.</p>
2.11	<p>Is it possible to designate a third party to perform the download of ICSRs?</p>	<p>A MAH (EU QPPV or appointed deputy) can register one or more users of a third party and grant them with the appropriate access rights so they will be able to perform the download of ICSRs associated with that MAH.</p>

Reference	Question	Answer
2.12	<p>When an MAH submits a change to the XEVMPD, what is the timeframe for the change to be reflected in the EVWEB download tool?</p> <p>Does this mean that if a product is acquired on for example May 1st, the XEVMPD entry is done by Company A by May 5th, and the EVWEB access is updated to reflect this change by May 8th? Would Company A be able to download on May 8th, all ICSRs for this product from May 1st or May 8th only?</p>	<p>The eLearning video EVM3c explains that dates for ICSR downloads are based on the date of classification of any suspect substance or product reported in the ICSR against Art 57/xEVMPD.</p> <p>The ICSR download is possible the day after a new XEVMPD submission is marked as 'Validated by EMA' (up to a week from submission date, provided that the required information is suitable for validation).</p> <p>The organisation that is marked as the XEVMPD owner HQ has access to ICSR data which can be a different organisation to the one that submitted the XEVMPD data (e.g. data submitted by affiliate).</p> <p>The access to ICSRs is not time restricted so the export of ICSRs received prior to the new XEVMPD entry is also supported.</p>
2.13	<p>The EVM3c training module indicates that ICSRs cannot be downloaded after they have been archived. Is it possible for an MAH to request that ICSRs are moved back into an active state so that the cases can be downloaded?</p>	<p>The archiving of each download request will be performed after 30 days. The ICSRs remain available for download if the MAH makes another request.</p>
2.14	<p>When an MAH submits an ICSR to the EMA, will that ICSR also appear for download in EVWEB? Is there a way to filter these cases out?</p>	<p>The ICSR download function automatically excludes same sender ICSRs from the download.</p>

Reference	Question	Answer																						
2.15	<p>Are users restricted to see the downloads that they have requested for themselves?</p> <p>Is it possible for an EVWEB user to see what has been downloaded by other users for that same company setup e.g. can everyone in Company A HQ see what other users in COMPANY A HQ have downloaded?</p>	<p>The ICSR download manager shows all requests made by the same organisation, therefore a user with the appropriate rights can see requests made by other users within their organisation.</p>																						
2.16	<p>For what time period is archived downloads available for retrieval?</p>	<p>The results of download requests in EVWEB are saved for 30 days.</p>																						
2.17	<p>Will local NCAs also be reporting non-serious cases to EudraVigilance?</p> <p>Can a MAH expect non-serious cases from NCAs to also be available for export from EVWEB?</p>	<p>The EudraVigilance submission requirements for valid unsolicited and solicited ICSRs reported by healthcare and non-healthcare professionals [DIR Art 107(3), 107a(4)] are as follows:</p> <table border="1" data-bbox="1077 794 1848 1197"> <thead> <tr> <th>Origin</th> <th>Adverse reaction type</th> <th>Time frame</th> </tr> </thead> <tbody> <tr> <td colspan="3" style="text-align: center;">Marketing authorisation holders</td> </tr> <tr> <td rowspan="2">EU</td> <td>All serious</td> <td>15 days</td> </tr> <tr> <td>All non-serious</td> <td>90 days</td> </tr> <tr> <td>Non-EU</td> <td>All serious</td> <td>15 days</td> </tr> <tr> <td colspan="3" style="text-align: center;">Competent authorities in Member States</td> </tr> <tr> <td rowspan="2">EU</td> <td>All serious</td> <td>15 days</td> </tr> <tr> <td>All non-serious</td> <td>90 days</td> </tr> </tbody> </table> <p>ICSR downloads include both serious and non-serious as per the above reporting requirements (see also the EudraVigilance Access Policy revision 3).</p>	Origin	Adverse reaction type	Time frame	Marketing authorisation holders			EU	All serious	15 days	All non-serious	90 days	Non-EU	All serious	15 days	Competent authorities in Member States			EU	All serious	15 days	All non-serious	90 days
Origin	Adverse reaction type	Time frame																						
Marketing authorisation holders																								
EU	All serious	15 days																						
	All non-serious	90 days																						
Non-EU	All serious	15 days																						
Competent authorities in Member States																								
EU	All serious	15 days																						
	All non-serious	90 days																						

Reference	Question	Answer
2.18	Are there means (other than looking at the export history) of tracking or having an overview of what ICSRs have been downloaded by an MAH?	Apart from L2B requests (ICSRs including case narratives), ICSRs exported by an MAH are not tracked.
2.19	When EU assessment is present, will two assessments by the reporter and the MAH, be also present or not?	In accordance with the specific data elements as defined in the EudraVigilance Access Policy (revision 3), the information as provided by the sender, will be provided in the ICSRs exported.
2.20	The published material by the EMA states that an overview of duplicate masters with their linked duplicates can be made available to an MAH. Can you please provide details on how we can obtain/request this overview and what details it provides?	The "Master" ICSR (mastericsr) cases are included as part of the ICSR download in EVWEB. The "Master" includes a reference to the associated duplicates using the world-wide unique case identifiers of the duplicates. In addition, an EVDAS query which will show MAHs which of their cases are under a master is being developed and will be released after November 2017. The EMA will communicate closer to the time when it will be released. For technical details related to the specifications of master cases, please refer to the EU ICH E2B (R3) ICSR Implementation Guide.
2.21	If a masterichicsr is deleted because it is no longer valid (i.e. they are not true duplicates), would the MAH receive nullification for the deleted masterichicsr?	Nullification ICSRs are included for both masters and non-masters. Master cases can only be nullified by the EMA, and once they are nullified, the underlying duplicates will be reclassified so that they are no longer grouped together.

Reference	Question	Answer
2.22 (new)	<p>For stakeholder group III, access level 2B, will there be a difference in access based on which level the individual cases are coded (substance vs product)?</p> <p>Example:</p> <p>Company A, Product A, substance Paracetamol</p> <p>Company B, Product B, substance Paracetamol</p> <p>1: If a case is coded on Product A, can Company B get access to level 2a data?</p> <p>2: If yes to 1, then can Company B get access to all level 2b data (after formal request)?</p> <p>If a case is coded on Paracetamol, we presume that both Company A and Company B can access level 2A data. Can both company A and B get access to all level 2B data (after formal request)?</p>	<p>Both EVWEB and EVDAS will provide access to MAHs at the level of the substance using the highest level in the hierarchy of the XEVMPD. This is known as the 'Active substance high level'. MAHs with a product containing an active substance can access levels 2A and 2B for the cases where the substance (or the product containing the substance) is coded as suspect/interacting and this is regardless of the product and regardless of the sender of the ICSRs.</p> <p>For the examples on paracetamol, both companies A and B will have access to level 2A and 2B for the cases where paracetamol is coded as suspect/interacting. Moreover, Company A will have level 3 access for the cases they have sent and Company B will have level 3 access for the cases they have sent. For the MLM cases, company A and B will get also level 3 access.</p> <p>Please note that the level 2B 'request' is automated in the system (EVWEB). Companies will have to select the reason for the request and confirm their agreement with the confidentiality undertaking. These steps are fully integrated in EVWEB and no stand alone or separate request has to be submitted to the EMA.</p>
2.23 (new)	<p>Will the ICSR batch download functionality only include ICSRs with an active substance for which a MA is hold in EEA but exclude all ICSR submitted by another MAH or by the MAH itself?</p>	<p>ICSR export function will exclude all the ICSRs submitted by their own organisation. It will however include all ICSRs submitted by any other organisation that matches the active substances for which they hold an EEA MA.</p>

Reference	Question	Answer
2.24 (new)	Once we have submitted in EVWEB using manual data entry, will the submission be in R3 format? - so this means if we move to gateway submission in the future the submission must be R3 too, as we cannot go back?	EVWEB will create E2B (R3) messages only. If you then implement a pharmacovigilance system that only supports E2B (R2) submissions this will mean that follow-up submissions will be in the less well-structured E2B (R2) format. Organisations are requested not to do this as this reduces the quality of the information between versions of an ICSR
2.25 (new)	Which active substances / products' information will we be able to access as MAH in the Levels 1 / 2A / 2B / 3?	The details of what information will be displayed at Level 1 and Level 2 are described in the EudraVigilance Access policy http://www.ema.europa.eu/ema/pages/includes/document/open_document.jsp?webContentId=W_C500218300 <u>As a quick summary:</u> Level 3 gives full access to the information as submitted Level 2 gives the verbatim substance and product information even if unrecoded Level 1 gives access to the product name for CAPs and substance name for products authorised through other procedures and will give no access to unclassified product and substance information e-Learning course is here: https://www.youtube.com/watch?v=WfuogTpCFWM&feature=youtu.be
2.26 (new)	How can Narratives be downloaded? Do we need to take one of the training sessions in person to get access to Narratives (Level 2B?)	Access to Level 2B is granted by the QPPV or deputy QPPV within your organisation. The following eLearning course shows how to make a Level 2B request: https://www.youtube.com/watch?v=huVGOfhx9Ug

Reference	Question	Answer
2.27 (new)	Can you confirm that ICSR downloaded on active substance level will only include ICSRs sent to EMA by NCAs and not include ICSRs from other MAHs for the same active substance?	The EudraVigilance access Policy gives access to all EEA data regardless of the original sender.
2.28 (new)	Is the confidentiality agreement to access case narratives a one-time process or does it has to be signed for every request?	Each request requires the confirmation of the confidentiality undertaking.
2.29 (new)	Some EEA agencies have stated that they will be forwarding cases to EV in local language. Can you confirm that all data fields in EV will be in English with the exception of E.i.1.1a Reaction/Event as Reported by the Primary Source in Native Language and H.5.r Case Summary and Reporter's Comments in Native Language (the latter of which would not be available to MAHs anyway via EV download with level 2A access).	The ICSRs will be made available to MAH as reported to EudraVigilance and in line with the EudraVigilance Access policy
2.30 (new)	Is it possible to exclude ICSRs with other MAHs tradenames from ICSR download for a specific active substance?	No, the information is matched against active substances.
2.31 (new)	If a narrative is downloaded via L2B access is it allowed including this in the company safety database?	This is the choice of the MAH concerned; the MAH will need to ensure that EU data protection legislation is adhered to when storing this data in global systems.

