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2025

Module VI

Collection, Management, and Submission of Reports of Suspected Adverse Reactions to Medicinal Products

Version 1.0

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Module VI - Collection, Management, and Submission of Reports of Suspected Adverse Reactions to Medicinal Products

List of Abbreviations

ICSR:	Individual Case Safety Report
LOE:	Lack of Efficacy
MAH:	Marketing Authorization Holder
PSUR:	Periodic Safety Update Report

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VI.A. Introduction

This module addresses the requirements related to the collection, data management, and reporting of suspected adverse reactions (serious and non-serious) associated with medicinal products for human use authorized in Lebanon.

The guidance provided in this Module does not address the collection, management, and reporting of events or patterns of use, which do not result in suspected adverse reactions (e.g., asymptomatic overdose, abuse, off-label use, misuse or medication error) or which do not require to be reported as individual case safety report or as Emerging Safety Issues. This information may, however, need to be collected and presented in periodic safety update reports for the interpretation of safety data or for the benefit risk evaluation of medicinal products. In this aspect, guidance provided in Module VII applies.

VI.A.1. Terminology

The definitions provided hereafter shall be applied for the purpose of this Module. Some general principles presented in the ICH-E2A and ICH-E2D guidelines should also be adhered to; they are included as well in this chapter.

You can refer to the ICH website for more information: https://www.ich.org/index.html.

- **Abuse:**

  This corresponds to the persistent or sporadic, intentional, excessive use of a medicinal product, which is accompanied by harmful physical or psychological effects.

- **Adverse Drug Reaction:**

  An adverse drug reaction is a response to a medicinal product that is noxious and unintended. This includes adverse reactions which arise from:

  - The use of a medicinal product within the terms of the marketing authorization;
  - The use outside the terms of the marketing authorization, including overdose, off-label use, misuse, abuse and medication errors;
  - Occupational exposure.

- **Adverse Event:**
  An untoward medical occurrence after exposure to a medicine, which is not necessarily caused by that medicine.

- **Causality Assessment:**

  In accordance with the ICH-E2A guideline, the definition of an adverse reaction implies at least a reasonable possibility of a causal relationship between a suspected medicinal product and an adverse event. An adverse reaction, in contrast to an adverse event, is characterized by the fact that a causal relationship between a medicinal product and an occurrence is suspected. For regulatory reporting purposes, as detailed in the ICH-E2D guideline, if an event is spontaneously reported, even if the relationship is unknown or unstated, it meets the definition of an adverse reaction. Therefore, all spontaneous reports notified by healthcare professionals, patients or consumers are considered suspected adverse reactions, since they convey the suspicions of the primary sources, unless the reporters specifically state that they believe the events to be unrelated or that a causal relationship can be excluded.

- **Individual Case Safety Report (ICSR):**

  This refers to the format and content for the reporting of one or several suspected adverse reactions in relation to a medicinal product that occur in a single patient at a specific point in time. A valid ICSR should include at least one identifiable reporter, one single identifiable patient, at least one suspect adverse reaction, and at least one suspect medicinal product.

- **Life Threatening:**

  Life-threatening refers to a reaction in which the patient was at risk of death at the time of the reaction; it does not refer to a reaction that hypothetically might have caused death if more severe.

- **Medicinal Product:**

  A medicinal product is characterized by any substance or combination of substances:

  - Presented as having properties for treating or preventing disease in human beings; or
  - Which may be used in or administered to human beings either with a view to restoring, correcting, or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.

- **Misuse:**

  This refers to situations where the medicinal product is intentionally and inappropriately used, not in accordance with the authorized product information.

- **Occupational Exposure:**

  This refers to the exposure to a medicinal product, as a result of one ‘s professional or non-professional occupation.

- **Off-label Use:**

  This relates to situations where the medicinal product is intentionally used for a medical purpose, not in accordance with the authorized product information.

- **Overdose:**

  This refers to the administration of a quantity of a medicinal product given per administration or cumulatively, which is above the maximum recommended dose according to the authorized product information. Clinical judgement should always be applied.

- **Primary Source:**

  The primary source of the information on a suspected adverse reaction(s) is the person who reports the facts. Several primary sources, such as healthcare professionals and/or a consumer, may provide information on the same case. In this situation, all the primary sources’ details, including the qualifications, should be provided in the case report, with the primary source(s) section repeated as necessary in line with the ICH-E2B(R2) guideline.

