**General Directorate of Pharmacy and Pharmaceuticals**

# GUIDELINE FOR PHARMAVOVIGILANCE INSPECTIONS

**Turkey Pharmacovigilance Center**

PHARMACOVIGILANCE INSPECTIONS

# PHARMACOVIGILANCE INSPECTIONS

Pharmacovigilance inspections are conducted in accordance with the provisions of the "Regulation concerning the Monitoring and Evaluation of the Safety for Medicinal Products for Human Use" that was issued in the official gazette, dated 22 March 2005 and numbered 25763.

To ensure that marketing authorization holders comply with pharmacovigilance regulatory obligations and to facilitate compliance, the General Directorate of Pharmacy and Pharmaceuticals, Turkey Pharmacovigilance Center (TUFAM) conducts pharmacovigilance inspections. Inspections may be performed in cases of suspicion of non-compliance in addition to those performed on a routine basis. The results of an inspection will be provided to the marketing authorization holder who will be given the opportunity to comment on the findings. The results will be used to help the marketing authorization holders improve compliance and may also be used as a basis for enforcement action. The scheduling and conduct of these inspections will be performed within the frame of routine programs and/or driven by risk analysis criteria.

## 1. Types of Inspection

### a) Routine inspections

Routine inspections are conducted at time intervals specified by the Ministry.

### b) Targeted inspections

Targeted inspections may be required when one or more of the following arise:

• Triggers for the inspection are identified which do not relate to specific concerns about a product safety or actual non-compliance e.g.:

o The marketing authorization holder has not previously been inspected.
o The marketing authorization holder has placed their first product on the market.
o The marketing authorization holder has recently been or are involved in a merger or takeover process.
o The marketing authorization holder has changed their system significantly (for ex: establishment of new database system, contracting out reporting activities to Contract Pharmacovigilance Institutions, etc).

Triggers for the inspection are identified which relate to specific concerns about a product's safety or actual non-compliance e.g. significant issues relating to:

o Failure to fulfill or delays in implementation of follow-Up measures or specific Obligations relating to the monitoring of product safety, identified at the time of the marketing authorization.
o Delays in expedited or periodic reporting.
o Incomplete reporting.
o Submission of poor quality or incomplete Periodic Safety Update Reports (PSURs)
o Inconsistencies between reports or other information sources.
o Change in risk-benefit balance or failure to communicate change in risk-benefit balance.
o Previous inspection experience.
o Information of the relevant company received from other authorities.
o Poor or non-timely follow-up to requests for information from the Ministry.
o Providing information to the public on public-related pharmacovigilance issues without notifying the Ministry in advance or concurrently.
o Product withdrawal with little or no advance notice to the Ministry.

The above are examples and/or other issues may trigger a targeted pharmacovigilance inspection.

### c) Pharmacovigilance system inspections

These inspections are designed to review the systems, personnel, facilities in place and their compliance with pharmacovigilance obligations. They may use products as examples to test the system. They may be routine or targeted.

**d) Product specific investigations**

These inspections focus specifically on a given product and are usually targeted as a result of triggers that have been identified.

**e) Inspections of Contractors**

Any contracted institution carrying out pharmacovigilance activities in whole or in part, on behalf of or in conjunction with the marketing authorizaiton holder may be inspected, in order to confirm their capability to support the marketing authorizaiton holder's compliance with pharmacovigilance obligations.

**f) Unannounced inspections**

Inspections may also be conducted without announcement in advance in addition to being conducted with announcement beforehand.

## 2. Inspection Procedures

The inspection procedures depend on the nature (routine/targeted) of the inspection and the conditions of inspection request.

### 2.1 Preparation for the Pharmacovigilance Inspection

The Ministry sends a letter to the Company, stating that a routine pharmacovigilance inspection is planned to be performed and requests the authorization holder to submit the "**Summary of Pharmacovigilance Systems (SPS) Document**" that summarizes the pharmacovigilance system, for which an outline is attached, to facilitate planning and preparation. No SPS is required for unannounced inspections.

