Guide for Reporting Adverse Reactions to Marketed Drugs

Guide for Pharmaceutical Industry in Nigeria

This document has been prepared to serve as a guideline to those reporting adverse drug reactions. It represents the National Pharmacovigilance Centre/NAFDAC’s current thinking on the safety, quality and efficacy of medicines. NPC/NAFDAC reserve the right to request for any additional information to establish the safety, quality and efficacy of a medicine and may make amendments in keeping with the knowledge which is current at the time of consideration of safety data.

NATIONAL PHARMACOVIGILANCE CENTRE (NPC),
NAFDAC NIGERIA
Introduction

The decision to approve a drug is based on its having a satisfactory balance of benefits and risks within the conditions specified in the product labeling. This decision is based on the information available at the time of approval. The knowledge related to the safety profile of the product can change over time through expanded use in terms of patient background and the number of patients exposed. In particular, during the early post marketing period the product might be used in settings different from clinical trials and a much larger population might be exposed in a relatively short timeframe.

Once a product is marketed, new information will be generated, which can have an impact on the benefits or risks of the product; evaluation of this information should be a counting process, in consultation with regulatory authorities. Detailed evaluation of the information generated through pharmacovigilance activities is essential for all products to ensure their safe use. The benefit risk balance can be improved by reducing risks to patients through effective pharmacovigilance that can enable information feedback to the users of medicines in a timely manner.

This guide is intended to assist the MAH during the post marketing period in reporting adverse drug reactions (ADRs) associated with medicines and in the management of safety data, which arise during clinical trials. It is not intended to be used in the light of safety data to arise, during clinical trials.

For the purpose of these guidelines, “Authority” refers to the National Agency for Food and Drug Administration and control (NAFDAC) and the NPC refers to National Pharmacovigilance Centre, at NAFDAC.

DEFINITIONS AND TERMINOLOGY

2.1 Adverse event/experience

"is any untoward medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a casual relationship with this treatment”.

The term “adverse event” is a broad one that encompasses “adverse drug reactions” and other unwanted occurrences which may be related to the use of the drug but they may not necessarily be caused by the drug.
2.2 The World Health Organization’s definition for Adverse Drug Reaction (ADR) is:

THE 1972 WHO Definition of ADR.

“a response to a medicine which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease, or for the modification of physiological conditions”.

2.3 Serious Adverse Drug Reaction is:

"any untoward medical occurrence that at any dose:
- Results in death,
- Is life-threatening,
- Requires patient hospitalization or prolongation of existing hospitalization,
- Results in persistent or significant disability/incapacity, or
- Causes congenital anomaly/birth defect
- Requires an intervention to prevent permanent impairment or damage”.

The term “life-threatening” refers to a reaction in which the patient was at risk of death at the time of the reaction.

2.4 Serious Unexpected Adverse Reaction is:

"an adverse reaction, not previously documented i.e. that is not identified in nature, severity or frequency in the risk information which is not consistent with domestic labeling or market authorization, or expected from characteristics of the drug”.

Reports that add significant information on specificity or severity of already documented serious ADR constitute unexpected reaction.
2.5 Healthcare professional

For the purpose of reporting suspected adverse reaction “health care professionals” are medical practitioners, pharmacists, nurses and traditional herbal healers.

When reports originate from pharmacists or nurses, further information about the case should, where possible, be sought from a medical practitioner responsible for the patient. Furthermore, if there is more than one reporter, the health care professional directly involved with the patient’s care and who provides the most complete and clinically relevant information, will be considered the primary reporter.

2.6 Adverse Drug Reaction case Report

Is a detailed record of all relevant data associated with the use of a medicine in a subject or patient.

2.7 Spontaneous Report

Is a communication to a company, regulatory authority or other organization that describes a suspected adverse drug reaction in a patient given one or more medicines, and which does not derive from a study.
2.8 Reportable Adverse Reaction – Minimum Information

A reportable ADR requires the following minimum information:

- An identifiable source (reporter) of the information. This should include the name or initials and address of the reporter and the reporter’s qualification (for e.g. doctor, pharmacist, nurse or traditional herbal healers).
- An identifiable patient may be identified by surname or initials of surname or by a reference number.
- Suspected products(s)
- Suspected reactions(s)

Follow up information should be actively sought and submitted as soon as it becomes available. Case reports should be clearly labeled as “initial” or “follow up” reports. In the follow up report, specific reference should be made to the initial report, preferably by including the manufacturer’s number specific to the report.

