Book review

Guide to Paediatric Clinical Research

Edited by Klaus Rose & John N. van den Anker.

Published by Karger, 2007, 138 pages, HB, price €65.50/\$83.75.

ISBN 978-38055-8201-8

It is widely acknowledged that the discovery, development and regulation of medicines specifically for children has lagged sadly behind that for adults. This had led to an underdeveloped regulatory process for paediatric licence applications and a practical response from those responsible for prescribing medicines to children, namely extrapolation from adult data to determine efficacy and safety for paediatric medication in many disease areas. The problem could only be tackled by a combined approach from industry, academics, regulators and healthcare practitioners responsible for paediatric therapeutics. This is what has happened, with the USA taking a lead and Europe, rather belatedly, following.

This slim volume (137 pages including index) is an excellent summary of how this is evolving. Its multiauthorship reflects the integrated approach required, with representation from pharmacy, clinical pharmacology, industry, various paediatric specialties, nursing and patient interest groups. Unfortunately, there is no contribution from the European Medication Agency which could have put the European regulations in perspective with comments on progress on real-time applications.

The 15 chapters are short and cover the main areas of interest and controversy: historical background, regulatory change, challenges of ethics and clinical research, consent and assent, paediatric formulations, blood and tissue sampling, studies in neonates, studies in protocol design and novel methodologies. The latter two chapters will probably be of most interest to the clinical pharmacologist. They explore the requirements of the Paediatric Plan as laid down in European Legislation and offer a useful decision tree approach to deciding which paediatric studies are essential and which can be extrapolated from adult data. They touch on the vexed question of 'what is a child' in terms of arbitrary age limits compared with physiology development, and the equally vexed question of whether if (ever) it is ethical to conduct healthy normal volunteer studies to determine kinetics and early tolerability in children who cannot expect to benefit from the study. This leads to a brief description of sparse sampling techniques in population kinetics, and alternative novel designs such

as enrichment approaches, concentration-controlled designs, placebo-withdrawal and randomized placebo phased designs. All these approaches are aimed at extracting the maximal amount of data with minimal exposure of children to unnecessary risk. The downside, as stated, is that some knowledge of and confidence about the position and shape of the concentration-response curve is required which, if inadequate, could lead to an incorrect decision or failure to achieve the primary kinetic and dynamic end-points. It will be extremely interesting to see whether the regulatory bodies accept the inclusion of these designs in the Paediatric Plans.

The other area of special interest to clinical pharmacologists is the organization of paediatric research networks across Europe which aim to recruit children to studies in diseases of low incidence and to study innovative methodologies for recruitment, such as sequential enrolment, continual assessment methods, and *in silico* modelling simulation.

In conclusion, the only serious issue I would raise with this book is the title, which should be a *Guide to Paediatric Clinical Research with Medicinal Products*. Otherwise it is an excellent summary of the current state of knowledge for those in the field and an accessible introduction for the newcomer.

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RECEIVED

5 June 2007

ACCEPTED

8 June 2007

PUBLISHED OnlineEarly

31 August 2007