#### 2.1.1 SPS Document

The SPSs should be prepared and submitted by the marketing authorization holders to the Ministry within 6 weeks at maximum. In some cases, this period may be shorter. The SPS should be short and brief and should not exceed 25 pages, excluding the attachments, where applicable. The SPSs should be prepared as separate copies for each inspector and submitted to the Ministry in printed form and also in electronic form (email or CD-ROM).
Where applicable, plans, drafts and graphs may be used to facilitate explanations.

In cases where some sections in the SPS are not applicable for the marketing authorization holder, the relevant section should include the phrase "not applicable" (for ex: if there are no "activities/functions - those directly or indirectly related to pharmacovigilance - that are out-sourced in Turkey" in the section **"Agreements with the third parties"** included in the SPS attachments, it's enough to write "not applicable" here).

The following should be considered in preparing the SPS document: if there's only a single pharmacovigilance system in the company, irrespective of the source of adverse events, it's appropriate to prepare a single SPS. If the company has different pharmacovigilance systems, multiple SPSs should be prepared. Accordingly, multiple inspections for the same marketing authorization holder may be performed to inspect the different systems.

### 2.1.2 Inspection Plan

After the SPS is reviewed by the Ministry, the inspection plan is established that outlines the planned meetings to be held for the purposes of and in the scope of the inspection, and sent to the marketing authorization holder. Inspection activities should be explained in detail in the inspection plan. The inspectors may make modifications in this plan prior to/during the inspection to achieve the objects of the inspection.

## 2.2 Conduct of the Pharmacovigilance Inspection

### 2.2.1 Opening Meeting

On the first day, an opening meeting must take place between the inspectors and the inspectees. In this meeting, the method of inspection should be introduced and discussed. In particular, the following points should be covered:

· The scope of the inspection is described.
· The Inspector outlines the inspection regulations and describes the methods and procedures to be used to conduct the inspection,
· The activities and personnel to be interviewed that are described in the Pharmacovigilance Inspection Plan are determined and inspection logistics is provided.
· It's re-confirmed that the resources, documents and facilities required by the inspectors are available.
· The time and date for the closing meeting and any interim meetings is determined.
· Appropriate site personnel should provide the requsted information about the marketing authorization holder and/or supporting contractors.

### 2.2.2 Conduct of Inspection/data collection and record of observations

The following documents should be submitted to the inspectors. When necessary, the inspectors may also request other documents related to the inspection.

**a) Legal and administrative aspects**
· Documentation of the responsible parties for pharmacovigilance/drug safety activities
· Identifying the Drug Safety Associate at the marketing authorization holder's site
· Availability of documentation on all suspected adverse events
· Contractual documentation with respect to any pharmacovigilance/drug safety responsibilities being out-sourced by the marketing authorizaiton holder
· Where applicable, special requirements for reporting of adverse events to the Ministry or for monitoring safety (for ex: post-authorisation commitments and compliance with Risk Management Plans);
· Preparation and submission of PSURs/ SPCs (including revisions)
· Collection and reporting of spontaneous adverse effects
· Collection, follow-up and reporting of pregnancy exposure
· Collection, follow-up and reporting of information on paediatric population exposure, if any

· Submission of any other information relevant to the evaluation of the risks and benefits of a medicinal product to the Ministry, particularly information concerning post-authorisation safety studies (including those in the Risk Management Plan)

**b) Organizational structure**

**(i) Quality system and Standard Operating Procedures (SOP) for pharmacovigilance activities**

- Documentation of SOPs and instructions to cover all aspects of pharmacovigilance/drug safety. These SOPs and instructions should include, but are not limited, to the following activities:

    - Collection and management of pharmacovigilance data (from consumers, healthcare professionals, medical information departments, medical representatives, quality departments, regulatory affairs departments, legal departments, manufacturing sites, sub contractors, etc.):

o Causality assessment
o Determination of seriousness and listedness/expectedness and whether adverse effect reports are expeditable
o Coding
o Avoidance of duplicate reporting
o Ensuring reporting compliance
o Identifying and tracking initial and follow-up reports
o Ensuring an adequate and complete follow-up
o Handling of reports to and from other organizations
o Handling of reports relating to comparator, product or placebo
o Ensuring completeness of the information contained in databases.

