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BOOK REVIEW

Therapeutic Risk Management of Medicines

Stephen J Mayall and Anjan K Banerjee. Elsevier, 1st Edition, 2014. Print Book ISBN: 9781907568480, eBook ISBN: 9781908818270

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When asked to review this book just before the summer I happily accepted. As a researcher with a keen interest in the impact of regulatory decisions on clinical practice I expected this book to increase my understanding of risk management of medicines around the globe, following the dramatic changes in the field of pharmacovigilance in the past decade. Moreover, I expected the authors to pinpoint areas where the implementation of pharmacovigilance activities as now required by regulators was less than straightforward.

Then, I got the book, all 401 pages of it, including a positive appraisal—including some critical notes—by no less than Ralph Edwards. So, what could I still add on this impressive-looking book? Well, let me give it a try.

The book is divided into four parts. In part 1 the authors provide a historic overview of key safety issues that have shaped the current risk management system. This overview is perhaps not comprehensive, but thorough and to the point. The concept that "risks of a medicinal product need to be placed in the context of its benefits, rather than just assessed in isolation" is introduced in chapter 2 as a basic principle of therapeutic risk management. And, although the book further focuses on identification and management (with the aim to minimize) of known and unknown risks, it is clearly written from the concept that risk management should consider this balance between risks and benefits. Very appropriately, the authors describe in chapter 15 the challenges in assessing this benefit–risk balance and how to present or communicate these often disparate and uncertain entities to respective stakeholders. In this first part of the book the principles of risk management in Europe and the USA are presented, with a relatively short chapter on risk management in the rest of the world. The European Union Risk Management Plan (EU-RMP) forms the basis of risk management approaches in Canada and Australia, and even Japan has its own requirements but follows a similar approach. Risk management approaches in the enormous emerging markets of China and India remain rather elusive, but it is of interest to note that Brazil has similar requirements to an EU-RMP (see, for example, Table 6.1 of the book). The book continues with its focus on risk management approaches in Europe and the USA, which is understandable as these regions have the most developed requirements.

The second and third parts are the reason you want to buy this book. Part 2 addresses what the safety concerns are that need to be addressed in the EU-RMP safety specification or what level of pharmacovigilance activities are required for the USA. The concept of routine pharmacovigilance (i.e., collection and interpretation of spontaneously reported adverse events, signal management, etc.), and the need for and design of additional pharmacovigilance activities, i.e., post-authorization safety studies (PASS), are detailed. Chapter 9 is an important chapter that describes how to analyze whether and what type of risk-minimization activities are required. The authors emphasize the need for careful planning. They promote the use of a multi-step approach, in particular the Failure Modes and

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Effects Analysis (FMEA) model that is followed by a Criticality Analysis, together known as FMECA. This approach basically describes the various steps of the treatment process, where the process may go wrong, and what the likelihood and severity are of these potential failures. This will then result in a prioritization of the risks that risk minimization should be aimed at. The authors—who are recognized experts in the field of risk management, but also paid consultants—warn against "lazy thinking". They argue that copying another drug's risk minimization approach, even of a similar drug, should be avoided. Although closely copying what others may have done is usually not a good strategy for anything, it does seem to make sense that class-related drugs would have similar risk management plans (RMPs) and risk minimization activities, if only to reduce confusion by healthcare professionals. Nevertheless, it is understood that class-related medicinal products could have, for example, different pharmacokinetics properties. Thus, this could result in the need for a dose adaptations in patients with renal impairment for one product but not for another. Obviously, there is a balance between starting over with a fresh mind and mindlessly copying someone else's program. This part of the book also describes in an excellent manner available risk minimization tools and where they fit in EU and USA regulatory frameworks and healthcare context. The third part of the book describes (challenges around) the implementation and evaluation of effectiveness of risk minimization activities. The chapter on evaluation is co-written by Meredith Smith, a senior drug safety officer of a large pharmaceutical company. It provides a good grasp on what levels of process and outcome the impact of risk minimization activities can and should be measured. It also gives examples of strategies, designs, and data collection methods that are suitable for such evaluation (summarized, for example, in Table 11.2). The authors identify some critical areas, such as the low response to surveys used to evaluate the impact of risk minimization tools and poor representation of certain geographic areas, and also that not all required evaluations were carried out. In addition, although risk minimization evaluation should ideally include a priori thresholds that determine success, these are often not specified. In chapter 12 very practical and useful considerations are provided on how to implement pharmacovigilance and risk minimization activities; the authors clearly show their hands-on experience with the topic.

The final part of the book addresses potential future developments in risk management. It is a bit of an eclectic collection of chapters, including discussing Development RMPs (DRMP) that address pharmacovigilance activities before the drug is launched. Other chapters on the commercial importance of risk management (the most interesting suggestion of which is that registries can both monitor uptake of a new medicinal product in a "correct" population from a third-party payers perspective as well as monitor safe use of the product following labeling restrictions), learnings on risk management from other industries, and future developments are less relevant for the planning and design of risk management. Beyond doubt, the most attractive chapter is chapter 15, which addresses, as mentioned, "benefit risk assessment and public communication".

In general, this is a well-written, sturdy hardcover book that fits well with its main use as a reference book in my view. However, I have two practical aspects that I did not like that much about the print version of the book. The authors provide many references to regulator's guidance documents, but these are lengthy uniform resource locator (URL) addresses that are not easy to look up, as you cannot just click on them in the print. This might not be an issue with the ebook. The second downside is that the print version is in black and white only and particularly the many graphics (which are in various shades of gray) are not all as crisp as they could be.

In conclusion, this is a must-have book for those working in the field of therapeutic risk management of medicines. It provides an interesting read but is mostly a very practical reference book on how to set up an RMP or to check whether you have covered all topics when developing your own RMP. It is very useful as a training book for new pharmacovigilance officers, but it is also useful for experienced staff (including regulators) to reflect on how they address risk management in their own company. The book considerably increased my understanding of risk management of medicines around the globe (albeit predominantly in Europe and USA), amply meeting my first expectation. However, it did not fully answer my second question of whether implementation of new pharmacovigilance activities on a regional or global scale has been successful.

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