EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Information Management

Monitoring of medical literature and the entry of relevant information into the EudraVigilance database by the European Medicines Agency

Inclusion and exclusion criteria for processing of Individual Case Safety Reports

Draft prepared by Project Maintenance Group 1 of the governance structure for pharmacovigilance	24 February - 6 March 2015
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Note: Revision 1 contains the following:

- Update of section 2.1. Report Type to add in exclusion criteria for animal, *in vitro* and toxicology studies.
- Update of the diagrams to make the process flow easier to follow
- Addition of Annex I which collates all the exclusion criteria and the relevant terms in the tracking sheets

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1. Introduction

Only valid[1] Individual Case Safety Reports (ICSRs) qualify for reporting. All literature records should therefore be screened, reviewed and assessed to make sure that the minimum criteria for reporting for reports of suspected adverse reactions are met.

This document describes inclusion/exclusion criteria that have been prepared in support of the screening, review and assessment of scientific and medical literature and recording of activities as outlined in chapter 2.4. of 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). The inclusion/exclusion criteria are based on the principles set out in the guideline on good pharmacovigilance practices: Module VI – Management and reporting of adverse reactions to medicinal products in the latest version (EMA/873138/2011) and are to be regularly reviewed taking into account the experience gained as part of the medical literature monitoring activities.

The steps to decide on the inclusion or exclusion of literature for the reporting of suspected adverse reactions are outlined below.

Processes following completion of the review of the literature records in relation to inclusion/exclusion criteria are defined in the "Detailed guide regarding the monitoring of medical literature and the entry of relevant information into the EudraVigilance database by the European Medicines Agency" and apply accordingly.

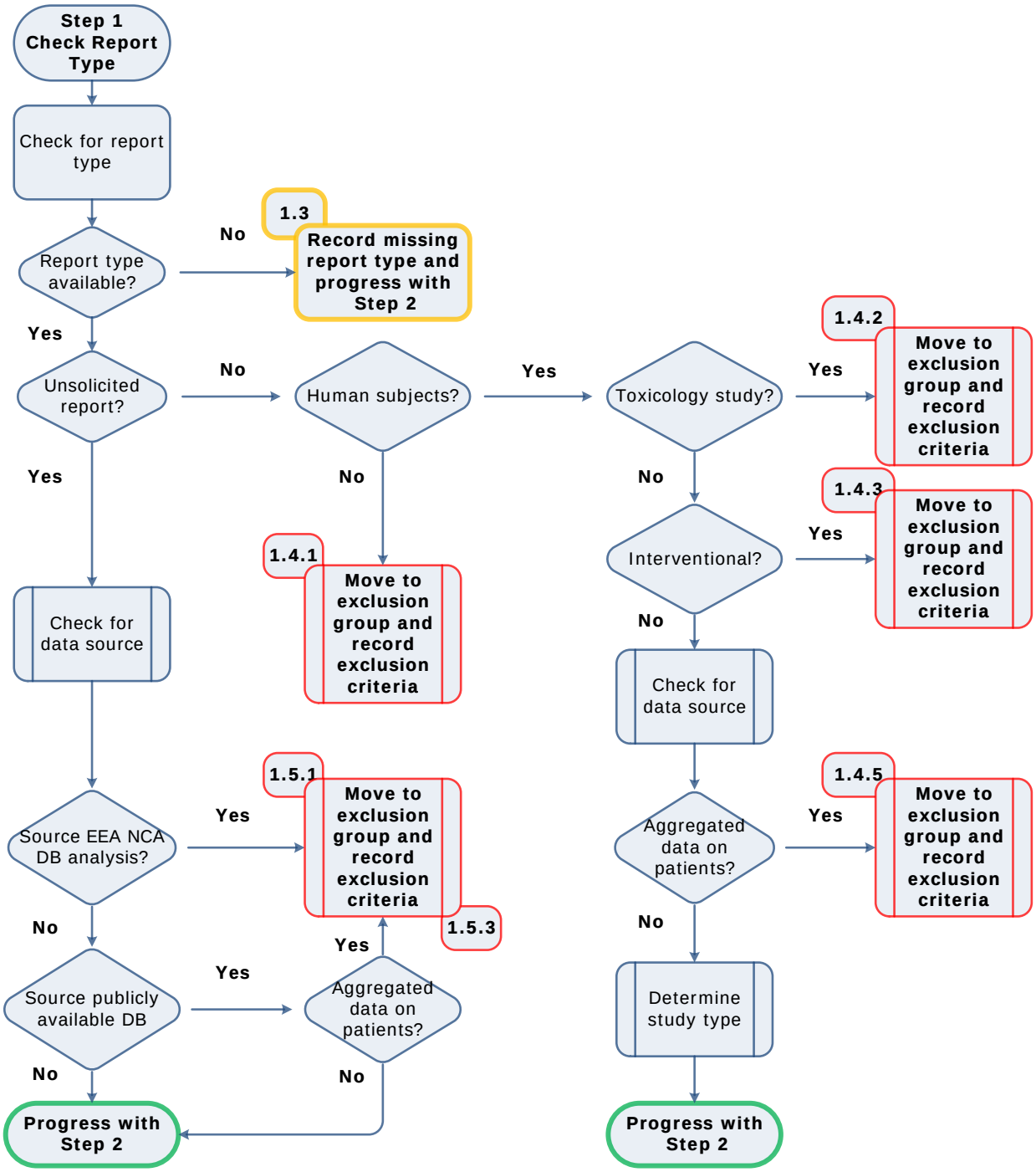
Note: Missing information as referred to in the following steps will be handled in line with chapter 3.3, "Follow-up of individual cases" of the detailed guide.

[1] GVP Module VI., chapter VI.B.2. Validation of reports

2. Inclusion/Exclusion Criteria

2.1. Report Type

Step 1 refers to the determination of the report type.