- Review, validation and follow-up of suspected adverse reactions
- Data Management (accurate storage and retrieval of information, tracking of reports and ensuring timeliness, compliance with requirements of confidentiality)
- Expedited reporting to the Ministry
- Monitoring of worldwide scientific literature
- Preparation and submission of Periodic Safety Update Reports
- Management of requests for information by the Ministry
- Management of urgent safety restrictions and type II variations
- Updating of core safety information/summary of product characteristics
- Signal detection/trend analysis activities
- Management of communications with the Ministry
- Production of Risk Management Plans

· Organisational charts to identify the key personnel
· Control of SOPs and other procedural documentation, including writing, review, approval, updating, distribution and implementation
· Review of Quality Control processes and documentation
· Review of corrective and preventive action processes and documentation
· Auditing of the pharmacovigilance system:
    o Determine that audits of key pharmacovigilance/drug safety activities are being carried out and which organisation is in charge
    o The processes for communicating and addressing internal audit findings
    o Audit of contractors/sub-contractors
    o Qualification and training of internal auditors.

**(ii) Drug Safety Associate**

· Documentation identifying the Drug Safety Associate along with qualifications and training, brief job description, brief curriculum vitae.
· Documentation of Drug Safety Associate and contact details in the quality system
· Verification that the Drug Safety Associate has adequate (direct, timely) access to all relevant pharmacovigilance/drug safety information
· Verification that the Drug Safety Associate has sufficient authority within the company to make amendments to the pharmacovigilance system in order to ensure compliance
· Documentation for delegation of tasks
· Verification of the assignment of a representative when the Drug Safety Associate is absent, and notification of this assignment to the Ministry and implementation of this process.

**(iii) Resources and training of Personnel**.

· Interview of personnel involved in any pharmacovigilance activity (including medical representatives, medical information, regulatory affairs, legal, clinical trial and product quality personnel)
· Documentation of job description, qualifications and training of individuals involved in any stage of pharmacovigilance/safety evaluation process
· Documentation on policies and procedures for training of personnel
· Allocation of deputies to key personnel

**c) Facilities and computer systems**

· Computer systems in use
· Data flow and collection system
· System for the archiving and retrieval of documents
· Archiving facilities
· Controlled access to the archives

**d) Safety data obtained from other departments: Quality defects/Medical information, Legal information etc.**

To be considered but not limited to:
· Quality defects and complaints should be examined to establish whether there are quality defects that could lead to adverse reactions or whether there may be a quality defect reported that could be the cause of actual or potential adverse reactions and vice versa.
· Handling of medical information and legal information should also consider the potential for adverse reaction identification,
· Information collected by the Marketing and Regulatory Affairs Departments.

**e) Review of data/documents**

The following are examples of testing that may be performed (this list may be changed by the Ministry depending on the inspection to be performed)

· Confirmation that potential adverse effects from any source (e.g. product complaints, information enquiries, medical representatives, post-marketing studies) have been processed appropriately. This may include a review of compliance reports.
· Determination of seriousness
· Determination of listedness/expectedness
· Causality assessment
· Consistency and correctness of coding with terminologies used and internal procedures
· Quality and completeness of the medical review
· Quality of the information included in case summaries

· Adequacy of follow-up measures taken
· Adequacy of follow-up information collection and reporting
· Any specific questions raised in the inspection request
· Submission of expedited and periodic reports to the Ministry. Have all relevant reports been submitted within the correct timeframes?
· Have all relevant cases (all serious adverse effects and all non-serious adverse effects, unlisted adverse effects) been discussed or included in the line listings of the PSUR covering the relevant time period?
· Have specific requests in Assessment Reports (e.g. for the presentation and submission of data) been appropriately addressed?
· Can serious adverse effects/adverse events be identified in the listings of non-serious adverse effects/adverse events?
· Has the output from literature searches been appropriately reviewed?
· Can specific literature cases be retrieved from the database?
· Have new safety issues arising from post-authorisation studies, conducted worldwide, been reported promptly to competent authorities?
· Adequacy of quality control process and follow-up measures taken (corrective action process).

