Risk Based Monitoring for Pharmaceutical Safety

Yannick BARDIE, MSc, PhDf, President of Intelligence in Life™

www.intelligenceinlife.org

Introduction

Recent accidents have raised public awareness regarding the need for transparency and safety in the evaluation of health products. The case of VIOXX® can be identified as the most representative industrial, global, contemporary pharmaceutical accident similar to that of thalidomide in 1953 and Distilbene in 1977.

The works presented in this chapter focus on one of current societal issues: how can the quality and the safety of health products available on the market be guaranteed to every citizen? This topic is directly related to the notion of pharmacovigilance and in the broader sense that of surveillance and strategic foresight (SF).

Pharmaceutical accidents of the industrial era bring about issues related to the implementation of a security system in this area, similarly to what already exists in the areas of civil nuclear, space and aerospace.

The main topic of pharmacovigilance concerns the surveillance of drugs and the prevention against the risk of adverse effects resulting from their use whether this risk is potential or supported by proof.

It constitutes a guarantee that remains valid throughout the lifetime of a drug[1]. It thus comes under the umbrella of the science concerned with the detection, assessment, understanding and prevention of adverse effects or any other problem related to drugs[2]..

System and clinical trial project organization analysis

According to Rasmussen[3], the study of risk management involves an analysis of sociotechnical systems. The understanding of the roles, actions and strategies of the system actors requires the knowledge of the requirements and constraints of the system to which they belong.

Within the context of a clinical trial project organization[4], one can make a distinction between external business and IS strategies to this organization and internal business and IS strategies.

Figure 5.2 highlights the interactions within each area as well as between external, internal levels and cross-domain interactions.

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[1] 1 http://social-sante.gouv.fr/soins-et-maladies/medicaments/la-surveillance-des-medicaments/article/la-pharmacovigilance.

[2] 2 This can easily be widely extended to the medical device, for which the designation medical devices vigilance is appropriate.

[3] RASMUSSEN J., Risk Management in a Dynamic Society: A Modelling Problem, Safety Science, 1997.

[4] The project is a single process that consists of a set of coordinated and controlled activities, comprising start and end dates, undertaken with the purpose of achieving a goal in accordance with specific requirements, including time, cost and resources constraints (according to the ISO 10006:2003 standard and reformulated by the AFNOR as the X 50-105 standard).

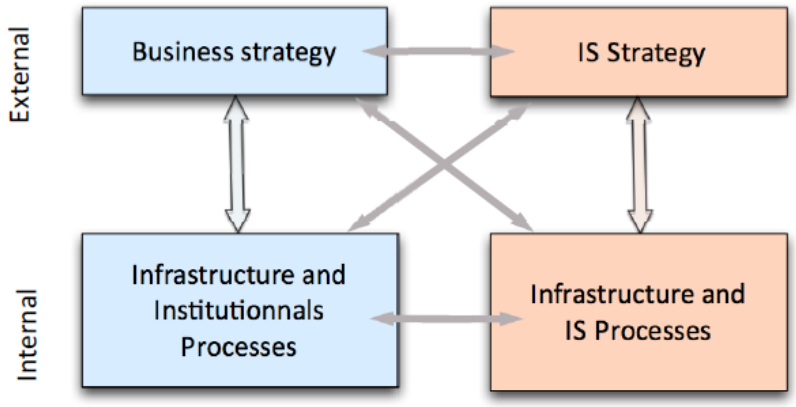

Figure 5.2. *Information system business areas interactions*

The process of monitoring however focuses on the issue of risk management (risk-based monitoring [RBM] – transposition at the level of the ISO 31000:2009 standard onto risk management). This has been the subject of studies, two of which serve as references to institutions: OPTIMON and ADAMON that are cited by the FDA and the EMA and destined to proponents of clinical trials.

OPTIMON (monitoring optimization)[5] observes that monitoring, in the current state, is not optimal and relies on an analytical grid including three steps:

(1) definition of the topic(s) for study;
(2) identification of one or several conditions of increased risk and
(3) determination of the risk level.

ADAMON[6] is a proposal for a tool able to systematize risk assessment and for the implementation of measures targeted for quality management.

On the other hand, we have focused on the concept of weak signals: the designation weak signals introduces a parallel between the fields of electromagnetism, electronics and that of information and decision systems that multiply as part of the company's management framework[7]. Analogously to generalized or specialized types of computing platforms affected by the civil and military surveillance of space areas, strategic foresight can rely on a device equivalent to a radar (radio detection and ranging) in order to capture primary, emerging information of unclear origins.

It is likely that weak signals are particularly significant in specific procedures that organizations can implement so as to increase the probability of being capable of releasing warnings in the presence of an emerging event?