Reference	Question	Answer
2.32 (new)	Regarding EVWEB, Will it be possible to download the ICSRs by sorting according to country of occurrence?	A filter for Primary source country is available in EVWEB.
2.33 (new)	During ICSR Download from the EudraVigilance, will only products specific to the company of the person logged into EudraVigilance be downloaded if no other settings are selected?	The ICSR download is linked to the Organisation Headquarter ID, only users registered under the HQ can make L2 download requests and it will be for all products in the XEVMPD associated with that HQ.
2.34 (new)	Can you precise if nullflavor will be used in ICSRs from EVWEB to mask date values (i.e. date of batch transmission) or UCUM values?	The EU and ICH implementation guides indicate for which fields and what types of nullflavor are permitted.
2.35 (new)	Will all elements not available for level 2.A users will be masked in ICSRs by Nullflavor?	In most situations the data elements will not be populated in the XML if no access is permitted. If a field is mandatory according to the XSD schema a nullflavor will be used.
2.36 (new)	<p>Can we copy and paste from EVWEB? We anticipate a low volume so I am trying to find a bridging manual work around without having to validate the xslt converter.</p> <p>Import into EVWEB? WebSpace? Is this part of EVWeb interface? So: export from EVWEB, import into WEBSpace and chose to see as RTF or HTML? Where can I find information on this?</p>	<p>E2B (R3) files can be imported into the EVWEB workspace and can then be printed in human readable formats.</p> <p>Please see the EVWEB user manual for more details: http://www.ema.europa.eu/ema/pages/includes/document/open_document.jsp?webContentId=W C500229855</p>

Reference	Question	Answer
2.37 (new)	Will ICSRs be re-routed as single ICSR messages only or can we expect to receive messages with multiple ICSRs?	ICSRs will be re-routed individually as single XML files.
2.38 (new)	Will EMA follow-up on missing ACKs on re-routed ICSRs? Incl. after one or more resubmissions?	<p>The EU Implementation Guide has been updated to capture the retries that will be attempted; the following is proposed:</p> <p>“NCAs should return acknowledgements for rerouted ICSRs within 48 hours of the initial receipt. If no acknowledgement is received within 48 hours, EudraVigilance will automatically resubmit the re-routed ICSRs.”</p> <p>First submission is 48 hours; second attempt is 24 hours third attempt is 24 hours. If not it is 6 days before service desk contacts the NCA EudraVigilance will resubmit ICSRs up to a maximum of three attempts following the initial re-routing if no acknowledgement has been returned.</p> <p>After the maximum number of resubmissions has been reached, the NCA will be contacted to confirm if they are experiencing technical issues.”</p>
2.39 (new)	Will current MedDRA versions be accepted in the new XCOMP environment? And will XCOMP be updated with every MedDRA release?	Yes, current version and one previous version (20.0 and 19.1) and XCOMP will be updated with every MedDRA release.
2.40 (new)	How will MAHs be notified that an ICSR sent to EV is merged into a "master case"?	Master cases will be made available to MAHs through the download ICSRs function
2.41 (new)	Are the re-routing rules from EV to NCA considering transmission date or receipt date?	<p>Re-routing is based on the primary-source country, further details are available in the EU Implementation guide:</p> <p>http://www.ema.europa.eu/ema/pages/includes/document/open_document.jsp?webContentId=WC500165979</p>

Reference	Question	Answer
2.42 (new)	Will an MAH be able to download an ICSR coming from an ATU program running in France concerning an Active substance not yet granted a licence but maybe reportable to FDA?	If a product does not have a valid marketing authorisation approved in the EEA access will not be provided according to the EudraVigilance access policy
2.43 (new)	What is the criteria allowing EMA to identify a MAH product? The Owner identifier/registration organisation ID? The MAH Code? The MAH Name?	Entries in the XEVMPD through the use of the field Owner HQ identifier are used to establish the link between the logged on user/organisation and what ICSRs they have L2 access.

Reference	Question	Answer
2.44 (new)	<p>If an MAH identifies case reports under the signal detection process, that requires access to the case narrative, they will be able to retrieve the ICSRs from the EVWEB ICSR export screen using the filter Level 2B – please confirm that the download process will bypass the automatic removal of ICSRs cases sent to EV by the MAH in question (as per NCA case download)?</p> <p>If one or many of the ICSRs retrieved under level 2B access needs to be added to an MAH’s own safety database (because the ADR was missing for example), are there any issues for adding the case narrative component from these ICSRs to the MAH’s database ? (it is stipulated that for the NCA downloads, case narratives will be stripped out for PII considerations)</p> <p>If it is a missing ICSR that requires submitting to other non-EEA Regulatory Agencies and/or Licence partners, we may end exposing the original case narrative downloaded from EudraVigilance – does the Agency have any concerns on this action?</p>	<p>1) L2B requests require that the requester enters the worldwide case ID(s) for the ICSR(s) required, same sender (Level 3) ICSRs will be excluded from such requests as these WW case IDs should be in the requester’s own database and therefore there is no need to request them.</p> <p>However, if the requester wishes to view their own cases in EudraVigilance this can be done through a search for the case in the ICSR search section of EVWEB, from there the requested can view the whole case without having to complete the reason for the request and data protection obligation form.</p> <p>2) The MAHs will need to ensure that European Data protection obligations are applied to any European data made available to non-EEA regulatory bodies or other organisations</p>

Reference	Question	Answer
2.45 (new)	If we see that upon download not all ICSRs get created as R3 ICSRs upon creation – what action should an MAH undertake to report this issue to EMA given we are not able to identify the specific ADR (NB. I did see this during the pilot testing)	The ICSR download function automatically excludes same sender (L3) ICSRs from the download.
2.46 (new)	Is it possible to extract for one high level substance group and for one signal all corresponding narratives? (level 2B) (by batch)	Yes. Level 2B requests can be made by entering a list of worldwide unique case identifiers for which the corresponding ICSRs can be downloaded in one zipped file.
2.47 (new)	Is L2B access (EVWEB) for subcontractors restricted to a limited period of time?	The EU QPPV and trusted deputy will have the ability to grant and remove a user's Level 2B access. User access permissions are managed by the EU QPPV/Deputy QPPV through the secure area of EudraVigilance under "manage your profile"
2.48 (new)	The agency cases that the MAH will retrieve in EudraVigilance will have their narrative in English? Or in the local language of the case?	The EMA will not be translating any cases. The narrative, which is only available with level 2B access or for MLM cases, will be in whatever language it was sent to EudraVigilance. MLM cases always have the narrative in English.

Reference	Question	Answer
2.49 (new)	<p>In relation to the search of cases in EVWEB using the new system.</p> <p>We would appreciate some guidance on the following scenario: a MAH had recently obtained an approval for a new indication with the corresponding new dosing and dosage form.</p> <p>The active substance that has already been approved some time ago. Therefore, it is possible that performing a cases search only using the name of the active substance, it will return on an elevated number ICSR items and most of them not applicable for the referred new indication/medicinal product.</p> <p>Please clarify if it would be possible to narrow this "active substance search" with the help of the following filters as "indication for use" and/or "new dosage form" and "dosing" characteristics in order to make a difference in reference to the rest of medicinal products containing the same "active substance"?</p>	<p>The download function is based on the EudraVigilance Access Policy L2A. Access is based on the active substance for medicinal products, for which a MAH holds a marketing authorisation.</p> <p>The dosage form field in ICSRs is currently a free text field and therefore a filter would be an unreliable way of identifying specific products. The indication stated on ICSR is captured as reported by the primary source which may not match the MedDRA terms of licenced indication; it is also therefore unreliable to trust as a filter.</p> <p>The country of the primary source can however be used to exclude countries where a product is not available on the market, however it should be noted that a patient is still able to obtain medicinal products by crossing borders.</p>
2.50 (new)	<p>Which format are Narratives downloaded? Excel, Word, XML?</p>	<p>The narratives will be exported in E2B(R3) format</p>

Reference	Question	Answer
2.51 (new)	If I understand correctly, EMA is no more re-routing ICSRs from NCAs to MAHs. If MAH is going to retrieve the ICSRs sent to EV from all NCAs, will it be still mandatory to send ACKs messages?	MAHs should not send acknowledgements for ICSRs downloaded from EudraVigilance
2.52 (new)	If case was submitted to a NCA prior to 22 November 2017 and needs to be nullified after 22 Nov, should the nullification be sent to the EMA?	For post-authorisation ICSRs the nullification should be sent to EudraVigilance, for clinical trial cases previously sent to an NCA the nullification should be sent to the NCA
2.53 (new)	Currently, we receive the cases by brand name from Health Authorities (i.e. Spanish Health Authorities). From 22-Nov-2017, we should upload the cases from EudraVigilance. If the brand name is not mentioned in these cases, should we assume that we are the owner of these products?	Yes, if there is no brand name mentioned in a case & you market the product in that territory, then you cannot exclude ownership & should assume that the case may be related to your product.
2.54 (new)	Please confirm that the ICSR form will only show case narratives for the MAH originated ICSRs, for non-MAH originated ICSRs you need to request case narratives from EVWEB using level 2b access?	ICSR forms level 1 and 2a do not contain the narrative. The narratives are provided in the ICSR form level 3 and in level 2b access in EVWEB. For more information about the ICSR form, please consults the ICSR form manual http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2017/06/WC500229803.pdf

Reference	Question	Answer
2.55 (new)	Is it possible to copy & paste WWID's from the line listing (EVDAS) where case narratives are not visible and thereby need to be requested under level 2b from EVWEB?	It is possible to copy and paste WW case IDs one by one, delimiters need to be used when pasting a list of case IDs. Further guidance will be provided in the near future.
2.56 (new)	Will the EVWEB view in production open in internet explorer?	The supported browsers to be used to access EVWEB in production as of November 2017 will be: Google Chrome, Internet explorer and Mozilla Firefox.
2.57 (new)	Is there a limitation of numbers that the QPPV can designate to have Level 2b access from the EV registration screen? Is this number separate to those people registered as EVDAS scientific role?	There is no limit for the number of users the QPPV can designate to have level 2b access, it is just a user permission. This is a separate permission for the EVWEB interface only; it has no connection to EVDAS roles.
2.58 (new)	Please confirm the pre-requisite that a person NOT registered for EVDAS scientific can still have Level 2b access providing they are registered in EV at HQ level?	This is a separate permission for the EVWEB interface only and requires that the user is registered at HQ level
2.59 (new)	How will this work with regards to QPPV oversight and accessing EVWEB to download ICSRs with case narratives – will the prompt screen still appear upon request for the user to confirm that the download is for the purposes of signal detection activities?	The individual user that has been granted L2B access by the QPPV will themselves have to agree to the confidentiality undertaking and also provide the reason for the request

Reference	Question	Answer
2.60 (new)	<p>In tests files loaded from EVWEB test module there is no batch number (N.1.2) available and the date of batch transmission (N.1.5) is masked by a nullflavor, so they had to be manually added into the files in order to be processed in the database.</p> <p>Will it be the same in production environment?</p>	<p>The access policy does not give access to these fields of the original data, therefore they are currently not provided.</p> <p>This request is being reviewed and the generation of automated text to populate these fields is being planned to support the upload process by MAHs.</p>

3. Medical Literature Monitoring

Reference	Question	Answer
3.1	Will the MLM list of substances stay the same or change?	The MLM list of substances monitored by the Agency remains unchanged.
3.2	Presumably the access will still be linked to XEVMPD data. One of the eLearning videos said this would be updated each night—is that right?	All MAHs already have, and will continue to have, full access to all MLM cases for substances that the Agency is monitoring and for which the company holds a marketing authorisation in the EEA.
3.3	Can the MAH continue to use their XML filters to retrieve valid ICSRs?	The MAH will need to set up a new filter.

