



National Agency for Food & Drug Administration & Control (NAFDAC)

Pharmacovigilance Directorate

NAFDAC Good Pharmacovigilance Practice Guideline

Chapter 5 Adverse Reaction Reporting

CHAPTER 5 ADVERSE REACTION REPORTING	4
5.1 Purpose	4
5.2 Scope	4
5.3 Definitions	4
5.4 Structures and Processes.....	9
5.4.1 Collection of Individual Safety Reports	9
5.4.2 Sources of Report.....	10
5.4.2.1 Unsolicited report.....	10
5.4.2.1.1 Spontaneous reports	10
5.4.2.1.2 Literature reports.....	11
5.4.2.1.3 Reports from non-medical sources	12
5.4.2.1.4 Information on suspected adverse reactions from the internet or digital media	12
5.4.2.2 Solicited reports	12
5.4.2.2.1 Adverse Reaction Reports from Post-Authorisation Studies.....	13
5.4.2.2.2 Reports from other Post-Marketing Initiatives: Surveys, Registries and Organised Data Collection Systems	14
5.4.2.2.3 Reports from patient support programmes and market research programmes	14
5.4.2.3 Contractual Agreements.....	15
5.4.3 Validation of reports	15
5.4.4 Follow-up of reports	17
5.4.5 Reporting of Individual case safety reports (ICSRs)	18
5.4.6 Reporting timelines.....	19
5.4.6.1 Serious Adverse Reactions.....	19
5.4.6.2 Significant Safety Issues	20
5.4.7 Tabulated summary of reporting requirements).....	20
5.4.8 Reporting format	21
5.4.9 Data management	21
5.4.10 Quality management.....	22
5.5 Special situations	23
5.5.1 Use of a medicinal product during pregnancy or breastfeeding	23
5.5.1.1 Pregnancy.....	23
5.5.1.2 Breastfeeding.....	24
5.5.2 Use of a medicinal product in a paediatric or elderly population	24

5.5.3 Reports of overdose, abuse, off-label use, misuse, medication error or occupational exposure.....24

5.5.4 Lack of therapeutic efficacy.....25

5.5.5 Suspected adverse reactions related to quality defect or Substandard and falsified medicinal products...25

5.5.6 Suspected transmission via a medicinal product of an infectious agent 25

5.5.7 Emerging safety issues.....26

5.5.8 Donated Medicinal Products.....26

5.5.9 Period between the submission of the marketing authorisation holder application and the granting of the marketing authorization 27

5.5.10 Period after suspension, revocation or withdrawal of Marketing Authorisation 27

5.5.11 Period during a public health emergency 28

CHAPTER 5 ADVERSE REACTION REPORTING

5.1 Purpose

This chapter of the GVP guides the implementation of the legal requirements outlined in the Good Pharmacovigilance Practice Regulation, Section 11, specifically for marketing authorization holders and NAFDAC regarding the collection, data management, and submission of individual reports of suspected adverse reactions (serious and non-serious) related to medicinal products authorized for human use in Nigeria. It details the expectations for the collection, validation, follow-up, management, and submission of Individual Case Safety Reports (ICSRs) for these medicinal products. The provisions in this chapter are in line with ICH E2D and ICH E2B(R3) standards, reflecting internationally recognized best practices as described in EMA GVP Module VI.

5.2 Scope

This Chapter applies to:

- Marketing Authorisation Holders (MAHs)
- Applicants for marketing authorisation
- Contracted pharmacovigilance service providers
- Healthcare professionals and other reporters
- The National Pharmacovigilance Centre

These requirements apply to all suspected adverse reactions occurring:

- In Nigeria
- Outside Nigeria (foreign reports)
- In organised data collection systems (e.g., registries, post-authorisation studies)

5.3 Definitions

Adverse Event (AE): An adverse event is any untoward medical occurrence in a patient exposed to a medicinal product and which does not necessarily have a causal relationship with the medicinal product. An adverse event can therefore be any unfavourable and unintended sign (for example, an abnormal laboratory finding), symptoms, or disease temporally associated with the use of a medicinal product, whether or not considered causally related to this medicinal product

Adverse Reaction: An Adverse Reaction is a response to a medicinal product which is noxious and unintended. A response to a medicinal product means that a causal relationship between the medicinal product and the adverse event is at least a reasonable possibility.

Adverse reactions may arise from use of the medicinal product within or outside the terms of the marketing authorisation. Use outside the marketing authorisation includes, but is not limited to:

- Off-label use
- Overdose
- Misuse

- Abuse
- Medication errors
- Occupational exposure

For regulatory reporting purposes, if an adverse event is spontaneously reported, even where the causal relationship is unknown or not explicitly stated, it should be treated as a suspected adverse reaction.

Causality: the likelihood that a medicinal product is responsible for an observed adverse event. In accordance with ICH-E2A, 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 characterised by the fact that a causal relationship between a medicinal product and an occurrence is suspected.

For regulatory reporting purposes, as detailed in ICH-E2D, 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 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.

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 authorised product information. Clinical judgement should always be applied.

Off-label use: This relates to situations where the medicinal product is intentionally used for a medical purpose not in accordance with its approved labeling or product information

Misuse: This refers to situations where the medicinal product is intentionally and inappropriately used not in accordance with the terms of the marketing authorisation.

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

Occupational exposure: This refers to the exposure to a medicinal product as a result of one's professional or non-professional occupation. It does not include the exposure to one of the ingredients during the manufacturing process before the release as a finished product.

Medication error: This is an unintended failure in the drug treatment process that leads to, or has the potential to lead to harm to the patient.

Falsified medicinal product: This relates to any medicinal product with a false representation of:

- its identity, including its packaging and labelling, its name or its composition as regards any of the ingredients, including excipients and the strength of those ingredients;
- its source, including its manufacturer, its country of manufacturing, its country of origin or its marketing authorisation holder; or
- its history, including the records and documents relating to the distribution channels used.

This definition does not include unintentional quality defects and is without prejudice to infringements of intellectual property rights.