2.9 Blinded Study Report

Study participants and/or the investigators are unaware of the identity of the intervention.

2.10 Periodic Safety Update Reports (PSUR)

Is an update of the world-wide safety experience of a medicine at defined times post-registration, as determined from the international birth date. Each safety update report should cover the period of time since the last update report. The PSUR should be compiled in accordance with the requirements of the ICH E2C (CPMP/ICH/288/95) Expert Group on Clinical Safety Data Management: Periodic Safety Update Reports for Marketed Drugs.
A line listing provides key information but not necessarily all the details customarily collected on individual cases. Reactions are classified by body system for the most serious-presenting sign or symptom. The headings usually included are:

- **Country**
- **Source** *(physician, literature, etc)*
- **Age**
- **Sex**
- **Dose of drug**
- **Duration of treatment** *(prior to event); time to onset*
- **Description of reaction** *(as reported)*
- **Patient outcome** *(for e.g., fatal, resolved, e.t.c)*
- **Comment**
- **Company Reference Number**

In some instances, depending on the type or source, ADR reports should be presented as line listings. A line listing serves to help the Authority to identify cases that it might wish to examine more completely by requesting full case reports.
PROCEDURES FOR REPORTING

3.1 GENERAL PRINCIPLES

3.1.1 Who to report to:

All reports required by these guidelines should be sent to the NPC at the address, NAFDAC CHQ, Plot 2032 Olusegun Obasanjo Way, Wuse Zone 7 Abuja.

3.1.2 Route of Notification:

Reports may be sent by post to NAFDAC offices nationwide or electronically to pharmacovigilance@nafdac.gov.ng or nafdac_npc@yahoo.com.

3.1.3 Follow-up reports:

After initial receipt of an adverse reaction report, a notice of acknowledgement will be sent to the applicant quoting the number assigned to the case report. Any follow-up correspondence from the applicant, relating to the same case report should be cross-referenced to the assigned database number or to an appropriate unique number assigned by the applicant (relating specifically to the initial notification). This is the only reliable way to minimize the duplication of reports submitted by applicants.

3.1.4 Internal Pharmacovigilance system:

(i) The applicant should ensure that it has in place an appropriate system for pharmacovigilance that will provide for the proper management of safety data for its medicines and to ensure that appropriate action can be taken when necessary. It is strongly recommended that the applicant has available, in Nigeria, a full-time qualified person(s) responsible for pharmacovigilance, both for pre and post-marketing surveillance. This person(s) should have experience and training in all aspects of pharmacovigilance and, if not a health care professional, should have access to a medically qualified person.

(ii) The managing director of a pharmaceutical company must nominate a specific individual(s) responsible for pharmacovigilance activities. The NPC must be informed who the person(s) is that will assume responsibility for all matters pertaining to pharmacovigilance, including the person(s)
contact details (postal and email addresses and telephone and fax numbers).

(iii) Responsibilities of the MAH’s pharmacovigilance officer should include:

- The establishment and maintenance of a system which ensures that information about all suspected adverse reactions, which are reported to the company or organization, including to medical representatives and clinical research associates, is collected and collated such that it is accessible at a single point.
- Serving as a contact person to NAFDAC and, in particular, the NPC for all matters relating to pharmacovigilance.
- The preparation of the following for submission to the authority
  - Adverse drug reaction reports
  - Periodic Safety Update Reports (PSURs), when necessary
  - Company-sponsored pre and post-registration reports
  - On-going pharmacovigilance evaluation during the post-registration period.
- Ensuring that any request from the authority for additional information deemed necessary for evaluation of the risk-benefit ratio of a medicine, is provided to the authority promptly and fully.

3.1.5 Report Format and Details:

(i) **Pre-registration**: A Serious Adverse Event/Reaction (SAE) shall be reported in the same format as that of a post-registration, but must include the details of the study, when and where approved. Applicants may use their in-house Adverse Event report forms to submit such reports, provided all the data elements are included on the form in a clearly readable format.

(ii) **Post-registration**: reporting can be done using the adverse reaction report form available from the NPC (Appendix I), or applicants may use their in-house report forms, provided all the necessary data elements are included in the form in legible format.

(iii) Applicants should submit ALL the relevant information available at the time of initial notification of an adverse drug reaction report, i.e., not only the minimum information required for a report. The attachment of discharge summaries, post-mortem reports, relevant laboratory data and other additional clinical data, is encouraged.
(iv) The original words/description (verbatim) used by the initial reporter to describe the adverse reaction should be provided. The full name of the medicinal substance including brand and generic name must be provided.

