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Global pharmacovigilance management in a borderless age

Abstract

It has been a decade since GVP guidelines were issued in Japan. In these years, the expected roles of drug safety management representatives have significantly changed. Furthermore, globalization of business requires pharmacovigilance (PV) operations to be managed globally. This article discusses keys to success in implementing a global PV management scheme from three points of view; (1) PV strategy development, (2) discussion model for PV management scheme, and (3) global PV system development.

Introduction

In Japan, multiple efforts on post-marketing drug development have been made from the Edo period, in order to promote proper use of medicines. The biggest turning point for drug safety issues in Japan was the issue of Good Vigilance Practice (GVP) guidelines in 2004 in association with the 2002 revision of the Pharmaceutical Affairs Act. GVP guidelines define standards of post marketing activities and are asking pharmaceutical companies for collection, analysis and reporting of safety information on their drugs. With the guidelines, compliance with GVP added to the requirements to obtain a drug marketing authorization in Japan and pharmaceutical companies became required to establish an internal scheme to manage drug safety information for marketed products.

Increasing importance of PV operation

It has been a decade since GVP guidelines were issued in Japan . In these years, the expected roles of drug safety management representatives have significantly changed. The initial focus was proper case reporting to the authorities complying with the guidelines. Today, the scope has expanded to a proactive practice to maximize patient benefit by promoting the proper use of drugs and risk minimization based on the pharmacovigilance (PV) perspective, such as benefit-risk evaluation.

Major factors of PV operations change include:

- External factors
  - An increase in safety data that is publically accessible by consumers, healthcare providers, payers, etc. (e.g. EudraVigilance system by the European Medicines Agency)
  - Introduction of new regulations (e.g. Risk Management Plan; RMP)
- Internal factors
  - An increase in importance of accountability in line with requirements to be transparent
  - An increase in demand for integrated / consistent safety report through a product lifecycle (e.g. Development Safety Update Report; DSUR)

In this article, we would like to discuss three steps that pharmaceutical companies should take, to comply with the environmental changes; (1) PV strategy development, (2) discussion model for PV management scheme, and (3) global PV system development.

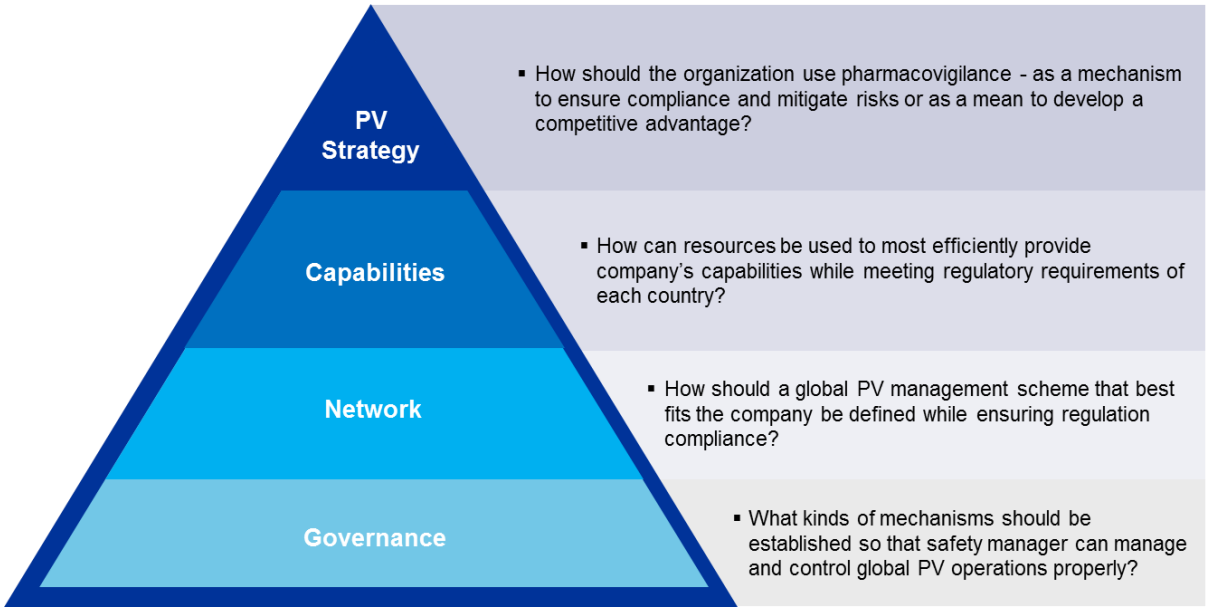
1. PV strategy development: Define items to be achieved through PV operations

As drug development and marketing are globalized, pharmaceutical companies are required to collect, assess and report adverse events in all the countries where clinical trials are conducted and/or products are marketed, following each authority's instructions. In establishing global PV management scheme, pharmaceutical companies need to understand that there is no definitive model as the role allocation among global affiliates is expected to be defined based on their own global strategies on purpose of PV unitization such as:

- Define PV as a mechanism to assure compliance and hedging risks
- Define PV as a tool to provide richer safety information to increase competitiveness

Figure 1 illustrates a Deloitte framework for the discussion of a PV business model that is developed based on our experience with several pharmaceutical clients. After a corporate level PV strategy is defined / clarified, required capabilities, network (global PV management scheme) and governance functions are to be discussed.

Figure 1: PV business model discussion framework



2. Discussion model for PV management scheme: Hub & Spoke model

As discussed, a global PV management scheme can be discussed once a corporate level PV strategy has been developed. Based on our experience working with several pharmaceutical clients, we believe the Hub & Spoke model (Figure 2) is an effective way to discuss the global PV management scheme.