Active substance: Any substance or mixture of substances intended to be used in the manufacture of a medicinal product and that, when used in its production, becomes an active ingredient of that product intended to exert a pharmacological, immunological or metabolic action with a view to restoring, correcting or modifying physiological functions or to make a medical diagnosis.

Excipient: Any constituent of a medicinal product other than the active substance and the packaging material; E.g. colouring matter, preservatives, adjuvants, stabilisers, thickeners, emulsifiers, flavouring and aromatic substances.

Medicinal product: A medicinal product is characterised 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.

Primary source, healthcare professional, consumer

In accordance with ICH-E2B, the primary source of the information is the person who reports the facts about an ICSR. Several primary sources, such as healthcare professionals and/or consumers, may provide information on the same case. In this situation, all the primary sources' details, including the qualifications, should be provided in the ICSR and the "Primary source(s)" section should be repeated as necessary in line with ICH-E2B (See 5.4.3 Validation of reports)

In accordance with the ICH-E2D,

- 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 confirmation

A consumer may provide medical documentation (e.g., laboratory or other test data) that supports the occurrence of a suspected adverse reaction and which indicates that an identifiable healthcare professional suspects a causal relationship between a medicinal product and the reported adverse reaction. Similarly, a report may be notified by a medically qualified patient, friend, relative or carer of the patient. In these situations, the reported information is considered medically confirmed. In the same way, where one or more suspected adverse reactions initially reported by a consumer are subsequently confirmed by a healthcare professional, the ICSR should be considered medically confirmed. It should be updated at the case level in line with ICH-E2B(R2), or at adverse reaction level in accordance with ICH-E2B(R3) for each subsequently medically confirmed suspected 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 (NOTE: The term “life-threatening” in the definition of “serious” refers to an AE/ADR in which the patient was at risk of death at the time of the AE/ADR; it does not refer to an AE/ADR that hypothetically might have caused death if it were more severe);
- requires inpatient hospitalisation or results in prolongation of existing hospitalisation;
- results in persistent or significant disability/incapacity;
- is a congenital anomaly/birth defect;
- is an important medical event as described below

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

Where one or more serious suspected adverse reactions are reported in an ICSR, the information on the seriousness should be documented at the case level in line with ICH-E2B(R2) or for each suspected adverse reaction in accordance with ICH-E2B(R3), depending on the ICH-E2B format used for the ICSR electronic submission.

Unexpected Adverse Event / Adverse Reaction

An Unexpected Adverse Event (AE) or Unexpected Adverse Reaction (ADR) is an adverse event or adverse reaction, the nature, severity, specificity, or outcome of which is not consistent with the applicable regional or local product information (e.g., Summary of Product Characteristics (SmPC) or Prescribing Information).

An AE/ADR shall be considered unexpected if:

- It is not listed in the current regional or local product labelling; or
- Its nature, severity, specificity, or clinical outcome is not consistent with the description in the product labelling; or
- It is reported with a fatal outcome, unless the product labelling explicitly states that the reaction may be associated with a fatal outcome.

Where there is uncertainty as to whether an AE/ADR should be classified as expected or unexpected it shall be treated as unexpected for regulatory reporting purposes.

Adverse reactions described in product information for the pharmacological class (so-called “drug-class ADRs”) shall not automatically be considered expected for a specific medicinal product unless they are explicitly included in the applicable product labelling for that product.

For individual case safety reporting (ICSR), the term “unexpected” applies in relation to the approved product information. The term “unlisted” refers to the Company Core Safety Information (CCSI) and is not used for regulatory ICSR expectedness assessment.

Individual case safety report (ICSR)

This refers to the format and content for the submission of an individual report of 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 (see 5.4,3 validation of report).

Marketing Authorisation Holder: An entity authorised by the Agency to manufacture, import, receive as donation, distribute or sell a medicinal product in Nigeria

MedDRA (Medical Dictionary for Regulatory Activities): An internationally standardised medical terminology developed under the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). MedDRA is used for the coding, retrieval, analysis, and reporting of medical information relating to human medical products. In Individual Case Safety Report (ICSR) management, it provides a common terminology for coding reported adverse events, signs and symptoms, diagnoses, investigations and other relevant medical concepts, thereby promoting consistency in case processing, safety data analysis, signal detection and regulatory reporting.

MedDRA is organised into a five-level hierarchy, progressing from more specific medical concepts to broader groupings:

1. **Lowest Level Term (LLT):** The most specific level, containing terms that represent how a medical concept may be reported or expressed. Each LLT is linked to a Preferred Term.

2. **Preferred Term (PT):** Represents a single, distinct medical concept and is the principal level used for coding and analysing reported events.
3. **High Level Term (HLT):** Groups related Preferred Terms.
4. **High Level Group Term (HLGT):** Groups related High Level Terms into broader medical categories.
5. **System Organ Class (SOC):** The broadest level, grouping terms by organ system, aetiology, purpose or other defined categories. MedDRA has 27 SOCs, including *Cardiac disorders* and *Nervous system disorders*.

Parent report: A parent report is the original Individual Case Safety Report (ICSR) that contains information about a suspected adverse event for a specific patient.

Solicited reports: Solicited reports are adverse event reports derived from organized data collection systems, where reporting of events is actively sought.

5.4 Structures and Processes

This section highlights the general principles in relation to the collection, recording and reporting of reports of suspected adverse reactions associated with medicinal products for human use as it concerns the Marketing Authorisation Holder (MAH). The definitions provided in 5.3 above should be followed.

5.4.1 Collection of Individual Safety Reports

- 5.4.1.1 The Marketing Authorisation Holder should take appropriate measures to collect and collate all reports of suspected adverse reactions associated with medicinal products for human use originating from unsolicited or solicited sources. The pharmacovigilance 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 and submission to the Agency.
- 5.4.1.2 The system should ensure the collection and recording of all reports of suspected adverse reactions brought to its attention by health care professionals or consumers or occurring in the context of a post-authorization study. Marketing Authorisation Holders should not refuse to consider reports of suspected adverse reactions received from patients and healthcare professionals.
- 5.4.1.3 Marketing Authorisation Holders should establish mechanisms enabling the traceability and follow-up of adverse reaction reports while complying with data protection principles. Pharmacovigilance data and documents relating to individual authorised medicinal products should be retained as long as the product is authorised and for at least 10 years after the Marketing Authorisation Holder has ceased to exist.

