Medical Literature Monitoring Service Contractor Work Instruction (MLM WIN-04)

Title: WIN on Performing Follow-Up for MLM ICSRs		
Applies to: Staff members in EMA and its contractors		
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1. Changes since last revision

WIN formatted as per the agency current template.

LMTT replaced with LiEMA throughout the document.

Under Section 5.1, in step 1, process to be followed in LiEMA has been added.

Under Section 5.2, in step 1, process to be followed in LiEMA has been added.

2. Records

All attempts for follow-up are stored in Document Management System (DMS) for each ICSR.

Electronic copy of this WIN will be stored in DMS.

No paper copies are archived.

3. Scope

The aim of this WIN is to outline the process to follow up with author for the potential and confirmed ICSR(s).

4. Definitions

Term	**Definition**
EEA	European Economic Area

Term	Definition
DMS	Document Management System
DocID	DocID is the unique ID generated by LiEMA for each literature reference(s) in the tracking tool.
EMA	European Medicines Agency
EudraVigilance	The European data-processing network and management system, which has been developed according to internationally agreed standards and which allows the EMEA to manage the electronic data exchange of Individual Case Safety Reports (ICSRs) and to support the EU pharmacovigilance activities at Community level.
Individual Case Safety Report (ICSR)	An ICSR is an electronic report, which provides the most complete information related to an individual case at a certain point of time. An individual case is the information provided by a primary source to describe suspected adverse reaction(s) related to the administration of one or more medicinal products to an individual Patient at a particular point of time.
LiEMA	LiEMA is a reference management system that provides literature safety surveillance and reference management capabilities.
MLM	Medical Literature Monitoring

5. Instructions

General Principles

In accordance with the detailed guide regarding the monitoring of medical literature and the entry of relevant information into the EudraVigilance database by the European Medicines Agency (EMA/161530/2014), one attempt for follow-up is made with the primary author for confirmed serious and non-serious cases based on a risk-based approach.

This refers to individual cases, where either the outcome is unknown or pre-defined clinical information (EMA/409859/2015) is missing regarding important medical events (IME).

Follow-up is also sought for both serious & non-serious potential cases reactions where the reviewer(s) suspect, or are certain, that there was an adverse drug reaction, but not all the minimum reporting criteria for a valid ICSR are present in the literature article.

Personal data that could be used to identify the patient, such as name, initials or date of birth must NOT be requested as a part of follow-up. Any personal data received during follow-up that could be used to identify the patient is to be anonymized to ensure full compliance of the EU data protection legislation. It should NOT be entered in the ICSR.

Any attempt to obtain follow-up information is documented and a check for potential duplicates in EudraVigilance is performed in the context of processing of any new follow-up information.

Follow-up methods applied are tailored towards optimizing the collection of missing information with the aim of encouraging the primary author(s) to submit new information relevant for the scientific evaluation of a particular safety concern.

5.1. Initiating Follow-up Process for Serious & Non-Serious Valid ICSRs

Step	**Action**
1. Assess the need for follow-up	During case processing, review information in serious and non-serious ICSR(s) and determine if any additional information is required. For example, this could include following up for an unknown outcome or information regarding test results where they were implied but not provided. In LiEMA, under Documents section, navigate to 'Request Documents' tab, click 'Request Follow-Up (CP)' to mark that the follow up has been initiated with the author.
2. Create entry in follow-up tracker	Create row in the follow-up tracker saved on the DMS and enter: • DocID • Substance Group Number • Author • Author e-mail address • Valid ICSR = Y
3. Select relevant questions from library on a risk-based approach	Access the follow-up question library in the follow-up tracker. In the follow-up tracker, select the standardised questions which need to be sent, copy & paste the questions into column F 'follow-up questions to be asked'. Save the follow-up tracker on the DMS.
4. Medical Review	Physician reviewing the case checks the follow-up questions requested by the case processor and adds or updates the questions based on their medical judgement (as required). The Medical Reviewer will update LiEMA for the 'Correctness of FUP request content'
5. Follow-up sent	Using the template in Annex 1, prepare the follow-up form in e-mail format and paste the questions into the left-hand column of the table. Send the e-mail from EMAMLM@syneoshealth.com Update the follow-up tracker to indicate that the follow-up has been sent out and save the follow up e-mail in the DMS. The expected date is auto populated to '30 days' time. Amend if necessary.

5.2. Follow-up Process for Potential ICSRs

Step	**Action**
1. Potential ICSR identified	Following review of the literature reference, if there is still an unconfirmed but potential ICSR, the reviewer will initiate a follow up request in LiEMA. In LiEMA, under Documents section, navigate to 'Request Documents' tab, click 'Author Follow Up' to mark that the follow up has been initiated with the author.

Step	Action
2. Create entry in follow-up tracker	Create row in Follow-up tracker saved on the DMS, and enter: • DocID • Substance Group • Author • Author e-mail address • Valid ICSR = Potential
3. Select relevant questions from library on a risk-based approach	Access the follow-up question library in the follow-up tracker. Select questions to be sent to confirm the ICSR, and any other relevant information, copy paste into column F 'follow-up questions to be asked'. Save the follow-up tracker on the DMS.
4. Follow-Up sent	Using the template in Annex 2, prepare the follow-up form in email format and paste the questions from the follow-up tracker into the left-hand column of the table. Send the email from EMAMLM@syneoshealth.com Update the follow-up tracker to indicate that the follow-up has been sent out and save the follow up email in the DMS. The expected date is auto populated to '30 days' time.

