April 15, 2021

1. **Facilities and equipment for post-authorization pharmacovigilance**

2. **Training of personnel for post-authorization pharmacovigilance**

3. **Managing contractual agreements for pharmacovigilance**

Dr. Varun Sharma

Senior Projects Leader, Pharmacovigilance
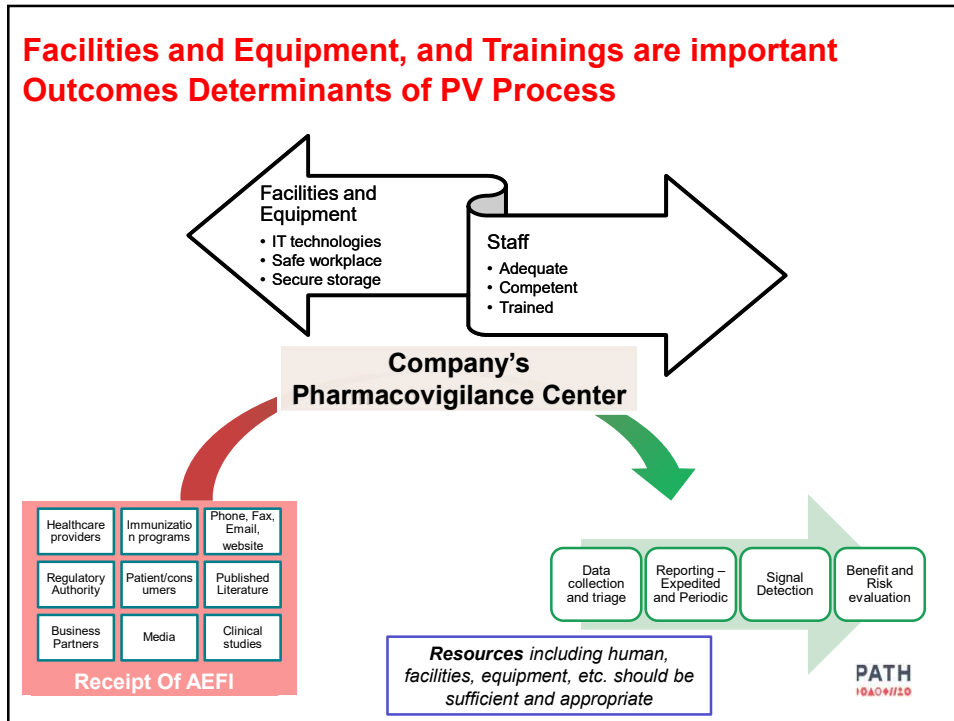
PATH

Pharmacovigilance System

System used by an organization to fulfil its <u>legal tasks and responsibilities</u> in relation to pharmacovigilance and designed to <u>monitor the safety</u> of authorized medicinal products and detect any <u>change to their risk-benefit balance</u> .