- 5.4.1.4 Concerning the collection and recording of reports of suspected adverse reactions, Marketing Authorisation Holders' responsibilities apply to reports related to medicinal products for which ownership cannot be excluded based on one the following criteria:
- medicinal product name
 - active substance name
 - pharmaceutical form
 - batch number
 - route of administration
- 5.4.1.5 The Marketing Authorisation Holder shall ensure that any information on suspected adverse reactions related to at least one of the active substances of its medicinal products authorised in Nigeria, and identified by any company within the same corporate group (including parent, subsidiary or affiliated companies) outside Nigeria, is promptly made available to the MAH. This obligation also applies where the MAH has entered into contractual or commercial agreements with external partners outside Nigeria (e.g. licensing, co-marketing, distribution or pharmacovigilance agreements). In such cases, appropriate arrangements shall be made to ensure the timely exchange of safety information and compliance with reporting requirements.
- 5.4.1.6 All notifications that contain pharmacovigilance data should be recorded and archived in compliance with the applicable data protection requirements of the Agency (See Nigeria Data Protection Act, 2023).

5.4.2 Sources of Report

5.4.2.1 Unsolicited report

5.4.2.1.1 Spontaneous reports

A spontaneous report is unsolicited communication by a healthcare professional, or consumer that describes one or more suspected adverse reactions in a patient who was given one or more medicinal products and that does not derive from a study or any organised data collection systems where adverse event reporting is actively sought. Concerning this, the following situations should also be considered as spontaneous reports:

- 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' organisations to their members, or class action lawsuits should be considered spontaneous reports.
- Unsolicited consumer adverse reaction reports should be handled as spontaneous reports irrespective of any subsequent “medical confirmation”.

- Reports of suspected adverse reactions, which are not related to any organised data collection systems and (i) which are notified through medical enquiry/product information services or (ii) which are consequent of the distribution of information or educational materials;
- Marketing Authorisation Holders shall record all reports of suspected adverse reactions originating from within or outside Nigeria, which are brought to their attention spontaneously by healthcare professionals, or consumers. In this context, Marketing Authorisation Holders may consider utilising their websites to facilitate the collection of reports of suspected adverse reactions by providing adverse reaction forms for reporting, or via e-reporting or appropriate contact details for direct communication.

5.4.2.1.2 Literature reports

The scientific and medical literature is a significant source of information for the monitoring of the safety profile and of the benefit-risk balance of medicinal products, particularly in relation to the detection of new safety signals or emerging safety issues. Marketing Authorisation Holders are therefore expected to maintain awareness of possible publications through a systematic literature review of widely used reference databases (e.g. Medline, Excerpta Medica or Embase) no less frequently than once a week. The Marketing Authorisation Holder 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. In addition, Marketing Authorisation Holders should have procedures in place to monitor scientific and medicinal publications in local journals in countries where medicinal products have a marketing authorisation, and to bring them to the attention of the Agency as appropriate.

Reports of suspected adverse reactions from scientific and medical literature, including relevant published abstracts from meetings and draft manuscripts, should be reviewed and assessed by Marketing Authorisation Holders to identify and record ICSRs originating from spontaneous reports or non-interventional post-authorisation studies.

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. Valid ICSRs should be submitted in accordance with the time lines and modalities detailed in section 5.4.6 Reporting Timelines

One case should be created for each single patient identifiable based on characteristics provided in section 5.4.3 Validation of Report. Relevant medical information should be provided and the publication author(s) should be considered as the primary source(s).

5.4.2.1.3 Reports from non-medical sources

If a Marketing Authorisation Holder becomes aware of a report of suspected adverse reactions originating from a non-medical source, for example the lay press or other media, it should be handled as a spontaneous report. Every attempt should be made to follow-up the case to obtain the minimum information that constitutes a valid ICSR (section 5.6 Validation of reports) The same reporting timelines should be applied as for other spontaneous reports (see section 5.4.6 Reporting Timelines)

5.4.2.1.4 Information on suspected adverse reactions from the internet or digital media

Marketing Authorisation Holders should regularly screen the internet or digital media under their management and responsibility, for potential reports of suspected adverse reactions. In this aspect, digital media is considered to be company sponsored if it is owned, paid for and/or controlled by the Marketing Authorisation Holder. The frequency of the screening should allow for potential valid ICSRs to be reported to the Agency within the appropriate reporting timelines based on the date the information was posted on the internet site/digital medium.

If a Marketing Authorisation Holder 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 reporting as ICSR.

Unsolicited cases of suspected adverse reactions from the internet or digital media should be handled as spontaneous reports. The same reporting timelines as for spontaneous reports should be applied (see section 5.4.6 Reporting Timelines)

In relation to cases from the internet or digital media, the identifiability of the reporter refers to the existence of a real person, that is, it is possible to verify the contact details of the reporter (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.

5.4.2.2 Solicited reports

As defined in ICH-E2D, Solicited reports of suspected adverse reactions are those derived from organised data collection systems, which include clinical trials, non-interventional studies, registries, post-approval named patient use programmes, other patient support and disease management programmes, surveys of patients or healthcare providers, compassionate use or

named patient use, or information gathering on efficacy or patient compliance. Reports of suspected adverse reactions obtained from any of these data collection systems should not be considered spontaneous.

