Medical Literature Monitoring Service Contractor Work Instruction (MLM WIN-07)

Title: WIN on MLM Duplicate Management Process		
Applies to: Staff members in EMA and its contractors		
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1. Changes since last revision

WIN formatted as per the agency's current template.

LMTT replaced with LiEMA throughout the document.

Complete WIN updated as per the new technology system

2. Records

Electronic copy of this WIN will be stored in Document Management System (DMS).

No paper copies are archived.

3. Scope

The aim of this WIN is to outline the process for performing quality control activities for all the workstream activities.

4. Definitions

Term	Definition
Business day	Monday – Friday, including Bank Holidays
CAPA	Corrective Action, Preventive Action

Term	Definition
DMS	Document Management System
EMA	European Medicines Agency
FTA	Full Text Article
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
XML	eXtensible Markup Language

5. Instructions

General Principles

Quality Control (QC) activities will be undertaken for the following workstream activities:

- Review of articles
- Management of follow-up activities
- Processing of ICSRs
- Submission of ICSRs

100% Quality Control for all records will be undertaken for:

- Management of follow-up activities (weekly basis)
- Processing of ICSRs (per case)
- Submission of ICSRs (weekly basis)

Weekly meetings with EMA will be scheduled to discuss quality finding(s) and inconsistencies.

The MLM team will follow internal procedures for any non-compliance related to lateness in sharing of serious ICSRs to EMA and transmission of ICSRs to EudraVigilance.

From full production phase onwards, quality control activities for Screening and Review workstreams described above were performed at 5% sample on a monthly basis until mid-Dec 2021 and post that quality control activities only for Review workstream is performed at 10% sample with no change in quality control activities for screening workstream, unless performance issues are deemed unsatisfactory.

If the monthly major quality scores for Review are below 99.5% consecutively for two weeks, the monthly sample size will increase from 10% to 12%, 15%, 20% as per the EMA MLM Process and Quality Control Plan.

Note: Minor quality percentage for the review workflow will not have any impact on the above percentage for the minor error.

Quality Control of Potentials and Full Text Article (FTA) Management:

During the review step, literature references which cannot be assessed as valid ICSR(s) or gets excluded due to missing information are marked as potential ICSRs in LiEMA.

To determine, if a potential ICSR is a valid ICSR, either a follow-up e-mail is sent to author to obtain more information, or an FTA is obtained, and a final assessment is made further.

In scope: Quality Control of pre-assessed potential ICSRs in LMTT

5.1. Quality Control: Review of Literature References

The literature review which is being quality controlled should be performed in accordance with:

MLM SOP-01 – Medical Literature Monitoring Screening and Reviewing Process

MLM WIN-02 – Reviewing MLM Literature

Step	**Action**
1. Login to LiEMA	Login LiEMA by entering your work e-mail address and select 'QC role' associated with your e-mail address. Click 'Continue'.
2. Retrieval of records	Upon successful login, click 'Quality Control Advanced' and under 'Quality Metric Name', select the quality metrics as configured in the system. Select 'Start Date (Selection Date)'– 'End Date (Selection Date) for a date for which quality control of the literature references needs to be performed. Click 'Apply Filters'. List of literature references will be displayed as per the selected quality metric. Note: Whenever volume permits, this activity should be performed on a daily basis, for a 10% sample of the previous day reviewed data.
3. Review of records	Click on each Doc ID to perform the quality control of the reviewed literature reference. Under Reference page, click 'QC' icon (highlighted in red) next to the active substance name that needs to be QC reviewed. Review the record and assess the information within LiEMA.

Step	Action
	Once all the fields have been reviewed, select appropriate 'QC Assessment'. If all entries are acceptable, with no errors, select 'No QC Error' under QC assessment. Click 'Save'. If any of the entry is incorrect and acceptable, select 'QC error, no correction required', type of error(s) as 'Minor error(s)' and enter the number of errors identified. Enter the QC comments/findings in 'Description of minor errors' and click 'Save'. For any DocID, which fail Review QC, select 'QC error, correction required', select 'type of error(s)' and enter the 'number of errors identified', as appropriate. Enter the QC comments/findings in 'Description' section based on the error identified and click 'Save'. A notification will be sent by the system to the respective reviewer detailing the QC result and will be visible to the respective reviewer under 'References' tab. The reviewer must action QC finding in LiEMA on the same business day and once it has been actioned, select check box for 'Errors Corrected'. Click 'Save'. Repeat the above-mentioned steps for all the entries retrieved from the quality metric.