Step – 1 Report Type	Action
1.1	Check for the type of report in accordance with GVP Module VI, chapter VI.B.1.
1.2	If the report type is available, progress with Step 1.4
1.3	If the report type cannot be determined, record the report type as missing and progress with step 2.
1.4	Check if the literature record refers to a spontaneous (unsolicited) report as defined in GVP Module VI, chapter VI.B.1.1.1. Is the report unsolicited? If No, proceed with step 1.4.1 If Yes, proceed with step 1.5
1.4.1	If the literature record is not a spontaneous report i.e. refers to a solicited report, proceed as follows: • If the literature record refers to an animal study or an *in vitro* study, the record can be excluded from ICSR reporting (GVP Module VI, chapter VI.C.1). The literature record is to be moved to the exclusion group with the exclusion criteria to be recorded.
1.4.2	• If the literature record refers to a toxicology study, the record can be excluded from ICSR reporting (GVP Module VI, chapter VI.C.1). The literature record is to be moved to the exclusion group with the exclusion criteria to be recorded.
1.4.3	• If the literature record refers to an interventional study, the record can be excluded from ICSR reporting (GVP Module VI, chapter VI.C.1). The literature record is to be moved to the exclusion group with the exclusion criteria to be recorded.
1.4.4	– If the literature record refers to solicited reports other than interventional studies, check the data source for the literature record.
1.4.5	• If the literature record refers to aggregated data on patients, move the literature record to the exclusion group and record the exclusion criteria.
1.4.6	√ If the literature record refers to one or more individual and identifiable patients, move literature record in inclusion group and record inclusion criteria.
1.5	If the literature record refers to a spontaneous report (unsolicited communication, which does not derive from a study or any organised data collection systems where adverse event reporting is actively sought), proceed as follows:
1.5.1	• If the data source refers to literature ICSRs, which are based on an analysis from a competent authority database within the EU, the literature record can be excluded from ICSR reporting (GVP Module VI, chapter VI.C.2.2.3.). The literature record is to be moved to the exclusion group with the exclusion criteria to be recorded.

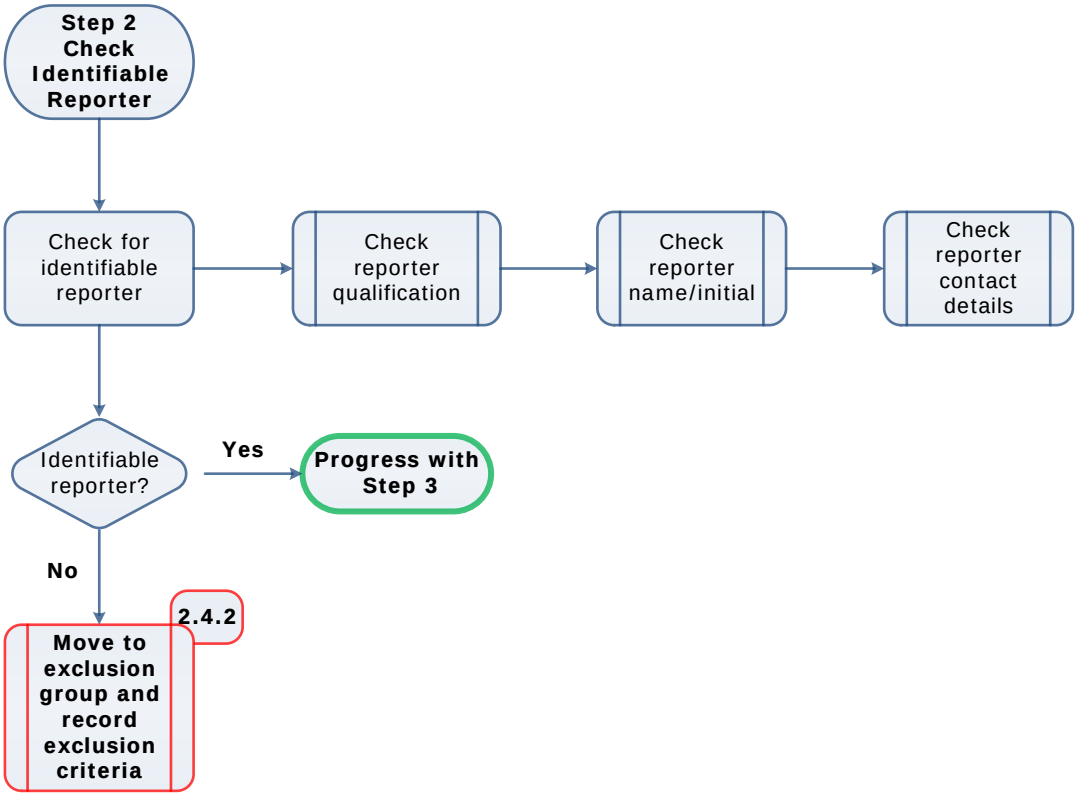
Step – 1 Report Type	Action	
1.5.2	√	If the data source refers to literature ICSRs, which are based on the analysis from a competent authority database outside the EU, the ICSR reporting requirements remain (GVP Module VI, chapter VI.C.2.2.3.). Progress with Step 2 and record inclusion criteria.
1.5.3	•	If the literature record present data analyses from publicly available databases[2] and/or describes a systematic retrospective records review, which describes adverse reactions, which occur in a group of patients with a designated medicinal product with the aim of identifying or quantifying a safety hazard related to a medicinal product, the literature record can be excluded from ICSR reporting. The literature record is to be moved to the exclusion group with the exclusion criteria to be recorded.
1.5.4	√	If the literature record present spontaneous reports where the individual patient(s) can be associated with one or more suspected adverse reaction(s) related to one or more suspect/interacting medicinal products, the ICSR reporting requirements remain (GVP Module VI, chapter VI.B.2.). Progress to Step 2. Move literature record in inclusion group and record inclusion criteria.

[2] This includes Vigibase: http://who-umc.org/DynPage.aspx?id=98082&mn1=7347&mn2=7252&mn3=7322&mn4=7326

2.2. Identifiable Reporter

Step 2 refers to the determination of one or more identifiable reporters.

In the case of a published study or published individual case, the reporter would be the investigator or first author, and details on publication and trial type should also be provided[3].



Step – 2 Identifiable Reporter	Action
2.1	Check if the literature record refers to one or more identifiable reporter (primary source) as outlined in GVP Module VI, chapter VI.B.2 based on at least one of the criteria outlined under point 2.2 to 2.4.
2.2	Check if the reporter qualification (e.g. physician, pharmacist, other healthcare professional, lawyer, consumer or other non-healthcare professional) can be determined.
2.2.1	√ If the reporter qualification can be determined, record inclusion criteria.
2.2.2	• If the reporter qualification cannot be determined, record missing information and proceed with step 2.3.