For the purpose of safety reporting, solicited reports should be classified as study reports, and should have an appropriate causality assessment, to consider whether they refer to suspected adverse reactions and therefore meet the minimum criteria for reporting (see section 5.4.3 validation of reports)

5.4.2.2.1 Adverse Reaction Reports from Post-Authorisation Studies

- 5.4.2.2.1.1 MAHs shall report all serious suspected adverse reactions occurring in post-authorisation studies undertaken in Nigeria of which they become aware, in accordance with the reporting timelines for serious adverse reactions specified in this Guideline.
- 5.4.2.2.1.2 Where non-serious suspected adverse reactions from such studies meet the minimum criteria for a valid Individual Case Safety Report (ICSR), they shall be reported in accordance with the applicable timelines.
- 5.4.2.2.1.3 MAHs shall establish and maintain mechanisms to collect complete and comprehensive case information and to evaluate such information to enable meaningful medical assessment and determination of reportability of valid suspected adverse reactions related to the studied (or supplied) medicinal product.
- 5.4.2.2.1.4 MAHs shall exercise due diligence in:
 - Establishing appropriate pharmacovigilance systems for organised data collection activities;
 - Following up reports to obtain clinically relevant and outcome information;
 - Seeking, where possible, the causality assessment of the primary source regarding the role of the studied (or supplied) medicinal product in the reported adverse event.
- 5.4.2.2.1.5 Where the primary source's causality assessment is not available, the MAH shall perform its own medical assessment based on the available information to determine whether there is a reasonable possibility of a causal relationship. Where such a reasonable possibility exists and the minimum reporting criteria are fulfilled, the report shall be submitted to the Agency in accordance with the requirements of this Guideline.
- 5.4.2.2.1.6 Where a post-authorisation study is initiated and conducted independently of the MAH of the medicinal product, and is not sponsored, managed or financed by the MAH, the primary responsibility for reporting adverse

reactions to the Agency rests with the investigator in accordance with applicable research and regulatory requirements.

5.4.2.2.1.7 However, where the MAH becomes aware of a suspected adverse reaction arising from such a study that meets the minimum criteria for a valid ICSR, the MAH shall ensure that the case is assessed and reported to the Agency in accordance with the timelines specified in this Guideline.

5.4.2.2.1.8 MAHs should, where feasible, request that investigators notify them of serious suspected adverse reactions occurring in studies involving their medicinal products.

5.4.2.2.2 Reports from other Post-Marketing Initiatives: Surveys, Registries and Organised Data Collection Systems

5.4.2.2.2.1 MAHs may be involved in post-marketing initiatives that result in the collection of information relating to their medicinal products, including but not limited to:

- Patient support and disease management programmes;
- Surveys of patients or healthcare professionals;
- Programmes designed to gather information on efficacy or patient compliance;
- Market research programmes;
- Voluntary patient or disease registries.

Such activities constitute organised data collection systems and reports arising from them are considered solicited reports. These activities may involve the receipt of information on adverse events.

5.4.2.2.2.2 MAHs shall establish and maintain systems to collect complete and comprehensive case information from such programmes and to evaluate that information in order to determine:

- Whether the minimum criteria for a valid Individual Case Safety Report (ICSR) are fulfilled; and
- Whether there is a reasonable possibility of a causal relationship between the medicinal product and the reported adverse event.

5.4.2.2.2.3 Where the minimum reporting criteria are met and a reasonable possibility of a causal relationship cannot be ruled out, the event shall be classified as a suspected adverse reaction and processed and reported in accordance with the reporting requirements and timelines specified in section 5.4.6 Reporting Timelines.

5.4.2.2.3 Reports from patient support programmes and market research programmes

- 5.4.2.2.3.1 A patient support programme is an organised system where a Marketing Authorisation Holder receives and collects information relating to the use of its medicinal products. Examples are post-authorisation patient support and disease management programmes, surveys of patients and healthcare providers, gathering information on patient compliance, or compensation/reimbursement schemes.
- 5.4.2.2.3.2 A market research programme refers to the systematic collection, recording and analysis by a Marketing Authorisation Holder of data and findings about its medicinal products relevant for marketing and business development.
- 5.4.2.2.3.3 Safety reports originating from those programmes should be considered as solicited reports. Marketing Authorisation Holders should have the same mechanisms in place as for all other solicited reports to manage that information and report valid cases of adverse reactions, which are suspected to be related to the medicinal product concerned.

5.4.2.3 Contractual Agreements

The marketing of many medicines increasingly takes place through contractual agreements between two or more companies, which may market same product in the same or different countries/region. Arrangements vary considerably with respect to inter-company communication and regulatory responsibilities. Overall, this can be a complex issue. In such relationships, it is very important that explicit licensing/contractual agreements specify the processes for exchange of safety information, including timelines and regulatory reporting responsibilities. Safety personnel should be involved in development of any agreements from the beginning. Processes should be in place to avoid duplicate reporting to the regulatory authority, e.g. assigning responsibility to one company for literature screening. Whatever the nature of the arrangement, the MAH is ultimately responsible for regulatory reporting. Therefore, every reasonable effort should be made between the contracting partners to minimize the data exchange period to promote compliance with MAH responsibilities.

5.4.3 Validation of reports

- 5.4.3.1 Only valid ICSRs qualify for submission. All reports of suspected adverse reactions should therefore be validated to make sure that the minimum criteria for reporting are included in the reports before submitting them to the Agency (see ICH-E2D). The minimum criteria are:
 - One or more identifiable reporter (primary source), characterised by qualification (e.g. physician, pharmacist, other healthcare professional, lawyer, consumer or other non-healthcare professional) name, initials or address. Whenever possible, contact details for the reporter should be recorded so that follow-up activities can be performed. However, if the reporter does not wish to provide contact details, the ICSR should still

be considered as valid providing the organisation who was informed of the case was able to confirm it directly with the reporter. All parties providing case information or approached for case information should be identifiable, not only the initial reporter.

- One single identifiable patient characterised by initials, patient identification number, date of birth, age, age group or gender. The information should be as complete as possible.
- One or more suspected substance/medicinal product (see 5.3 Definitions).
- One or more suspected adverse reaction (see 5.3 Definitions) If the primary source has made an explicit statement that a causal relationship between the medicinal product and the adverse event has been excluded and the MAH agrees with this, the report does not qualify as a valid ICSR since the minimum information is incomplete. The report does not also qualify as a valid ICSR if it is reported that the patient experienced an unspecified adverse reaction and there is no information provided on the type of adverse reaction experienced. 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. For instance a marketing authorisation holder is made aware that a patient was hospitalised or died, without any further information. In this particular situation, medicinal judgment should always be applied in deciding whether the notified information is an adverse reaction or an event. For example, a report of sudden death would usually need to be considered as a case of suspected adverse reaction and reported.

