Guideline on Pharmacovigilance audits

NATIONAL MEDICINES REGULATORY AUTHORITY
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Content

Pharmacovigilance audits

1. Requirement to perform an audit for MAHs

- In order to ensure their internal compliance with the pharmacovigilance regulations, company standards and quality system requirements MAHs have the following requirements:
  - local manufactures Sri Lanka are required to perform regular risk-based audit(s) of their pharmacovigilance system, including quality system.
  - for Imported medicinal products, the MAH abroad is required to perform regular risk-based audit(s) of their pharmacovigilance system including quality system for both:
    - central pharmacovigilance process (i.e process conducted by global team) and
    - affiliate pharmacovigilance process (i.e process conducted by their local representative in Sri Lanka).

2. Scope of the required audits

Upon designing audit strategy, the MAH should cover the governance, risk management and all parts of the pharmacovigilance system including:

- all pharmacovigilance processes and tasks;
- the quality system for pharmacovigilance activities;
- interactions and interfaces with other departments, as appropriate;
- pharmacovigilance activities conducted by affiliated organizations or activities delegated to another organization (e.g. regional reporting centers, MAH affiliates or third parties, such as contract organizations and other vendors).

3. The risk-based approach to pharmacovigilance audits

The risk-based approach to audit planning focuses on the areas of highest risk to the MAH's pharmacovigilance system, including its quality system. This is a non-prioritized, non-exhaustive list of examples of risk factors that could be considered for this purpose:

- changes to legislation and guidance;
- major re-organization or other re-structuring of the pharmacovigilance system, mergers, acquisitions (this may lead to a significant increase in the number of products for which the system is used);
- change in key managerial function(s);
- risk to availability of adequately trained and experienced pharmacovigilance staff, e.g. due to significant turn-over of staff, deficiencies in training processes, re-organization, increase in volumes of work;
- significant changes to the system since the time of a previous audit, e.g. introduction of a new database(s) for pharmacovigilance activities or of a significant upgrade to the existing database(s), changes to processes and activities in order to address new or amended regulatory requirements;
- first medicinal product of the MAH authorized in Sri Lanka;
- medicinal product(s) on the market with specific risk minimization measures or other specific safety conditions such as requirements for additional monitoring;
- criticality of the process: how critical is the area/process to proper functioning of the pharmacovigilance system. When deciding when to audit an affiliate or third party, the MAH should consider the nature and criticality of the pharmacovigilance activities that are being performed by an affiliate or third party, in addition to considering the other factors included in this list;
- outcome of previous audits, e.g. has the area/process ever been audited (if not, then this may need to be prioritized depending on criticality); if the area/process has previously been audited, the audit findings are a factor to consider when deciding when to re-audit the area/process, including the implementation of agreed actions;
- identified procedural gaps relating to specific areas/processes;
- other information relating to compliance with legislation and guidance, for example: information from compliance metrics, from inspections, from complaints, from other external sources, e.g. audits;
- other organizational changes that could negatively impact on the area/process, e.g. if a change occurs to a support function (such as information technology support) this could negatively impact upon pharmacovigilance activities.

- historical areas with insufficient past audit coverage, and high risk areas identified by specific requests from management and/or persons responsible for pharmacovigilance activities.

4. Selection of Auditor

4.1. Qualifications, skills and experience of auditors

Auditors should demonstrate and maintain proficiency in terms of the knowledge, skills and abilities required to effectively conduct and/or participate in pharmacovigilance audit activities.

The proficiency of auditor/ audit team members will have been gained through a combination of education, work experience and training and, as a team, should cover knowledge, skills and abilities in:

- audit principles, procedures and techniques;
- applicable laws, regulations and other requirements relevant to pharmacovigilance;
- pharmacovigilance activities, processes and system(s);
- management system(s);
- organizational system(s).

4.2. Audits undertaken by outsourced audit service providers

Ultimate responsibility for the operation and effectiveness of the pharmacovigilance system resides within the MAH. Where the MAH decides to use an outsourced audit service provider to implement the pharmacovigilance audit the following should be considered:

- the MAH should ensure that the has outsourced auditor has appropriate qualifications, skills and experience as described above;
- the requirements and preparation of the audit risk assessment, the audit strategy and audit program and individual audit should be specified to the outsourced service providers, by the MAH, in writing;
- the scope, objectives and procedural requirements for the audit should be specified to the outsourced service provider, by the MAH, in writing;
- the MAH should obtain and document assurance of the independence and objectivity of outsourced service providers;

- the outsourced audit service provider should also follow the requirements in this guidance as well as the principles detailed in EMA GVP Module on Pharmacovigilance audit

The MAH may also decide to use an outsourced service provider to conduct risk assessment and/or design audit strategy and audit program. In all cases ultimate responsibility for the effectiveness of the pharmacovigilance audit resides within the MAH.

5. Responsibilities of the MAHs regarding pharmacovigilance audits

- **Audit Planning**:
  - The MHAs should follow a risk based approach for planning pharmacovigilance audits and this risk assessment as well as the audit plan should be documented.
  - The MAHs should ensure the independence and objectivity of the pharmacovigilance auditor and this should be documented.
  - The MAH should ensure that written procedures are in place regarding the planning, conduct, reporting and actions of individual audits including the timeframes for all the steps.
- **After the audit conduct**:
  - the MAH shall ensure that the auditor prepares an audit report with the findings and they are graded as critical, major or minor in order to indicate their relative criticality to risks impacting the pharmacovigilance system. This audit report should be communicated in a timely manner to the management and relevant parties, including those responsible for pharmacovigilance systems.
  - Based on the audit findings, the MAH shall ensure that an appropriate plan detailing the root cause analysis as well as corrective and preventative actions and appropriate implementation time frame is prepared.
  - The MAH should ensure that agreed corrective and preventative actions are implemented and monitored in a systematic way and evidence of completion of actions is recorded. Follow-up audits should be carried out as deemed necessary, in order to verify the completion of agreed actions.

- **Audit & PSMF**
  - The MAHs should ensure that a list of all scheduled and completed audits is kept in the annex to the pharmacovigilance system master file (PSMF). The dates and results of audits and follow-up audits shall be documented.
  - MAH shall place a note concerning critical and major audit findings of any audit relating to the pharmacovigilance system in the PSMF. Once the corrective and preventive actions have been fully implemented and verified with an objective evidence, the note of these findings may be removed from the PSMF.
- **Role of the QPPV/ LSR:** should receive pharmacovigilance audit reports, and provide information to the auditors relevant to the risk assessment, including knowledge of status of corrective and preventive actions. The QPPV/ LSR should also be notified of any audit findings relevant to the pharmacovigilance system in Sri Lanka.

For more guidance on the structure and process for pharmacovigilance audits, refer to the *EMA Guideline on good pharmacovigilance practices (GVP) Module IV* .

In the context of pharmacovigilance, the risk to public health is of prime importance. For audit planning risk can be assessed at the following stages:

- strategic level audit planning resulting in an audit strategy (long term approach and includes a list of audits that could reasonably be performed usually for a period of 2-5 years), which should be endorsed by upper management;
- tactical level audit planning resulting in an audit program (one or more audits planned for normally for a year including their audit objectives, and the scope). It should be prepared in line with the long term audit strategy.
- operational level audit planning resulting in an audit plan for individual audit, prioritizing audit tasks based on risk and utilizing risk-based sampling and testing approaches, and reporting of audit findings in line with their relative risk level and audit recommendations in line with the suggested grading system.