How can one design structured, reticulate and pro-active instruments at the internal organizational level that allow this organization to explore its external environment to acquire, distribute and use forward-looking information for the purpose of anticipating plausible future changes? How can in fine disaster be made unlikely to happen?[8]

[5] "OPTIMON STUDY", 2013, available at https://ssl2.isped.u-bordeaux2.fr/optimon/Default.aspx.
[6] "ADAMON STUDY", 2013, available at sur http://ctj.sagepub.com/content/6/6/585.full.pdf+html
[7] COHEN K., CYERT RICHARD M., "Theory of the Firm", Prentice-Hall Int., New York, vol. XVIII, no. 2, pp. 21–33, 1975.
[8] FRITZ C., "Disaster", Contemporary Social Problems, pp. 651–694, 1961.

Propositions :

Based on the interactions between fields described, Henderson[9] describes and categorizes strategies making use of information technology as levers for decision making and, in which the IS plays a critical role in the transformation of the institutional process (see Figure 5.10).

Alignment, according to this model, can be achieved by the following four strategies:

1. implementation strategy (the external institutional business strategy induces the implementation of infrastructures and internal processes and the IS infrastructure follows);
2. technological influence (the external business strategy generates external changes in IS strategies (standards) that in turn induce changes in infrastructures and internal IS processes);
3. technological operation (it is the external IS strategy and its technological breakthroughs that drive internal processes and infrastructures);
4. technological implementation (the infrastructure of the global external IS influences and improves the quality of the institutional process).

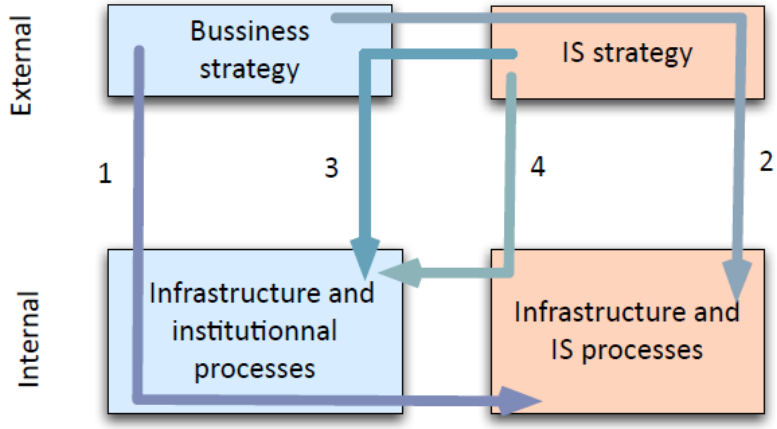

Figure 5.10. *Alignment strategies*

Within the pharmacovigilance context, the process of aligning information systems according to objectives and business strategy is, in our view, a major challenge. The specificity and sensitivity of pharmacovigilance will depend on the quality of the strategic alignment. European and American authorities preferentially advocate strategy because of the evolution of information technology in connection with the notion of integrity.

[9] HENDERSON J.C., VENTRAKAMAN N., "Strategic in Transforming Organizations", New York Oxford University Press, pp. 97–117, 1992.

As a matter of fact, the issue related to integrity covers various dimensions,which are as follows:

– the integrity of voluntary participants (patients and subjects) to medical research and end users of health solutions; in the field of studies, which is biomedical research and in particular in the area of clinical trials, the integrity of participants is crucial. The possibility of conducting a clinical trial is under the control of ethics committees or people protection committees as well as pharmacovigilance authorities;

– the integrity of the research and development processes of data used for security analyses. The integrity of the data generation process is supported by the study protocol framework. This is the process of data generation where the early stages of the production of weak signals can be found[10];

– the integrity of actors (in a moral sense) within the organizations conducting health solutions development projects;

– data integrity (source documentation namely the PMR, clinical, monitoring, surveillance and pharmacovigilance).

Operational Changes Foreseen

Unlike “standard” monitoring that consists of checking 100% of source data (at the investigation center) and in identifying source data transcription errors (in the patient’s medical record) in the CRF in paper or electronic form, RBM is intended to optimize and reduce onsite monitoring. The intensity of onsite data verification will therefore be adapted to the risk level, preset at the beginning of the study in the risk management plan (by type of test, medication, development stage, by country, etc.) but also through adaptation during testing, according to the risk signals perceived in the databases created. Among other things, this will make it possible to optimize onsite monitoring, and therefore to decrease the time spent at site, and as a result, the cost allocated to global monitoring (almost 30% of the budget of a study are dedicated to monitoring).

Conclusion

On a neo-institutional level, how will monitoring be structured in governmentality? How and by whom will be carried out control, static and dynamic organizational management in clinical research under the framework of the new European regulation on clinical trials? Will we witness resistance to change? Will we witness resistance and conflicts when implementing information systems able to manage risk-based monitoring? As such, will we observe resistance to change during the implementation of such systems? How can acceptance be guaranteed by the actors? Would such IS be chosen by managers? Is it technologically and sociotechnologically possible to develop safe computer, cybernetics tools in the field of the clinical evaluation of health products?

[10] H.I.A., “Managing strategic surprise by response to weak signals.”, California Management Review, vol. XVIII, no. 2, pp. 21–33, 1999.