  In accordance with the ICH-E2D guideline:

  - A healthcare professional is defined as a medically-qualified person such as a physician, dentist, pharmacist, nurse, coroner, or as otherwise specified by local regulations;
  - A consumer is defined as a person who is not a healthcare professional, such as a patient, lawyer, friend, relative of a patient, or carer.

  Medical documentations (e.g., laboratory or other test data) provided by a consumer that support the occurrence of the suspected adverse reaction, or which indicate that an identifiable healthcare

professional suspects a reasonable possibility of a causal relationship between a medicinal product and the reported adverse event/reaction, are sufficient to consider the spontaneous report as confirmed by a healthcare professional.

If a consumer initially reports more than one reaction and at least one receives medical confirmation, the whole report should be documented as a spontaneous report confirmed by a healthcare professional and be reported accordingly. Similarly, if a report is submitted by a medically qualified patient, friend, relative of the patient, or carer, the case should also be considered as a spontaneous report confirmed by a healthcare professional.

- **Seriousness of an Adverse Reaction:**

Seriousness as described in ICH-E2A, a serious adverse reaction corresponds to any untoward medical occurrence that at any dose results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent, or significant disability or incapacity, or is a congenital anomaly/birth defect.

The characteristics/consequences should be considered at the time of the reaction to determine the seriousness. For example, life-threatening refers to a reaction in which the patient was at risk of death at the time of the reaction; it does not refer to a reaction that hypothetically might have caused death if more severe.

Medical judgment should be exercised in deciding whether other situations should be considered serious. Some medical events may jeopardize the patient or may require an intervention to prevent one of the above characteristics/consequences. Such important medical events should be considered serious.

VI.B. Structures and processes

VI.B.1. Collection of individual case safety reports

Marketing Authorization Holders (MAHs) should have in place the appropriate tools to collect all reports of suspected adverse reactions associated with medicinal products originating from unsolicited or solicited sources.

In this regard, a pharmacovigilance system should be developed to allow the acquisition of sufficient information for the scientific evaluation of those reports. The system should be designed so that it helps

to ensure that the collected reports are authentic, legible, accurate, consistent, verifiable, and as complete as possible for their clinical assessment. All notifications that contain pharmacovigilance data should be documented and archived in compliance with the applicable data protection requirements.

The system should also be structured in a way that allows for reports of adverse events and suspected adverse reactions to be validated in a timely manner and exchanged with the national competent authority within the legal submission time frame.

In accordance with the ICH-E2D, two types of safety reports are distinguished in the post-authorization phase: reports originating from unsolicited sources and those reported as solicited.

VI.B.1.1. Unsolicited reports

VI.B.1.1.1. Spontaneous reports

As defined in ICH-E2D, a spontaneous report is an unsolicited communication by a healthcare professional, or consumer, to a competent authority, MAH, or other organization that describes one or more suspected adverse reactions in a patient who was given one or more medicinal products. The below should be considered as a spontaneous report:

- Stimulated reporting that occurs consequent to a direct healthcare professional communication, publication in the press, questioning of healthcare professionals by company representatives, communication from patients' organizations to their members, or class action lawsuit;
- Unsolicited consumer adverse reactions report, irrespective of any subsequent "medical confirmation," should be handled as a spontaneous report;
- Reports of suspected adverse reactions, which are not related to any organized data collection systems and which are notified through medical enquiry/product information services or which are consequent of the distribution of information or educational materials;
- Unsolicited reports of suspected adverse reactions collected from the internet or digital media;
- Reports of suspected adverse reactions from non-interventional post-authorization studies related to specified adverse events for which the protocol does not require their systematic collection
- Reports of suspected adverse reactions from compassionate use or named patient use conducted in countries where the systematic collection of adverse events in these programs is not required.

VI.B.1.1.2. Literature reports

The medical literature is an important source of information for the monitoring of the safety profile and of the risk-benefit balance of medicinal products, particularly in relation to the detection of new safety signals or emerging safety issues.

1. MAHs should monitor possible articles through a systematic literature review of reference databases (e.g., Medline, Excerpta Medica, or Embase) no less frequently than once a week.
2. The MAH should ensure that the literature review includes the use of reference databases that contain the largest reference of articles in relation to the medicinal product properties, and that the search is also conducted in local journals in countries where medicinal products have a marketing authorization, including Lebanon.
3. Reports of suspected adverse reactions from the medical literature, including relevant published abstracts from meetings and draft manuscripts, should be reviewed and assessed by MAHs. Submission is restricted to ICSRs pertaining exclusively to medicinal products authorized for marketing in Lebanon.