The lack of any of these four elements means that the case is considered incomplete and does not qualify for reporting. The Marketing Authorisation Holder is required to exercise due diligence in following up the case to collect the missing data elements. Reports, for which the minimum information is incomplete, should nevertheless be recorded within the pharmacovigilance system for use in on-going safety evaluation activities.

When the missing information has been obtained (including for example when the medicinal product causal relationship with the reported adverse event is no longer excluded), the ICSR becomes valid for submission.

- 5.4.3.2 When collecting reports of suspected adverse reactions via the internet or digital media, the term “identifiable” refers to the possibility of verification of the existence of a reporter and a patient.
- 5.4.3.3 When the Marketing Authorisation Holder is made aware that the primary source may also have reported the suspected adverse reaction to another concerned party, the report should still be considered as a valid ICSR. All the relevant information necessary for the detection of the duplicate case should be included in the ICSR.

- 5.4.3.4 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. In this situation, the opinions of both the consumer and the healthcare professional should be included in the narrative section of the ICSR.
- 5.4.3.5 For solicited reports of suspected adverse reactions (see section 5.4.2.2 Solicited Report), where the receiver disagrees with the reasonable possibility of a 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 narrative section of the ICSR.
- 5.4.3.6 the same principle applies to the ICSR seriousness criterion, which should not be downgraded from serious to non-serious simply because the MAH disagrees with the seriousness reported by the primary source.

5.4.4 Follow-up of reports

- 5.4.4.1 When first received, the information in suspected adverse reaction reports may be incomplete. These reports should be followed up as necessary to obtain supplementary detailed information significant for the scientific evaluation of the cases. This is particularly relevant for monitored events of special interest, prospective reports of pregnancy, cases notifying the death of a patient, cases reporting new risks or changes in the known risks. This is in addition to any effort to collect missing minimum information (see section 5.4.3 for Validation of Report). Any attempt to obtain follow-up information should be documented.
- 5.4.4.2 The provision in ICSRs of information on the patient's age is important in order to be able to identify safety issues occurring specifically in the paediatric or elderly population. Reasonable efforts should be made to follow-up on ICSRs where information on the patient's age or age group is initially not reported by the primary source
- 5.4.4.3 Similarly, for suspected adverse reactions related to biological medicinal products, the definite identification of the concerned products with regard to their manufacturing is of particular importance. Therefore, all appropriate measures should be taken to clearly identify the names of the products and their batch numbers. With respect to this, it is recommended to specify in the case narrative if information on the batch number has been requested, when it is missing in the initially submitted ICSR.
- 5.4.4.4 Follow-up methods should be tailored towards optimising the collection of missing information. This should be done in ways that encourage the primary source to submit new information relevant for the scientific evaluation of a particular safety concern. The use of targeted specific forms in the local language should avoid requesting the primary

source to repeat information already provided in the initial report and/or to complete extensive questionnaires, which could discourage future spontaneous reporting. Therefore, consideration should be given to pre-populating some data fields in those follow-up report forms to make their completion by the primary source easy.

- 5.4.4.5 When information is received directly from a consumer suggesting that an adverse reaction may have occurred, if the information is incomplete, attempts should be made to obtain consent to contact a nominated healthcare professional to obtain further follow-up information. When such a case, initially reported by a consumer, has been confirmed totally or partially by a healthcare professional, this information should be clearly highlighted in the ICSR.
- 5.4.4.6 For suspected adverse reactions relating to biological medicinal products, the definite identification of the concerned product with regard to its manufacturing is of particular importance. Therefore, all appropriate measures should be taken to clearly identify the name of the product and the batch number
- 5.4.4.7 For some cases, it may not always be possible to perform follow-up activities taking into account that the reporter information may have been anonymised in accordance with local legal requirements or due to provisions that allow for anonymous reporting, for example in case of medication error with harm and the reporter does not wish to disclose an identity. These cases should be considered valid for submission as ICSRs, providing that the notified organisation was able to confirm them directly with the primary sources and that the other minimum criteria for reports validation are satisfied

5.4.5 Reporting of Individual case safety reports (ICSRs)

- 5.4.5.1 Only valid ICSRs (see sections 5.4.3 Validation of Report) should be reported. The clock for the reporting of a valid ICSR starts as soon as the information containing the minimum reporting criteria has been brought to the attention of the Marketing Authorisation Holder, including medical representatives and contractors. This date should be considered as day zero. It is the first day when a receiver gains knowledge of a valid ICSR, irrespective of whether the information is received during a weekend or public holiday. Reporting timelines are based on calendar days.
- 5.4.5.2 Where the Marketing Authorisation Holder has set up contractual arrangements with a person or an organisation, explicit procedures and detailed agreements should exist between the Marketing Authorisation Holder and the person/organisation to ensure that the Marketing Authorisation Holder can comply with the reporting obligations. These procedures should in particular specify the processes for exchange of safety information, including timelines and regulatory reporting responsibilities and should avoid duplicate reporting to the Agency.
- 5.4.5.3 For ICSRs described in the scientific and medicinal literature (see section 5.4.2.1.2 Literature Reports), the clock starts (day zero) with awareness of a publication containing the minimum information for reporting. Where contractual arrangements are

made with a person/organisation to perform literature searches and/or report valid ICSRs, detailed agreements should exist to ensure that the Marketing Authorisation Holder can comply with the reporting obligations.

- 5.4.5.4 When additional significant information is received for a previously reported case, the reporting time clock starts again for the submission of a follow-up report from the date of receipt of the relevant follow-up information. For the purpose of reporting, significant follow-up information corresponds to new medical or administrative information that could impact on the assessment or management of a case or could change its seriousness criteria; non-significant information includes updated comments on the case assessment or corrections of typographical errors in the previous case version.