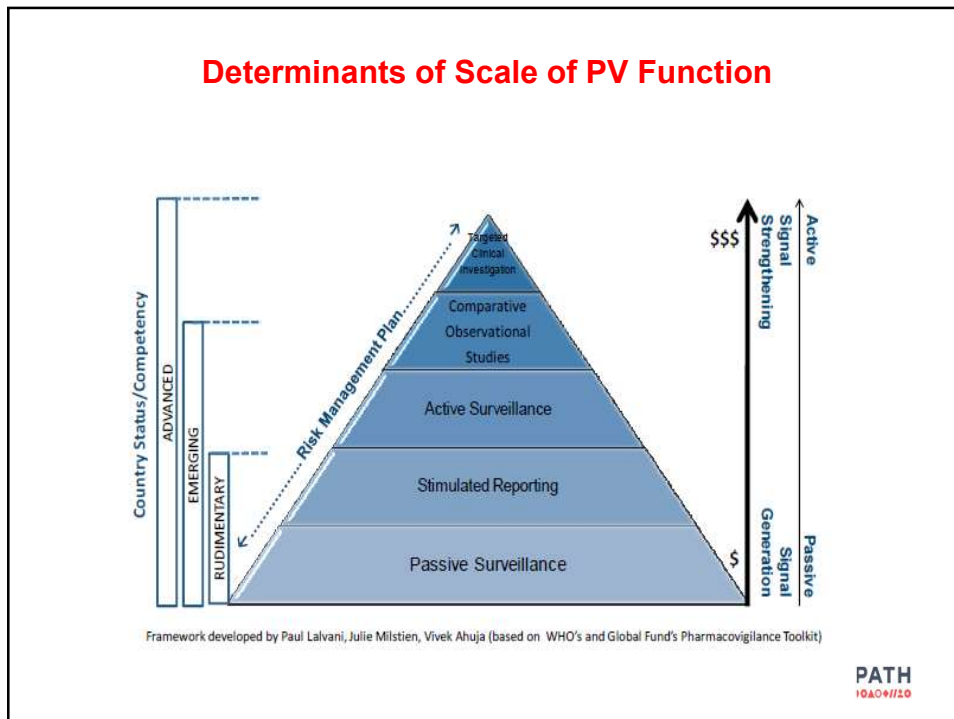**PATH**

Facilities and Equipment, and Trainings are important Outcomes Determinants of PV Process

Facilities and Equipment
• IT technologies
• Safe workplace
• Secure storage

Staff
• Adequate
• Competent
• Trained

Company's Pharmacovigilance Center

Healthcare providers	Immunization programs	Phone, Fax, Email, website
Regulatory Authority	Patient/consumers	Published Literature
Business Partners	Media	Clinical studies

Receipt Of AEFI

| Data collection and triage | Reporting – Expedited and Periodic | Signal Detection | Benefit and Risk evaluation |

Resources including human, facilities, equipment, etc. should be sufficient and appropriate

PATH

3

Determinants of Scale of PV Function

Country Status/Competency

ADVANCED
EMERGING
RUDIMENTARY

Risk Management Plan

Targeted Clinical Investigation

Comparative Observational Studies

Active Surveillance

Stimulated Reporting

Passive Surveillance

Active Signal Strengthening

Passive Signal Generation

$$$

$

Framework developed by Paul Lalvani, Julie Milstien, Vivek Ahuja (based on WHO's and Global Fund's Pharmacovigilance Toolkit)

PATH

4

2

Determinants of Scale of PV Activities

Planning is important

Your organization's pharmacovigilance activities will probably increase with time

- ❑ **New products and territories** get added to company businesses

- ❑ **Higher sales** translate into more prescriptions and therefore wider population exposure

- ❑ **New pharmacovigilance regulations** in various countries

- ❑ **Strict enforcement** and stricter penalties for noncompliance, frequent safety related actions

- ❑ **Increased awareness** among patient population regarding safe use of drugs/vaccines

PATH

5

Planning for Set-up/Enhancement of PV Function

Dependencies

❑Number of countries and plans for expansion to others?

❑Current products, and in pipeline?

❑Type: drugs/vaccines/medical devices?

❑Plans for WHO pre-qualification?

❑Number of adverse events (AE) currently received from all sources? Any ignored source of AE data?

❑Current level of trainings of personnel?

❑Upcoming requirements for Periodic report submission?

❑Signal detection activity undertaken? Risk management plans?

❑Current Quality Control and Quality Assurance functions?

❑Current PV activities undertaken?

PATH

6

Considerations for Set-up/Enhancement

QPPV

Adequately qualified, and experienced

Available 24X7; Back up person availability

May be outsourced/shared

Support of a medically qualified person

Considerations for Set-up/Enhancement (contd.)

Product/Vaccine Safety Committee / Interdepartmental networking

PSC – Interdepartmental senior level committee

Documented proofs for interactions with other departments like marketing, manufacturing quality assurance

Considerations for Set-up/Enhancement (contd.)

The pharmacovigilance system	Organizational chart
	Adequate staff, including medical reviewer and Quality Control
	System to collect, collate, validate and follow up Adverse Events from all sources
	Mechanism for regulatory reporting – expedited and periodic
	Monitor compliance
	Adequate, safe and secure storage spaces
	PV database to store and retrieve data efficiently when needed
	Business continuity plan and a disaster recovery plan (Back-up systems)

9

Considerations for Set-up/Enhancement (contd.)

