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Book reviews

Excipient Toxicity and Safety

M.L. Weiner, L.A. Kotkoskie (editors), Marcel Dekker, New York, Basel, 2000, 370 pages, ISBN 0-8247-8210-0

Sooner or later every pharmaceutical scientist comes across a situation where the safety of a particular excipient is unclarified for the intended use in a formulation. It is obvious, that new excipients, which have not been used in humans must be subject of basic toxicological studies and specific safety investigations on the pertaining product. But often things are not so clear, especially when excipients have been used before for other purposes, via other application routes, with significantly different doses etc. At that point development teams always struggle how to go ahead and guidance was rare in that area. Here the new book can be of great value as it presents a comprehensive and modern compilation of the scientific background, the scope and interpretation of toxicological test systems and clinical evaluation and the relevant position of the regulatory bodies.

After a short introduction into types of excipients, a chapter on purity of excipients makes aware of their ubiquitous potential as a source of contamination. Hidden under the headline of 'History of excipient safety and toxicity' you then find a very compressed but informative source on GRAS (generally recognized as safe) excipients, typical 'excipient safety issues' from the past. I like this part as it is not so much an issue of history but of basis background knowledge to learn about the major 'events' in the field and the still open questions with some excipients in use.

The regulation of pharmaceutical excipients and the development of safety evaluation guidelines are subject of the next two, very informative chapters.

The different exposure routes are now reviewed separately in five consecutive contributions. This is the part of the book, where you have the chance to find specific information for your particular problem without being forced to read or browse through the full text. Surprisingly (or not?) the chapter on oral exposure is the shortest, although this pathway is clearly the most important one.

Toxicokinetics, hazard identification, exposure assessment and risk assessment are the contents of the following chapters. These considerations put the pure data gathered in the formal toxicological studies into the necessary context and the chapters are stimulating to think about twice. For me, the last chapter on 'Harmonisation of excipient standards' does not fit so well to the book, it deals in length with case studies on excipient specifications without a real message.

The book does not answer specific questions on typical excipients or excipient classes, nor does it refer to a professional selection of information sources, be it databases or traditional handbooks and literature. This is a major weakness of the monography and left me disappointed when I tried to get specific information on some actual issues of excipient safety evaluations. Cyclodextrins are not mentioned at all, no news on colorants are available and the persistent quest for new, safe surfactants for parenteral use is not touched at all. Magnesium stearate on the contrary is indexed more than ten times, as it was used as an example for harmonization. By chance I found a comprehensive and well written chapter on the BSE (bovine spongiform encephalitis) problem and how authorities handled it, but the index gave no hint on gelatin, BSE, or prions at all.

Consequently, the use of the book can not be recommended for those, who would like to know whether a specific excipient is applicable in a certain formulation. You have to ask: how shall I test an excipient in a specific situation, or: are the available data adequate and sufficient? With that scope, the book closes a real gap in pharmaceutical development literature (primarily for industrial use) and it does it very well. Toxicologists as well as pharmaceutical staff will find stimulating information. Also regulatory and quality assurance functions should refer to the book as a solid source of background information for upcoming decisions on excipients.

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High Throughput Screening: The Discovery of Bioactive Substances

John P. Devlin (editor), (ARRT International, Inc), Marcel Dekker, New York 1997, 712 pages, US$ 165.00, ISBN 0-8247-0067-8

The intention of this book is to facilitate the start with high throughput screening discovery (HTS) mode in the bio-based industrial environment, as well as to promote the adaption of these technologies within the academic commu-