If several medicinal products are mentioned in the publication, only those that are identified by the publication's author(s) as having at least a possible causal relationship with the suspected adverse reaction should be considered for literature review by the concerned MAHs.

If the product source, brand, or trade name is not specified in the publication, and the MAH cannot exclude its ownership of the suspected medicinal product based on the medicinal product name, active substance name, pharmaceutical form, batch number or route of administration, in this case the MAH should assume that it was its own product, yet the report should indicate that the specific brand was not identified.

One case should be created for each single identifiable patient in line with the characteristics provided in VI.B.2. Relevant medical information should be recorded, and the first publication author (or the corresponding author, if designated) should be considered as the primary source of information. Details about the co-authors do not need to be documented among the primary sources of information.
In summary, the purpose of literature Screening is to identify and capture ICSRs, signals, and safety data from external sources. Only valid cases should be reported, for that, you must complete the case details and, if needed, contact the author or source to obtain all required information.

If you are not sure whether the information relates to your product, you still report it unless you can prove otherwise. You may exclude a case only if you can confirm that it is not linked to your product. Examples:

- The API mentioned does not belong to your brand.
- The dosage form described is not marketed in your country.

VI.B.1.1.3. Reports from non-medical sources

If a MAH is made aware of a report of suspected adverse reactions originating from a non-medical source, for example, the media and news, it should be managed as a spontaneous report.

Necessary steps should be undertaken to follow up on the case to obtain the minimum information that constitutes a valid ICSR.

VI.B.1.1.4. Information on suspected adverse reactions from the internet or digital media

MAHs should regularly screen the internet or digital media under their management or responsibility (i.e., owned, paid for, and/or controlled by MAH), for potential reports of suspected adverse reactions. The frequency of the screening should allow for potential valid ICSRs to be submitted to the national competent authority within the appropriate regulatory submission time frames based on the date the information was posted on the internet/media source (day 0 for reporting). MAHs may also consider monitoring their websites to collect reports of suspected adverse reactions.

On the other hand, if a MAH becomes aware of a report of suspected adverse reaction described in any non-company-sponsored digital medium, the report should be assessed to determine whether it qualifies for submission as an ICSR.

In relation to cases from the internet or digital media, the identifiability of the reporter refers to the possibility of verification of the existence of a real person based on the information available, e.g., an email address under a valid format has been provided. If the country of the primary source is missing, the country where the information was received, or where the review took place, should be used as the primary source country.

VI.B.1.2. Solicited reports

As defined in ICH-E2D, solicited reports of suspected adverse reactions are those derived from organized data collection systems, which include clinical trials, non-interventional studies, registries, post-approval named patient use programs, other patient support and disease management programs, surveys of patients or healthcare professionals, compassionate use or name patient use, or information gathering on efficacy or patient compliance.

Necessary attempts should be made to follow up on the case to obtain the minimum information that constitutes a valid ICSR.
With regard to the submission as ICSRs, solicited reports should be classified as study reports. They should have an appropriate causality assessment to consider whether they refer to suspected adverse reactions and therefore meet the minimum validation criteria. The submission of those ICSRs should be done following the same modalities and time frames as for other spontaneous reports.

VI.B.2. Validation of reports

Only valid ICSRs qualify for submission. All reports of suspected adverse reactions should be validated before submitting them to the national competent authority to ensure that the minimum criteria are included in the reports.

Four minimum criteria are required for ICSRs validation:

a. **One or more identifiable reporter (primary reporter):**

This is characterized by parameters such as qualification (e.g., physician, pharmacist, other healthcare professional, lawyer, consumer, or other non-healthcare professional), name, initials, or address (e.g., reporter's organization, department, street, city, state or province, postcode, country, email, phone number). Local data protection laws might apply.

The term 'identifiable' indicates that the organization notified about the case has sufficient evidence of the existence of the person who reports the facts based on the available information. In addition, ICSR is not valid for submission unless information concerning the qualification and the country is available for at least one reporter.