(v) Additional information, not available at the time of initial report, should be provided in the form of follow-up reports.

(vi) The applicant is required to submit the name or initials, address and telephone number of the initial reporter on the adverse drug reaction case report form. In the case of a report from a clinical trial, the trial site at which the reaction occurred needs to be submitted in addition to other information requested.

3.1.6 Overdose:

Reports of overdose should be submitted only when the overdose was associated with an adverse reaction. Suspected adverse reactions, associated with an overdose, should be reported, as well as other reactions. This should include reports which indicate that taking of the suspect medicine led to suicidal intention and subsequent overdose of the suspect medicine, or other medication.

3.1.7 Teratogenicity and congenital anomalies:

Reports on congenital anomalies or teratogenicity should give details on:

- Age and sex of the infant.
- Follow-up reports for the infant which should be considered as follow-up to the initial report.
- The birth date or the date on which pregnancy was terminated which should be the event onset date.
- Date and/or duration of *in utero* exposure where possible.
- Any adverse reaction experienced by the mother which must be considered a new initial case report and should be submitted on a separate report form.

3.1.8 Product defects:

If an adverse event is suspected to be due to a product defect, it should be reported in the same manner as a suspected adverse reaction. The batch number of the suspected medicine should be included in the report. MAH should inform the Authority whether the implicated products have been tested for quality and what, if any, corrective actions are being taken to enable NAFDAC undertake necessary corrective measures.

3.1.9 Drug Interactions:
Any drug interaction which results in adverse reaction should be reported as an adverse reaction in the prescribed manner.

3.1.10 Another Applicant’s Product:

Spontaneous reports: If a pharmaceutical company receives a report of a suspected adverse reaction to a medicine marketed by another MAH, the report should promptly be forwarded to the MAH of that medicine. The company to whom the event was originally reported should not forward such reports to the Authority. The MAH is required to submit the report to the Authority with the same time constraints applicable to other reports.

3.1.11 Confidentiality:

Strict confidentiality will be maintained by the MAH Authority and NPC regarding the identities of the patient and the reporter involved in a suspected ADR report.

3.1.12 Lack of Efficacy reports:

Lack of efficacy applies to registered medicines only. The batch number of the suspected medicine should be included in the report. If the report of “lack of efficacy” is for an unapproved indication, the event is still reportable.

4.0 POST-REGISTRATION ADVERSE DRUG REACTION REPORTS

Adverse drug reactions occurring in Nigeria are considered “domestic” ADR reports, while those occurring outside Nigeria are considered “foreign” ADR reports. To facilitate the processing of ADR reports, it would be helpful if the reporter indicated whether the report is domestic or foreign.

4.1 Domestic Adverse Reaction Reports

(i) All serious, suspected adverse drug reactions, occurring in Nigeria with any medicine, must be reported by the MAH within 15 calendar days after first notification.

(ii) All non-serious, unexpected, suspected adverse drug reactions, occurring in Nigeria with any medicine, must be reported by the MAH within 60 calendar days after first notification.

4.2 Foreign Adverse Reaction Reports
(i) Foreign individual case reports should not be forwarded to the Authority on a routine basis, but should be reported in the context of a specific safety issue or on specific request by the Authority.

(ii) The MAH should inform the Authority of any action relating to their product safety that has been taken by a foreign agency including the basis for such action, within **(3) three calendar days** of first knowledge.

(iii) These guidelines also apply to medicines on which an application for registration has been submitted.

**4.3 Periodic Safety Update Reports (PSURs):**

(i) PSURs should be submitted in the following situations:
   - Whenever requested by the Authority.
   - When the submission of PSURs is a condition for registration of a new medicinal product or a range of medicinal products. Submission of PSURs is mandatory for drug molecules within the first ten years of marketing authorization. Reports should be submitted on a periodicity of 6 months for the first 2 years, annually for the 3 following years, and every five years, at the time of renewal of registration.
   - As part of a submission to amend the conditions of registration when the PSUR contains information supporting the amendment.
   - When a new medicinal product is **submitted to the Authority for registration** and when the product has already been marketed elsewhere, PSURs should be sent to the Authority within **30 days** of submission of registration documents. When a pharmaceutically finished/packaged medicine is listed, the MAH should submit a periodic safety update report every 6 months for the 2 year listing period. This constitutes one of the prerequisites for the renewal of listing.
   - When a clinical trial is being conducted on a product which is already registered in other countries.