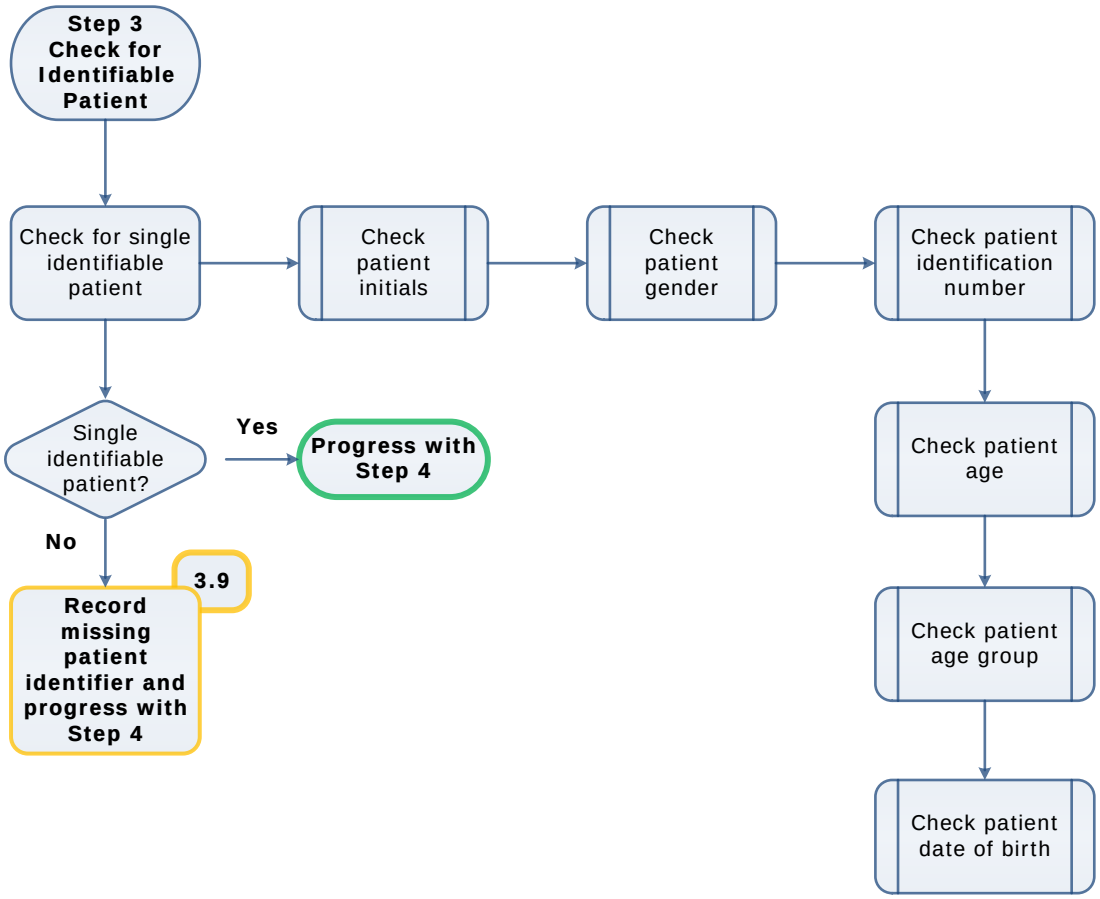
[3] ICH Harmonised Tripartite Guideline / Maintenance of the ICH Guideline On Clinical Safety Data Management: Data Elements For Transmission of Individual Case Safety Reports: E2B(R2): http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E2B/Step4/E2B_R2__Guideline.pdf

Step – 2 Identifiable Reporter	Action
2.3	Check if the reporter name or initials can be determined.
2.3.1	√ If the reporter name or initials can be determined, record inclusion criteria.
2.3.2	• If the reporter name or initials cannot be determined, record missing information and proceed with step 2.4.
2.4	Check the reporter address[4] (contact details) can be determined to ensure that follow-up activities can be performed.
2.4.1	√ If the reporter address/contact is available record inclusion criteria.
2.4.2	• If reporter address/contact is not available record missing information.
2.5	If one or more identifiable reporter can be determined through at least one of the aforementioned criteria(steps 2.2 to 2.4), progress with step 3.
2.6	If no identifiable reporter can be determined based on any of the aforementioned steps, move the literature record to exclusion group and record exclusion criteria.

[4] For Spain at least one of the data elements reporterstate (ICH E2B (R2) A.2.1.2e) or reporterpostcode (ICH E2B (R2) A.2.1.2f) should be populated.

2.3. Identifiable Patient

Step 3 refers to the determination of an identifiable patient.

