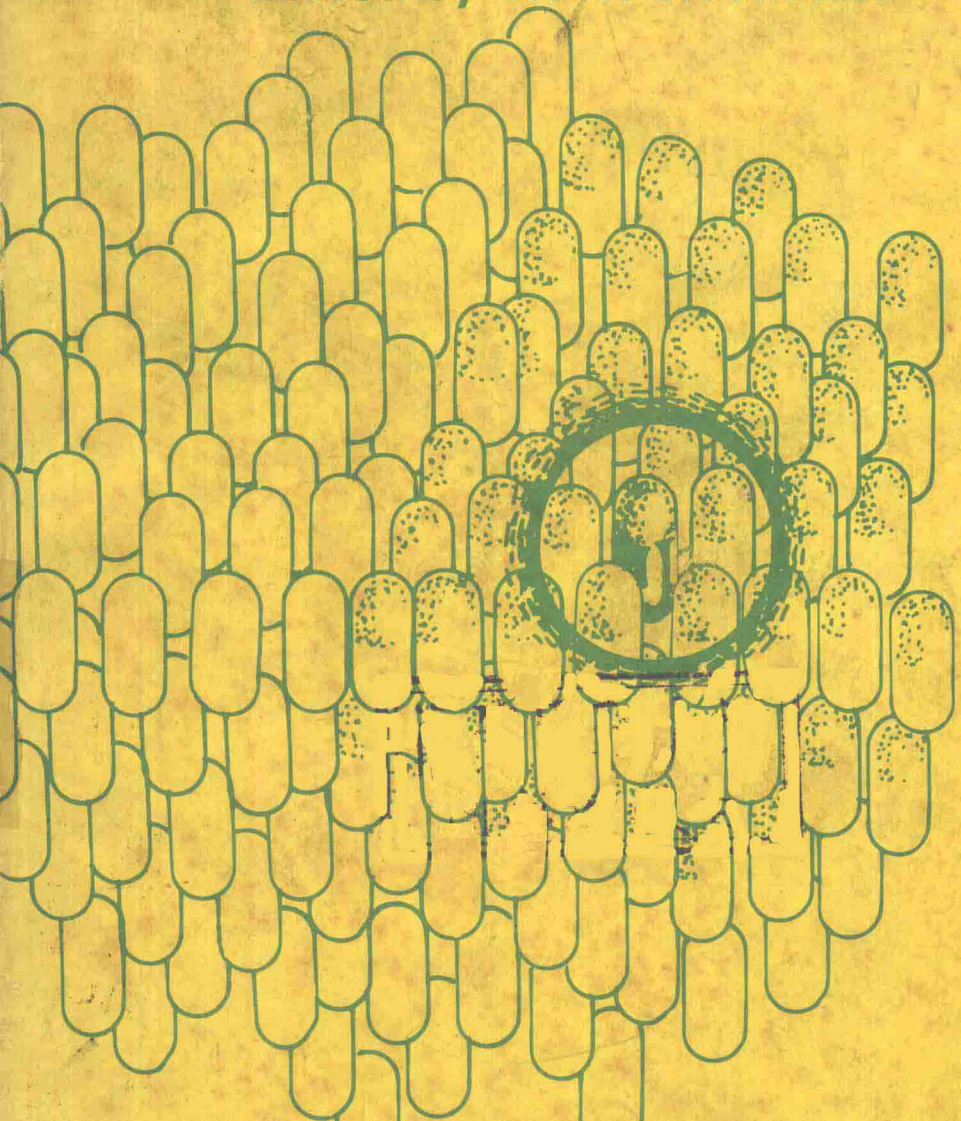
Monitoring for Drug Safety

Edited by W. H. W. Inman



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EDITED BY

W. H. W. Inman

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For my girls
June, Stella, Rosemary, Charlotte
and in memory of Valerie

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Foreword

The quickening pace of developments in new pharmaceutical products since World War II has almost inevitably, one might say, been associated with new legislation. Broadly speaking, the laws and regulations have been aimed, as in the Medicines Act in Great Britain, towards three objectives – the safety, the efficacy and the quality of products made available to the public. Each of these objectives has required the ingenuity, skill and patience of all those involved – from chemical and biological laboratories through the pharmacological and toxicological testing procedures, the pilot trials, the controlled clinical trials, the marketing and the collection of data about adverse reactions. All this has not only made a heavy demand on those responsible for achieving each of the three objectives, it has also imposed great responsibilities on those overseeing the processes in the various Government agencies all over the world. The public is perhaps too casual in its acceptance of all the care mobilized in their interest before new or, indeed old, medicines reach them. Perhaps the publication of this important review will widen appreciation of what has been and is going on, mostly successfully, behind the scenes. I certainly hope so.

