



Practical Considerations

Andrea Lohée, Pharm-AD
DCVMN training on PV,
May 2017



Overview

- Composition of a PV department
- Subcontracting
- Safety data exchange agreements



Size and workload of a classical PV department

- For a large vaccine manufacturer: 50 -100 staff if all in-house, can (theoretically) handle:
 - 3-5 DSURs/PSURs per month
 - 3 – 5 large development programs
 - Multiple audits/inspections per year
 - 100K – 200K reports/year
 - 5 – 10 important RMPs
 - Several important safety crises/year



Professional profiles

- Safety departments are frequently divided in 2 groups:
- A case management group or operations group
 - Collect safety reports
 - Feeds report into database
 - Provides aggregate listing or tables
- A safety evaluation group (now also called benefit) risk group)
 - Performs clinical review of individual reports
 - Performs signal detection and evaluation
 - Leads risk management activities



Professional profiles

- For case management: Varied professional backgrounds (eg languages to life sciences)
- For safety evaluations: mix of life sciences and medical backgrounds
- In addition: administrative support, IT profiles (for database functions), potentially legal support, quality control functions
- Management: frequently (bit not necessarily medical function)



Subcontracting PV activities

- Current challenges in industry
- PV operating models
- Core PV activities
- How to make model more efficient?
- Selecting the CRO
- Benefits
- Potential negative effects



Subcontracting PV activities

PV operating models

Current challenges in industry

- Increased complexity in PV due to fast growing environment, advances in technology and changing regulatory requirements
- Increasing focus on compliance systems and experienced talent
- Increasing costs for the maintenance of the infrastructure necessary
- Volume fluctuations



Subcontracting PV activities

PV operating models

PV operating models

Find right balance between:

- Efficiency
- Compliance
- Quality
- Effectiveness
- In-house expertise



Subcontracting PV activities

PV operating models

Driven by

- Budget constraints
- Product portfolio and case volume
- Geographical aspects
- Infrastructure
- Growth perspectives
- Company culture
- Availability of skilled pr
- ...



Subcontracting PV activities

How to make models more efficient

How to make models more efficient?

- Internal optimisation
 - Personnel
 - Tools
 - Processes
- Outsourcing
 - Full outsourcing
 - Partial outsourcing



Subcontracting PV activities

Core PV activities

Operational activities

- Collection of safety reports
- Case processing and submission (including QC)
- Preparation and submission of aggregate reports
- Preparation and submission of RMPs, REMs
- Literature monitoring
- Signal management
- PSMF

Managerial activities

- Procedural aspects (SOPs, PSMF)
- Contractual arrangements with 3rd parties
- Auditing
- Compliance oversight
- Regulatory intelligence
- Training
- System updates
- Forecasts



Subcontracting PV activities

Core PV activities

Collection of ICSRs

- Direct reports (single collection point/call centre)
- License partners
- Health authorities
- Medical information
- Literature (global & local)
- Social media
- Organised data collection (SMPs/protocols)



Subcontracting PV activities

Core PV activities

Processing of ICSRs

- Case intake (booking-in)
- Case triage
- Data entry
- QC
- Medical review
- Reporting (HA, partners, EC, etc)
- Case filing and storage
- Archiving



Subcontracting PV activities

Core PV activities

Periodic reports & RMPs

- Planning
- Preparation
- Stakeholders review
- QC
- Implementation & distribution
- Storage



Subcontracting PV activities

Core PV activities

Signal detection & benefit risk evaluation

- Detection of signals
- Assessment of signals
- Risk evaluation
- Risk minimisation
- Documentation



Subcontracting PV activities

Core PV activities

Systems and tools

- Safety database hosting
- Clinical database hosting
- Signal detection tools
- Eudravigilance
- MedDRA license
- WHO-DD license
- xEVMDP information



Subcontracting PV activities

Core PV activities

Managerial roles

- QPPV
- PSMF (including maintenance)
- SOP development and maintenance
- Training
- SDEA
- Regulatory intelligence
- Quality management & compliance oversight
- Auditing



Subcontracting PV activities

Selecting the CRO

Given the increasing scrutiny from authorities on the pharmacovigilance activities, great care must be taken to determine which elements of the PV activities can be delegated to a service provider.