Reference	Question	Answer
3.4 (new)	<p>It was specified in the module “Medical literature monitoring by EMA (EV-M7)”, that we can access to the MLM cases either via Single case downloading, General bulk downloading, or MLM bulk downloading.: For the “Single case downloading”, we have to enter the reference of the case in order to download a single MLM case.</p> <p>So normally we should be aware of the case previously? So, the query should be already done via ICSR download?</p> <p>So, what is the real interest of the “Single case downloading”?</p> <p>What is the interest of downloading MLM cases via General bulk downloading?</p> <p>We could download them via “MLM bulk downloading”, in this way we will only have the MLM cases without the other cases that were submitted to the agency via HCP/patient. Could you please clarify this point?</p>	<p>Since different stakeholders have different requirements, the Agency is making various methods of accessing the MLM cases available. You will need to decide which method is most convenient for you.</p>

4. Guideline on good pharmacovigilance practices: Module VI – Management and reporting of adverse reactions to medicinal products

Reference	Question	Answer
4.1	Should literature articles always be provided with a case, or is this only on request?	<p>Copies of literature articles do not need to be routinely submitted. A copy of the article should only be submitted upon request as stated in GVP Module VI, Chapter VI.C.6.2.3.2 Suspected adverse reaction reports published in scientific literature:</p> <p>“Upon request of the Agency, for specific safety review, a full translation in English and a copy of the relevant literature article shall be provided by the marketing authorisation holder that transmitted the initial report, taking into account copyright restrictions [IR 28(3)].</p>
4.2	Can an initial report be submitted as an amendment e.g. if a case is classified as ‘invalid and not submitted, but on further review found to be valid (with no new information received) could this be submitted as an amendment or would it be a late case?	<p>Amendment reports apply to valid ICSRs which have already been submitted to EudraVigilance. In this example the report was initially considered non-valid and upon further review found to be valid (with no new information received).</p> <p>The valid ICSR should be submitted as initial report. The clock for the submission starts as soon as the information containing the minimum criteria has been brought to the attention of the organisation; i.e., when the case was initially received.</p> <p>For further reference:</p> <p>GVP VI Chapter VI.B.7, Submission of individual case safety reports (ICSRs) states the following:</p> <p>“The clock for the submission of a valid ICSR starts as soon as the information containing the minimum criteria has been brought to the attention of the national or regional pharmacovigilance centre of a competent authority or of any personnel of the marketing authorisation holder, including medical representatives and contractors. This date should be considered as day zero.”</p>

Reference	Question	Answer
4.3	If a follow-up is required by a MAH on a case that was submitted to EudraVigilance by an NCA, does the MAH follow-up directly with the NCA or with EudraVigilance?	GVP VI Rev 2 Chapter VI.C.2.2. Responsibilities of marketing authorisation holder in EU states the following: "For ICSRs made accessible to marketing authorisation holders from the EudraVigilance database in accordance with REG Art 24(2) and in line with the EudraVigilance access policy, the routine request for follow-up by the marketing authorisation holders is not foreseen. If the follow-up of an ICSR is necessary for a specific situation, a justification should be provided with the request, which should be addressed directly to the sender organisation of the ICSR."

Reference	Question	Answer
4.4	<p>With the introduction of null flavour data elements in ICH E2B (R3), what is the Agency's expectation on submitting follow-up report when the follow-up query is sent after initial report submission?</p> <p>For example, if a report was initially submitted with a null flavour data element response of UNK, NI or NASK (per company default) then MAH updates the responses to ASKU after the follow-up query is sent. Is there an expectation for the MAH to submit follow-up reports to indicate all these null flavour field responses have now been changed to ASKU? Would this follow-up submission be considered "Amendment"?</p>	<p>The batch number for biological medicinal products is one of the main data elements, where the outcome of the follow-up is important to be notified.</p> <p>For example, an ICSR should be submitted as amendment report to EudraVigilance with the applicable null flavour (UNK) where the information (e.g. batch number of a vaccine) was asked but the primary source did not respond to the request for information</p> <p>Where the information (e.g. batch number of a vaccine) is asked for and is provided by the primary source, a follow-up should be submitted to EudraVigilance based on this new information. Where the primary source confirms that the information is not available, the applicable nullflavor (ASKU) is also to be submitted as follow-up.</p> <p>For reference please also see :</p> <p>GVP VI Rev 2 App VI.1.2: Follow-up of ICSRs by competent authorities in Member States with involvement of marketing authorisation holders. <i>Step 11.2: MAH to "Inform NCA that it was not possible to obtain follow-up information."</i></p> <p>And GVP VI Rev 2 Chapter VI.B.7.3, Amendment report:</p> <p>"There may be instances, where a valid report which has already been submitted may need to be amended for example when, after an internal review or according to an expert opinion some items have been corrected, (such as adverse event/reaction terms, seriousness, seriousness criteria or causality assessment) but without receipt of new information that would warrant submission of a follow-up report. (...) These submissions are considered as amendment reports."</p> <p>For further information on the use of nullflavor refer to the EU ICSR Implementation Guide (chapter I.C.3.7 Usage of nullflavor flags)</p>

Reference	Question	Answer
4.5	If we do not have permission to follow up, which null flavour should be used? Where FU is received and a null favour is updated to actual new information, is this the only time you would expect a FU report to be submitted? Or should this be done regardless of what the null flavour field is updated to e.g. No Information?	<p>The ICSR should be created or updated in accordance with the data that has been initially provided and received. See question 4.4.</p> <p>No permission to F-UP, UNK (“A proper value is applicable, but not known”), or NI (“No information whatsoever can be inferred from this exceptional value”) are example of nullFlavors that may be used.</p> <p>From GVP VI Chapter VI.C.6.2.2.7. Follow-up information: “NCAs and MAHs “should submit follow-up ICSRs if significant new medical information has been received. Significant new information relates to, for example, a new suspected adverse reaction, a change in the causality assessment, and any new or updated information on a case that impacts on its medical interpretation. Therefore, the identification of significant new information requiring to be submitted always necessitates medical judgement. (...)”</p> <p>For further details see also question 4.4.</p>
4.6	What are the reporting and download rules of ICSRs after go-live of the new EV system for the below scenario?	Please refer to the answers as provided in Figure 1. Response to question ID 4.6.

Figure 1. Response to question ID 4.6

	Scenarios	ICSR reporting – current state	Simplified reporting – post 22 November 2017	EVWEB ICSR download
a)	<p>Both companies have marketing authorisations in the EU and each handles their reporting.</p>	<p>Both partners report to the individual countries in the EU where they are the MAH;</p> <p>Scenarios for reporting to EudraVigilance:</p> <p>Partners both report to EudraVigilance for countries outside the EU or</p> <p>Partner reports to EudraVigilance in countries outside EU on behalf of the other company</p>	<p>Is it OK for both partners to report to EudraVigilance or should one company do this on behalf of the other? (Or is either OK?)</p> <p>Answer - The partnership agreement should clearly define which party performs reporting to EudraVigilance. This should also be clearly documented in the pharmacovigilance system master files (PSMF) of both parties.</p> <p>In such situations where an agreement is in place one party can perform the reporting.</p> <p>If no agreement is in place both parties can report. However it is strongly encouraged that the same worldwide unique case identifier is used.</p>	<p>Should one partner download (helps avoid duplication) or should both companies download?</p> <p>Answer - For downloading of data from EudraVigilance it is up to each organisation how they wish to organise themselves for reporting obligations outside the EU and for performing data analysis.</p> <p>However, it should be noted that ICSRs submitted by one party will form part of the downloads made by the other company as the ICSR export only excludes ICSRs made by the same headquarter sender.</p>
a)	<p>Both companies have marketing authorisations in in the EU but market in different Member States and one partner reports on behalf of the other.</p>	<p>One company reports all cases on behalf of the other</p>	<p>Can the partner continue to report on behalf of the organisation?</p> <p>Answer - See above for scenario a)</p>	<p>As above</p> <p>Answer - See above for scenario a)</p>

	Scenarios	ICSR reporting – current state	Simplified reporting – post 22 November 2017	EVWEB ICSR download
c)	One company reports on behalf of the partner which holds a EU marketing authorisation; note the company is not a MAH in any EU country	The company reports on behalf of the partner.	<p>Can the organisation continue to report on behalf of the partner?</p> <p>Answer – From a technical point it is recommended to establish a virtual affiliate under the MAH so that all the cases can be submitted by the other party under the MAH’s Headquarter ID.</p> <p>If this is not followed, the ICSRs will appear for EudraVigilance download by the MAH when they perform an export.</p>	<p>Partner as the MAH to access and download the ICSRs, or can we do that for them through delegation?</p> <p>Answer - Only the MAH has access to the data. Another party would only have access if the MAH gives a user from the other party access to EudraVigilance, this would give the user access to all the MAH’s ICSRs for all their products.</p>

Reference	Question	Answer
4.7 (new)	Does the EMA require a deletion notification for a ICSR originally reported to a NCA only prior to 22 Nov 2017 if it is determined after 22 Nov 2017 that a deletion is required?	Nullifications for ICSRs that were previously sent to NCAs should be submitted to EudraVigilance after 22 November