If information on the reporter's qualification is missing, the notification should be considered by default as a consumer report. If information on the reporter's country is not available, the country where the notification was received or where the review took place should be used in the ICSR. Whenever possible, contact details for the reporter should be recorded to facilitate follow-up activities. However, if the reporter does not wish to provide contact information, the ICSR should still be considered valid as long as the notified organization can confirm the case directly with the reporter.

To enable duplicate detection activities, all parties providing case information or approached for case information should be recorded in the ICSR (not only the initial reporter). When the information is based on second-hand or hearsay, the report should be considered invalid until it can be verified directly with the patient, the patient's healthcare professional, or a reporter who had direct contact with the patient.

b. One single identifiable patient:

This is characterized by at least one of the following qualifying descriptors: initials, medical record number (from general practitioner, specialist, hospital, or investigation), date of birth, age, age group, gestation period, or gender.

The term 'identifiable' refers to the possibility of verification of the existence of a patient based on the available information. The information should be as complete as possible in accordance with local data protection laws.

An ICSR should not be considered valid for submission unless information is available for at least one of the patient qualifying descriptors. Furthermore, in the absence of a qualifying descriptor, a notification referring to a definite number of patients should not be regarded as valid until an individual patient can be characterized by one of the aforementioned qualifying descriptors for creating a valid ICSR.

c. One or more suspected substance/medicinal product:

Interacting substances or medicinal products should also be considered suspect.

d. One or more suspected adverse reactions:

If the primary source has made an explicit statement that a causal relationship between the medicinal product and the reported adverse reaction has been excluded, and the MAH agrees with this assessment, the report does not qualify as a valid ICSR since the minimum information for validation is incomplete (there is no suspected adverse reaction).

The report also does not qualify as a valid ICSR if it is reported that the patient experienced an unspecified adverse reaction and there is no information on the type of adverse reaction.

Similarly, the report is not valid if only an outcome (or consequence) is notified and:

(i) No further information about the clinical circumstances is provided to consider it as a suspected adverse reaction; or

(ii) The primary source has not indicated a possible causal relationship with the suspected medicinal product.

The lack of any of the four elements means that the case is considered incomplete and does not qualify for submission as an ICSR. However, MAHs should make a necessary attempt to follow up on the case to obtain the missing data elements. Reports, for which the minimum information is incomplete, should be recorded within the pharmacovigilance system for use in ongoing safety evaluation activities. When the missing information has been obtained (including, for example, when the medicinal product's causal relationship with the reported adverse reaction is no longer excluded), the ICSR becomes valid for submission.

VI.B.3. Follow-up of reports

When first received, information contained in suspected adverse reaction reports may be incomplete or unclear. As a result, follow-up activities are often necessary to obtain supplementary information that is critical for the scientific and regulatory evaluation of individual cases. Follow-up is particularly important for monitored events of special interest, prospective pregnancy reports, cases involving patient death, or reports suggesting new risks or changes to known risks.

The objectives of follow-up activities are to complete and validate the case, clarify unresolved or evolving outcomes, and collect additional, specific, and clinically relevant information required to support a robust scientific assessment. This includes enabling an accurate evaluation of seriousness, causality, and appropriate case classification.

Follow-up should be initiated whenever minimum information is missing or unclear, when the seriousness, outcome, or timeline of the adverse event (AE) is insufficiently documented, or when additional data are required for scientific assessment or regulatory reporting. Follow-up may also be necessary if new or evolving information becomes available during case processing. These activities are conducted in addition to efforts aimed at collecting missing minimum criteria required for report validation.

Reasonable efforts should be made to obtain key demographic information, particularly the patient's age or age group, as this is essential for identifying safety concerns specific to pediatric or elderly populations. When such information is not initially reported, follow-up attempts should be undertaken and documented accordingly.

Follow-up should continue for as long as needed to finalize the case. Activities may cease once the case is considered complete and medically assessable, or when all reasonable attempts to obtain additional information have been exhausted and appropriately documented.

For suspected adverse reactions related to biological medicinal products, precise product identification is of particular importance. All appropriate measures should be taken to clearly identify the product name and batch number. When batch information is missing from the initial Individual Case Safety Report (ICSR), it is recommended that the case narrative explicitly document that batch details were requested as part of follow-up activities.