A Major error is defined as either a clearly incorrect decision (assessing an article as confirmed or potential when it is not, or vice versa) or an identical error by the same user for over 3 records for a week.

When a Major error has been identified, the QC personnel is responsible for discussing the identified errors with the responsible reviewer and supporting in refresher training (if required).

100% of that user's records will then be reviewed for 1 business day to assess the impact of the refresher training.

A minor error is defined as an error where the literature reference has been excluded correctly but with an incorrect selection of suboptimal exclusion criteria.

5.2. Quality Control: Management of Follow-up Activities

The follow-up activities which are being quality controlled should be performed in accordance with:

MLM SOP-01 – Medical Literature Monitoring Screening and Reviewing Process

MLM SOP-02 – Processing of Medical Literature Monitoring ICSRs

MLM WIN-02 – Reviewing MLM Literature

MLM WIN-03 – Processing and submitting ICSRs in EVWEB

MLM WIN-04 - Performing Follow-Up for MLM ICSRs

Step	**Action**
1. Login to LiEMA	Login LiEMA by entering your work e-mail address and password. Click 'Sign in'.
2. Retrieval of Follow-up status	Upon successful login, under 'Reports' select 'Report type' as 'Daily ICSR Report' and click 'Export'.
3. Review of Follow-up status	To review all FTA requests, filter in column H. Ensure that column K has a date entered or is blank. Ensure column L has a 'full text receive date' entered. Where column L is blank and a date has been entered in column K, ensure a follow-up e-mail is sent to receive the latest expected receipt date. Additionally, review the follow-up requested date (if required) and ensure that the date of follow-up is not historic. If the date has passed, this must be communicated to the review team who will update the literature reference to record the follow-up closure. To review all follow-up request with author, filter in column H. Ensure that column K has a date entered or is blank. Ensure column L has a 'full text receive date' entered. Where column L is blank and a date has been entered in column K, ensure a follow-up e-mail is sent to the author. Additionally, review the follow-up requested date (if required) and ensure that the date of follow-up is not historic. If the date has passed, this must be communicated to the review team who will update the literature reference to record the follow-up closure. Undertake the same process for the Daily Sum Screen report and ensure that when a literature reference has been assessed as a potential ICSR (follow-up requested with author), the case has been followed-up and the date to receive the follow-up has not surpassed. Additionally, follow-ups requested for confirmed ICSRs should undergo a quality check in the Quality Control workflow. The Quality Control personnel must check the follow-up questions, which will be sent to the author for the confirmed ICSR. If it is consistent with the case, LiEMA will be updated accordingly. If the follow-up questions are incorrect, the Quality Control personnel must update LiEMA, and feedback should be provided to the concerned case processor to correct the follow-up questions that needs to be sent to the author.

5.3. Quality Control: Processed ICSRs

Within Medical Literature Monitoring, all the processed ICSRs must be quality controlled. The purpose of this review is to assess the quality of the processed ICSR(s).

The ICSR processing activities which are being quality controlled should be performed in accordance with:

MLM SOP-02 – Processing of Medical Literature Monitoring ICSRs

MLM WIN-03 – Processing and submitting ICSRs in EVWEB

MLM WIN-06 – MLM Duplicate Management Process

Step	**Action**
1. Login to LiEMA	Login LiEMA by entering your work e-mail address and password. Click 'Sign in'.
2. Retrieval of cases	Upon successful login, select 'QC 1 pending' cases. Click 'Case ID hyperlink' for ICSR that needs to be quality controlled.
3. Review of cases	Import the XML file into EVWEB. Assess the information within XML against the source information. If any finding(s) is identified, that is incorporated in the appropriate section(s) of QC1 form. Once all the sections have been reviewed, select 'Decision' as appropriate and send the case either to Medical Review or Submission workflow. Click 'Submit'. Post medical review, quality control personnel will update QC 2 form and ensure that Medical Reviewer comments have been addressed appropriately and correctness of follow up request is correct. If the entry is acceptable, with no errors, select 'Error type' as 'No error'. If it is not acceptable, select 'Error type' as either 'Major', 'Medium', 'Minor' or "To discuss'. For cases, which fail ICSR QC, the QC personnel must enter the finding(s) in the appropriate sections of QC 2 form within LiEMA. The QC Personnel must correct the case (if required) and once corrected, mark Error type as 'Resolved' and populate 'Error resolved' date.

Step	Action
	Repeat the above-mentioned steps for all the cases that are quality controlled.

The definitions of major/medium/minor errors are based on those provided in Annex I of the Detailed guide regarding the EudraVigilance data management activities by the European Medicines Agency. However, they have been adapted taking into consideration the character of literature cases and it's an internal quality control process.