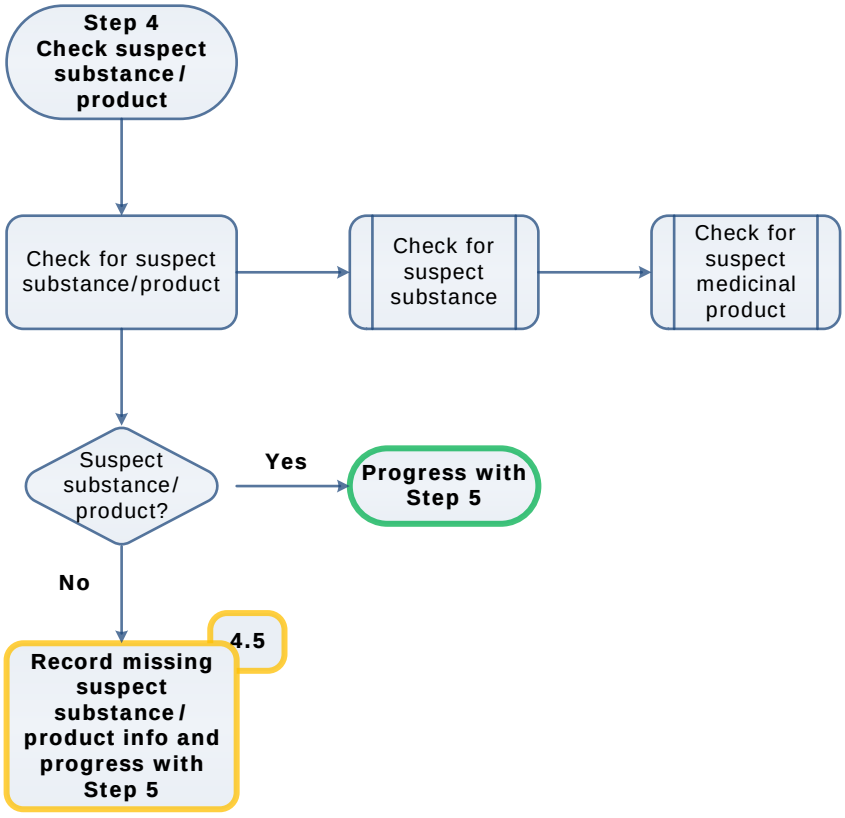


Step – 3 Identifiable Patient	Action
3.1	Check if the literature record refers to one or more identifiable patient as outlined in GVP Module VI, chapter VI.B.2. based on at least one of the criteria outlined under point 3.2 to 3.7.
3.2	Check if the patient initials can be determined
3.2.1	√ If the patient initials can be determined, record inclusion criteria.
3.2.2	• If the patient initials cannot be determined, record missing information and proceed with step 3.3.
3.3	Check if the patient gender can be determined.
3.3.1	√ If the patient gender can be determined, record inclusion criteria.
3.3.2	• If the patient gender cannot be determined, record missing information

Step – 3 Identifiable Patient	Action
	and proceed with step 3.4.
3.4	Check if a patient identification number can be determined.
3.4.1	√ If the patient identification number is available record inclusion criteria.
3.4.2	• If patient identification number is not available record missing information and proceed with step 3.5.
3.5	Check if the patient age can be determined.
3.5.1	√ If the patient age can be determined, record inclusion criteria.
3.5.2	• If the patient age cannot be determined, record missing information and proceed with step 3.6.
3.6	Check if a patient age group can be determined.
3.6.1	√ If the patient age group is available record inclusion criteria.
3.6.2	• If patient age group is not available record missing information and proceed with step 3.7.
3.7	Check if a patient birth date is provided.
3.7.1	√ If the patient birth date is available record inclusion criteria.
3.7.2	• If patient birth date is not available record missing information.
3.8	If one or more identifiable patient can be determined through at least one of the aforementioned criteria (steps 3.2 to 3.7), progress with step 4.
3.9	If no identifiable patient can be determined based on any of the aforementioned steps, record accordingly and progress with step 4.

2.4. One or more suspected substance / medicinal product

Step 4 refers to the identification of one or more suspected/interacting substance(s) or medicinal product(s) subject to the monitoring in accordance with Article 27 of Regulation (EC) No 726/2004.

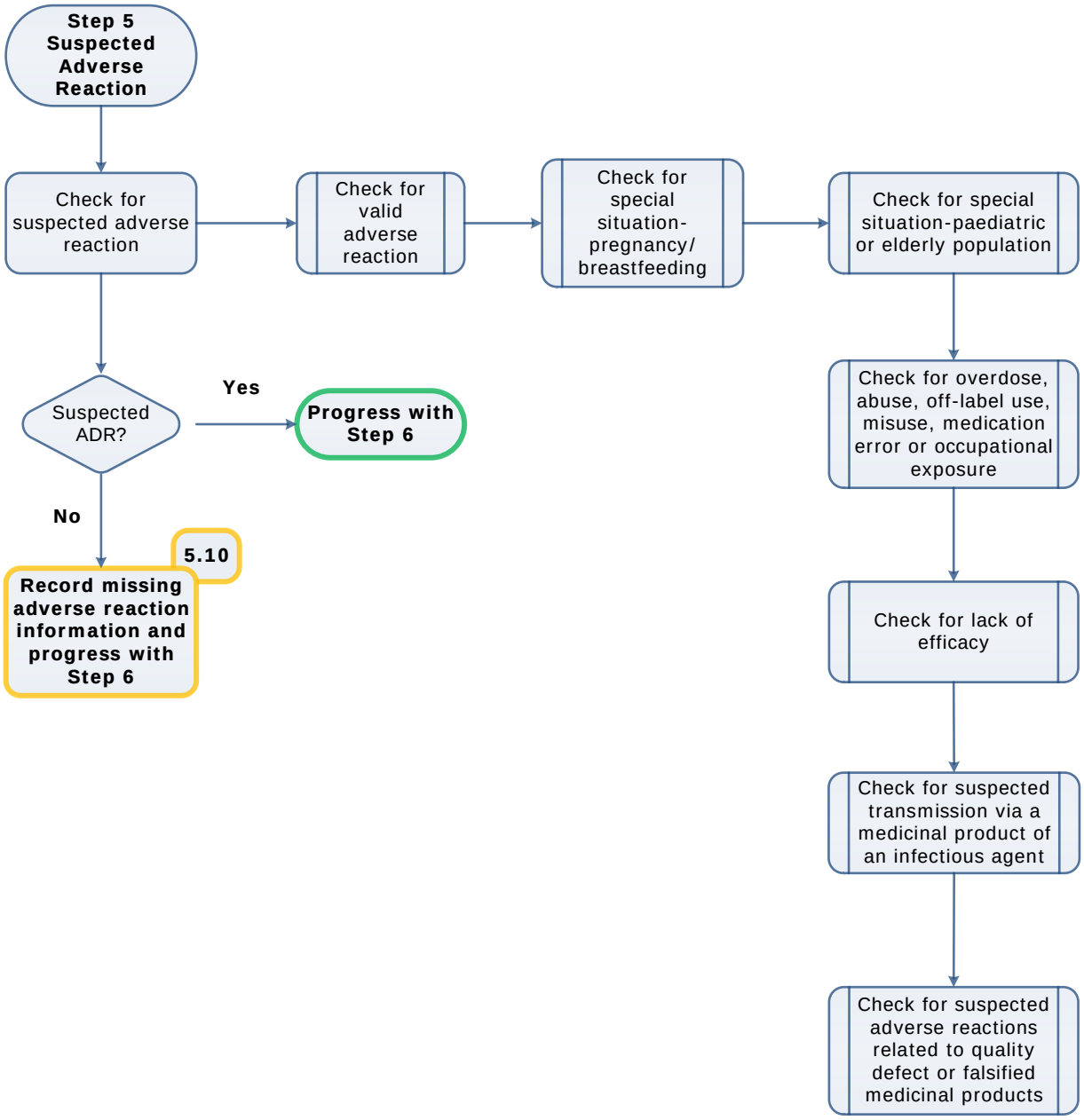


Step – 4 Suspect substance / medicinal product	Action
4.1	Check if the literature record refers to one or more suspected/interacting substance/medicinal product as outlined in GVP Module VI, chapter VI.B.2.
4.2	Check if a suspected/interacting substance(s) can be determined (in relation to the substance groups subject to the literature monitoring by the Agency).
4.2.1	√ If a suspected/interacting substance(s) can be determined, record inclusion criteria.
4.2.2	• If a suspected/interacting substance(s) cannot be determined, record missing information.
4.3	Check if a suspected medicinal product can be determined (in relation to substance groups subject to the literature monitoring by the Agency).
4.3.1	√ If a suspected/interacting medicinal product(s) can be determined, record inclusion criteria.