Reference	Question	Answer
4.8 (new)	<p>What is the expectation of the EMA for an ICSR originally reported to a NCA only prior to 22 Nov 2017 and downgraded due to follow-up information received to no longer require submission "by itself" after 22 Nov 2017?</p> <p>Should such downgrades be directed to EMA after 22 November 2017?</p>	<p>Follow ups that need to be submitted in accordance with the requirements specified in GVP module VI should be submitted to EudraVigilance after 22 November</p>
4.9 (new)	<p>We understand that cases exported from EV will not have narratives.</p> <p>When we need to report these cases outside of Europe, is it expected that we write our own narrative for the cases, or is it acceptable to request the full case narratives (L2B access?) for all cases that we will need to report elsewhere?</p>	<p>Under the conditions of the access policy (Level 2B) requests for the case narrative should only be made for in the context of reviewing a signal.</p> <p>The EMA is not in a position to advice on non-EEA requirements for creating and provision of case narrative.</p> <p>Please note that EU data protection legislation applies to all EEA ICSRs that are being transmitted to organisations located outside of the EEA.</p>
4.10 (new)	<p>Regarding Module VI: Amendment is a significant data clean up, with an initial receipt date equal to last significant information.</p> <p>Do amendments must be included into compliance metrics as for significant follow ups?</p>	<p>Serious and non-serious cases which have already been submitted to EudraVigilance may need to be amended when, after an internal review or according to an expert opinion some items have been corrected, without receipt of new information that would warrant for the submission of a follow-up report.</p> <p>Where the amendment significantly impacts on the medical evaluation of the case, an ICSR should be resubmitted and information on the amendment should be explained in the case narrative.</p> <p>For example, an amendment of the MedDRA coding due to a change in the interpretation of a previously submitted ICSR may constitute a significant change and therefore should be resubmitted as amendment report.</p>

Reference	Question	Answer
4.11 (new)	Where are the current guidelines specifying the revised reporting guidelines for MAHs to report ICSRs for serious and non-serious cases to the EMA after November 22nd?	<p>Information is already provided in chapter VI.C.4 of GVP VI Rev 1.:</p> <p>Once the functionalities of the EudraVigilance database specified in Article 24(2) of Regulation (EC) No 726/2004 are established, the following requirements, detailed in Articles 107(3) and 107a (4) of Directive 2001/83/EC, shall apply within 6 months of the announcement by the Agency to valid unsolicited and solicited ICSRs reported by healthcare professionals and non-healthcare professionals.</p> <p>This is independently of the condition of use of the suspected medicinal product and of the expectedness of the adverse reaction.</p> <p><u>a. Serious ICSRs</u></p> <ul style="list-style-type: none"> • Marketing authorisation holders shall submit all serious ICSRs that occur within or outside the EU, including those received from competent authorities outside the EU, to the EudraVigilance database only. • Competent authorities in Member States shall submit to the EudraVigilance database all serious ICSRs that occur in their territory and that are directly reported to them. <p><u>b. Non-Serious ICSRs</u></p> <ul style="list-style-type: none"> • Marketing authorisation holders shall submit all non-serious ICSRs that occur in the EU to the EudraVigilance database only. • Competent authorities in Member States shall submit all non-serious ICSRs that occur in their territory to the EudraVigilance database.

5. Reporting to National Competent Authorities in the EEA

Reference	Question	Answer
5.1	Will MAHs receive EU ICSRs reported by NCAs ONLY from the EMA?	<p>For the detailed legal provisions on the simplified reporting rules please refer to the announcement of the EMA Management Board on the confirmation of full functionality of the EudraVigilance database and GVP Module VI Chapter VI.C.2.1, Responsibilities of Member States which states the following:</p> <p>“Each Member State shall have in place a system for the collection and recording of unsolicited and solicited reports of suspected adverse reactions that occur in its territory and which are brought to its attention by healthcare professionals, consumers, or marketing authorisation holders [DIR Art 101(1) and 107a(1)].</p> <p>In this context, competent authorities in Member States shall establish procedures for collecting and recording all reports of suspected adverse reactions that occur in their territory [IR Art 15 (2)]. Marketing authorisation holders shall submit ICSRs to EudraVigilance in accordance with the provisions set out in Dir Art 107(3) and further detailed in VI.C.4.”</p> <p>In addition, Article 107a, paragraph 4 states the following:</p> <p>“Member States shall, within 15 days following the receipt of the reports of serious suspected adverse reactions referred to in paragraph 1, submit the reports electronically to the EudraVigilance database. They shall, within 90 days from the receipt of reports referred to in paragraph 1, submit reports of non-serious suspected adverse reactions electronically to the EudraVigilance database. Marketing authorisation holders shall access those reports through the EudraVigilance database”.</p>

Reference	Question	Answer
5.2	With reference to question 3.1: What about local systems like PV Networks in Italy?	<p>The Italian Medicines Agency will not receive any more the Italian ICSRs directly by the MAHs because they shall submit ICSRs to EudraVigilance in accordance with the provisions set out in Dir Art 107(3) and further detailed in VI.C.4."</p> <p>Suspected ADR reporting forms for healthcare professionals and consumers are available on the website of AIFA and a reporter can send the filled ADR reporting form directly to the Responsible of Pharmacovigilance (RPhV) of the local structure to which the reporter belongs. The reporter can find the addresses of the RPhV to this link http://www.agenziafarmaco.gov.it/it/responsabili. The RPhV is the user responsible for the data entry process in the National Pharmacovigilance Database (NPhVD) and after few days all cases (serious and non-serious) registered in the NPhVD are and will be automatically transmitted and uploaded in EV.</p> <p>The online reporting modality has also been made available to the public at this link www.vigifarmaco.it.</p> <p>Healthcare professionals and consumers may also report adverse events and/or medication errors to the MAHs. If a MAH receives an ADR report, it will have to transmit the report only to EV as specified by regulations.</p> <p>We think to leave the visibility of data in the NPhVD to the MAHs (only for their products) in order to handle the duplicates and/or follow-up.</p>
5.3	Do Spanish non-serious cases require a Spanish narrative?	<p>Where suspected adverse reactions are reported by the primary source in narrative and textual descriptions in an official language of the Union other than English, the original verbatim text and the summary thereof in English shall be provided by the marketing authorisation holder [IR 28(4)].</p> <p>In practice, for ICSRs reported in Spain, the original verbatim text reported by the primary source in Spanish should be included in the ICSRs. This is applicable to serious and non-serious cases. For non-serious cases there is no need to create a case narrative if not provided by the primary source.</p>

Reference	Question	Answer
5.4 (new)	<p>Does EMA plan to include additional national requirements and specialties within the E2B file for submission to EMA into official EMA guidelines, e.g. ICSRs occurring in Spain to contain a Spanish narrative?</p> <p>As we do not have reporting obligations to local authorities any longer we expect the EMA requirements to be the driving set of rules for a compliant E2B file.</p>	<p>In accordance with Article 28 (3)(m) of the Commission Implementing Regulation (EU) No 520/2012, a case narrative shall be provided, where possible , for all cases with the exception of non-serious cases.</p> <p>With regard the provision of information in the local language the following requirement from Article 28 (4) of the Commission Implementing Regulation (EU) No 520/2012 applies: Where suspected adverse reactions are reported by the primary source in narrative and textual descriptions in an official language of the Union other than English, the original verbatim text and the summary thereof in English shall be provided by the marketing authorisation holder.</p> <p>In practice, the original verbatim text reported by the primary source in an official language of the Union other than English should be included in the ICSR, if it is requested by the Member State where the reaction occurred or by the Agency. The ICSR should be completed and submitted in English if not otherwise requested.</p> <p>The case narrative in the local language and the summary thereof in English should be provided in serious ICSRs submitted to EudraVigilance if requested by the competent authority of the Member State where the reaction occurred. If not otherwise requested, the narrative should be provided in English.</p>

Reference	Question	Answer
5.5 (new)	Does the EMA expect that ICSRs provided by NCA to EMA be made available in English language in all E2B free text fields?	<p>With regard the provision of information in the local language the following requirement from Article 28 (4) of the Commission Implementing Regulation (EU) No 520/2012 applies: Where suspected adverse reactions are reported by the primary source in narrative and textual descriptions in an official language of the Union other than English, the original verbatim text and the summary thereof in English shall be provided by the marketing authorisation holder.</p> <p>In practice, the original verbatim text reported by the primary source in an official language of the Union other than English should be included in the ICSR, if it is requested by the Member State where the reaction occurred or by the Agency. The ICSR should be completed and submitted in English if not otherwise requested.</p> <p>In accordance with Article 28 (4) of the Commission Implementing Regulation (EU) No 520/2012, Member States may report case narratives in their official language(s).</p> <p>For those reports, case translations shall be provided when requested by the Agency or other Member States for the evaluation of potential signals. For suspected adverse reactions originating outside the EU, English shall be used in the ICSR.</p>
5.6 (new)	What are the EMA expectations for translation of ICSRs received at NCA, e.g. could the MAH be involved into translation of ICSRs originally reported to a NCA?	<p>In accordance with Article 28 (4) of the Commission Implementing Regulation (EU) No 520/2012, Member States may report case narratives in their official language(s). For those reports, case translations shall be provided when requested by the Agency or other Member States for the evaluation of potential signals. For suspected adverse reactions originating outside the EU, English shall be used in the ICSR [IR 28 (4)].</p>

6. Guideline on good pharmacovigilance practices: Module IX - Signal Management

Reference	Question	Answer
6.1 (updated)	What is the frequency of signal detection using EudraVigilance?	Please refer to revision 1 of GVP IX, which is being finalised and will be published in advance of the go-live.
6.2	Are there recommendations for thresholds when a more detailed analysis/discussion should be done?	<p>The eRMR provides the EudraVigilance data and the disproportionality analysis, but it does not state which DEC's should be further analysed.</p> <p>MAHs should exercise scientific rationale when deciding which DEC's from the eRMR deserve further analysis. This should be based on the knowledge of the safety profile of the medicinal product (including closely related terms that are labelled), exposure, patient population, previous assessments etc.</p> <p>Statistical signal detection has to be complemented with clinical and scientific assessment and judgement as a SDR is not the same as a validated signal and there could be real safety signals that do not show as SDRs (~ 50% of the signals raised from EV data did not appear as SDRs).</p>
6.3	<p>Are there specific criteria for a risk-based approach?</p> <p>Is it sufficient to search the EV database only for specific drugs/active substances for which in the own signal detection process (using global safety database) signals were detected?</p>	<p>Article 18 of the Commission Implementing Regulation 520/2012 states that MAHs, NCAs and the Agency shall ensure the continuous monitoring of the EudraVigilance database with a frequency proportionate to the identified risk, the potential risks and the need for additional information.</p> <p>The risk-based approach therefore applies to the frequency for monitoring EudraVigilance. Please also see question 6.1 'What is the frequency of signal detection using EudraVigilance?'</p> <p>Using EudraVigilance to consult specific Drug Event Combinations for signal strengthening cannot be considered a 'continuous monitoring' of the database.</p>