**f) Recording inspection observations**

All inspection observations should be documented. If appropriate, copies should be made of records containing inconsistencies or illustrating non-compliance.At the end of the inspection, the inspectors should review all observations to determine which are to be reported as non-compliance or as quality system deficiencies. The inspector should ensure that these are documented in a clear, concise manner and are supported by objective evidence.
All reported observations (findings) should be identified with reference to specific requirements of the regulations or other related documents against which the inspection has been conducted. The names and titles of persons interviewed or present during the inspection meetings and the details of the inspected organisation should be documented.

### 2.2.3 Inspection Close-up Meeting

At the end of the inspection, the inspector(s) should conduct a closing meeting with the inspectee. The Drug Safety Associate, his deputy or other responsible persons for pharmacovigilance activities should attend the meeting. The purpose of the closing meeting is:

· To summarise inspection findings and observations to ensure that the results of the inspection are clearly understood and that there is no misunderstanding by either the inspectors or the inspectees,
· To provide the inspected party with an opportunity to correct any misconceptions made by the inspector or to supply additional information in response to the findings.
· To request copies of any documents that may be required by the inspector, (e.g. to assist with the preparation for other activities associated with the inspection).

An inspection may consist of visits to more than one location. If appropriate, a closing meeting may be held at each location inspected.

## 2.3 Preparation of the Inspection Report

After the final document requested from the authorization holder is received following inspection (generally within 30 days), the inspection report is prepaered in accordance with Appendix 2. For inspections involving multi-facilities, generall inspection data is prepared in accordance with Appendix 3. For writing the Pharmacovigilance Brief Report presented in Appendix 4, data to be included in Appendix 5 will be used.

This report relates to observational data obtained by the inspectors during the inspection. The inspection report is also sent to the marketing authorization holder.

## 2.4 Follow-up of Inspection Results

Where an inspection reveals non-compliances the Marketing authorizaiton holder will be required to prepare an action plan to correct the non-compliances and avoid their recurrence. The marketing authorizaiton holder may be required to provide reports including evidence of the progress and completion of the action plan. There may be re-inspection at an appropriate time to verify the progress and success of these remedial actions.

# 3. Administrative Measures and Regulatory Actions

In the event of non-compliance with pharmacovigilance requirements, regulatory options include the following:

• Education and Facilitation
Marketing authorization holders may be informed of non-compliance and advised on how this can be remedied.
• Inspection
Non-compliant marketing authorization holders may be re-inspected to determine the extent of non-compliance and to ensure compliance is achieved.
• *Warning*
The Ministry may issue a formal warning reminding marketing authorization holders of their pharmacovigilance regulatory obligations.
• Naming non-compliant marketing authorization holders
The Ministry may consider making public a list of marketing authorization holders found to be seriously or persistently non-compliant.

- Urgent Safety Restriction:

The Ministry will proceed according to the Regulation and Guideline on the Modifications in Medicinal Products for human use, which have been authorized or submitted for authorization.

- Variation of the Marketing Authorisation:

The Ministry will procced according to the Regulation and Guideline on the Modifications in Medicinal Products for human use, which have been authorized or submitted for authorization.

- Suspension of the Marketing Authorization:

The Ministry will proceed according to the Regulation on Authorization of Medicinal Products for Human Use.

- Revocation of the Marketing Authorization

The Ministry will proceed according to the Regulation on Authorization of Medicinal Products for Human Use.

**Appendix-1: Pharmacovigilance system summary (PSS) document**

**Section 1: Contact Information**

| **Authorization Holder** | |
|---|---|
| Name | |
| Address | |
| Telephone numbers | |
| Website | |
| **Drug Safety Associate** | |
| Name and other duties | |
| The address of place of duty | |
| Place where pharmacovigilance activities are conducted | |
| **Number of products authorized/approved in Turkey** | |
| | |

**Section 2: The structure of the Company and Pharmacovigilance Operational Model**

1. Give a brief profile of the Company to include the following information.

    - Company Affiliates/worldwide presence.
    - The list of Company's expertise products and therapeutical field/fields (authorized/approved products and products submitted for authorization/approval)
    - Recent merger or purchases (together with the effects on and relation with pharmacovigilance)

Company's response:

2. Brief summary on conduct of pharmacovigilance activities in the Company.

Company's response:

Section 3: Pharmacovigilance System

1. The summary of the pharmacovigilance activities conducted at the pharmacovigilance departments in Turkey and global pharmacovigilance departments, if any.