5.4.6 Reporting timelines

5.4.6.1 Serious Adverse Reactions

- 5.4.6.1.1 The marketing authorization holder (MAH) and any individuals authorized to distribute medical products should maintain records of all suspected serious adverse reactions reported in Nigeria. They are required to inform the Agency of these incidents within fifteen (15) days of receiving the information.
- 5.4.6.1.2 All serious ARs should be reported as soon as possible and in no later than fifteen (15) calendar days from receipt by the MAH. The clock for serious ARs starts (as day 0) on the day that the four minimum data elements in relation to the AR report are received.
- 5.4.6.1.3 The reporting time clock is considered to begin again when a MAH receives additional clinical or medically relevant information for a previously reported serious AR. This information must be reported as soon as possible and in no later than fifteen (15) calendar days after receipt of the additional information.
- 5.4.6.1.4 If MAH receives additional information about a case initially classified as non-serious that indicates the case should be re-classified (e.g. from non-serious to serious), the MAH must report the case as soon as possible, and in no later than 15 calendar days after receipt of the information that led to the change in classification.
- 5.4.6.1.5 For suspected serious AR cases occurring in Nigeria that are identified through screening the worldwide literature, the clock starts (day zero) when the MAH becomes aware of a publication containing the four minimum data elements. It is preferable that a copy of the relevant published article (in English or an English summary/translation) is provided to the Agency at the time the initial AR report is made. However, if the article is not available at this time, it must be provided to the Agency within 15 calendar days of submission of the AR report. Where difficulty is experienced in meeting the 15 calendar days requirement for submission of the article, the Agency must be notified in writing prior to the 15 day period ending.
- 5.4.6.1.6 The Marketing Authorisation Holder (MAH) should report to the Agency any action relating to their product safety that has been taken by a regulatory authority outside

Nigeria, including the basis for such action, as soon as possible but not later than fifteen (15) calendar days of first knowledge.

5.4.6.2 Significant Safety Issues

- 5.4.6.2.1** Significant safety Issues (SSIs) are newly identified safety concerns that may require action or further evaluation. They include issues that may impact the benefit-risk profile of a product and warrant immediate or expedited communication to regulatory authorities
- 5.4.6.2.2** Any significant safety issue identified by the MAH must be reported to the Agency as soon as possible, within 7 calendar days, the regulatory reporting time clock starts from the time of awareness of the issue by any personnel of the MAH. This is considered to have occurred when the MAH's review and analysis have been completed and a conclusion is drawn that a significant safety issue has occurred or when the MAH becomes aware of the actions of an overseas regulatory authority.
- 5.4.6.2.3** These situations are different from the reporting of Adverse reactions, where the MAH is allowed up to 15 calendar days to confirm and follow-up on details before submitting an individual serious Adverse Reactions to the Agency.

5.4.7 Tabulated summary of reporting requirements)

TYPE OF ADR REPORT	TIME FRAME FOR REPORTING	FORMAT
Local reports		
Fatal or Life-threatening Unexpected	Notified within 7 calendar days followed by a complete report with 8 additional calendar days	Initial notification Email to pharmacovigilance@nafdac.gov.ng and andadr@nafdac.gov.ng notification Industry e-Reporting
Serious Unexpected/Expected	As soon as possible but not later than 15 days	Industry e-Reporting
Non-serious (Expected /Unexpected)	90 days	Industry e-Reporting

Foreign reports (spontaneous/ published/ study):		
Serious unexpected	As soon as possible but not later than 15 days	ADR/CIOMS forms
Serious Expected	30 Calendar days	Line lists
Non-serious (Expected /Unexpected)	90 Calendar days	Line lists, PSUR
Notification of change in Nature, Severity or Frequency or Risk factors	15 days	Detailed report (including Publications)
New information impacting the benefit-risk profile of the product including international regulatory decisions	Notified as soon as possible within 7 calendar days followed by a complete report within 8 additional calendar days	Detailed report (including Publications)s Included in next update of PSUR/PBRER

5.4.8 Reporting format

- 5.4.8.1 Adverse reactions can be reported using the adverse reaction reporting form available from the Agency. The MAH may also use its in-house reporting forms, provided all the necessary data elements are included in the form in a legible format. Discharge summaries, post-mortem reports, relevant laboratory data and other additional clinical data should be attached.
- 5.4.8.2 Electronic submissions may also be required by the Agency using the ICH-E2B format for electronic reporting or any other format prescribed by the Agency.

5.4.9 Data management

- 5.4.9.1 Electronic data and paper reports of suspected adverse reactions should be stored and treated in the same way as other medical records with appropriate respect for confidentiality regarding patients' and reporters' identifiability. Confidentiality of patients' records including personal identifiers, if provided, should always be maintained. Identifiable personal details of reporting healthcare professionals should be kept in confidence.

- 5.4.9.2 In order to ensure pharmacovigilance data security and confidentiality, strict access controls should be applied to documents and to databases to authorised personnel only. This security measure extends to the complete data path. In this aspect, procedures should be implemented to ensure security and non-corruption of data during data transfer.
- 5.4.9.3 When transfer of pharmacovigilance data occurs within an organisation or between organisations having concluded contractual agreements, the mechanism should be such that there is confidence that all notifications are received; in that, a confirmation and/or reconciliation process should be undertaken.
- 5.4.9.4 Correct data entry, including the appropriate use of terminologies, should be verified by quality assurance auditing, either systematically or by regular random evaluation. Data entry staff should be instructed in the use of MedDRA terminologies, Industry E-reporting and their proficiency confirmed.
- 5.4.9.5 Data received from the primary source should be treated in an unbiased and unfiltered way and inferences as well as imputations should be avoided during data entry or electronic transmission. The reports should include the verbatim text as used by the primary source or an accurate translation of it.
- 5.4.9.6 Electronic data storage should allow traceability (audit trail) of all data entered or modified, including dates and sources of received data, as well as dates and destinations of transmitted data.
- 5.4.9.7 A procedure should be in place to account for identification and management of duplicate cases at data entry and during the generation of aggregated reports.