Reference	Question	Answer
6.4 (updated)	<p>An MAH with numerous well established medicinal products approved will want to perform signalling using EVDAS in a six-month interval for these products.</p> <p>To distribute the workload and to avoid reviewing all medicinal products in the same month, these reviews are intended to get scheduled in a way that an equal number of medicinal products get reviewed each month based on eRMRs for six-month periods.</p> <p>Is there an expectation that the first review for each medicinal product starts with an eRMR for a period starting with the same month, i.e. June 2017 or is it acceptable to use an eRMR starting with June 2017 for a medicinal product reviewed in December, an eRMR starting with July for a product reviewed in January, and so on?</p>	<p>The request for flexibility is acknowledged.</p> <p>Further guidance on practical aspects of transitional arrangements for MAHs will be published closer to the start of the new process.</p>
6.5 (new)	<p>Regarding the expectation for the MAH to screen product information within EU for signals already potentially addressed: where can the MAH will find this information?</p>	<p>Please refer to revision 1 of GVP IX, which is being finalised and will be published in advance of the go-live.</p>

Reference	Question	Answer
6.6 (new)	When the signal notifications form used for a standalone notification will be available for the MAH? What kind of information should be provided in this form?	The standalone signal notification form is being finalised together with GVP IX revision 1 and will be made available before the new process for MAHs starts.
6.7 (new)	For a combination product, do you expect us to screen the products individually and then screen the combination product?	When a combination of substances is considered a unique active substance high level, routine signal detection in EudraVigilance can be performed using the combination. Nevertheless, safety information for the single ingredients may be relevant during the analysis of safety data related to the combination so MAHs may take the opportunities provided in EV to retrieve the data for other active substances, including single ingredients used also in combinations.
6.8 (new)	Based on the information published on the European medicines web-portal (see IX.C.8.), the signal was not recently addressed by (a) competent authority (ies) of (a) Member State(s) or by PRAC. What do you mean by "Recently"?	Please refer to revision 1 of GVP IX, which is being finalised and will be published in advance of the go-live.
6.9 (new)	Do you plan to adapt/update the PBRER format according to the new process of SD (sections dealing with signals)?	The availability of EudraVigilance for MAHs and the new signal management process does not modify the format and the PSUR process. The PSUR should contain all validated signals for which the evaluation is finished or ongoing at the PSUR DLP. This is regardless of the source of the signal or the actions taken with the signal. Data from EudraVigilance should be considered when preparing the PSUR as another source of safety information. As stated in the GVP Module VII, PSURs shall be based on all available data.

Reference	Question	Answer
6.10 (new)	Is it expected from MAHs of generic products to use eRMR/ EVDAS for signal detection and further tracking? OR EVDAS be used for validation only?	All MAHs without distinction shall monitor EudraVigilance data according to Commission Implementing Regulation (EU) No 520/2012. Please also refer to the information on transitional arrangements published on the Agency's signal management webpage http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000587.jsp&mid=WC0b01ac0580727d1b)
6.11 (new)	From an NCA perspective, what is the average number of signals per eRMR? a) Statistical? b) Potential? c) Validated?	EMA publishes every year the Annual Report on EudraVigilance for the European Parliament, the Council and the Commission. The 2016 annual report can be retrieved in the following link: http://www.ema.europa.eu/docs/en_GB/document_library/Report/2017/03/WC500224056.pdf The 2016 annual report states the following: "In 2016, the Agency's Signal Management Team reviewed in detail a total of 2,076 potential signals (i.e. drug-event pairs from screening of the EudraVigilance database, medical literature, information received from other regulatory authorities etc.) for substances included in centrally authorised medicinal products. Overall the major source of EMA potential signals in 2016 continues to be EudraVigilance, from which 82.7% of potential signals originated. The number of confirmed signals prioritised and assessed by the PRAC in 2016 was 94, compared with 102 in 2015. Of these 94 signals, 48 were validated by the Agency and 46 were validated by the MSs in the course of ongoing ADR reports monitoring through screening of reaction monitoring reports, ADR reports, medical literature and other safety data; overall 66% included data from EudraVigilance as their source." For further information on the EudraVigilance activities, please consult the 2016 annual report: http://www.ema.europa.eu/docs/en_GB/document_library/Report/2017/03/WC500224056.pdf
6.12 (new)	Please clarify what is meant by TME?	TME is described in the guideline 'Screening for adverse reactions in EudraVigilance' published in Dec 2016: http://www.ema.europa.eu/docs/en_GB/document_library/Other/2016/12/WC500218606.pdf

Reference	Question	Answer
6.13 (new)	Can you please confirm that MAHs have a grace period between 22 Nov and 22 Feb to fully implement their processes around signal detection with EVDAS?	Please refer to the information published on the Agency's signal management webpage (http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000587.jsp&mid=WC0b01ac0580727d1b)
6.14 (new)	Due to the enhanced collaboration between EMA and WHO, the EudraVigilance data will be included in VigiBase. Would it, therefore, be acceptable that the MAH monitors VigiBase instead of EudraVigilance to fulfil the request of monitoring EudraVigilance data?	Commission Implementing Regulation (EU) No 520/2012 explicitly requires that MAHs monitor the data available in EudraVigilance, not VigiBase. Of note, the transfer of data from EudraVigilance to VigiBase will only concern ADRs occurring in the EU and from 22 November 2017. The EudraVigilance access policy describes the levels of access for the different stakeholders. MAH can have access to level 2a (228 E2B data fields) and Level 2B (230 E2B data fields). WHO is provided with level 2C (134 E2B data fields).
6.15 (new)	Following publication of the EMA letter on the monitoring of the EudraVigilance database by marketing authorisation holders on 20-Jul-2017, could you please clarify whether for the one-year pilot period, all the MAHs of active EEA licenses for the active substances included in the 'List of medicinal products under additional monitoring' are required to monitor EudraVigilance and inform EMA/NCA of validated signals or whether this only applies for the MAHs of the products present in the 'List of medicinal products under additional monitoring' and for which the approved PI includes a black triangle?"	The pilot will concern all <u>active substances</u> included on the 'additional monitoring list' in force as of 22 November 2017. Please refer to the information published on the Agency's signal management webpage (http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000587.jsp&mid=WC0b01ac0580727d1b)

Reference	Question	Answer
6.16 (new)	How many days after a standalone notification, PRAC informs the QPPV about a signal "non- confirmation" or "confirmation"?	Please refer to revision 1 of GVP IX, which is being finalised and will be published in advance of the go-live.
6.17 (new)	How should we obtain the originator's labelling for reviewing for signal detection purposes? Will there be guidance?	Please refer to revision 1 of GVP IX, which is being finalised and will be published in advance of the go-live.
6.18 (new)	Are MAHs expected to re-validate non-confirmed signals? If yes, should they be sent to PRAC through one of the communications routes?	Please refer to revision 1 of GVP IX, which is being finalised and will be published in advance of the go-live.
6.19 (new)	Can we have an example of the EPITT?	EPITT is database used by EMA and NCAs to track information on various pharmacovigilance processes including validated signals. Information on signals assessed by PRAC is published on the Agency's website.
6.20 (new)	Would you know when the Standalone Form will be published?	The standalone signal notification form is being finalised together with GVP IX revision 1 and will be made available before the new process for MAHs starts.
6.21 (new)	Will we be able to see the reason for non-confirming a signal in the report sent to the QPPV including the confirmed and non-confirmed signals?	Please refer to revision 1 of GVP IX, which is being finalised and will be published in advance of the go-live.
6.22 (new)	Have you identify which products will be included in the pilot phase in EVDAS	Please refer to the information published on the Agency's signal management webpage (http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000587.jsp&mid=WC0b01ac0580727d1b).

7. Signal detection and use of the MAH pharmacovigilance queries dashboard in EVDAS

Reference	Question	Answer
7.1	Regarding the selection of the active substances to query the EVDAS reports, are MAHs able to select substances only for their own medicinal products?	<p>No. MAHs can select any active substance to retrieve eRMRs and line listings from EVDAS. This access is based on Level 1 access according to the EudraVigilance Access Policy. Different levels of access depending on the product for which the MAHs hold a marketing authorisation is provided for the ICSR form.</p> <ul style="list-style-type: none"> • ICSR form level 1 if the MAH does not have a product for the specific substance • ICSR form level 2a if the MAH has a product for the specific substance • ICSR form level 3 if the case has been previously submitted by the MAH and for the MLM cases. <p>Access to EudraVigilance data in EVDAS for MAHs is provided at the level of the 'active substance high level', which is the highest grouping in the hierarchy of the XEVMPD.</p>
7.2	Are MAHs able to view data in the EVDAS reports on only the MAH's product(s), or does the MAH view the data for all MAH's for the "active substance"?	<p>Access to EudraVigilance data in EVDAS for MAHs is provided at the level of the 'active substance high level'. EudraVigilance provides data based on all ICSRs submitted to the EudraVigilance Post-Authorisation Module (EVPM) by any organisation for the selected active substance, where the substance (corresponding medicinal product) is reported as suspect or interacting.</p> <p>The eRMR and line listings are based on level 1 access according to the EudraVigilance Access Policy and the output-fields are the same regardless of the substance and regardless of the MAH querying the database.</p> <p>When retrieving ICSR forms from the link provided in the case line listing, different levels of access (level 1, 2A and 3) as per the EudraVigilance Access Policy are provided depending on the MAHs and the medicinal products for which they hold a marketing authorisation in the EEA. (See question 7.1)</p> <p>The case line listing and ICSR form provide the reference to the world-wide unique case identifier to facilitate case reconciliation within the MAHs databases where necessary.</p>