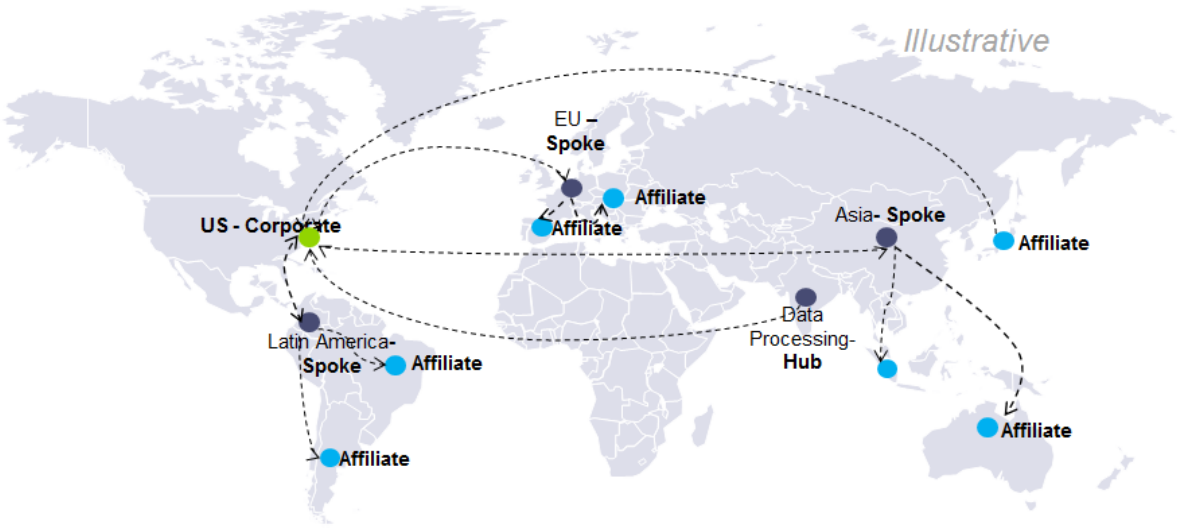
In this model, we divide PV functions into four parts: Corporate, Spoke, Hub and Affiliates, and then consider the functional allocation within a global network:

- Corporate
  - Pipeline management
  - Benefit-risk assessment
  - Signal detection
  - Information transmission
- Spoke
  - Oversee regulation compliance status of affiliates in designated regions
  - Support for standardization and sophistication of case assessment quality in designated regions
  - Act as an affiliate
- Affiliate
  - Collect, evaluate and report adverse events identified in the country
  - Communicate closely with local authorities
- Hub
  - Data processing using outsourcing providers (e.g. CROs)
    *Central information management of products / studies for outsourcing

For the effective utilization of the Hub & Spoke model to define the optimal global PV management scheme for now and the future, we recommend to make the following points clear beforehand:

- Countries with own presence and license of each product (sold as own product or licensed-out which means no reporting responsibilities)
- Market maturity and regulation austerity of each country

Figure 2: Example of Hub & Spoke model



3. Global PV system development: Points for system implementation

As a next step, PV system infrastructure is to be developed once a PV strategy and a global PV management scheme are defined. In this step, the system infrastructure needs to be well-designed to properly support the global operation governance.

Until recently, pharmaceutical companies had installed and maintained different PV systems that best comply with regulations in each country and case information had been shared by intersystem coordination and/or people's efforts. In Japan, regardless of multinational or domestic, many companies had adopted systems considering PMDA's reporting requirements and usability.

Today, many companies are adopting a single PV system for global use, trying to build a single database for safety information. In addition to complying to local regulations, performing benefit-risk assessment to minimize risks is a primary objective of PV that requires central case information management in a timely manner. It is true that the coming enforcement of the ICH guideline E2B (R3) in April 2016 is a definitive trigger of system replacement, but it seems that the essential purpose of this in recent years is to achieve the primary PV objective.

As of September 2013, many pharmaceutical companies are working on adopting single PV database globally, including Japan and some are expected to complete the implementation in 2014. Apparently these companies share two pivotal considerations:

- Communication among international affiliates, which can especially be a challenge when introducing a system globally
- System functionalities to comply with Japan-specific customs in reporting process

Not limited to pharmaceutical industry, major companies have had to invest great deal of resources in the global implementation of the ERP (Enterprise Resource Planning) package system, which integrates major business functions such as finance, accounting, human resources, personnel affairs, production, procurement, stock control and sales. Although PV is a single part of business function, implementation of PV system demands substantial investment in terms of human resources due to the two challenges described above.

Based on our extensive experience, we believe that it is crucial to address the following points for successful implementation of a single global database:

- Well-understood objectives of system implementation:
  Different from conventional PV systems used in Japan which has high degree of usability, global system requirements usually primary prioritize database integration and compliance with regulations. Thus, a company must make affiliates understood that the new system intends to comply with regulations of various countries and manage risks globally and optimize system requirements
- Global communication
  Since a multinational vendor is often commissioned for global system implementation, assigning project members that are capable to handle international communication and tightly manage a complex project are crucial

Conclusion

To sum up, the sound foundation for a global PV management scheme is created through PV strategy development, discussion of a PV management scheme, and global PV system development. Establishing a global PV management scheme enables firms to realize the primary objective of PV operations, which is to maximize patient benefit by promoting proper use of drugs and risk minimization. In the near future, it is expected that PV will play a wider and more sophisticated role, and naturally, enhancement of activities such as benefit-risk assessment becomes a key to achieve competitive advantage and to expand market share.

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