5.4.10 Quality management

- 5.4.10.1 The Marketing Authorisation Holders 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 reporting and case archiving. Correct data entry, including the appropriate use of terminologies should be quality controlled, either systematically or by regular random evaluation. Conformity of stored data with initial and follow-up reports should be verified by quality control procedures, which permit for the validation against the original data or images thereof. In this aspect, the source data (e.g., letters, emails, records of telephone calls that include details of an event) or an image of the source data should be easily accessible. The whole process should be monitored by quality assurance audits.
- 5.4.10.2 Clear written standard operating procedures should guarantee that the roles and responsibilities and the required tasks are clear to all parties involved and that there is provision for proper control and, when needed, change of the system. This is equally applicable to activities that are contracted out to third parties, whose procedures should

be reviewed to verify that they are adequate and compliant with applicable requirements.

- 5.4.10.3 Personnel directly performing pharmacovigilance activities, should be appropriately trained in applicable pharmacovigilance legislation and guidelines in addition to specific training in report processing activities for which they are responsible and/or undertake. Other personnel who may receive or process safety reports (e.g. clinical development, sales, medical information, legal, quality control) should be trained in adverse event collection and reporting in accordance with internal policies and procedures.

5.5 Special situations

5.5.1 Use of a medicinal product during pregnancy or breastfeeding

5.5.1.1 Pregnancy

- 5.5.1.1.1 Reports, where the embryo or foetus may have been exposed to medicinal products (either through maternal exposure or transmission of a medicinal product via semen following paternal exposure), should be followed-up in order to collect information on the outcome of the pregnancy and development of the child after birth. When an active substance (or one of its metabolites) has a long half-life, this should be taken into account when assessing the possibility of exposure of the embryo, if the medicinal product was taken before conception.
- 5.5.1.1.2 Not infrequently, pregnant women or healthcare professionals will contact either competent authorities or the marketing authorisation holder to request information on the teratogenicity of a medicinal product and/or experience of use during pregnancy. Reasonable attempts should be made to obtain information on any possible medicinal product exposure to an embryo or foetus and to follow-up on the outcome of pregnancy (see 5.4.4 Follow Up).
- 5.5.1.1.3 Reports of exposure to medicinal products during pregnancy should contain as many detailed elements as possible in order to assess the causal relationships between any reported adverse events and the exposure to the suspected medicinal product. In this context, the use of standard structured questionnaires is recommended.
- 5.5.1.1.4 Individual cases with an abnormal outcome associated with a medicinal product following exposure during pregnancy are classified as serious reports and should be reported, in accordance with the requirements outlined in section 5.4.5 Reporting of ICSRs. 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.

- 5.5.1.1.5 Other cases, such as reports of induced termination of pregnancy without information on congenital malformation, reports of pregnancy exposure without outcome data or reports which have a normal outcome, should not be reported as ICSR since there is no suspected adverse reaction. These reports should, however be collected and discussed in the periodic safety update reports (see Chapter 6).
- 5.5.1.1.6 However, in certain circumstances, reports of pregnancy exposure with no suspected reactions may necessitate to be submitted as ICSR. This may be a condition of the Certificate of Registration or stipulated in the risk management plan; 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).
- 5.5.1.1.7 A signal of a possible teratogen effect (e.g. through a cluster of similar abnormal outcomes) should be notified immediately to the Agency.

5.5.1.2 Breastfeeding

- 5.5.1.2.1 Suspected adverse reactions which occur in infants following exposure to a medicinal product from breast milk should be reported to the Agency in line with the guidance provided in section 5.4.5. Reporting on ICSRs.

5.5.2 Use of a medicinal product in a paediatric or elderly population

- 5.5.2.1 The collection of safety information in the paediatric or elderly population is important. Reasonable attempts should therefore be made to obtain and submit the age or age group of the patient when a case is reported by a healthcare professional, or consumer in order to be able to identify potential safety signals specific to a particular population. General guidance in section 5.4.4 follow up of reports should be applied.

5.5.3 Reports of overdose, abuse, off-label use, misuse, medication error or occupational exposure

- 5.5.3.1 For the purpose of these guidelines, medication error refers to any unintentional error in the prescribing, dispensing, or administration of a medicinal product while in the control of the healthcare professional or consumer.
- 5.5.3.2 Reports of overdose, abuse, off-label use, misuse, medication error or occupational exposure with no associated adverse reaction should not be reported as ICSRs. They should be considered in periodic safety update reports as applicable. When those reports constitute safety issues impacting on the benefit-risk balance of the medicinal product, they should be notified to the Agency.
- 5.5.3.3 Reports associated with suspected adverse reactions should be routinely followed-up to ensure that the information is as complete as possible with regards to the symptoms,

treatments, outcomes, context of occurrence (e.g., error in prescription, administration, dispensing, dosage, unauthorised indication or population, etc.).

5.5.4 Lack of therapeutic efficacy

- 5.5.4.1 Reports of lack of therapeutic efficacy should be reported within 15 calendar days and followed-up if incomplete unless the reporter has specifically stated that the outcome was due to disease progression and was not related to the medicinal product.
- 5.5.4.2 Clinical judgment should be used when reporting cases of lack of therapeutic efficacy. For example, an antibiotic used in a life-threatening situation where the medicinal product was not in fact appropriate for the infective agent should not be reported. However, 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, should be reported within 15 days.
- 5.5.4.3 For vaccines, cases of lack of immunogenic effect should be reported, in particular with the view to highlight potential signals of reduced immunogenicity in a sub-group of vaccinees, waning immunity, or strain replacement. With regard to the latter, it is considered that spontaneously reported cases of lack of immunogenic effect by a healthcare professional may constitute a signal of strain replacement. Such a signal may need prompt action and further investigation through post-authorisation safety studies as appropriate. General guidance regarding the monitoring of vaccines failure, provided in the Report of CIOMS/WHO Working Group on Vaccine Pharmacovigilance, may be followed.