To ensure pharmacovigilance data security and confidentiality, strict access controls must be implemented so that only authorized personnel can access documents and databases. These security measures should apply across the entire data lifecycle. Information received from primary sources must be handled in an unbiased and unfiltered manner, and assumptions, imputations, or interpretations should be avoided during data entry or electronic submission. Procedures must also be in place to identify and manage duplicate cases both at data entry and during the generation of aggregated reports.

The Standard Operating Procedure (SOP) should clearly define follow-up standards, including the frequency of follow-up attempts, the number of attempts required per case, the overall duration of follow-up, and the timing of initiation (e.g., immediately after case validation, at predefined intervals, or following case evolution). These parameters should be risk-based and proportionate to the seriousness and clinical relevance of the case.

All follow-up attempts must be documented, regardless of whether a response is received. Documentation should include the date and method of follow-up (written, verbal, or electronic), the information requested, and the outcome of each attempt. A lack of response does not negate the requirement to document the follow-up effort.

When follow-up is conducted verbally, the information obtained must be validated by repeating key details and explicitly requesting confirmation from the reporter. The discussion should be clearly summarized and recorded in the case documentation.

Overall, follow-up activities should be focused, case-specific, and clinically relevant, avoiding unnecessary or repetitive requests. All follow-up must be conducted in compliance with data protection requirements, confidentiality obligations, and ethical standards.

VI.B.4. Case narratives

In addition to the structured data element, the MAH should provide the case narrative within the case report. The objective of the narrative is to summarize all relevant clinical and related information, including patient characteristics, therapy dates, medical history, clinical course of the event/s, diagnosis, and adverse reactions including the outcome, laboratory evidence (including normal ranges), and any other information that supports or refutes an adverse reaction (e.g., challenge information). The narrative should serve as a comprehensive, stand-alone "medical story". Care should be taken by the MAH to ensure that the information in the narrative (e.g., patient identifiers, adverse reactions, indication, and medical conditions) is accurately captured in the appropriate data fields.

Abbreviations and acronyms should be avoided, with the possible exception of laboratory parameters and units. Key information from supplementary records, including summarized relevant autopsy or post-mortem findings, should be included in the report, and their availability should be mentioned in the narrative and supplied on request.

VI.B.5. Quality management

MAHs should have a quality management system in place to ensure compliance with the necessary quality standards at every stage of case documentation, such as data collection, data transfer, data management, data coding, case validation, case evaluation, case follow-up, ICSR submission, and case archiving.

Correct data entry, including the appropriate use of terminologies, should be quality controlled, either systematically or by regular random evaluation. Activities that are contracted out to third parties should be documented and reviewed to verify that they are adequate and compliant with applicable requirements. Staff directly performing pharmacovigilance activities should be appropriately trained in applicable pharmacovigilance legislation and guidelines, in addition to specific training in report processing activities under their responsibility. Staff should be trained on standards and terminologies, and their proficiency confirmed. Other personnel who may receive or process safety reports (e.g., clinical

development, sales, medical information, legal, quality control) should be trained in adverse events/reactions collection and submission to the pharmacovigilance department in accordance with internal policies and procedures.

VI.C. Operation of reporting activities

VI.C.1. Scope of Reporting

The scope of reporting, originating within Lebanon, should include all of the following:

- All suspected adverse reactions;
- Special situations such as: overdose, abuse, misuse, medication error, occupational exposure, off-label use, quality defects, counterfeit products, interaction of medicines should be reported only if associated with adverse reaction(s):
    - All reports with adverse events/reactions to be reported according to their seriousness timeline. If the associated event is serious, the reporting timeline is 15 days. If the associated event is not serious, the reporting timeline is 90 days (Table 2);
- For the lack of therapeutic efficacy cases, there is no need for reporting when the reporter has specifically stated that the outcome was due to disease progression and was not related to the medicinal product;
- In certain circumstances, reports of lack of therapeutic efficacy with no suspected adverse reactions may need to be submitted within 15 days. Medicinal products used in critical conditions or for the treatment of life-threatening diseases, vaccines, and contraceptives are examples of such cases.
- Any suspected transmission of an infectious agent via a medicinal product should be considered a serious adverse reaction. If no other criterion is applicable, the seriousness of this ICSR should be considered as an important medical event. This also applies to vaccines.