Reference	Question	Answer
7.3	<p>Medicinal products are currently entered via an affiliate registration in our EudraVigilance set-up.</p> <p>For the purpose of retrieval of safety information from EudraVigilance, do the medicinal products automatically roll-up to the headquarter ID for an MAH?</p>	<p>The users registered with the headquarter organisation ID can have L2A/B access as this is based on the XEVMPD data, which is linked to a headquarter organisation ID.</p> <p>Affiliates therefore can only have L1 or L3 access.</p>
7.4	Can MAH users of EVDAS retrieve data for multiple active substances at the same time?	EVDAS users can select different active substances at the same time to retrieve data when using the fixed reference period eRMR, the line listing and the active substance grouping reports. The ad-hoc reference period eRMR only allows for the selection of one substance each time the report is run; this is to protect the performance of the system.
7.5	Can the users filter the data in EVDAS using MedDRA?	The MedDRA hierarchy including SMQs level 1 broad and narrow can be used to filter the data in the eRMRs and in the case line listings. The MedDRA prompt is not mandatory.
7.6	Which one is the best eRMR report to use when monitoring substances every two weeks?	<p>The eRMR allows for the continuous monitoring of the EudraVigilance database. For the best use of the eRMR, the frequency of monitoring should be in line with the eRMR reporting period, as the eRMR will highlight the new cases since the last review.</p> <p>To monitor substances every 2 weeks, the ad-hoc reference period eRMR report should be used. This report allows for the selection of the reporting period between 1 to 105 days.</p> <p>On the contrary, the fixed reference period eRMR is designed to monitor the substances every 6 months as this eRMR contains a default reference period of 6 months.</p>
7.7	Does the line listing retrieved from the hyperlink in the number of cases in the eRMR contain always the same cases as stated in the eRMR, even if the line listing is retrieved on a different day?	Users should always take into account that EVDAS is updated every night. The hyperlinks in the eRMR to retrieve the case line listings work even if the eRMR has been exported in Excel/PDF. By clicking on the hyperlinks, EVDAS runs the line listings 'in situ' and provides the data according to the most updated information in EVDAS. Therefore if users retrieve eRMRs and line listings on different dates, the number of cases may be different (e.g. if nullification and de-duplications have occurred).

Reference	Question	Answer
7.8	When calculating the Reporting Odds Ratio (ROR) in the eRMR, is the type of product (e.g. vaccines) taken into consideration for the calculations?	The ROR is provided for each of the drug-event combinations in the eRMR and does not take the type of medicinal products into account for the calculation. The ROR is calculated using as background parameters all the medicinal products and all the spontaneous suspected reactions reported to the EVPM. Reports from studies (observational from the EVPM and interventional clinical trials from EVCTM) are not included in the calculation of the ROR. The calculation of the ROR is described in the guideline ' screening of adverse reactions in EudraVigilance '.
7.9	Are the RORs for special populations calculated on all active substances?	<p>The fields provided in the eRMR are stable and the output contains always the same elements regardless of the substance.</p> <p>Statistical calculations of the ROR for paediatrics and geriatrics are always provided in the eRMR; this is per drug-even combination providing that ICSRs have been submitted within these populations to support the calculations. Statistical calculations of the ROR for special populations are described in the guideline 'screening of adverse reactions in EudraVigilance'.</p>
7.10	<p>What type of drug-event combinations MAHs should further analyse and review following the screening of the eRMR?</p> <p>Is the expectation that MAHs will always review special population statistics? Or products with no paediatric indication should paediatric SDRs be further analysed?</p>	<p>Statistical signal detection should always be combined with medical and clinical judgment and input. MAHs should decide which drug-event combinations should be further evaluated following the screening of the eRMR.</p> <p>This decision should be based, amongst others, on the knowledge of the medicinal product, identified risks, potential risks and missing information. GVP IX, GVP Addendum I and the guideline on 'screening for adverse reactions in EudraVigilance' provide general principles for signal detection.</p> <p>Regarding the SDRs for special populations, EVDAS calculates the relative RORs using the age reported in the ICSRs. SDRs in the paediatric population for medicinal products/substances without a paediatric indication may be highlighting safety issues related to the off-label use of the medicinal product in the paediatric population.</p>

Reference	Question	Answer
7.11	If we access cases that are not in the MAH database, is there an expectation that we will add the cases to the MAH database (if we determine they are the MAH's)?	MAHs should follow the established procedures when they receive information on a case that they are not aware of.
7.12	When selecting the active substance, can it be filtered by route of administration (e.g. topical, injection, oral, etc.)?	<p>EVDAS filters are described in detailed in section 'MAH pharmacovigilance queries dashboard' slides 42-101 of the eLearning module: EVDAS training for Marketing Authorisation Holders (EV-M5b).</p> <p>There is no filter for the route of administration. Information on the route of administration can be found in the outputs: eRMR (slide 151), Line listing (slide 156) and ICSR form (slide 165), described in the EVDAS training for Marketing Authorisation Holders (EV-M5b).</p>
7.13	Can we use the ad hoc reference period capability for our 6 month reviews instead of the fixed reference period?	Slide 84 of the eLearning module EVDAS training for Marketing Authorisation Holders (EV-M5b) , states that the reference period of the ad hoc eRMR is restricted to 3 months and 2 weeks in the past from the day the report is run. The users are therefore able to define the reference period as being as short as a single day or as long as 105 days. In other words users cannot get an eRMR with a reference period of 6 months using the ad hoc eRMR, they need to use the fixed reference period.
7.14	In the context of credential to be used to retrieve outputs from EVDAS, once an eRMR is exported, is it necessary to be registered with EVDAS to retrieve line listings via the hyperlink?	Yes, it is necessary to be registered into EVDAS to obtain the line listings associated with the eRMRs.
7.15	In the context of credentials to be used to retrieve outputs from EVDAS, once a line listing is exported, is it necessary to be registered with EVDAS to retrieve ICSR via the hyperlink?	<p>To retrieve the ICSR forms via the hyperlink in the case line listing, the EVDAS user can click on the hyperlink and access the individual case. To do so the EVDAS user also needs to enter the EVWEB credentials.</p> <p>Signal management teams, where experts do not have a EVDAS scientific user profile, can access ICSRs directly from EVWEB, for which they need to be also registered.</p>

Reference	Question	Answer
7.16	What documentation do MAHs need to have/keep with regards to the signal detection and management activities when monitoring EudraVigilance?	MAH need to retain documentation related to the management of signals including signal detection activities using EudraVigilance data; this should be in line with the pharmacovigilance procedures described in the MAH's PSMF.
7.17 (new)	When you download an eRMR, you can distribute to others who can see it for assessment but it seems they won't be able to click link to see line listing (i.e. would you need to go back to person with access to EVDAS?). When will we be able to test EVDAS platform and various process scenarios in the test environment?	In order the access data from EVDAS and retrieve line listings from the hyperlinks provided in the eRMR, the users must have credentials to use EVDAS. No EVDAS training environment will be available.
7.18 (new)	Question related to EVDAS: will there be any test or example system outputs prior to go-live (i.e. excel format eRMR) for configuring or testing systems for managing the data?	Outputs of EVDAS, eRMR's, Line listings and ICSR forms are fully described in the eLearning EVDAS training for Marketing Authorisation Holders (EV-M5b)
7.19 (new)	For generic drugs, do all the MAH should query EVDAS or only the MAH of the innovator drugs?	All MAHs without distinction shall monitor EudraVigilance data according to Commission Implementing Regulation (EU) No 520/2012.
7.20 (new)	Is it possible for a company to only use the statistical query in EVDAS and to stop to perform a statistical test in his own database?	MAHs should determine and decide the relevant processes and activities in order to comply with their pharmacovigilance obligations and the European legislation.

Reference	Question	Answer
7.21 (new)	When will the list of HLSA registered in EVDAS available for all MAHs?	This will be made available on 22 November 2017.
7.22 (new)	Question about " ADRREPORTS.EU portal" we can find information on reports of suspected side effects (also known as suspected adverse drug reactions) for authorised medicines in the European Economic Area (EEA). What if my product (NAP) is not there? Why is it not there? Should I contact EMA helpdesk?	Please contact EMA helpdesk (https://servicedesk.ema.europa.eu).
7.23 (new)	Will it be based on the companies XEVMPD products including formulation or just active ingredient?	Access to EudraVigilance data for MAHs is provided at the level of the 'active substance high level'. Following the analysis of the data, MAHs should consider the relevant information for the safety of their products.
7.24 (new)	Is there a test area available we can log into and have a look around and familiarise with EVDAS?	No EVDAS training environment will be available. Users can access EVDAS on 22 November 2017

Reference	Question	Answer
7.25 (new)	Can we run an eRMR on all active substance high levels or only the ones including an active substance for which we are MAH?	<p>Access to EudraVigilance data in EVDAS for MAHs is provided at the level of the 'active substance high level'. EudraVigilance provides data based on all ICSRs submitted to the EudraVigilance Post-Authorisation Module (EVPM) by any organisation for the selected active substance, where the substance (corresponding medicinal product) is reported as suspect or interacting.</p> <p>The eRMR and line listings are based on level 1 access according to the EudraVigilance Access Policy and the output-fields are the same regardless of the substance and regardless of the MAH querying the database.</p> <p>When retrieving ICSR forms from the link provided in the case line listing, different levels of access (level 1, 2A and 3) as per the EudraVigilance Access Policy are provided depending on the MAHs and the medicinal products for which they hold a marketing authorisation in the EEA.</p>
7.26 (new)	For a defined eRMR, for one High Level Active Substance, would it be possible de performs only the analysis on the indication/population/route of administration covered by the Marketing Authorisation of the concerned MAH?	<p>The eRMR will provide the number of cases (during the reporting interval and in total) per route of administration (when reported) for the DEC. This will take into account the three most frequent routes of administrations as reported.</p> <p>The eRMR will also provide the number of cases per drug-event combination when the route of administration has not been reported.</p> <p>This will be irrelevant for substances with only one authorised route of administration but more relevant for substances with several routes of administrations.</p> <p>This information should be put in the context of the number of cases during the period and cumulative</p>

Reference	Question	Answer
7.27 (new)	Training Module EV- M5b Jan 2017: Is a MAH able to view data in the eRMR for the MAH's product(s) only, or can the MAH view the data for all MAHs for the selected active substance (MAH's product), if there is more than one MAH for this substance?	<p>Access to EudraVigilance data in EVDAS for MAHs is provided at the level of the 'active substance high level'. EudraVigilance provides data based on all ICSRs submitted to the EudraVigilance Post-Authorisation Module (EVPM) by any organisation for the selected active substance, where the substance (corresponding medicinal product) is reported as suspect or interacting.</p> <p>The eRMR and line listings are based on level 1 access according to the EudraVigilance Access Policy and the output-fields are the same regardless of the substance and regardless of the MAH querying the database.</p> <p>When retrieving ICSR forms from the link provided in the case line listing, different levels of access (level 1, 2A and 3) as per the EudraVigilance Access Policy are provided depending on the MAHs and the medicinal products for which they hold a marketing authorisation in the EEA.</p>
7.28 (new)	<p>You informed us that EVDAS will be available from 22 November 2017.</p> <p>What will be the dates of the first fixed period e-RMR pre-generated by EMA? Will it be 01Jun2017-30 Nov2017?</p>	<p>EMA is currently evaluating different options; one option is to provide an eRMR on 22 November 2017 with a reference period from 1 May 2017 to 31 October 2017.</p> <p>Alternatively, an eRMR can be provided on 1 Dec 2017 covering the reference period from 1 June to 30 November 2017.</p> <p>These options will be confirmed in due course.</p>