5.5.5 Suspected adverse reactions related to quality defect or Substandard and falsified medicinal products

- 5.5.5.1 When a report of suspected adverse reactions is associated with a suspected or confirmed substandard and falsified medicinal product, a valid ICSR should be reported. The seriousness of the ICSR is linked to the seriousness of the reported suspected adverse reactions in accordance with the definitions provided in section 5.3 Definitions.
- 5.5.5.2 In addition, to protect public health, it may become necessary to implement urgent measures such as the recall of one or more defective batch(es) of a medicinal product from the market. Therefore, Marketing Authorisation Holders should have a system in place to ensure that reports of suspected adverse reactions related to substandard and falsified medicinal products are investigated promptly and that confirmed quality defects of substandard and falsified products are notified to manufacturer and to the Agency.

5.5.6 Suspected transmission via a medicinal product of an infectious agent

- 5.5.6.1 For the purposes of reporting, any suspected transmission of an infectious agent via a medicinal product should be considered as a serious adverse reaction and such cases should be reported within 15 days in accordance with requirements outlined in section 5.4.6 Reporting Timelines. If no other criterion is applicable, the seriousness of this ICSR should be considered as important medicinal event. This also applies to vaccines.
- 5.5.6.2 In the case of medicinal products derived from human blood or human plasma, haemovigilance procedures may also apply. Therefore the Marketing Authorisation Holder should have a system in place to communicate suspected transmission via a medicinal product of an infectious agent to the manufacturer, the relevant blood establishment(s) and the Agency. Any organism, virus or infectious particle (e.g. prion protein transmitting transmissible spongiform encephalopathy), pathogenic or non-pathogenic, is considered an infectious agent.
- 5.5.6.3 A transmission of an infectious agent may be suspected from clinical signs or symptoms, or laboratory findings indicating an infection in a patient exposed to a medicinal product. Emphasis should be on the detection of infections/infectious agents known to be potentially transmitted via a medicinal product, but the occurrence of unknown agents should also always be considered.
- 5.5.6.4 In the context of evaluating a suspected transmission of an infectious agent via a medicinal product, care should be taken to discriminate, whenever possible, between the cause (e.g. injection/ administration) and the source (e.g. contamination) of the infection and the clinical conditions of the patient at the time of the infection (immuno-suppressed /vaccinee).
- 5.5.6.5 Confirmation of contamination (including inadequate inactivation/attenuation of infectious agents as active substances) of the concerned medicinal product increases the evidence for transmission of an infectious agent and may therefore be suggestive of a quality defect for which the procedures detailed in 5.5.5 Suspected adverse reactions related to quality defect or Substandard and falsified medicinal products should be applied.
- 5.5.7 Emerging safety issues**
 - 5.5.7.1 Events/observations may occur in relation to an authorised medicinal product, which may have major impacts on the risk-benefit balance of the product and/or on patients or public health. They may require urgent attention of the agency and could warrant prompt regulatory action and communication to patients and healthcare professionals. These important new evidences should be considered as emerging safety issues. They should be notified to the Agency in accordance with the requirements provided in GVP Module IX Signal Detection. This is in addition to the ICSR submission requirements detailed in section 5.4.5 Reporting of ICSR when the emerging safety issue refers to a single case of suspected adverse reactions.

5.5.8 Donated Medicinal Products

- 5.5.8.1 Where medicinal products are supplied through donation programmes (e.g. by governments, international organisations, or non-governmental organisations), all suspected adverse reactions associated with such products shall be subject to the same reporting requirements and timelines as those applicable to authorised medicinal products in Nigeria.
- 5.5.8.2 The MAH, where one exists for the donated product in Nigeria, shall be responsible for the collection, assessment and reporting of all valid Individual Case Safety Reports (ICSRs) in accordance with the requirements specified in this Chapter.
- 5.5.8.3 In situations where there is no identifiable MAH in Nigeria, the overall responsibility for the collection, assessment and reporting of suspected adverse reactions to the Agency shall rest with the entity or person authorised to receive the donated product in Nigeria (e.g. government agency, public health programme, or designated implementing partner).
- 5.5.8.4 Such entity or person shall ensure that:
- all reports meeting the minimum criteria for a valid ICSR are submitted in accordance with the timelines specified in this Chapter;
 - appropriate mechanisms are in place for the collection, documentation, follow-up and transmission of adverse reaction reports; and
 - relevant safety information received from healthcare professionals, patients, or donor organisations is promptly evaluated and reported as required.
- 5.5.8.5 Where safety information relating to donated products is received from international partners or donor organisations, such information shall be promptly reviewed and, where applicable, submitted to the Agency as ICSRs or as significant safety information in line with this Guideline.

5.5.9 Period between the submission of the marketing authorisation holder application and the granting of the marketing authorization

- 5.5.9.1 In the period between the submission of the MAH application and the granting of the Marketing Authorisation information (quality, non-clinical, clinical) that could impact on the benefit-risk balance of the medicinal product under evaluation may become available to the applicant (see section 5.5.7 Emerging Safety Issues). It is the responsibility of the applicant to ensure that this information is immediately submitted to the Agency.

5.5.10 Period after suspension, revocation or withdrawal of Marketing Authorisation

- 5.5.10.1 The Marketing Authorisation Holder shall continue to collect any reports of suspected adverse reactions related to the concerned medicinal product following the suspension of a marketing authorisation. Where a Certificate of Registration is withdrawn or revoked, the former Marketing Authorisation Holder is encouraged to continue to

collect spontaneous reports of suspected adverse reactions originating within the country to facilitate the review of delayed onset adverse reactions or of retrospectively notified cases.

5.5.11 Period during a public health emergency

- 5.5.11.1 A public health emergency is a public health threat duly recognised either by the World Health Organization (WHO) or the Federal Ministry of Health. In the event of a public health emergency, regular reporting requirements may be amended. Such arrangements will be considered on a case-by-case basis and will be appropriately notified on the Agency's website.