Advanced Mechanisms	Signal detection mechanism may need special software
	Literature monitoring and online monitoring may need additional investments
	Risk Management Plans may need to be developed

10

Considerations for Set-up/Enhancement (contd.)

Database

Any database used to collect safety data, where the data is ultimately going to be submitted to a health authority must be **secure** and **validated**

The integrity of the database and the data must be assured

PATH

11

Considerations for Set-up/Enhancement (contd.)

Trainings

Internal and external trainings

Trainings of PV staff and all company employees

Mechanism to track trainings

PATH

12

Considerations for Set-up/Enhancement (contd.)

Outsourcing PV activities, Managing Business partners	PV activities may be outsourced Updated outsourcing agreements should be available Safety data exchange agreements with business partners should be signed

PATH

13

Considerations for Set-up/Enhancement (contd.)

Audits	Train internal teams for PV audits External auditors may also be engaged

PATH

14

Considerations for Set-up/Enhancement (contd.)

SOPs and Work Instructions

SOPs and WIs for each pharmacovigilance process

Reflective of the local regulations and the applicable international guidelines

Updated from time to time

PATH

Facilities and Equipment: Key points

❑ The organization should:

- o have **adequate facilities** and equipment such as office space, information technology (IT) systems and (electronic) storage space
- o they should be located, designed, constructed, adapted and maintained so as to suit their **intended purpose**
- o ensure that the critical ones are subjected to appropriate **checks**, qualification and/or validation activities to prove their suitability for the intended purpose
- o have processes in place to keep awareness of the valid terminologies in their **valid versions** and
- o keep the **IT systems** up-to-date accordingly

PATH

Trainings

17

Training of Staff

The staff being the critical aspect, their training on the PV requirements becomes essential.

❑ Organization's responsibility:

- o Provide initial and continued training
- o Maintain training plans and records
- o ensures that staff has appropriate qualifications, understanding of relevant PV requirements as well as experience
- o Ensure that staff
  - o receives and is able to seek information on the course of action once s/he becomes aware of a safety concern
  - o understands processes to be used in case of urgency

18

Criticality of Training in Pharmacovigilance

❑ Regulations and regulatory guidelines mandate having suitably trained staff for PV

❑ Managing complex systems and processes

- Primary objective of PV is patient safety and requires specific training **for efficient and effective execution**.
- Well-planned job specific trainings **help organization realize its goals and objectives** by covering the gaps between current and desired job performance levels and competencies of its employees
- Trainings can help in **problem solving**, **increasing productivity** and prepare for and **respond to future changes**

PATH

19

Choice of trainings and management system

Questions

- How much training is required?
- Are external trainers are required?
- Who should undergo which type of training?
- whether all personnel should receive the same set of trainings?
- What should be topics of trainings?
- whether there should be a separate function in the company which manages the trainings

Solution depends on

- Business model – regions/countries
- Product portfolio – Number of authorizations, type of products
- Job descriptions
- Workload - number of AEFI cases received, number of periodic reports to be generated, literature searches to be done, etc.
- Staff attrition
- Changing regulations or new regulatory requirements
- Specific training requirements

PATH

20

Topics for Trainings

❑ Training of pharmacovigilance staff

    ❑ Training on organizational requirements like computer systems, corporate policies, mission, safety in workplace, etc.

    ❑ Job specific pharmacovigilance trainings, including SOPs

    ❑ Tailored to suit the job role and responsibilities of an employee and support continuous enhancement of skills

❑ Training of other company employees

    ▪ All employees trained to identify and report any AE coming to their notice to the PV department on an expedited basis

    ▪ Additional trainings for staff from other departments indirectly involved in PV activities. E.g., sales, regulatory affairs, legal affairs, quality assurance, etc.