Step – 4 Suspect substance / medicinal product	Action
4.3.2	• If a suspected/interacting medicinal product(s) cannot be determined, record missing information.
4.4	If one or more suspected/interacting substance/medicinal product can be determined through at least one of the aforementioned steps (4.2 to 4.3), progress with step 5.
4.5	If no suspected substance(s)/medicinal product(s) can be determined based on the aforementioned steps, record accordingly and progress with step 5.

2.5. One or more suspected adverse reaction(s)

Step 5 refers to the identification of one or more suspected adverse reaction(s).

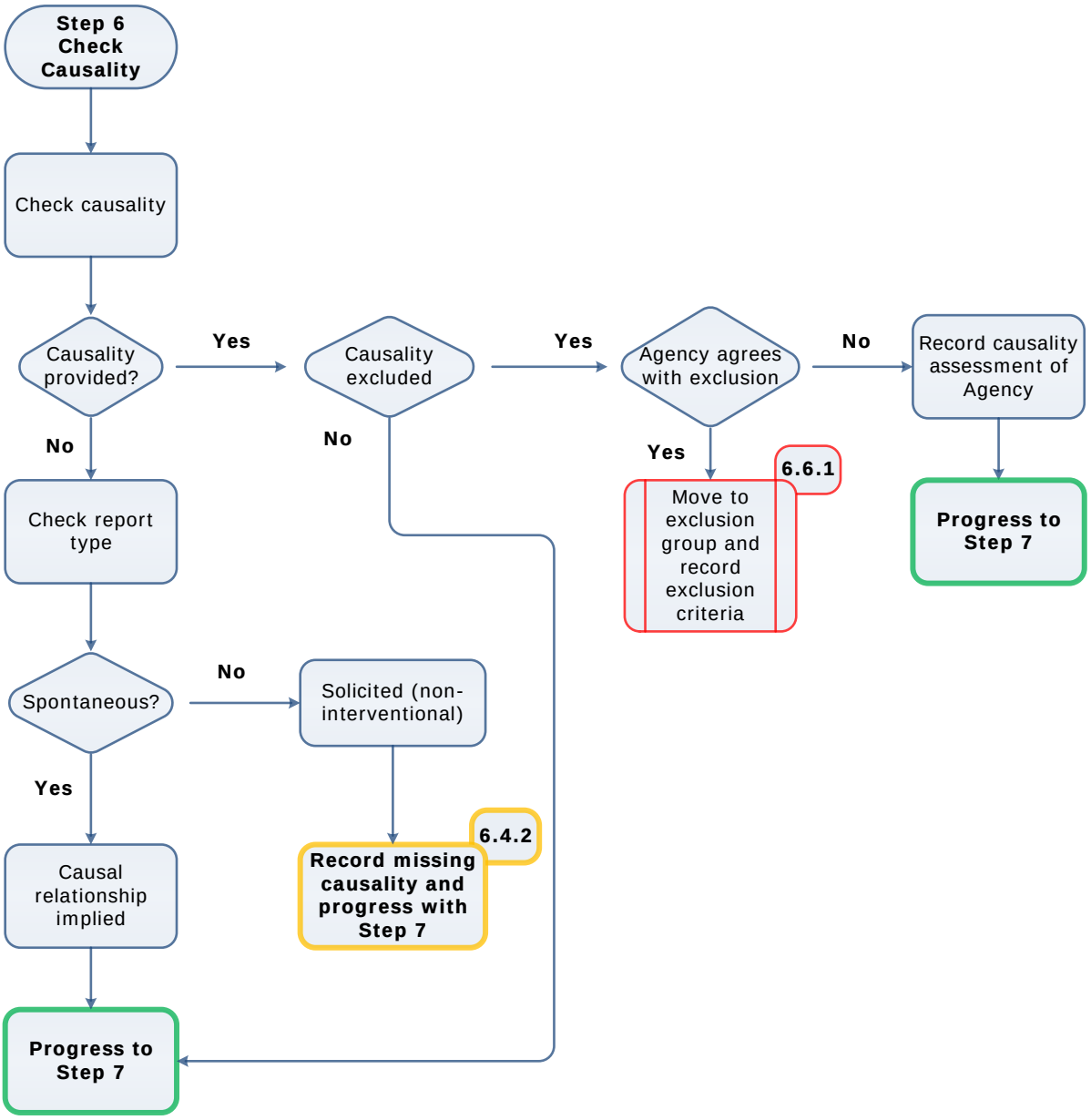


Step – 5 Suspect adverse reaction	Action
5.1	Check if the literature record refers to one or more suspected/adverse reaction as outlined in GVP Module VI, chapter VI.B.2.
5.2	Check for suspected adverse reaction in accordance with GVP Module VI, chapters VI.A.2.1. and VI.B.2. (fourth bullet point)

