

Recent Publications

American Hospital Formulary Service Drug Information: 89

The American Hospital Formulary Service Drug Information, which is published by the American Society of Hospital Pharmacists, prides itself as "the most comprehensive authoritative source of evaluative drug information". It is certainly one of the most frequently updated. Every year, for the past thirty years, a new annual edition has been published to assure the claim that it covers virtually every single drug entity available in the United States. The task, which involves over 250 independent clinicians and pharmacists in the review process, is formidable and, since the unwieldy loose-leaf format was replaced by a single bound volume in 1984, it has become a prime source of reference far beyond North America.

Its organization, which is determined by a practical, and not overly elaborate, pharmacologic-therapeutic classification, is admirable for the busy clinicians for whom it is primarily intended. If the trend to include introductory commentaries at the beginning of each set of individual drug monographs is sustained, it will compete strongly with many of the established textbooks on clinical pharmacology.

Reference: *AHFS Drug Information 89*. American Society of Hospital Pharmacists, Inc., 4630 Montgomery Avenue, Bethesda, MD 20814. ISBN 0 930530-89-6.

Medicines: regulation, research and risk

No drug regulator and no executive working in an internationally-based pharmaceutical company can operate effectively without a sound working knowledge of the processes by which medicinal products are controlled within the major national markets. There is no shortage of information of a more or less ephemeral nature in the weekly trade press, but it is not so easy to find comprehensive and readable accounts of how the statutory and regulatory provisions that determine these processes have evolved. This book provides a valuable introduction to the complexities of relevant law in the industrial-

ized English-speaking countries and in Japan, together with a brief guide to the European Directives concerning medicines as they stood at the end of 1987.

As an important bonus it also includes a series of informed essays and commentaries on matters of the moment ranging from the costs of pharmaceutical research, product patent life, product liability, and orphan drugs, to mechanisms for monitoring marketed products. The topics are wide-ranging and the reader will be hard-pressed to find them presented in a more readily-assimilable form.

Reference: *Medicines: regulation, research and risk*. Ed. Griffin, J.P., D'Arcy, P.F., Harron, D.W.G. Queen's University of Belfast, 1989 ISBN 0 85389 325 X

Pyrrolizidine alkaloids

This book disposes of the dogma that herbal and other traditional medicines may be assumed to be safe on the basis of long and apparently uneventful usage. Many of these preparations contain alkaloids that are known to be toxic and, among these, the pyrrolizidines have long been associated with the development in man of veno-occlusive hepatic disease and the development of cirrhosis. However, it is accidental poisoning with these substances that poses the greatest danger. In many regions plants containing them in high concentrations contaminate staple crops and constitute a threat to farm animals, particularly during the dry season. A large outbreak of human poisoning was recently reported from Afghanistan following a prolonged period of drought.

In experimental studies in animals they have produced acute and chronic toxic changes in the liver, lungs and central nervous system and they possess a dose-related potential to induce teratogenic, fetotoxic and mutagenic changes. This book draws together information cited in over 500 published studies and it provides the most comprehensive overview of the biological properties of these substances that has yet been compiled.

Reference: *Pyrrolizidine alkaloids*. *Environmental Health Criteria*, No. 80. World Health Organization, Geneva (1988) ISBN 92 4 15480 2

Guidelines for improving children's prescription medicine use

Ten independent studies of the attitudes of children in the United States of America towards their medicines have shown that, even in the case of those on anticancer therapy, almost half of them fail to comply with instructions. A report entitled "Children and America's Other Drug Problem", which discusses these findings, has been issued by the National Council on Patient Information and Education, a body that represents consumers, health-care professionals, government and industry, and which receives active support from the Food and Drug Administration and the American Medical Association. Its message, issued in the form of guidelines on how to inculcate a more responsible attitude in children towards their medicines, is directed primarily to clinicians and it draws on much expert advice from professionals with extensive practical experience of the many facets of the problem.

Reference: *Children and America's Other Drug Problem*. National Council on Patient Information and Education, 666 Eleventh Street, NW, Suite 810, Washington, DC 20001, USA.

Predicting carcinogenicity

One of the most challenging and complex tasks in toxicology today is to determine which of the daunting array of established laboratory models are most reliably predictive of the consequences to man of exposure to biologically active substances. In 1981, the International Programme on Chemical Safety, in collaboration with the National Institute of Environmental Health Sciences of the USA, initiated a large inter-laboratory collaborative study of short-term assays proposed as alternatives or supple-

ments to the classical long-term cancer bioassays performed in rodents. The first phase of the study, completed in 1985, which was directed to the identification of one or more *in vitro* eukaryotic tests suitable to complement the *Salmonella* mutation assays, has resulted in a proposal that a standardized chromosomal aberration assay should be developed for this purpose (1).

The second phase of the study appraises the results obtained when two structurally-related carcinogen/non-carcinogen pairs of compounds were subjected to a wide range of *in vivo* assays. The results, now published in two volumes (2), indicate that short-term *in vivo* tests are of value, less as primary screens, but rather to identify genotoxins most likely to present a carcinogenic hazard to man.

Much still remains to be explored regarding the relative advantages and disadvantages of short-term *in vivo* and *in vitro* models as indicators of genotoxicity. Particularly for those toxicologists concerned primarily with new drug development, the strategies for investigating non-genotoxic mechanisms of chemical carcinogenesis remain largely open to debate. The work accomplished thus far in this project indicates that, if answers are to be supplied, they are most likely to emerge through organized international collaborative efforts.

References

1. Progress in Mutation Research. Vol. 5. *Evaluation of short-term tests for carcinogens*. Ed. Ashby, J., de Serres, F.J., Draper, M. et al. Elsevier (1985). ISBN 0 444 80615 6
2. International Programme on Chemical Safety. *Evaluation of short-term tests for carcinogens*. Vols. 1 & 2. Eds. Ashby, J., de Serres, F.J., Shelby, M.D. et al. Cambridge University Press on behalf of the World Health Organization, Geneva (1988). ISBN 0 521 34152 3 (Vol.1): 0 521 34153 1 (Vol.2).