PATH

21

Timing for Trainings

❑ Training new company employees

    ▪ PV department:

        ▪ Elaborate and appropriate trainings

        ▪ Specific training plan made for employee after considering previous job experience and current job expectations

        ▪ Not all employees, even those recruited for the same pharmacovigilance activity, would require the same level of training

    ▪ Other departments: Induction training to included PV basics

❑ Retraining

    ▪ Personnel who score less than required in an assessment test

❑ Refresher training

    ▪ All personnel already on the job

    ▪ The topics can be varied and could include critical SOPs and applicable regulations

    ▪ scheduled depending on the complexity of the process and identified need

❑ New SOP or regulatory requirements

    ▪ To be done as soon as possible

PATH

22

Assessment of Training Effectiveness

❑ Tool to ensure that the knowledge from the training was absorbed

❑ Can help identify areas needing more emphasis or retraining

❑ Should be conducted at the end of each training session or as soon as possible.

❑ Should not take more than a few minutes to conduct

❑ A 'pass percentage' can be defined

❑ Even in cases where self training is required, an assessment of that topic can be planned.

PATH

23

Managing the Trainings

❑ Develop Training SOP

❑ Prepare role-based training plan

❑ Prepare standard slide deck

❑ Document each training

- The golden rule is to document every training
- All training records should be signed and dated by the trainer and the trainee
- In case of self training, 'self' should be written in space for trainer
- In case of online instructor led training, a scan of the training record form should be printed and filed
- Good practice to prepare individual training file

Topic	QPPV	PV Manager	PV Associate	Medical Reviewer
ICH…	+	+	+	+
Medical assessment ..	+			+
Data entry..		+	+	
Etc.	+	+		

PATH

24

12

Challenges

❑PV is a relatively new subject in some countries

    ❑Less options for academic courses
    ❑Appropriate trainers may not be readily available

❑Employees located at different geographies – timings (for lengthy topics/courses), language

❑Investments

- External trainers and courses
- procuring software for web-based trainings, management of trainings
- national/international travel

❑Lack of infrastructure

- Slow internet connections
- room to accommodate large number of trainees
- lack of equipment to conduct video/web-based trainings

PATH

25

Training of Personnel for PV: Key Points

o Initial and continued training are important

o Documenting training plans and records

o Targeted towards continuous improvement of relevant skills, application of scientific progress and professional development

o Process in place for post training assessment

o Training for non-PV team staff should be done

With proper planning and execution, the company can manage all its pharmacovigilance related compliance needs effectively and efficiently

PATH

26

Safety Data Exchange Agreements

27

Safety Data Exchange Agreements (SDEA)

An agreement which extends the terms of the Business Contract between Marketing Authorization Holder and Business Partner to describes the responsibilities of parties **to ensure that for the product(s) covered by the contract, regulatory reporting of safety data and other pharmacovigilance obligations are fulfilled** and the business interests of the parties relating to the safety of the product(s) are protected.

Marketing Authorization Holder is the primary entity legally responsible for Pharmacovigilance. The Manufacturer may or may not be the MAH in a particular country. (Distributers, local companies in foreign countries).

❑ Business partners only carrying out sales for MAH may only require simple agreement.

❑ Business partners more involved, e.g., distributer, co-marketing, co-developing or licensee, requires more detailed SDEA

28

Important Considerations for SDEA

Products and territories covered

Safety information to be communicated

- Direction of communication
- Language of communication
- Contact information
- Sources (solicited and unsolicited)
- Timelines (Serious and non-serious; define Day 0)
- Format
- Mode

PV activities primary responsibilities

- PVSMF
- Literature search
- Receipt, assessment and follow up of product complaints and AEFI cases
- Safety Database hosting
- Regulatory reporting – expedited and periodic
- Periodic reports generation - draft, review, timelines
- Signal detection
- Audits and inspections

PATH

29

ICSR Reconciliation with Business Partners

SOP driven

On a monthly basis

Provide CIOMS II line listing to all appropriate partners

Other party confirms the receipt of all the cases listed

Take appropriate action for missing cases

A Reconciliation tracker can be maintained to track & monitor the compliance.

PATH

30

Thank You

31