Vaccine Safety Monitoring and Pharmacovigilance Tools
Advanced Pharmacovigilance Mini E-Workshop
16-18 March 2020

dcvmn
Developing Countries Vaccine Manufacturers Network

PV Audit Checklist for facilitating PV System gap analyses

Proposal

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What is a Pharmacovigilance Audit?

General (Dictionary of Pharmacovigilance):

"A systematic and independent process by which activities and documentation can be assessed and evaluated against agreed procedures to establish levels of compliance, competence, effectiveness, and probity ..."

EU GVP Definition:

"A systematic, disciplined, independent and documented process for obtaining audit evidence and evaluating the evidence objectively to determine the extent to which the audit criteria are fulfilled (see ISO 19011 (3.1)2)."

Benchmarking, reviews of qualifications, risk assessment questionnaires, surveys or other activities in which evidence of fulfilment of pharmacovigilance requirements is not independently obtained and evaluated, would not be regarded as an audit.

HMA
Heads of Medicines Agencies

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

3 August 2015
EMA/228028/2012 Rev 1*

Guideline on good pharmacovigilance practices (GVP)
Module IV – Pharmacovigilance audits (Rev 1)

Purpose and Objectives of Audits

To ensure compliance with company procedures and local / global regulatory requirements

- Audits are mandatory (EU) or expected by Regulators

To ensure company regulatory obligations / commitments are met

To identify process / quality improvements

To detect system gaps

To prepare for regulatory inspections

To ascertain that pharmacovigilance staff / company staff have adequate / appropriate training

To assess delegation of legal responsibilities to vendors and contractural obligations

Types of Audits

- Pharmacovigilance system audits
- Pharmacovigilance process audits
- Company Affiliates (i.e., Country Offices, Local Operating Companies, Marketing Company)
- Licensing Partners / Business Partners / Distribution Partners

Pharmacovigilance System Audits
Systems approach focused on business processes /1

Case collection and processing

- Overall case processing and case quality
- AEFI assessment and triage
- AEFI coding
- Medical review
- Case narrative

Regulatory reporting / Regulatory functions

- Expedited reporting of individual case safety reports (7-day / 15-day reports)
- Periodic reporting (DSURs, PSURs)
- Labeling
- Regulatory Authority query management

Signal detection process / Safety surveillance

Risk management process

Literature search

Pharmacovigilance System Audits
Systems approach focused on business processes /2

- Medical Information
- Product Quality complaint handling / AEFI reconciliation
- Safety information flow from all applicable sources from initial receipt to reporting to external partners
- Safety database and electronic systems to support pharmacovigilance
- Skills and resource level

Pharmacovigilance System Audits
Systems approach focused on business processes /3

Structure of the company's pharmacovigilance organization

PV Quality Management

- Quality assurance and quality control processes
- Performance monitoring and metrics
- SOP
- Training
- Document retention / Archiving

Business continuity / Disaster recovery

Compliance with company procedures and global Pharmacovigilance regulations (e.g., ICH, EMA, FDA, national regulations)

Compliance with Marketing Partner agreements

- Ensure pharmacovigilance roles and responsibilities are defined and performed
- Ensure appropriate exchange of safety information

Audit Procedures

Preparation

- Audit agenda
- Identify and confirm all R / R of staff involved
- Obtain and review the documents requested by the auditors
- Prepare audit back-office
- Compile questions for relevant auditees

Opening Meeting – Meeting to kick-off the audit

- Explain the audit and QA plan / scope of the audit
- Confirm date / time still ok
- Explain the course of the audit
- Request further documents that could not be requested earlier

Audit conduct

- Interviews with the responsible staff on the processes / SOPS / workflows
- Document reviews
- Demonstration of activities
- Walk through the safety processing system (e.g., work area, file storage, archiving)

Closing / Exit meeting

- Discussion of preliminary results

Audit Report - Follow-up CAPAs

Audit Report

Issued within defined timelines

Executive Summary

Description of Objectives and Scope of audit

Observations:

- Clear description of conditions observed
- Reference or criteria as the basis for the observation
- Quantification / Examples for context as applicable
- Assessment of cause and effect
- Judgement / Rating – e.g. Critical, Major, Minor based on Company Rating Scale
- Process / Quality improvement opportunities

Rating of Audit / Inspection Findings

In general, 3 rating categories of findings:

- Critical
- Major
- Minor (Other)

Definitions (wording may vary slightly between different companies / Authorities):

- Critical: 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: 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: Deficiency in pharmacovigilance system, practices or processes that would not be expected to adversely affect the rights, safety or well-being of patients.

