Benchmarks: Alternative Methods in Toxicology. Edited by M. A. Mehlman. Princeton Scientific Publishing Co., Inc., Princeton, NJ, 1989 *(219 pp, $58.00)*.

With ten contributed articles from 18 authors and the editor, this book includes the multiple topics of toxicologic mechanisms, conventional testing and regulatory standards, and alternative methods to the use of animals in toxicology. The editor, M. A. Mehlman, bases the term "alternative" on the four R's, namely to 1) replace the use of animals, 2) reduce the number of animals, 3) refine existing procedures so that animals are subject to less pain and suffering, and 4) maintain responsibility to the public in design of alternative methods. With these objectives, the subjects discussed by the authors as alternatives extend to computerized artificial intelligence, in vitro tests for skin and eye irritancy, pharmacokinetic metabolism and excretion of compounds, genotoxicity, carcinogenicity, teratogenicity, systemic toxicity, and improved statistical interpretation of in vivo data to allow smaller test groups. The book succeeds in providing the reader with an overview of the diverse and complex approaches to conventional and alternative toxicology.

With greater orientation toward comprehensive toxicology than dermatopathology, some attention is given in the book to cutaneous irritancy and carcinogenicity. The Draize test for skin irritancy by toxic compounds has provided a standard of skin inflammation and corrosion that has been accepted by regulatory agencies for decades. However, current opinions from the civic and scientific communities have recognized and begun to address the need for improved indexes of skin irritancy to displace the Draize test. Two articles in the book describe the application of computerized artificial intelligence using Structure-Activity Relationships (SAR) of chemicals as skin and eye irritants. This fascinating and sophisticated alternative utilizes existing animal data of skin irritancy from known compounds to predict irritancy of novel compounds based on their similarity of chemical structures and activities. The SAR alternative is reported by Enslein to compare to the Draize test with predictive accuracy of 93% for topically applied hydrocarbons. In a related article by Rosenkranz and Klopman, SAR were used to predict correctly an equivalent activity to form skin tumors in mice for benz[e]aceanthrylene (a novel poly aromatic hydrocarbon, "PAH") as for benzo[a]pyrene (a known carcinogenic PAH) based on identical reactive groups in the two compounds. Although these kinds of alternatives are not considered absolute or independent substitutes for complex physiologic responses of animal models, they provide useful screening techniques that can reduce the numbers of animals needed for conclusive toxicologic classification. In fact, a consensus recognition is made by the authors that each new alternative method for toxicologic testing must always withstand the ultimate rigors of correlation to animal tests and validation by regulatory agencies. Most authors also favor basing conclusions on batteries of in vitro toxicologic assays with concurrent results to displace particular animal tests. Certain authors even extend design considerations for alternative toxicology to compensate for the limitations inherent in extrapolation to humans of results from toxicologic tests performed with animals.

Conspicuously absent from the book are cellular and molecular models of cutaneous inflammation from in vitro studies of immunodermatology. Although tremendous knowledge has been gained in recent years in the fields of cutaneous cytokines and immunology, no in vitro models of cutaneous inflammation are presented. Also absent are discussions of drug metabolism in skin, and in vitro models of percutaneous absorption using available culture systems for epidermal keratinocytes. One possible explanation for these exclusions is the current paucity of alternative systems for measurement of cutaneous penetration and irritancy in vitro that have been correlated and validated against in vivo standards. However, the editor notes in the preface that this volume is "the first in a series," and therefore future volumes will have opportunities to address these exciting and important subjects. By reference and allusion, the book makes new challenges to develop, correlate, and validate working models of skin not only as a site of toxic response, but also as a metabolically active organ through which toxic compounds may pass before translocation to other sites.

For focussed and specific considerations of conventional dermatotoxicology, other books are superior. However, the subject material in this book is intentionally broad, and addresses well the social, academic, governmental, and industrial aspects of conventional and alternative methods in toxicology. In this respect, the book provides a good perspective and reference point for assessment of specialized alternatives in cutaneous toxicology.

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Sterol Biosynthesis Inhibitors—Pharmaceutical and Agrochemical Aspects. Ellis Horwood Series in Biomedicine. Edited by D. Berg and M. Plempel. Ellis Horwood Ltd., Chicester, West Sussex, U.K., 1988 *(583 pp, $155.00)*.

This book is divided in three parts covering I) Chemistry, mode of action, toxicology, and general aspects on sterol biosynthesis inhibitors (SBI) (7 chapters) concerning piperazines, pyridines, pyrimidines, imidazoles, triazoles, morpholines, piperidines, and allylamines; II) the use of SBI in plant protection (6 chapters); and III) SBI compounds in human and animal mycoses (8 chapters) and aromatose inhibitors (1 chapter). Thirty-four authors contributed to this work.

In part I the chemistry of a large number of SBI compounds is reviewed, followed by an electronmicroscopic study, and a look at the mechanism of action of pyridines, pyrimidines, azoles, morpholines, and allylamines, as well as an approach for the development of new compounds and a review of toxicologic aspects of various compounds.

The mechanism of action of a large number of plant, human, and animal antifungals is described and discussed. In this respect the ergosterol biosynthesis or induced deficiency; the various aspects concerning sterols, cytochrome P-450, squalene epoxidase, fungistatic, and fungicidal activity; the relation between the mechanism of action and the activity; and general aspects on toxicology, hormonal influences, and teratogenic implications are exposed.

Part II deals in detail with various aspects of plant protection SBI in general. The use of a large number of fungicides in cereals, stone fruit, grapes, and peanuts is discussed, and special attention is drawn to the combination of two or more antifungals. The rationale of this is to avoid emergence of resistant strains and to cover a broader

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