Step – 5 Suspect adverse reaction	Action
5.2.1	√ If a 'valid' suspected adverse reaction can be determined, record inclusion criteria.
5.2.2	• If a suspected adverse reaction cannot be determined or if there is a reference to an unspecified adverse reaction and there is no information provided on the type of adverse reaction experienced, record missing information.
5.3.	Check for special situation - use of a medicinal product during pregnancy or breastfeeding in accordance with GVP Module VI, chapter VI.B.6.1.
5.3.1	√ If a suspected adverse reaction can be determined as a result of the use of a medicinal product during pregnancy or breastfeeding, record inclusion criteria.
5.3.2	• If literature record refers to induced termination of pregnancy without information on congenital malformation, record exclusion criteria (since there is no suspected adverse reaction).
5.3.3	• If literature record refers to pregnancy exposure without outcome data, record exclusion criteria (since there is no suspected adverse reaction).
5.3.4	• If literature record refers to pregnancy exposure with normal outcome, record exclusion criteria (since there is no suspected adverse reaction).
5.3.5	√ If a literature record refers to pregnancy exposure with no suspected adverse reaction if condition of the marketing authorisation or stipulated in the risk management plan, record inclusion criteria. Note: for example pregnancy exposure to medicinal products contraindicated in pregnancy or medicinal products with a special need for surveillance because of a high teratogenic potential (e.g. thalidomide, isotretinoin).
5.4	Check for special situation - use of a medicinal product in a paediatric or elderly population in accordance with GVP Module, chapter VI.B.6.2.
5.4.1	√ If the literature record refers to the use of a medicinal product in a paediatric or elderly population with one or more suspected adverse reactions, record inclusion criteria.
5.4.2	• If the literature record does refers to the use of a medicinal product in a paediatric or elderly population without a suspected adverse reaction, record exclusion criteria.
5.5	Check for special situation - reports of overdose, abuse, off-label use, misuse, medication error or occupational exposure in accordance with GVP Module VI, chapter VI.B.6.3.
5.5.1	√ If the literature record refers to reports of overdose, abuse, off-label use, misuse, medication error or occupational exposure with one or more suspected adverse reactions, record inclusion criteria.

Step – 5 Suspect adverse reaction	Action
5.5.2	• If the literature record refers to reports of overdose, abuse, off-label use, misuse, medication error or occupational exposure with no associated adverse reaction, record exclusion criteria.
5.6	Check for special situation - Lack of therapeutic efficacy in accordance with GVP Module VI, chapter VI.B.6.4.
5.6.1	√ If the literature record refers to lack of therapeutic efficacy with one or more suspected adverse reactions, record inclusion criteria.
5.6.2	√ If the literature record refers to reports of lack of therapeutic efficacy for a medicinal product used in critical conditions or for the treatment of life-threatening diseases, record in inclusion criteria. Note: Clinical judgement should be used when considering if other cases of lack of therapeutic efficacy qualify for reporting. For example, a life-threatening infection, where the lack of therapeutic efficacy appears to be due to the development of a newly resistant strain of a bacterium previously regarded as susceptible, is reportable.
5.6.3	• If the literature record does not refer to lack of therapeutic efficacy with one or more suspected adverse reactions, record exclusion criteria.
5.7.	Check for suspected transmission via a medicinal product of an infectious agent in accordance with GVP Module VI, chapter VI.C.2.2.5.
5.7.1	√ If the literature record refers to a suspected transmission via a medicinal product of an infectious agent, record inclusion criteria.
5.7.2	• If the literature record does not refer to a suspected transmission via a medicinal product of an infectious agent, record exclusion criteria.
5.8	Check for suspected adverse reactions related to quality defect or falsified medicinal products in accordance with GVP Module VI, chapter VI.C.2.2.4.
5.8.1	√ If the literature record refers to suspected adverse reactions related to quality defect or falsified medicinal products, record inclusion criteria.
5.8.2	• If the literature record does not refer to a suspected adverse reactions related to quality defect or falsified medicinal products, record in exclusion criteria.
5.9	If one or more suspected adverse reaction can be determined through one of the aforementioned steps (5.2 to 5.9), progress with step 6.
5.10	If no suspected adverse reaction can be determined based on the aforementioned steps, record accordingly and progress with step 6.

2.6. Causality



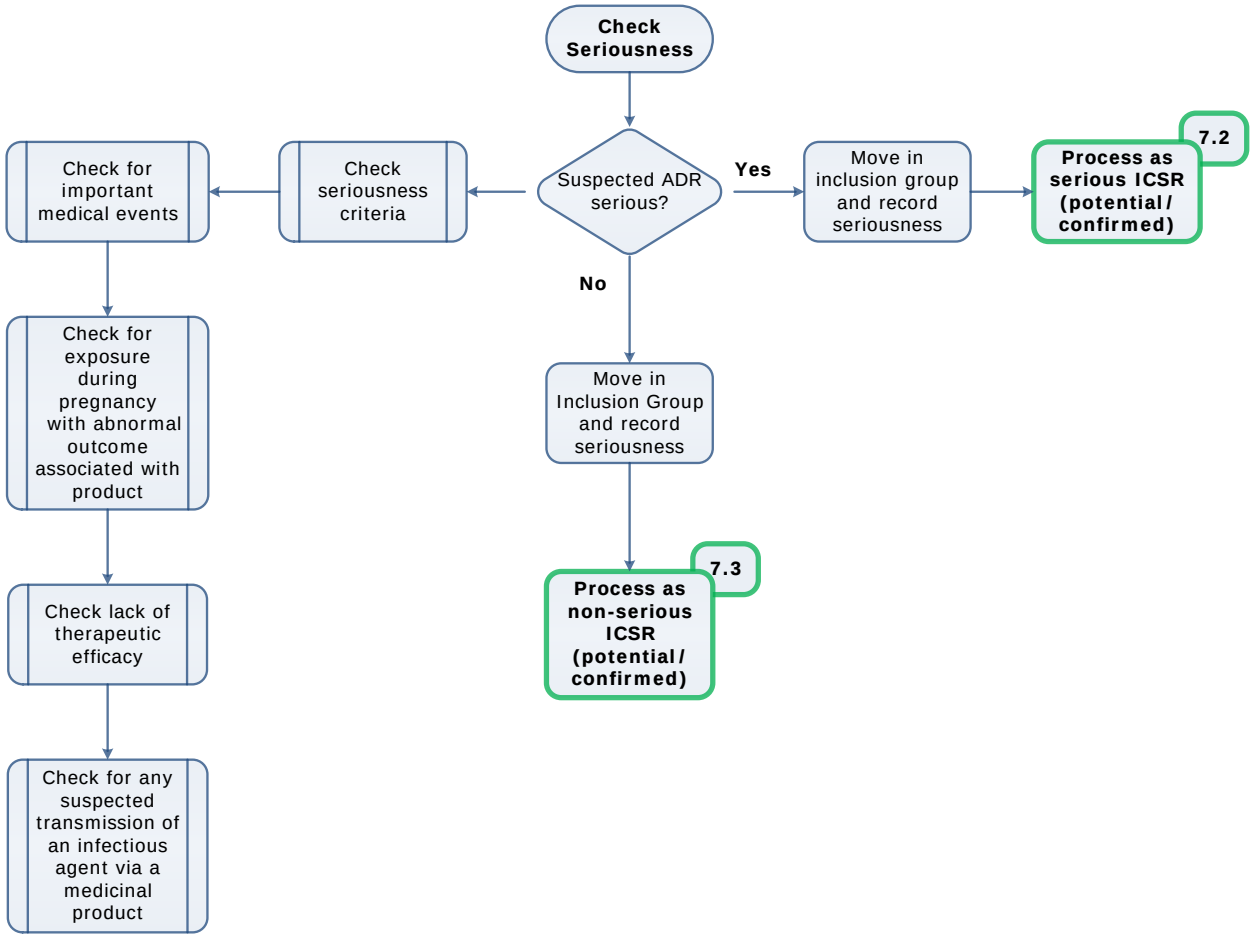
Step – 6 Causality	Action
6.1	Check if the literature record provides a causality assessment as outlined in GVP Module VI, chapters VI.A.2.1.1, VI.B.2 and VI.C.6.2.2.4.
6.2	Check if causality assessment has been provided.