(ii) The applicant should inform the Authority of any steps, which are taken, or to be taken, with regard to safety concerns raised in the periodic safety update report at the time of the submission.

**4.4 Case reports from published scientific literature:**

(i) MAH should report published suspected adverse drug reactions related to the active substance(s) of their medicinal products, as relevant to domestic adverse reaction report or foreign adverse reaction report in 4.1 and 4.2. A copy of the relevant published article should be provided.
(ii) If more than one medicine is mentioned in the literature report, only the MAH whose medicine is suspected of being the cause is required to submit a report. The suspect medicine is usually the one stated as such in the body or title of the article by the author(s).

4.5 Reports from post-registration studies:

(i) All suspected adverse reactions from post-registration studies taking place in Nigeria must be reported as domestic adverse reaction report according to 4.1. This applies to report from any type of clinical or epidemiological investigation, regardless of design or purpose, involving a medicinal product.

(ii) Investigators involved in post-registration studies, should be aware of what the definition of what constitutes a serious adverse drug reaction, as well as the distinction between ‘reactions’ and ‘events’.

(iii) In the case of post-registration studies, adverse “events” are usually systematically solicited. In cases where there is uncertainty as to whether or not an event is a reaction, the case should be reported as an adverse reaction. Events that are clearly related to the medicine should not be reported.

Attn:
(iv) If the manufacturer receives a report of a serious adverse drug reaction from the investigator who is blinded to individual patient treatment, the guidelines outlined in section 5.3 should be adhered to.

4.6 On-going Pharmacovigilance evaluation:

(i) MAH must inform the Authority, within 3 calendar days of first knowledge, whenever new evidence becomes available (nationally and internationally) that could significantly impact on the benefit/risk assessment of a medicine or which could be sufficient to consider changes to the conditions of registration of the medicine.

(ii) MAHs must report any change in the nature, severity or frequency of expected adverse drug reactions or any risk factors identified within 15 calendar days. The basis on which these assessments are made should be included.

(iii) Additional pharmacovigilance data, such as actual case reports, drug usage figures, the regulatory status of the product in other countries, independent pharmacoepidemiology studies, pre-clinical studies or significant product quality data may be requested by the Authority as the situation warrants.

4.7 Consumer Reports:
If a MAH receives an adverse drug reaction report from a consumer, the consumer should be advised to report this reaction through his/her medical practitioner, pharmacist nurse or dentist. If this approach fails, the MAH should attempt to obtain as much information as possible from the consumer. If the minimum information for reporting has been met, the case is considered reportable and should be forwarded.

4.8 Reports Relating to Pregnancy and Breast-Feeding:

The MAH must report suspected adverse drug reactions related to pregnancy or breast-feeding as specified in 4.1 and 4.2 regardless of whether the drug is contra-indicated in pregnancy and/or lactation. The MAH should ensure that pregnancies reports received in association with their drugs are followed until the outcome is known and reported.

5.0 PRE-REGISTRATION ADVERSE DRUG REACTION/EVENT REPORTS

This applies to reports from any type of clinical or epidemiological trial, regardless of design or purpose.

5.1 Adverse Drug Reaction Reporting for Clinical Trials:

(i) All fatal and life-threatening, unexpected adverse drug reactions occurring during clinical trials should be reported to the authority within 3 calendar days after first knowledge by the applicant. The initial notification must be followed by as complete a report as possible, within an additional 8 calendar days. This report must include an assessment of the importance and implication of the findings, including relevant previous experience with the same or similar medicines.

(ii) Serious, unexpected adverse drug reactions that is not fatal or life-threatening, which occur in clinical trials in Nigeria must be reported as soon as possible, and not later than 15 calendar days after first knowledge by the applicant.

   Attn:

   (iii) All suspected serious, unexpected adverse drug reaction reports originating from world-wide clinical trials site outside Nigeria for which the same medicine is being used in clinical trials in Nigeria should be reported within 15 calendar days.

(iv) Authority must be notified, within 15 calendar days after first knowledge by the applicant, when there is a suggestion of a change in the nature, severity or frequency of expected adverse drug reactions or when new risk factors are identified. The basis on which these assessments are made should be included.
(v) Any information, which may in any way influence the benefit-risk assessment of a medicine or which would be sufficient to consider changes in the administration of the medicine or in the overall conduct of a clinical trial, must be reported to the Authority. The applicant must submit this information to the Authority within (3) calendar days of first knowledge thereof. This could include individual case reports or a major safety finding from other sources.