This section should be filled out by summarizing how compliance with the applicable Regulations and Guidelines is achieved, and include the following sections:

- A summary of the pharmacovigilance activities conducted by the other Departments that cover pharmacovigilance activities (for ex: Medical Department, Authorization Department and quality control department).
- Procedure for spontaneous adverse effect reporting (review of data initiated upon achievement and expedited reporting. Flow charts may be used for this).
- Detailed description of the compliance monitoring activities.
- How PSURs are prepared and submitted to the Ministry.
- The list of routine tasks performed by the Drug Safety Associate.
- Description of how signal generation and SmPC modification prpcedures are performed.
- Risk Management Plans (RMP) (Is there a RMP generated for any product by the Company?).

Company's response:

**Section 4: Data-Processing Systems used in Pharmacovigilance**

1. Detailed description of the data-processing systems/databases used for collection, comparison and evaluation of suspected adverse effects (for ex: spontaneous reports and solicited reports).
2. Detailed description of data-processing systems used in Turkey for collection/monitoring of adverse effect reports, including databases used for medical information consultancy (charts may be used for describing the interaction between the systems).

Company's response:

3. Brief information on databases used for collection, comparison and evaluation of suspected adverse events reported within the last 5 years (if any).

Company's response:

**Section 5: Quality Control System**

1. Does the Company intend to maintain the same pharmacovigilance system for the 6 month-period following completion of SPS? If the answer is no, you are required to submit a summary of the intended changes.
2. Who's responsible for pharmacovigilance system inspections? Where and for how long are the inspection reports kept?

Company's response:

**Section 6: Training Records**

Description of the training record system including the job definitions, CVs and place of the training records of the key personnel involved in conduct of pharmacovigilance activities.

Company's response:

**Section 7: Archiving**

Brief description of archiving of pharmacovigilance documentation.

If a company has been contracted to store pharmacovigilance documentation, the name and address of the facility.

Company's response:

**Section 8: Questions and/or Comments related to Data requested by the Ministry and/or submitted by the Company**

Company's response:

**Appendices of the SPS document**

- All appendices should be numbered.
- Each page should include a header/footer to include the Company name, appendix number, appendix title and page number.
- Should your company be unable to produce appendices, please summarize the reason why the appendix cannot be prepared, in section 8 of the SPS.

| **Appendix number** | **Information Request** |
|---|---|
| **Key Personnel** | |
| **1** | Organisation chart with names and job titles for the Turkish pharmacovigilance departments. |
| **2** | Up-to-date C.V. and job description for the Drug Safety Associate and deputy Drug Safety Associate. |
| **3** | Organisation chart with names Medical Information department and contractor performing the medical information service. |
| **The Company's product portfolio** | |
| **4** | A list of all products authorized/licensed in Turkey<br><br>Please include the following information:<br>➢ Active ingredient(s).<br>➢ State whether the product is marketed in Turkey.<br>➢ Trade name in Turkey.<br>➢ Indicate the five products that generated the greatest number of adverse event reports in the year before completion of the SPS. |