Step – 6 Causality	Action
6.3	If causality is not excluded progress with step 7. NOTE: Reference is also made to GVP Module VI, chapter VI.B.2. where the following is stated: "A valid case of suspected adverse reaction initially submitted by a consumer cannot be downgraded to a report of non-related adverse event if the contacted healthcare professional (nominated by the consumer for follow-up information) disagrees with the consumer's suspicion (see VI.A.2.1.1.). In this situation, the opinions of both the consumer and the healthcare professional should be included in the ICSR. Guidance on the reporting of the medical confirmation of a case, provided in ICH-E2B(R2) Section A.1.14 ("Was the case medically confirmed, if not initially from a healthcare professional?") (see GVP Annex IV), should be followed. For solicited reports of suspected adverse reactions (see VI.B.1.2.), where the receiver disagrees with the reasonable possibility of causal relationship between the suspected medicinal product and the adverse reaction expressed by the primary source, the case should not be downgraded to a report of non-related adverse event. The opinions of both, the primary source and the receiver, should be recorded in the ICSR".
6.4	If causality has not been provided, check report type.
6.4.1	√ If the report type is spontaneous, the causal relationship is implied (see GVP Module VI, chapter VI.A.2.1.1). Record inclusion criteria and progress with step 7. Note: According to the GVP VI.B.1.1.2., for literature reports, "If multiple medicinal products are mentioned in the publication, only those which are identified by the publication's author(s) as having at least a possible causal relationship with the suspected adverse reaction should be considered by the concerned marketing authorisation holder(s)." If the report type is spontaneous in the literature and no causality is provided for a single or multiple medicinal products reported, the medicinal product(s) reported will be considered as suspect. Follow-up will be initiated for serious adverse reactions with the primary author to obtain feedback on the possible causal relationship. If a causal relationship is excluded for any of the reported medicinal products, proceed with step 6.6.
6.4.2	√ If report type is solicited and non-interventional, record missing causality and progress with step 7. Note: report type solicited and interventional has been excluded at step 1.
6.5	If causality has been provided, check if causality is excluded.
6.6	If causality is excluded, check in accordance with GVP Module VI, chapter VI.B.2 if Agency agrees with exclusion of the causal relationship.

Step – 6 Causality	Action
6.6.1	• If the Agency agrees with the exclusion of the causal relationship, move literature record in exclusion group and record the exclusion criteria. The process ends here.
6.6.2	√ If the Agency does not agree with the exclusion of the causal relationship, record the Agency's causality assessment in inclusion criteria and progress with step 7.

2.7. Seriousness

Step 7 refers to the determination of seriousness of the suspected adverse reaction(s).



Step – 7 Seriousness	Action
7.1	Check for seriousness as outlined in GVP Module VI, chapter VI.A.2.4.
7.1.1.	Check for any untoward medical occurrence that at any dose results in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a congenital anomaly/birth defect.
7.1.2	If none of the criteria under point 7.1.1 are met, check whether other situations should be considered as serious reactions exercising medical judgement. Check if the described medical events may jeopardise the patient or may require an intervention to prevent one of the above characteristics/consequences. The IME list as developed by the EV-EWG can be applied for guidance purpose only.

Step – 7 Seriousness	Action
7.1.3	Check individual cases with an abnormal outcome associated with a medicinal product following exposure during pregnancy; they are to be classified as serious reports in accordance with GVP Module VI, chapter VI.B.6.1. This especially refers to: – reports of congenital anomalies or developmental delay, in the foetus or the child; – reports of foetal death and spontaneous abortion; and – reports of suspected adverse reactions in the neonate that are classified as serious.
7.1.4	Check if the lack of therapeutic efficacy may require to be reported within a 15-day time frame (expedited reporting for serious adverse reactions) e.g. for medicinal products used in critical conditions or for the treatment of life-threatening diseases in accordance with GVP Module VI, chapter VI.B.6.4.
7.1.5	Check for any suspected transmission of an infectious agent via a medicinal product; they should be considered as a serious adverse reaction.
7.2.	√ If seriousness is confirmed, move literature record in Inclusion Group, record as serious and process as potential/confirmed serious ICSR (transmit to EV within 7 days of confirmation).
7.3	√ If seriousness is not confirmed, move literature record in Inclusion Group, record as non-serious and process as potential/confirmed non-serious ICSR (transmit to EV within 21 days of confirmation).