Reference	Question	Answer
7.29 (new)	<p>Training Module EV-M5b Jan 2017: "plenty of different routes".</p> <p>A priori: If a product with several routes of administration, the 3 most frequent are presented. Could you please confirm?</p>	<p>The eRMR will provide the number of cases (during the reporting interval and in total) per route of administration (when reported) for the DECAs.</p> <p>This will take into account the three most frequent routes of administrations as reported.</p> <p>The eRMR will also provide the number of cases per drug-event combination when the route of administration has not been reported.</p> <p>This will be irrelevant for substances with only one authorised route of administration but more relevant for substances with several routes of administrations.</p> <p>This information should be put in the context of the number of cases during the period and cumulative.</p> <p>See as an example an extract from an eRMR:</p>
7.30 (new)	Can we have eRMR with zero signals?	<p>If the question is referring to Signals of Disproportionate Reporting (SDR), the answer is potentially yes.</p> <p>This may relate to medicinal products with a very low reporting rate of ADRs and for which the ADRs reported have been commonly reported for the rest of the substances in the EudraVigilance database.</p>
7.31 (new)	How long will level 2B access be available for MAHs for a defined signal?	Level 2B is always available provided that the MAH users have been granted access by the EU QPPV and the user confirmed agreement with the confidentiality undertaken when requesting L2B access.
7.32 (new)	According to your experience, from the authorities' side, what is the mean time interval between e-RMR availability and signal validation?	The time to be dedicated for signal detection and assessment processes depends on many different variables including the substance and the number of cases received for the DECAs selected for review.

Reference	Question	Answer
7.33 (new)	Regarding EVDAS screening, should it be performed by specific PT or it can be done with the PT prompt free of PT's.?	The EDVAS dashboard allows performing queries using the MedDRA hierarchy. The prompt is not mandatory and therefore when it is not completed, the system will retrieve all the cases received in the EVPM for the selected active substance when it has been coded as suspect/interacting.
7.34 (new)	If it is not possible to search by dosage form or indication, how valuable can the results be for substances with totally different dosages and dosage forms (e.g. oral laxative vs injectable mineral supplement)?	Access to EudraVigilance data for MAHs is provided at the level of the 'active substance high level'. Following the analysis of the data, MAHs should consider the relevant information for the safety of their products.
7.35 (new)	For the line listing in EVDAS - is there a limit to the number of rows?	The current limit to display ICSR in the line listing is 100,000 cases. 2,738 cases can be exported in excel. 100,000 cases can be exported in csv.
7.36 (new)	When the EVDAS user manual will be published?	This will be published in October 2017
7.37 (new)	Have you planned to organize any webinar to explain EMA methodology on your signal assessment in order to allow the MAH to be more familiar and share your experience on this process	A DIA/EMA information day on Signal Management will take place at the EMA premises on 27th October 2017. See published Agenda: http://www.ema.europa.eu/docs/en_GB/document_library/Agenda/2017/02/WC500222156.pdf

Reference	Question	Answer
7.38 (new)	When using the fixed-period, users can select an eRMR containing multiple active substances. Is there a limit to how many active substances can be grouped in a single eRMR?	<p>There is no limit in the number of substances users can select in the prompt for the fixed eRMR, but the limit is in the output that is generated.</p> <p>This limit is 100,000 rows (= 100,000 drug-event combinations) and applies both to the eRMR report and the line listing.</p> <p>If the user selects substances that would generate an output larger than 100,000 rows, no results will be given and an error message will be displayed.</p>
7.39 (new)	What is the proper way to handle closely monitoring topics in point of view of signal management (over including them in PSUR)?	<p>The access to the EudraVigilance data by MAHs does not change the format of the PSURs.</p> <p>When analysing safety issues under close monitoring, MAHs should consider the cases held in EV as another source of information that may enhance the assessment of those issues.</p> <p>Topics requested by a regulator to be closely monitor should be reported in Section 15 of the PSURs as indicated in GVP Module VII.</p>
7.40 (new)	Will we have also the device technical complaints coding reflected in the eRMR if associated to an AE?	<p>The eRMR is an output from EV and contains the drug-event combinations as coded in the ICSRs.</p> <p>If cases related to medical devices are submitted to EV as ICSRs and coded with a suspect /interacting drug and suspected ADRs, the relevant drug-event combinations will appear in the eRMR.</p>
7.41 (new)	Do the MAH have the obligation to do the same signal detection exercise concerning the technical complaints in EVDAS?	<p>Medical devices have their specific legislations to be followed. If the complaint related to medical devices contains suspected ADRs, MAHs should follow the standard process for the signal management procedure.</p>

8. Technical Questions

Reference	Question	Answer
8.1	In the ICSR Implementation Guide it is mentioned that "When binary (base 64) data is submitted the deflate algorithm RFC 19513 should be used "DF". Will EMA support any other compression logic like GZ?	The EU implementation of "DF" matches the ICH E2B(R3) Implementation Guide (IG). If the ICH IG is updated then GZ will be implemented in EU as well.
8.2	When can we expect sample files having attachments?	Example files have been created and published on 26 June 2016.
8.3	What will be the sequence of attachment embedding in the ICH E2B (R3) file? Our interpretation is that it will be created using following sequence: Original Attachment > Compression with DF > Encoded to Base64.	Yes that is the normal approach as only base 64 notations can appear in the XML field.

Reference	Question	Answer
8.4	<p>In the latest EMA BFC package, there is change in the file downgrade-b4.xml starting from line 289. We are not able to find any documentation, in which this change is covered or explained.</p> <pre data-bbox="331 464 837 975"> <xsl:if test="\$XEVMPPD=1"><xsl:choose> <xsl:when test="string-length(hl7:code/@displayName) > 0 and string-length(hl7:code/@code) > 0 and hl7:code/@codeSystem ='SUB-code'"><xsl:value-of select="hl7:code/@displayName"/></xsl:when> <xsl:otherwise> <xsl:value-of select="hl7:name"/></xsl:otherwise></xsl:choose></xsl:if> <xsl:if test="\$XEVMPPD!=1"> <xsl:value-of select="hl7:name"/></xsl:if> </xsl:if> </pre>	<p>An organisation can choose between using the verbatim reported product and substance names and the classified XEVMPPD terms made by EMA for population of the ICH E2B (R2) data element.</p> <p>The setting can be applied in the BFC file "OIDs.xml":</p> <pre data-bbox="875 408 2047 507"> <!-- Use Recoded EudraVigilance product and substance names instead of verbatim term --><!-- set value to 1 to use EV recoding--><xsl:variable name="XEVMPPD"></xsl:variable><!-- EV product --> </pre>

Reference	Question	Answer
8.5 (new)	<p>Will the recoding for suspect drug substance or product names performed by EMA in the EudraVigilance database assign the corresponding MAH in B.4.k.4.3 / G.k.3.3. if this information is available?</p> <p>Does the EMA filter allow to define downloads based on product level, thus, allows for searches for fixed dose combinations to only list ICSR which actually contain the combination product?</p>	<p>The product and substance information reported in an ICSR is classified against data held in XEVMPD. The access policy is based on active substance; therefore MAHs will need to decide what action to take on the ICSRs downloaded based on the information as reported in the ICSR.</p>
8.6 (new)	<p>There is a discrepancy between wording in GVP VI and the EU HL7 Implementation Guide concerning the use of local language- GVP VI allows for original language to be provided only where this is requested by either the concerned member state CA or by EMA. The EU HL7 Implementation Guide simply states that the MAH 'shall provide the original verbatim text'.</p>	<p>The EU IG has been revised and published; the text has been brought in line with the revised GVP VI.</p>
8.7 (new)	<p>In tests files loaded from EVWEB test module there is no batch number (N.1.2) available and the date of batch transmission (N.1.5) is masked by a nullflavor, so they had to be manually added into the files in order to be processed into database. Will it be the same in production environment?</p>	<p>The access policy does not give access to these fields of the original data, therefore they are currently not provided. This request is being reviewed and the generation of automated text to populate these fields is being planned to support the upload process by MAHs.</p>

Reference	Question	Answer
8.8 (new)	Is there a R3 field viewer? So that we can see R3 files in human readable format to manually process?	Yes, EVWEB allows organisations to up load E2B (R3) files into the application (workspace), from the application it is possible to generate human readable outputs.
8.9 (new)	Have gateway validation rules to determine ACK and NACK from cases being transmitted been finalised for EMA? -.that is for R3 format ICSRs	EU implementation guide and published business rules excel sheets include the rules applied for ICSRs and what issues would generate a negative acknowledgement being returned.
8.10 (New)	Could you confirm "E2BR3/R2 XML Testing" is mandatory to obtain our activated access to production environment? Do we have to send you back R3 converted files in e2BR2 format?	If there is no significant change to the database, then it is not mandatory to perform testing with the EMA; however we strongly recommend that you perform some testing of your own in the XCOMP environment to ensure that you will still be able to transmit cases when the new system goes live.
8.11 (new)	If the safety database vendor performs E2B R3 related testing with EMA directly, does the MAH using the tested safety database version still have to perform full testing or is this limited to few test scenarios?	In this scenario, if you have installed the database without modification, then you would not have to perform full testing. If any modification has been done, testing with EMA is mandatory.
8.12 (new)	Once the implementation of the new R3 format of the safety database is done, MAH has to performance the testing with EMA. Are the places of the testing limited? First come and first served?	Currently up to 5 organisations can book a place to perform test in a week. This will be reviewed if testing requests increase.

Reference	Question	Answer
8.13 (new)	Do R3 test files on EMA web site contain any attachments? What is the coding/archive standard for embedded files since there were some issues over its version?	As described in the EU implementation guide the encoding is Base64 and the compression algorithm is Deflate RFC1951 for sending in the EU, however please note the current test files have used ZLIB RFC1950 compression. These test files are planned to be amended soon.
8.14 (new)	What is the maximum allowed embedded file size?	As described in the EU implementation guide the maximum size of any single attachment is 15Mb, the maximum ICSR XML file size permitted is 20Mb.