5.3. Monitoring of Responses

Step	Action
1. Monitoring Responses	Monitor the EMAMLM@syneoshealth.com inbox on a continuous basis throughout the day for responses received for follow-up e-mail(s) sent to author.
2. Triage Follow-Up	Once follow-up is received, acknowledge the e-mail by replying "Thank you" to the author for sharing the follow-up information. Review the responses to determine if the information is new information and requires a case update. If an update is required, determine the correct timeline based on the seriousness, i.e. a non-serious case getting upgraded to a serious case. Day zero is the day the follow up information is received. If no new information is received, save the follow-up e-mail in the DMS and update LiEMA. If a follow-up is received for a potential ICSR and the information confirms that an ICSR is present, LiEMA will be updated accordingly, and the source document will be saved in DMS.
3. Update case with new information	Process all new information as follow-up in accordance with WIN MLM-03 – Processing and submitting ICSRs in EVWEB
4. Archive e-mail	Save all relevant communication in DMS.
5. Updating LiEMA	If a follow-up response is not received for a potential ICSR within 30 calendar days, LiEMA will be updated with the missing information and actioned accordingly.

6. Reference documents

Not Applicable

7. Annexes

7.1. Annex 1 – Template for sending follow-up for valid ICSRs

Subject:

Our Reference: (Doc ID) Request for follow-up for Adverse Drug Reaction reported in literature.

Message body:

Dear Dr X,

I am writing to you on behalf of the European Medicines Agency's Medical Literature Monitoring service, regarding the following article which you recently published: <<insert full literature reference here>>.

THIS PARAGRAPH ONLY TO BE USED IF THE AUTHOR IS NOT FROM THE EEA: The European Medicines Agency is the agency of the European Union (EU) responsible for the scientific evaluation, supervision and safety monitoring of medicines in the EU, working with the regulatory agencies in all EU Member States and the World Health Organization. It is broadly equivalent to the Food and Drug Administration (FDA) or <<insert name of medicines regulator from author's country here>>.

We monitor the medical literature for reports of adverse drug reactions (ADRs), turn these into ADR reports and transmit them to regulatory authorities and pharmaceutical companies in the EU and to the World Health Organization. These are used in detecting possible signals that could lead to a change in the understanding of the risk-benefit balance of the medicines.

In your article, you describe a patient who experienced a reaction of <<insert verbatim term>> after taking << insert drugs here>>. To aid our pharmacovigilance assessors in their understanding of the reactions caused by these medicines, we would be grateful if you could provide a little more information regarding the [patient(s), drug(s) and the reaction(s)].

Any information that you can give us would help. Even approximate information is useful, so, for example, if you only know that the patient was overweight, rather than their exact weight, then that would still be helpful.

Please do not include any personal identifying information, which includes patient medical records or information such as the patient’s name/initials, Date of birth, Medical record number, Specialist record

number, Hospital record number or Investigation number.

<<Select questions from bank of questions>>

Question	Answer

With Best Regards,

<<Insert a name here>>

EMA Medical Literature Monitoring Service

7.2. Annex 2 – Template for sending follow-up for potential ICSRs

Subject:

Our Reference: (Doc ID) Request for follow-up for potential Adverse Drug Reaction reported in literature.

Message body:

Dear Dr X,

I am writing to you on behalf of the European Medicines Agency's Medical Literature Monitoring service, regarding the following article which you recently published: <<insert full literature reference here>>.

THIS PARAGRAPH ONLY TO BE USED IF THE AUTHOR IS NOT FROM THE EEA: The European Medicines Agency is the agency of the European Union (EU) responsible for the scientific evaluation, supervision and safety monitoring of medicines in the EU, working with the regulatory agencies in all EU Member States and the World Health Organization. It is broadly equivalent to the Food and Drug Administration (FDA) or <<insert name of medicines regulator from author's country here>>.

We monitor the medical literature for reports of adverse drug reactions (ADRs), turn these into ADR reports and transmit them to regulatory authorities and pharmaceutical companies in the EU and to the World Health Organization. These are used in detecting possible signals that could lead to a change in the understanding of the risk-benefit balance of the medicines.

In your article, you describe a patient who experienced a reaction of <<insert verbatim term>> after taking << insert drugs here>>. To aid our pharmacovigilance assessors in their understanding of the reactions caused by these medicines, we would be grateful if you could provide a little more information regarding the [patient(s), drug(s) and the reaction(s)].

Any information that you can give us would help. Even approximate information is useful, so, for example, if you only know that the patient was overweight, rather than their exact weight, then that would still be helpful.

Please do not include any persona identifying information, which includes patient medical records or information such as the patient's name/initials, Date of birth, Medical record number, Specialist record number, Hospital record number or Investigation number.

<<Select questions from bank of questions>>

Question	**Answer**

With Best Regards,

<<Insert a name here>>

EMA Medical Literature Monitoring Service