Appendix 1: Tracking sheet exclusion criteria

The following table summarises the exclusion criteria from the sections above and the matching exclusion criteria published in the sum_screen & sum_ICSR tracking sheets:

Step	Exclusion criterion	Tracking sheet term [additional comments]
1.4.1	• If the literature record refers to an animal study or an in vitro study, the record can be excluded from ICSR reporting (GVP Module VI, chapter VI.C.1). The literature record is to be moved to the exclusion group with the exclusion criteria to be recorded.	Animal Study or Toxicology / in vitro study as applicable
1.4.2	• If the literature record refers to a toxicology study, the record can be excluded from ICSR reporting (GVP Module VI, chapter VI.C.1). The literature record is to be moved to the exclusion group with the exclusion criteria to be recorded.	Toxicology / in vitro study
1.4.3	• If the literature record refers to an interventional study, the record can be excluded from ICSR reporting (GVP Module VI, chapter VI.C.1). The literature record is to be moved to the exclusion group with the exclusion criteria to be recorded.	Interventional study
1.4.4.1	• If the literature record refers to aggregated data on patients, move the literature record to the exclusion group and record the exclusion criteria.	Aggregated data on patients
1.5.1	• If the data source refers to literature ICSRs, which are based on an analysis from a competent authority database within the EU, the literature record can be excluded from ICSR reporting (GVP Module VI, chapter VI.C.2.2.3.). The literature record is to be moved to the exclusion group with the exclusion criteria to be recorded.	Aggregated data on patients
1.5.3	• If the literature record present data analyses from publicly available databases[5] which describe adverse reactions, which occur in a group of patients with a designated medicinal product with the aim of identifying or quantifying a safety hazard related to a medicinal product, the literature record can be excluded from ICSR reporting. The literature record is to be moved to the exclusion group with the exclusion criteria to be recorded.	Aggregated data on patients

[5] This includes Vigibase: http://who-umc.org/DynPage.aspx?id=98082&mn1=7347&mn2=7252&mn3=7322&mn4=7326

Step	Exclusion criterion	Tracking sheet term [additional comments]
2.2.2	• If the reporter qualification cannot be determined, record missing information and proceed with step 2.3.	Unidentifiable reporter [Potential]
2.3.2	• If the reporter name or initials cannot be determined, record missing information and proceed with step 2.4.	Unidentifiable reporter [Potential]
2.4.2	• If reporter address/contact is not available record missing information.	Unidentifiable reporter [If reporter is unidentifiable at both 2.2.2 & 2.3.2 too, then case is excluded]
3.2.2	• If the patient initials cannot be determined, record missing information and proceed with step 3.3.	Unidentifiable patient [only exclude if all patient identifiers (3.2.2 – 3.7.2) are missing]
3.3.2	• If the patient gender cannot be determined, record missing information and proceed with step 3.4.	Unidentifiable patient [only exclude if all patient identifiers (3.2.2 – 3.7.2) are missing]
3.4.2	• If patient identification number is not available record missing information and proceed with step 3.5.	Unidentifiable patient [only exclude if all patient identifiers (3.2.2 – 3.7.2) are missing]
3.5.2	• If the patient age cannot be determined, record missing information and proceed with step 3.6.	Unidentifiable patient [only exclude if all patient identifiers (3.2.2 – 3.7.2) are missing]
3.6.2	• If patient age group is not available record missing information and proceed with step 3.7.	Unidentifiable patient [only exclude if all patient identifiers (3.2.2 – 3.7.2) are missing]
3.7.2	• If patient birth date is not available record missing information.	Unidentifiable patient [If patient is unidentifiable at 3.2.2, 3.3.2, 3.4.2, 3.5.2 & 3.6.2 too, then case is excluded]
4.2.2	• If a suspected/interacting substance(s) cannot be determined, record missing information.	Suspected substance or medicinal product missing [only exclude in combination with 4.3.2]
4.3.2	• If a suspected/interacting medicinal product(s) cannot be determined, record missing information.	Suspected substance or medicinal product missing [only exclude in combination with 4.2.2]
5.2.2	• If a suspected adverse reaction cannot be determined or if there is a reference to an unspecified adverse reaction and there is no information provided on the type of adverse reaction experienced, record missing information.	Suspected adverse reaction missing [Potential if there is a reference to an unspecified adverse reaction and there is no information provided on the type of adverse reaction experienced]

Step	Exclusion criterion	Tracking sheet term [additional comments]
5.3.2	• If literature record refers to induced termination of pregnancy without information on congenital malformation, record exclusion criteria (since there is no suspected adverse reaction).	Termination of pregnancy – no ADR information
5.3.3	• If literature record refers to pregnancy exposure without outcome data, record exclusion criteria (since there is no suspected adverse reaction).	Pregnancy – outcome unknown
5.3.4	• If literature record refers to pregnancy exposure with normal outcome, record exclusion criteria (since there is no suspected adverse reaction).	Pregnancy – no ADR
5.4.2	• If the literature record does refers to the use of a medicinal product in a paediatric or elderly population without a suspected adverse reaction, record exclusion criteria.	Paediatric – no ADR Or Elderly – no ADR [select one as applicable]
5.5.2	• If the literature record refers to reports of overdose, abuse, off-label use, misuse, medication error or occupational exposure with no associated adverse reaction, record exclusion criteria.	Overdose – no ADR Abuse – no ADR Off-label use – no ADR Misuse – no ADR Medication error – no ADR Occupational exposure – no ADR [select one as applicable]
5.6.3	• If the literature record does not refer to lack of therapeutic efficacy with one or more suspected adverse reactions, record exclusion criteria.	Lack of efficacy (non-life-threatening)
5.7.2	• If the literature record does not refer to a suspected transmission via a medicinal product of an infectious agent, record exclusion criteria.	Suspected adverse reaction missing
5.8.2	• If the literature record does not refer to a suspected adverse reactions related to quality defect or falsified medicinal products, record in exclusion criteria.	Quality defect – no ADR Falsified medicines – no ADR [select one as applicable]
6.6.1	• If the Agency agrees with the exclusion of the causal relationship, move literature record in exclusion group and record the exclusion criteria. The process ends here.	Causality missing

Additional exclusion criteria

The following exclusion criteria may also be used in the tracking sheets. These do not meet any of the steps outlined above, but may be returned in our searches and need to be tracked:

- **Erroneous search result**

Occasionally a result may arise, that is unrelated to either active substances or adverse events and containing no ADR information. These are usually unrelated to medical matters at all. In these circumstances, the term "Erroneous search result" will be entered as the exclusion criterion.

- **Full text requested**

If a case cannot be confirmed or excluded on the basis of the data available at the time of searching and the full text article needs to be purchased, then the row will be marked as Potential, with "Full text requested" entered in the ‘Inclusion/exclusion criteria’ column.

- **Translation requested**

If an article requires translation before it can be assessed, then the row will be marked as Potential, with "Translation requested" entered in the ‘Inclusion/exclusion criteria’ column. A translation request does not stop the 7/21-day clock.

- **Article in press**

If there is insufficient information in the abstract to make a case; but the article cannot be obtained because it is still in press, it will be marked as Potential with the exclusion criterion "Article in press".