- ICSRs resulting from use of a medicinal product during pregnancy or breastfeeding:
    - Reports on pregnancy exposure should not be reported before the outcome is known;
    - Individual cases with an abnormal outcome associated with a medicinal product following exposure during pregnancy are classified and reported as serious cases. This especially refers to:

- Reports of congenital anomalies or developmental delay, in the fetus or the child;
- Reports of fetal death and spontaneous abortion; and
- Reports of suspected adverse reactions in the neonate that are classified as serious.

Other cases, such as reports of induced termination of pregnancy without information on congenital malformation, reports of pregnancy exposure without outcome data, or reports that have a normal outcome, should not be submitted as ICSRs since there is no suspected adverse reaction. These reports should, however, be collected and discussed in the PSUR.

- ICSRs resulting from the use of a medicinal product in a pediatric or elderly population;
- In some cases, such as donations (donations provided as contributions which are free of charge to support communities in need, excluding donations intended for research purposes), products supplied for personal use, or any other source of non-registered products used in Lebanon where the patient has had an adverse event/reaction, should be reported;
- In regard to adverse events occurring in studies (non-interventional studies, compassionate use, preapproval access programs, patient support programs, market research, global interventional studies), only domestic adverse events/reactions resulting from these studies should be submitted to the LNPVP and follow the seriousness criteria for reporting.

To highlight, Severity refers to the intensity or magnitude of a clinical event (e.g., mild, moderate, severe), whereas seriousness is defined by the outcome or consequences of the event (e.g., death, life-threatening condition, hospitalization, disability, or other medically important conditions)

VI.C.2. Timelines for submission of individual case safety reports

VI.C.2.1. Day zero determination

Day zero is the date on which a MAH becomes aware of a publication containing the minimum information for an ICSR to be reportable (Table 1). Awareness of a publication includes any personnel of that MAH, or third parties with contractual arrangements with the MAH.

In summary, Day zero is defined as the date on which the local team becomes aware of the information.

For products of multinational MAHs represented in Lebanon by a local distributor, Day zero for reporting purposes is the date on which the local distributor in Lebanon first receives and becomes aware of the relevant information.

As for the data identified from Digital Media:

- If information is published by the company's own MAH on digital platforms, Day zero starts from the publication date, not from the date the team becomes aware.

- If the information is posted on any digital platform NOT belonging to the MAH, then Day zero is the date the local team becomes aware of the published information.

It is sometimes possible to identify the date on which a record was available on a database, although with periodic literature searching, day zero for a reportable adverse reaction present in an abstract is taken to be the date on which the search was conducted.

For articles that have been ordered as a result of literature search results, day zero is the date when the minimum information for an ICSR to be valid is available. MAHs should take appropriate measures to obtain articles promptly to confirm the validity of a case.

Only valid ICSRs should be submitted. 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 any personnel of the MAH, including medical representatives and contractors. This date should be considered as day zero irrespective of whether the information is received during a weekend or a public holiday. The timelines for submission are based on calendar days.

Where the MAH has set up contractual arrangements with a person or an organization, agreements should exist between the MAH and the person/organization to ensure that the MAH can comply with the submission of valid ICSRs within the appropriate timeframes. These procedures should, in particular, specify the processes for the exchange of safety information, including the timelines and responsibilities for the regulatory submission of valid ICSRs.

For ICSRs described in the medical literature, the clock starts (day zero) when a publication containing the minimum criteria is brought to attention (Table 1). Where contractual arrangements are made with a person/organization to perform literature searches and/or submit valid ICSRs, detailed agreements should exist to ensure that the MAH can comply with its regulatory submission obligations.

When additional significant information is received for a previously submitted case, the clock for the submission of a follow-up report starts again from the date of receipt of the relevant follow-up information.

For ICSRs captured from digital media under the management or responsibility of the MAH, the clock starts (day zero) when the information was posted.

For ICSRs captured from digital media in non–company–sponsored digital medium, the clock starts (day zero) when the MAH becomes aware of the posted information.

Table 1: Day zero determination

ICSR Source	Day (0) *,**
Publications/Abstracts	Date when the MAH became aware of the publication containing the minimum information for a valid ICSR
Digital media under the management of the MAH	Date when the MAH becomes aware of the posted information
Digital media in a non-company-sponsored digital medium	Date when the MAH becomes aware of the posted information.