Even in models where the full operational activities are outsourced, the MAH or sponsor must remain fully aware of all its products benefit-risk profile and remains ultimately responsible for the safety of its products

Delegation of activities ≠ delegation of responsibilities



Subcontracting PV activities

Selecting the CRO

Selection of the CRO

- Reputation
- Safety database and signal detection systems used
- Literature screening (tools, databases and possibility to perform local monitoring)
- Quality assurance system and quality monitoring
- Robust documentation and filing system
- Strong structure and managerial oversight



Subcontracting PV activities

Selecting the CRO

- Define the activities that could be outsourced
- Define the activities that must remain in-house
- Define the volume of activities
- Benchmark and compare
- Audit the service provider prior to engaging in the outsourcing of activities



Subcontracting PV activities

Selecting the CRO

Points to consider

- Geographical aspects
- Cultural and linguistic aspects
- Level of expertise of the CRO (including therapeutic area)
- Services offered
- Flexibility in offers
- Volume capabilities (reactivity in case of peaks)
- Training requirements
- Procedural readiness (SOPs)



Subcontracting PV activities

Selecting the CRO

Points to consider

- Big CROs have also often high turnover rates → training!
- Small CROs have usually less turnover but less flexible in case of workload peaks



Subcontracting PV activities

Benefits

Benefits

- Converting fixed resource costs into variable, workload dependent charges
- Reduced costs related to IT & infrastructure
- Reducing the number of resources to recruit, manage and train
- Improving on-demand access to unique expertise, intellectual property, and multidisciplinary knowledge
- Increased capacity flexibility



Subcontracting PV activities Benefits

- Free management to focus its attention on core capabilities and business performance
- Innovation & leading practices to maintain & increase competitiveness
- Standardisation of processes



Subcontracting PV activities

Potential adverse effects

Potential adverse effects

- Loss of internal expertise
- Increased contracts & technical agreements and resources needed for set up and maintenance of these contracts
- Increased quality assurance and quality control required
- Resources for training and meetings
- Increased travel costs
- Standardisation of processes



Safety data exchange agreements

One of the major trends in the pharma world is the joint development and marketing of medicinal products.

This entails all sorts of commercial contracts and agreements with other companies.

In the frame of such contracts, safety data exchange agreements must be put in place in order to define each parties roles and responsibilities in the collection and handling of safety related information.



Safety data exchange agreements

For this reason, it is crucial that the PV department is made aware in an early stage of the negotiations of all commercial contracts that could potentially result in the collection of safety related information.

This requires clear and established processes between legal/commercial/manufacturing activities and safety.

The SDEA should be a stand alone document (annex to the commercial contract).



Safety data exchange agreements

Type of commercial contracts

Commercial contracts may cover a variety of activities and can be divided in a few major types:

- In licensing
- Out licensing
- Co-development
- Co-manufacturing
- Distribution where distributor is the MAH
- Distribution where distributor is not the MAH



Safety data exchange agreements

Type of commercial contracts

- Co-marketing
- Co-Promotion
- Joint ventures
- Stock piling
- Supply agreements
- Technology transfers
- Supply of products
- ...



Safety data exchange agreements

Due diligence

Due diligence

Prior to entering into a deal, it should be ensured that the other party is capable of performing the activities that will be covered under the deal.

This can be done via a standard questionnaire or an audit.

The questionnaire and/or audit should provide sufficient evidence that the 3rd party has the adequate means, knowledge and infrastructure to perform the activities as described in the SDEA



Safety data exchange agreements

Content of SDEAs

Content of SDEA

The SDEA must clearly identify the following:

- Parties involved
- Holder of the global safety database
- Type of information to be exchanged
- Format for exchange of information (e.g CIOMS I, line listings, etc)



Safety data exchange agreements

Content of SDEAs

- Timelines for exchange of information
- Need for reconciliations and frequency for these
- Language for exchange of information
- Responsibilities for expedited reporting
- List of contacts for the different activities
- Definitions



Safety data exchange agreements

Ongoing monitoring

Once an SDEA is in place, it may require adaptations over the time, mainly in deals like technology transfers where different steps can require exchange of different types of information.

It should also be ensured on a regular basis that the terms of the SDEA are followed by both parties.

Contracts should be reviewed on a regular basis and at least when changes in the organisation occur that could impact the terms and conditions of the SDEA.



Safety data exchange agreements

Other types of technical agreements

For contracts with 3rd party service provider and for which collection of safety information is expected, the exchange of safety information will usually be part of technical agreements and/or safety management plans.

These are specific to PV activities and not directly linked to a commercial contract.

A safety management plan will be required for any PV service provider or any service provider that could be in contact with safety information including:



Safety data exchange agreements

Other types of technical agreements

- PV service providers
- Call centers
- Service providers subcontracted for conducting patient/HCPs surveys
- CROs conducting studies
- Commercial/promotional activities with direct contact to patients/HCPs
- ...



Safety data exchange agreements

Other types of technical agreements

PV must be aware of any of these contracts to be able to determine whether safety information is likely to be obtained from the activities covered by these contracts so that no safety information is missed