It is therefore a great pleasure to introduce this book. It represents a collection of authoritative statements from many parts of the world about the present state of our knowledge and practice in testing new therapeutic agents. Indeed as far as I know nothing so extensive and detailed on the subjects covered has previously been available to the medical professions, the pharmaceutical industry and those concerned with statutory regulations related to the safety of medicines. So it seems likely to become a historic landmark in the field. The appearance of this work is also particularly timely because we have reached what will probably be seen in the future as a watershed in our thinking about the development of new medicines. Those concerned are moving from the notion of increasing dependence on animal toxicity testing before introducing new agents towards a growing realization that in the end the most important species for study is man himself. The biochemical differences which occur as a result of the processes of evolution in the very species we use in toxicity testing are also to be found in the idiosyncratic variations between individuals of our own species. The new knowledge of protein structure provided by the molecular biologists in the last two decades has brought a wider realization that we cannot expect the structure of the isoenzymes in animal tissues to be identical with those that occur in man. So, the next advance in safety of medicines, an advance all seek

and demand, is very likely to be based on more strenuous and better organized post-marketing surveillance. Such programmes will be logical developments from the procedures that have been devised in attempts to track down drug side-effects, wanted and unwanted.

The Editor of this volume has, of course, been a major figure in this field and is the author of invaluable papers about adverse reactions, which have appeared over the last two decades. He is now well known world-wide for his foresight and his persistence, and perhaps for his life style, which has resulted in his bringing the clinical skills of close observation and detective-like following up of clues to the problems of drug development rather than to clinical practice. I can with some authority say that the Clinical School of the University of Cambridge is proud that, when poliomyelitis restricted his mobility as a medical student, Dr Bill Inman was taken in by the then Regius Professor of Physic and given his clinical training in Addenbrooke's Hospital, Cambridge. I know Sir Lional Whitby, who in this way was adumbrating our new School, would be quite delighted with Inman's success in his chosen field – a success which can be measured by the wide-ranging contributions he has attracted from far and near.

All of us who know him and have contributed to this volume will wish its publication every success and hope that the ideas presented will stimulate more and more work in important interfaces between, on the one hand, molecular biology and medicine, and on the other, between the professions involved and the patients we all seek to help.

Sir John Butterfield, OBE
Cambridge
December 1979

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Acknowledgements

The enthusiastic response to my invitation to contribute to this book is symptomatic of the great interest and involvement in drug safety. Of fifty-nine people initially approached, forty-seven accepted, seven suggested a colleague who also accepted, and only five declined because of other commitments – rather remarkable statistics.

I would like to thank especially Dr John Marks who inspired me to undertake the task of editing this work, and many of the individual contributors who commented so helpfully on the detailed specification I prepared before embarking on it; also my close associates, Dr Gillian Greenberg, Dr Edmund Harris, Mr Frank Thomas and Dr Peter Weber, who gave invaluable advice with several of the sections, and my wife, June, who became the Editor's Secretary. I am indebted to Professor Dr G. Wagner, Editor of *Methods of Information in Medicine*, for permission to reproduce Professor David Finney's article on Statistical Logic which first appeared eight years ago, and Mr G. M. G. Tibbs, Secretary of the Royal College of Physicians and Dr A. Stuart Mason, Editor of the *Journal of the Royal College of Physicians*, for permission to reproduce Mr John Wilmer's article on English law.

ATTRIBUTION

Several authors have asked me to state that the opinions expressed in their articles are personal and do not necessarily represent the official policy of their organizations. This applies to the World Health Organization and the national drug-monitoring centres and to members of several of their advisory bodies. Rather than repeat this statement many times throughout the book, it should be regarded as applying to all the material submitted for publication.

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