Reference	Question	Answer
8.15 (new)	<p>Regarding the Download functionality.</p> <p>Considered the effect of the EMA re-coding ICSR data against the XEVMPD on receipt and implications for what the end-user would see as a result in any future download of this same re-coded ICSR data?</p> <p>Will the data in the product name remain as originally received from source? Or will the end user see a corrected version post re-coding against XEVMPD?</p> <p>If the latter statement is correct against what XEVMPD entry would we see the product name in the R3 message? (This is important to understand if there are multiple manufacturers of the same product)</p> <p>What happens if there is no supporting information to truly identify the correct MAH data (no formulation or route of administration) ? What is the default?</p>	<p>The EU implementation guide has been updated and includes further details on how drugs are classified against XEVMPD data.</p> <p>In accordance with the access policy L2 access will provide the verbatim text as received in EudraVigilance for the product and substance names.</p> <p>In addition, the as classified product/substance name will also be made available in a separate field.</p> <p>L2 access is given based on active substance(s).</p>

Reference	Question	Answer
8.16 (new)	<p>Regarding the Download functionality.</p> <p>If the product name that is being provided is the original verbatim what exactly does the re-coding do – is it only Active substance information that is being re-coded?</p> <p>The reason why it is important to understand this data and the potential effects of the re-coding, most commercial safety databases will try to match the product name against a centrally stored repository within the safety system itself and often if there is no match, the product remains un-coded upon upload in the safety system, as a consequence</p> <p>We would be forced to manually recode the product in this circumstance</p> <p>No match of the product also means that information such as causality does not appear in the front end upon upload again forcing a manual intervention to review the xml message for this information</p>	<p>The EU implementation guide has been updated and includes further details on how drugs are classified against XEVMPD data.</p> <p>Until ISO IDMP is implemented and can be used for ICSRs organisations will need to continue classifying reported verbatim product and substance names against their own product and substance dictionaries.</p>

Reference	Question	Answer
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8.17

(new)

Regarding the Download functionality.

One other consideration for you, will the filename for any download incorporate the date of download as part of the filename? this will help with managing reports where we may have potentially high volumes of reports upon download

The screenshot below is what we saw in the pilot and yes this is not production, but as you can see the filename does not provide any meaningful information that an MAH can make use of?

Name	Type	Compressed size	Password	Size	Ratio	Date modified
IC-HCSR-EVTEST-1000000858	XML Document	4 KB	No	33 KB	89%	17/11/2016 16:09
IC-HCSR-EVTEST-1000000860	XML Document	5 KB	No	40 KB	89%	17/11/2016 16:09
IC-HCSR-EVTEST-1000000877	XML Document	3 KB	No	13 KB	81%	17/11/2016 16:09
IC-HCSR-EVTEST-1000000878	XML Document	3 KB	No	16 KB	84%	17/11/2016 16:09
IC-HCSR-EVTEST-1000000864	XML Document	4 KB	No	33 KB	89%	17/11/2016 16:09

The data of creation of the XML file will be included within the XML files themselves using the field N.1.5

9. Testing procedures for Electronic Data Interchange (EDI) Partners

Reference	Question	Answer
9.1	We have not yet had any notification of testing dates from the EMA. Could you please let me know when to sign up for a testing slot?	<p>Following the launch of XCOMP on 26 June 2017, organisations can initiate testing. Only where major system changes are introduced by an organisation or the testing of E2B(R3) compliant systems is planned, EMA should be contacted to agree on a testing slot.</p> <p>Please refer to testing steps at the EudraVigilance: electronic reporting webpage and the EudraVigilance change management webpage.</p>
9.2	Is there any plan for EMA to provide any additional sample R3 files for organisations to validate the ICH E2B (R3) downgrade logic?	<p>Example files have been created and published on 26 June 2016.</p> <p>With the launch of the new test environment on 26 June 2017, organisations are able to produce their own ICH E2B (R3) test files through access to the new XCOMP EVWEB application.</p>
9.3	What constitutes an E2B (R3) compliant system? Does it have to have an E2B (R3) compliant safety database or is the capability to report in the E2B (R3) format sufficient to be an E2B (R3) compliant system?	<p>The system should be able to create, send and process ICSRs that support all the data elements and the file format as defined in the ICH E2B (R3) and the EU ICSR Implementation guides. Testing should be performed as outlined in the EU ICSR Implementation Guide.</p>
9.4 (new)	<p>If we are EV Post users, is it mandatory to do the test in xCOMP?</p> <p>If it is necessary, should we book an slot?</p>	<p>Yes, EVPOST users must test before being allowed to use EVPOST in production.</p> <p>To perform testing a testing slot needs to be booked with EMA.</p>

Reference	Question	Answer
9.5 (new)	<p>When will cases be available in ICSR download functionality in the test environment, so we can download and test BFC tool and upload to our safety database to ensure functionality?</p> <p>Will the usual roughly 10 scenarios be available?</p>	<p>Test ICSRs can already be downloaded from XCOMP, test files can be downloaded from the EudraVigilance pages on the EMA website.</p>
9.6 (new)	<p>If an organisation has already submitted ICSRs to EV and is planning to continue to submit ICSRs in E2B R2 format from November 2017, should testing with EMA be performed?</p>	<p>It is recommended that all organisations test submission to the XCOMP system.</p> <p>However, if you have not changed you R2 system there is no need to contact EMA for this testing; this can be performed in XCOMP.</p>
9.7 (new)	<p>For EVWEB user, I understand there is no need to book slot for testing. Is it correct?</p>	<p>That is correct.</p>
9.8 (new)	<p>Does the EMA backward/forward conversion tool require another tool to actually convert R3 to R2, correct?</p> <p>It at the very least requires an xslt converter and this tool is not qualified /approved by EMA, and therefore a company will need to validate it. We cannot use EMA conversion tool without any other tool, correct?</p> <p>Is there a plan to make a 'qualified by EMA' tool to convert R3 to R2?</p>	<p>It is correct that you need to use a XSLT processor such as Microsoft's MSXSL in order to perform the instructions in the XSLT BFC tool.</p> <p>It would be unusual for organisations to validate XSLT processors as organisations would not validate programing compliers such as for using Java programs.</p>

Reference	Question	Answer
9.9 (new)	<p>In the EudraVigilance: Electronic reporting states that Third party service providers should complete all the testing steps (1 through 6).</p> <p>If we are using EVWEB for transmission is that required? Or just testing in XCOMP without booking a timeslot is enough?</p>	<p>If you are only using EVWEB online forms for creating and sending ICSRs there is no need to perform testing. Only gateway organisations and EVPOST users need to perform the testing.</p> <p>It is recommended that EVWEB users follow the published eLearning courses and get familiar with XCOMP.</p>
9.10 (new)	<p>Would it be possible to download sample R3 files without accessing XCOMP? Can you share the files?</p>	<p>Sample R3 files are published on the EMA website, under the page 'EudraVigilance change management', section 'On the new EudraVigilance database, where can I find detailed information and guidance? (Updated July 2017)'.</p> <p>Please refer to the document 'EU reference instances' and 'EU E2B (R3) testing files'.</p>

10. Go-Live Planning

Reference	Question	Answer
10.1	<p>What are the plans and expectations for the actual changeover of the EudraVigilance database from the old structure to the new one?</p>	<p>The new EudraVigilance System will become operational on 22 November 2017.</p> <p>In preparation of the launch of new EudraVigilance system the Agency is in a process of developing a go-live plan in collaboration with the Pharmacovigilance Business Team, the EudraVigilance Expert Working Group (EV-EWG) and the Pharmacovigilance Risk Assessment Committee (PRAC).</p> <p>The go-live plan is going to be published on the EMA website (planned Q3 2017).</p>

Reference	Question	Answer
10.2 (new)	<p>Is there a grace period for MAHs to be able to get started with monitoring activities in order to be compliant with requirements? E.g. start 6 months after final publication of GVP Module IX.</p> <p>Would this be inclusive of 6 months from receiving access to a functional eRMR so that we can work out our processes?</p>	<p>Please refer to dedicated communication from the Agency on its website: (http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000587.jsp&mid=WC0b01ac0580727d1b).</p>
10.3 (new)	<p>What is the date that a live, fully functioning eRMR inclusive of working hyperlinks, dummy data if real data isn't feasible will be available to us? - whilst the published training material helps until end-users can run this process end to end ,the business process cannot be fully finalized</p>	<p>EVDAS will be available to the users on 22 November 2017</p>

Reference	Question	Answer
10.4 (new)	<p>27 October is the target for EMA training being offered on signal detection.</p> <p>Are there plans for offering any earlier training sessions ahead of the November Go Live date?</p> <p>We wish to allow sufficient time for training and any adjustments that may need to occur to our process as a result of the training.</p> <p>What can be done to provide signal detection training earlier in this roll-out as a way to help mitigate any compliance risks with the November timing?</p>	<p>There are no plans for other training sessions dedicated to signal detection. MAHs should use the training materials provided and make use of the webinars and info days programmed.</p>
10.5 (new)	<p>If the MAH has sent an initial report to the NCA before 22nd November 2017, can any subsequent follow-ups be sent to EudraVigilance after 22nd November 2017?</p>	<p>Yes, the EudraVigilance system will allow MAH to follow-up (after 22 Nov 2017) on ICSRs previously sent to NCAs (before 22 Nov 2017).</p>
10.6 (new)	<p>In case of nullification, do we need to make sure that a report previously submitted to Local NCA, is sent for nullification to EudraVigilance after 22 Nov 2016?</p>	<p>Yes, nullification of ICSRs, previously submitted to NCAs, should be sent to the EudraVigilance system as of 22 Nov. 2017.</p>

11. Others

Reference	Question	Answer
11.1 (new)	When will you publish the update Q&A integrating the Q&A of previous sessions?	The Q&A document is intended to be updated monthly with the different questions received from all stakeholders, in particular with questions raised during support webinars organised by EMA.
11.2 (new)	Will knowledge evaluation for e-learning be available for new users to get access to ICSR reporting in EudraVigilance or it is mandatory to undertake face-to-face training?	<p>The knowledge evaluation is intended for new non-commercial sponsors registering their organisation for the first time.</p> <p>There is no requirement for existing registered organisations using EVWEB to undertake the face-to-face training.</p> <p>Existing users of the system should follow the e-learning courses and do not need to take a competency assessment</p> <p>New MAHs registering for the first time and wish to use EVWEB for their submissions will need to ensure that one member of staff has attended the training course.</p>