Attn:
(vi) All serious adverse events must be included as part of the 6 monthly progress reports in a line listing format.

(vii) All non-serious unexpected suspected adverse drug reactions must be included as part of the 6 monthly progress reports in a line listing format only.

(viii) A clinical investigator, who has been approved by the Authority, must sign all reports originating from Nigeria. A copy of the original report should be submitted to the Authority.

(ix) If the sponsor of a clinical trial or the applicant for the trial does not agree with the causal association assigned by the initial reporter or the investigator, the reaction should still be reported.

(x) Expedited (rapid) reporting will be inappropriate for serious events from clinical trials that are considered not related to the study product. All cases judged by the clinical investigator or the sponsor, as having a reasonable suspected causal relationship to the medicine, qualify as adverse drug reactions.

5.2 Managing Blinded Therapy Cases:

(i) When a serious, unexpected, suspected adverse drug reaction occurs which results in death or, which is life-threatening, and is therefore judged reportable on an expedited (rapid) basis, it is recommended that the blind be broken only for that specific patient by the sponsor. It is also recommended that, when possible and appropriate, the blind be maintained for those persons, such as biometrics personnel, responsible for analysis and interpretation of results at the study’s conclusion.

(ii) When a fatal or other serious outcome is the primary efficacy endpoint in a clinical trial, the integrity of the clinical trial may be compromised if the blind is broken. Under these and similar circumstances, agreement should be reached in advance with the Authority concerning serious events that would be treated as disease-related and not subject to routine expedited (rapid) reporting. An independent data safety monitoring board should be established prior to
commencement of the trial, and its composition and terms of reference, should be submitted with the clinical trial application documents to the Authority for evaluation.

5.3 Post-study events:

Serious adverse events that occur after the patient has completed a clinical trial (including any post-treatment follow-up required according to the protocol) should be considered for expedited report purposes as though they were study reports. A causality assessment (see appendix II) and the determination of expectedness are needed for a decision on whether or not expedited reporting is required.

5.4 Protocol Design Details:

Attn:

(i) Each clinical trial protocol submitted to the Authority should include a risk management procedure, including unblinding procedures, for dealing with serious, unexpected events or reactions which may arise during the conduct of the trial and which could significantly impact on the safety of the study subjects.

(ii) There may be differences in the clinical safety profile for different presentations, for e.g., dosage form, formulation or delivery system of the pharmacologically active compound(s) or different indications/uses of a given product. All adverse reactions which qualify for reporting should be cross-referenced with all other dosage forms and uses for that product. The Investigator’s Brochure must therefore cover adverse drug reaction information that applies to all product presentations and uses.

5.5 Interpretation:

For the purpose of these guidelines, “Authority” refers to the National Agency for Food and Drug Administration and Control (NAFDAC) and the NPC refers to National Pharmacovigilance Centre at NAFDAC.
Appendix I

ADR Form

Appendix II

Causality Assessment Algorithm
(This is the assessment algorithm used by the WHO collaborating centre for International Drug Monitoring, Uppsala, Sweden.)

• **Certain**
  A clinical event, including laboratory test abnormality, occurring in a plausible time relationship to drug administration, and which cannot be explained by concurrent disease or other drugs or chemicals. The response to withdrawal of the drug (dechallenge) should be clinically plausible. The event must be definitive pharmacologically or phenomenological, using a satisfactory rechallenge procedure if necessary.

• **Probable/ Likely**
  A clinical event, including laboratory test abnormality, with a reasonable time sequence to administration of the drug, unlikely to be attributed to concurrent disease or other drugs or chemicals, and which follows a clinically reasonable withdrawal (dechallenge). Rechallenge information is not required to fulfill this definition.

• **Possible**
  A clinical event, including laboratory test abnormality, with a reasonable time sequence to administration of the drug, but which could also be explained by concurrent disease or other drugs or chemicals. Information on drug withdrawal may be lacking or unclear.

• **Unlikely**
  A clinical event, including laboratory test abnormality, with a temporal relationship to drug administration which makes a causal relationship improbable, and in which other drugs, chemicals or underlying disease provide plausible explanations.

• **Conditional/ Unclassified**
A clinical event, including laboratory test abnormality, reported as an adverse reaction, about which more data are essential for a proper assessment or the additional data under examination.

• **Inaccessible/ Unclassifiable**
  A report suggesting an adverse reaction which cannot be judged because information is insufficient or contradictory and it cannot be supplemented or verified.