| | |
|---|---|
| **Quality Control System** | |
| **5** | Standard operating procedures of other Departments that relate to pharmacovigilance (e.g. Medical Department, Quality Control, Regulatory Affairs). |
| **Reporting to Ministry – Compliance Statistics** | |
| **6** | Compliance with expedited reporting requirements to the Ministry for spontaneous reports.<br><br>For the last two years, please provide information per month to include:<br>➢ Total number of adverse event reports (non-serious and serious) received by company.<br>➢ Total number of adverse event reports submitted to Ministry on an expedited basis.<br>➢ Total number of late reports submitted to Ministry.<br>➢ Number of late reports as a percentage of the total number of expedited submissions to the Ministry. |
| **7** | Compliance with the requirement for PSURs to be submitted within 60 days of the data lock point.<br><br>For PSURs submitted to the Ministry in the last two years, please provide the following information:<br><br>➢ Product<br>➢ Data lock point<br>➢ Date submitted to the Ministry<br><br>If no PSURs have been submitted in the last two years, please provide information pertaining to the last five PSUR submissions to date. |
| **Third Party Agreements**<br>Service providers (e.g. contract organisations providing a medical information or pharmacovigilance service): | |
| **8** | Provide details of any activities/functions - those directly or indirectly related to pharmacovigilance - that are out-sourced in Turkey. |
| **Product related safety issues** | |
| **9** | Provide the list of any products that have been withdrawn from any global market in the last five years due to safety reasons (date of withdrawal, country of withdrawal, and reason). |
| **10** | Provide details of all Urgent Safety Restrictions, instigated by either the Company or a regulatory authority, in the last two years. |
| **Document requests to be submitted along with the SPS** | |
| **11** | Provide the relevant procedural documents relating to the following activities:<br><br>a) Processing of spontaneous adverse drug reactions reports |

| | |
|---|---|
| | b) Follow-up of individual cases<br>c) Reporting of expedited reports to the Ministry<br>d) Monitoring of compliance with 15-day requirements<br>e) PSUR preparation and submission<br>f) Signal analysis<br>g) Responding to medical information request |

**Appendix-2: Format of the Inspection Report**

**A. ADMINISTRATIVE INFORMATION**
A.1. PRODUCTS
A.2. MARKETING AUTHORISATION HOLDER
A.3. INSPECTION

**B. BACKGROUND AND GENERAL INFORMATION**
B.1. REASON FOR THE INSPECTION
B.2. SCOPE OF THE INSPECTION REQUEST

**C. DESCRIPTION OF INSPECTION AND FINDINGS**
C.1. CONDUCT OF THE INSPECTION
C.2. PERSONS MET DURING INSPECTION (Details can be included in an appendix)
C.3. FINDINGS RELATED TO THE PHARMACOVIGILANCE SYSTEM AND PRODUCT SPECIFIC ISSUES
C.3.1. Drug Safety Associate function
*C.3.1.1 Job description*
*C.3.1.2 Qualifications*
*C.3.1.3 Training*
*C.3.1.4. Deputising*
C.3.2. Organisational structure
*C.3.2.1 Pharmacovigilance system*
*C.3.2.2 Interfaces with sub-contractors*
*C.3.2.3 Interfaces with other departments of the company (Clinical Trials, medical information, quality complaints, legal etc.)*
C.3.3. SOPs
C.3.4. Personnel
*C.3.4.1 Job description*
*C.3.4.2 Qualifications*
*C.3.4.3 Training*
C.3.5. Databases
C.3.6. Adverse Event/Effect reporting
*C.3.6.1. General Overview of Adverse event reporting*
*C.3.6.2. Periodic Safety Update Reports*
*C.3.6.3. Post-authorisation safety surveillance study reporting overview*
*C.3.6.4. Procedures for trend analysis/signal generation*
C.3.7. Quality Control and Quality Assurance
*C.3.6.1. Quality Control*
*C.3.6.2. Quality Assurance*
C.3.8. Archiving
**D. SUMMARY AND EVALUATION OF FINDINGS AND CONCLUSIONS**
D.1. SUMMARY OF FINDINGS
D.2. CONCLUSIONS
D.3. RECOMMENDATIONS
D.4. CONCLUSIONS REGARDING THE RESPONSES FROM THE INSPECTEE

**E**. **SIGNATURE AND DATE**

**F. APPENDICES**

F.1. Response relating to the Marketing Authorization Holder or Comments from the inspectors of the response