**Day zero is to be calculated irrespective of whether the information is received during the weekend or a public holiday.*

*** When additional significant information is received for a previously submitted case, the clock for the submission of a follow-up report starts again from the date of receipt of the relevant follow-up information.*

VI.C.2.2. Reporting timeframes

- The submission of serious, valid ICSRs is required as soon as possible, but in no case later than 15 calendar days after initial receipt of the information. This applies to initial and follow-up information. Where a case initially sent as serious becomes non-serious based on new follow-up information, this information shall be submitted within 15 days; the submission timeframe for non-serious reports should then be applied to the subsequent follow-up reports.
- For the purpose of submission of ICSRs, significant follow-up information corresponds to new medical or administrative information that could impact the assessment or management of a case, or could

change its seriousness criteria. Non-significant information refers to updates such as revised comments on the case assessment or corrections of typographical errors in a previous case version; these do not need to be reported. The submission of non-serious valid ICSRs shall be submitted within 90 calendar days after initial receipt of the information. This applies to initial and follow-up information.

- Reports of lack of therapeutic efficacy for medicinal products used in critical conditions or for the treatment of life-threatening diseases, vaccines, contraceptives, or even those with **no** suspected adverse reactions may need to be submitted within a 15-day timeframe.
- Any suspected transmission of an infectious agent via a medicinal product should be considered a serious adverse reaction and submitted within a 15-day timeframe.
- Individual cases with an abnormal outcome associated with a medicinal product following exposure during pregnancy are classified as serious cases and reported within a 15-day timeframe.

Table 2 provides a summary of the reporting time frame for ICSRs in various scenarios.

Table 2: ICSRs reporting timeframes

Type of ICSRs	Reporting timeframe since day (0)
Serious ICSRs	15 days
Follow-up information for serious ICSRs*	15 days
Non-serious ICSRs	90 days
Significant Follow-up information for non-serious ICSRs	90 days
In certain circumstances, reports of lack of therapeutic efficacy with no suspected adverse reactions may need to be submitted within 15 days. Medicinal products used in critical conditions or for the treatment of life-threatening diseases, vaccines, and contraceptives are examples of such cases	15 days
Suspected transmission of an infectious agent via a medicinal product	15 days
Abnormal outcomes associated with a medicinal product following exposure during pregnancy are classified as serious.	15 days

**If a serious case becomes non-serious based on a new follow-up report, the information for this follow-up still needs to be submitted within 15 days. After that, the submission of subsequent follow-up reports should be sent as the non-serious follow-up time frame which is 90 days.*

VI.C.3. Report nullification

The nullification of a report should be used to indicate that a previously transmitted ICSR is considered completely void (nullified), for example, when the whole case was found to be erroneous.

VI.C.4. Report amendment

In some cases, an ICSR that has already been submitted may need to be amended. For example, 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. The same would apply where documentations mentioned in an ICSR, translations, or literature articles are requested by the national competent authority and are further sent as attachments in line with ICH E2B(R3). These submissions are considered as amendment reports.

VI.C.5. Modalities for submission of individual case safety reports

Based on the Ministerial Resolution MR #181 issued in 2021, MAHs should adhere to the internationally agreed ICH guidelines and standards and send the reports in XML format as specified in ICH E2B (R2 or R3) guidelines (https://www.moph.gov.lb/userfiles/files/Quality%26Safety/PharmacovigilanceSystemInLebanon/Karar%20181-2021.pdf).

All XML files should be sent to the following email: pv@moph.gov.lb.

VI.C.6. Period between the submission of the marketing authorization application and the granting of the marketing authorization

In the period between the submission of the marketing authorization application and the granting of the marketing authorization, information (quality, non-clinical, clinical) that could impact the risk-benefit balance of the medicinal product under evaluation may become available to the applicant. It is the responsibility of the applicant to ensure that this information is immediately submitted when the application is under assessment. During this period, the MAHs are not mandated to follow any reporting modality unless there is an emerging safety issue that needs to be communicated to the LNPVP.

VI.C.7. Period after suspension, revocation, or withdrawal of marketing authorization

The MAH shall continue to collect any reports of suspected adverse reactions related to the concerned medicinal product following the suspension of a marketing authorization till the expiry date of the last batch available locally

The time frames and submission requirements outlined in this module remain for valid ICSRs. Where a marketing authorization is withdrawn or revoked, the former MAH is encouraged to continue to collect spontaneous reports of suspected adverse reactions originating within Lebanon, to, for example, facilitate the review of delayed onset adverse reactions or of retrospectively notified cases till the expiry date of the last batch available locally.