**Comments on the Causality Assessment Algorithm**

**General**
While various causality terms are in use, the terms in this algorithm are the ones used most widely among countries participating in the WHO program. Some countries do not use all the terms, and many do not believe that a classification of “certain” is possible for a single report, while others make no distinction between “possible” and “probable”. These definitions have been accepted by countries that do use the terms.

While the terms “conditional/ unclassified” and “inaccessible/ unclassifiable” are not causality terms per se, they describe the status of ADR reports and therefore allow for practical communications about ADR issues.

**Certain**
It is recognized that very few reports will meet the criteria of this stringent definition, but this definition is useful because of the special value of such reports. It is considered that time relationships between drug administration and the onset and course of the adverse event are important in causality analysis. Also important is the consideration of confounding features (that is, the presence of other disease, drugs or chemicals). But due weight must be placed on the known pharmacological and other characteristics of the drug product being considered. Sometimes the clinical phenomena described will also be sufficiently specific to allow a confident causality assessment in the absence of confounding features and in the presence of appropriate time relationships, for example, penicillin anaphylaxis.

**Probable**
This definition has less stringent wording than the definition for “certain” and does not necessitate prior knowledge of drug characteristics or clinical adverse reaction phenomena. As stated, no rechallenge information is needed, but confounding drug administration or underlying disease must be absent.

**Possible**
This is the definition to be used when the administration of the drug in question is just one of several possible causes of the described clinical event.

**Unlikely**
This definition is intended to be used when it seems so plausible that the clinical event is attributable to something other than the drug in question.

**Appendix III**

**TABULATED SUMMARY OF REPORTING REQUIREMENTS**

**Post-Registration ADR Reports (registered medicinal products)**

<table>
<thead>
<tr>
<th>Type of ADR report</th>
<th>Time frame for reporting</th>
<th>Format</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local reports (spontaneous/published/study):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Serious (expected and unexpected)</td>
<td>15 days</td>
<td>ADR form #</td>
</tr>
<tr>
<td>• Non serious (unexpected)</td>
<td>15 days</td>
<td>ADR form #</td>
</tr>
<tr>
<td>• Non serious (expected)</td>
<td>No report</td>
<td>Not required</td>
</tr>
<tr>
<td>Foreign Reports (spontaneous/published/study):</td>
<td>On request or relating to specific safety issue</td>
<td></td>
</tr>
<tr>
<td>• Serious</td>
<td></td>
<td>As appropriate</td>
</tr>
<tr>
<td>Notification of Change in Nature, Severity or Frequency or Risk factors</td>
<td>15 days</td>
<td>Detailed report (including publications)</td>
</tr>
<tr>
<td>New information impacting on benefit-risk profile of product including international regulatory decisions</td>
<td>3 days</td>
<td>Detailed report (including publications)</td>
</tr>
</tbody>
</table>

# Applicant’s in-house ADR report form or NADEMC ADR report form.

**Pre-Registration ADR/ADE reports**

<table>
<thead>
<tr>
<th>TYPE OF ADR REPORT</th>
<th>TIME FRAME FOR REPORTING</th>
<th>FORMAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local Reports:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Fatal or life-threatening (unexpected)</td>
<td>3+8**</td>
<td>SAE form</td>
</tr>
<tr>
<td>• Other serious (unexpected)</td>
<td>15 days</td>
<td>SAE form</td>
</tr>
<tr>
<td>All (local &amp; foreign) report:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Event Description</td>
<td>Frequency</td>
<td>Reporting Requirement</td>
</tr>
<tr>
<td>----------------------------------------------------------------------------------</td>
<td>-----------------</td>
<td>------------------------------</td>
</tr>
<tr>
<td>Serious (unexpected and expected) events</td>
<td>6-monthly&quot;&quot;</td>
<td>Line listing</td>
</tr>
<tr>
<td>Non-serious unexpected reaction</td>
<td>6-monthly</td>
<td>Line listing</td>
</tr>
<tr>
<td>Notification of Change in Nature, Severity or Frequency of Risk factors</td>
<td>15 days and in 6 monthly report&quot;&quot;</td>
<td>Detailed report</td>
</tr>
<tr>
<td>New information impacting on risk-benefit profit of product or conduct of trial</td>
<td>3 days and in 6-monthly report&quot;&quot;</td>
<td>Detailed report</td>
</tr>
</tbody>
</table>

** 3+8 – initial notification to NAFDAC as soon as possible but within 3 calendar days followed by a complete report within 8 calendar days of the initial notification.

** REFERENCES**