F.2. Reference Texts

F.3. Documents requested prior to, during and after the inspection

F.4. Other appendices as required

**Appendix-3: Format of the general inspection data**

**A. ADMINISTRATIVE INFORMATION**
A.1. PRODUCTS
A.2. MARKETING AUTHORISATION HOLDER
A.3. INSPECTION

**B. GENERAL INFORMATION**
B.1. REASON FOR THE INSPECTION
B.2. SCOPE OF THE INSPECTION REQUEST
B.3. REFERENCE TEXTS

**C. DESCRIPTION OF INSPECTION AND FINDINGS (Critical and Major findings)**
*Include these headings as applicable:*
C.4.1. QP function
*C.4.1.1 Job description*
*C.4.1.2 Qualifications*
*C.4.1.3 Training*
*C.4.1.4. Deputising*
C.4.2. Organisational structure
*C.4.2.1 Pharmacovigilance system*
*C.4.2.2 Interfaces with sub-contractors*
*C.4.2.3 Interfaces with other departments of the company (Clinical Trials, medical information,quality complaints, legal etc.)*
C.4.3. SOPs
C.4.4. Personnel
*C.4.4.1 Job description*
*C.4.4.2 Qualifications*
*C.4.4.3 Training*
C.4.5. Databases
C.4.6. Adverse event/effect reporting
*C.4.6.1. Adverse effect reports*
*C.4.6.2. Periodic Safety Update Reports*
*C.4.6.3. Post-authorisation safety surveillance study reporting overview*
*C.4.6.4. Procedures for trend analysis/signal generation*
C.4.7. Quality Control and Quality Assurance
*C.4.7.1. Quality Control*
*C.4.7.2. Quality Assurance*
C.4.8. Archiving

**D. SUMMARY AND EVALUATION OF FINDINGS AND CONCLUSIONS**
D.1. SUMMARY OF FINDINGS
D.2. CONCLUSIONS
D.3. RECOMMENDATIONS

**E. SIGNATURE AND DATE**

**F. APPENDICES**
F.1. Inspection Report site 1
F.2. Inspection Report site 2
F.3. …….

**Appendix-4: Format of the Pharmacovigilance Brief Report**

**A. ADMINISTRATIVE INFORMATION**
A.1. NAME OF THE MARKETING AUTHORISATION HOLDER
A.1. NAME OF THE SITES INSPECTED WITH FULL ADDRESS
Is the site inspected:
- Part of the Marketing authorization holder company
- Sub-contactor/Contracted Pharmacovigilance Service Organization
- Other: _____ _

A.2. NAME AND ADDRESS OF THE SITE WHERE THE DRUG SAFETY ASSOCIATE IS LOCATED

A.3. INSPECTION REFERENCE NUMBER

A.5. NAMES OF THE INSPECTORS OR/AND "EXPERTS" PARTICIPATING IN THE INSPECTION.
A.6. DATE(S) OF INSPECTION

**B. BACKGROUND AND GENERAL INFORMATION**
B.1. SCOPE OF THE INSPECTION REQUEST

**D. SUMMARY AND EVALUATION OF FINDINGS AND CONCLUSIONS**
D.1. SUMMARY OF FINDINGS RELATED TO THE PHARMACOVIGILANCE SYSTEM AND PRODUCT SPECIFIC ISSUES
D.2. CONCLUSIONS ON THE ACCEPTABILITY OF THE PHARMACOVIGILANCE SYSTEM AND THE COMPLIANCE OF THE MARKETING AUTHORIZATION HOLDER WITH PHARMACOVIGILANCE OBLIGATIONS
D.3. RECOMMENDATIONS FOR FURTHER ACTIONS
**E. SIGNATURE AND DATE**

**Appendix-5: Classification of Inspection Results**

**Critical:** a deficiency in pharmacovigilance systems, practices or processes that adversely affects the rights, safety or well-being of patients or that poses a potential risk to public health or that represents a serious violation of applicable legislation and guidelines.

**Major:** a deficiency in pharmacovigilance systems, practices or processes that could potentially adversely affect the rights, safety or well-being of patients or that could potentially pose a risk to public health or that represents a violation of applicable legislation and guidelines.

**Minor:** a deficiency in pharmacovigilance systems, practices or processes that would not be expected to adversely affect the rights, safety or well-being of patients.