CAPAs
Corrective and Preventive Actions

CAPA development is one of the most important aspect of a successful audit

- Understand the observation and seek clarification
- Assess root cause / underlying issue
- Develop CAPAs that are
  - Specific: Action resolves the issue and aims to prevent reoccurrence
  - Achievable: Action that is realistic and in accordance with the Regulations
  - Time driven: Identify realistic timeframe for completion (based on the risk)
  - Accountable: Action has clear accountability defined

Processes of concern /1

Ongoing safety evaluation / Signal management

- Detection and evaluation
- Identification of change to benefit / risk
- Notification to authorities
- Completion of commitments

Risk Management System and Risk Minimization Commitments

- RMP in line with known safety concerns and the current risk management system for defined products
- Adherence to RMP commitments
- Regulatory safety requests and commitments
  - Awareness of requests
  - Tracking requests
  - Timetable for response
  - Content of response
  - Fulfilling commitments

Processes of concern /2

Registration activities	• Awareness of applications for marketing authorization
Third party obligations	• Identification of licensing partners • Adequacy of existing pharmacovigilance agreements • Procedures covering new licensing arrangements
Regulatory intelligence	• Awareness of changes to regulation
Safety database and associated systems	

The audit includes (but not limited) the evaluation of the following:

- Oversight Marketing Authorization Holder, including Safety Governance
- Roles and responsibilities of QPPV
- Responsibilities and organization of local Pharmacovigilance Department
- Quality Management Systems
  - Procedures
  - Quality Assurance
  - Quality Control
  - Record retention
- Back-up procedures
- Staff:
  - Training and training records
  - Job descriptions
  - Qualifications
  - PV experience
  - Staff not directly involved in PV activities
- SOPs including cross-functional SOPs
- Case processing of individual AEFIs incl. regulatory submission of AEFIs
- Aggregate reports
  - PSURs / Annual Reports
  - Timely submissions to NRA
- Signal identification and evaluation
- Risk Management Plans and updates
- Handling of urgent safety issues / crisis management
- Safety database
- Literature searches
- Medical information
- Compliance metrics
- Labeling:
  - Company Core Data Sheet (CCDS)/ Company Core Safety Information (CCSI)
  - Summary of Product Characteristics (SPC)
  - Patient Information Leaflet (PIL)
  - Process of updating and implementation of changes
- Contracts for external services
  - Contents and management
- Contracts with co-marketing, co-development, co-manufacturing
- Responses to safety inquiries from NRA
- Archiving

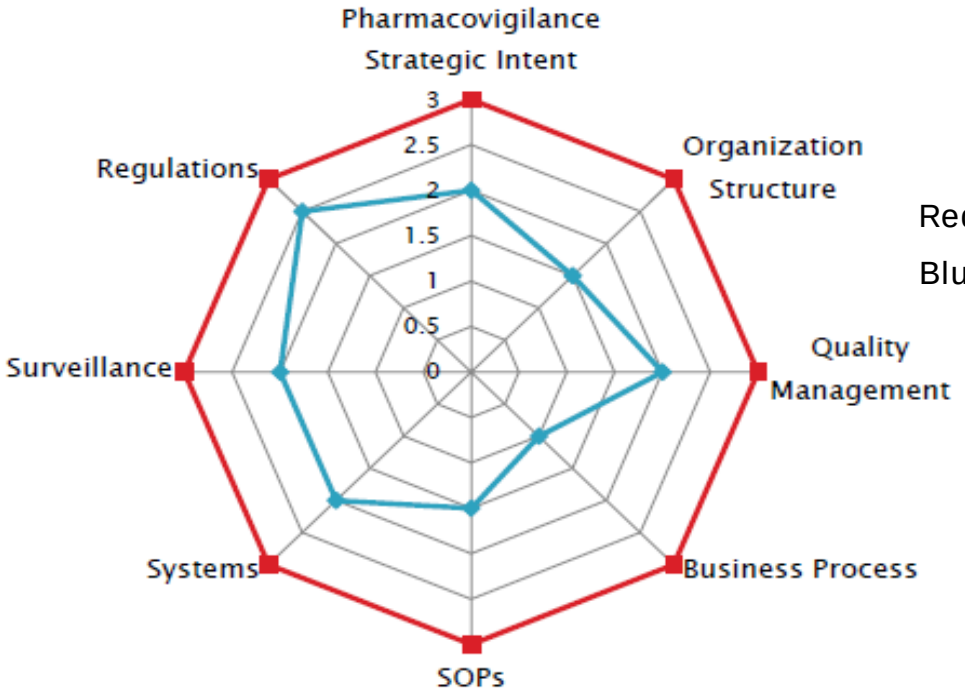
Audit Checklist

Pharmacovigilance audit activities should verify by examination and evaluation of objective evidence, the appropriateness and effectiveness of the implementation and operation of a PV system, including its quality system for PV activities.

- Audits provide company-wide awareness of Pharmacovigilance
- Utilize audit experience to build a structure of continuous improvement and audit / inspection readiness
- Audits support the company to establish the Pharmacovigilance Risk Profile

Company example visualizing gaps of the PV system (PV Risk Profile)

Jolley 2011



Red: Best Practices

Blue: Audit Results