A Major error is defined as an error which will impact the timelines (i.e. a serious case entered as non-serious), signal detection (missing or otherwise erroneous reactions or drugs), significantly poor quality in a case, e.g. test data completely omitted, narrative not containing relevant salient facts about the case. If there are multiple minor errors in a case or a consistent error by the same user for over 3 records are also considered as major errors.

Where a major error is identified, the Quality Control personnel will discuss the identified errors with the responsible case processor and support in refresher training (if required).

5.4. Quality Control: Processed ICSRs (EMA QC)

Within Medical Literature Monitoring, random quality check is performed by EMA for processed ICSR(s). The purpose of this review is to assess the quality of the processed ICSR(s).

Upon completion of the case processing, the MLM team should share the finalised serious and non-serious case(s) via an e-mail with EMA to perform the quality check.

Once the finalised cases have been reviewed, the EMA will provide feedback in 'EMA Quality Check' section of LiEMA. Feedback may also be provided by an e-mail.

Every business day, the MLM Quality Control team should search for ICSRs which have been reviewed by EMA and marked for error(s); if any. If there is any finding(s), review the finding and if any rationale needs to be provided, will be sent to EMA. If finding is correct, the relevant ICSR should be immediately corrected and re-transmitted.

Major and medium errors should be corrected as a priority, whereas minor errors should be corrected with the next transmission or with the current transmission if the case had not been transmitted prior to receipt of EMA feedback.

5.5. Quality Control: Submitting ICSRs to EudraVigilance

Quality Control for submission of ICSRs must be completed post submission of ICSR(s).

The purpose of this review is to assess whether the case was transmitted within the correct timelines and was sent to the correct recipient.

The ICSR submission activities which are being Quality Controlled should have been performed in accordance with:

MLM SOP-02 – Processing of Medical Literature Monitoring ICSRs

MLM WIN-03 – Processing and submitting ICSRs in EVWEB

Submission Quality Check must happen once the case has been transmitted in EudraVigilance and on the same day.

While reconciling daily submissions, search for cases with errors. Count should = 0. Then search for "Correct" cases. If n correct = n cases from LiEMA, stop.

If n correct < n cases from LiEMA, check reports with warnings.

Verify combined totals are correct and for the 'with warnings' cases, check the ACK to see what the warning was and if the case could be improved in the future or needs immediate changes.

If an ICSR contains any errors, this should be documented in LiEMA 'Submission Quality Check' step and the case must be re-transmitted on the same day.

For ICSRs which were transmitted to EudraVigilance without any error, 'Submission Quality Check' step is not required.

The daily report retrieved from the EVWEB ICSR area is saved in the DMS for future reference.

Step	**Action**
1. Login to LiEMA	Login LiEMA by entering your work e-mail address and password. Click 'Sign in'.
2. Retrieval of cases	Upon successful login, search for a case for which 'Negative Acknowledgement received'. Click 'Case ID hyperlink'.
3. Review of cases	Assess the information within LiEMA against the ICSR in EVWEB. If any updates are required, capture within 'Submitter Comments'. Once all sections have been reviewed, 'Error Type' is auto populated as 'Major'. Once, the case has been fixed with the error, incorporate 'Error resolved' date and click 'Submit'. Repeat the above-mentioned steps for any failed cases.

A Major error is defined as an error where an ICSR received an error in ACK or was transmitted to any recipient other than EudraVigilance (EVHUMAN).

5.6. Quality Control: 'Potential' LiEMA entries

For potential ICSR entries, 100% quality control must be performed to ensure the correctness of the decision taken by the reviewer.

The quality control of the 'Potential' entries must be performed no later than two business days of the initial review of LiEMA entry.

This activity must be undertaken by a designated team member who is trained on Quality Control of review workflow.

Step	Action
1. Login to LiEMA	Login LiEMA by entering your work e-mail address and select 'QC role' associated with your e-mail address. Click 'Continue'.
2. Retrieval of records	Upon successful login, search for a case for which 'Negative Acknowledgement received'. Click 'Case ID hyperlink'.
3. Review of cases	Assess the information within LiEMA against the source information. If any updates are required, capture within 'Submitter Comments'. Once all sections have been reviewed, 'Error Type' is auto populated as 'Major'. Once, the case has been fixed with the error, incorporate 'Error resolved' date and click 'Submit'. Repeat the above-mentioned steps for any failed cases.

6. Reference documents

Not Applicable

7. Annexes

Not Applicable