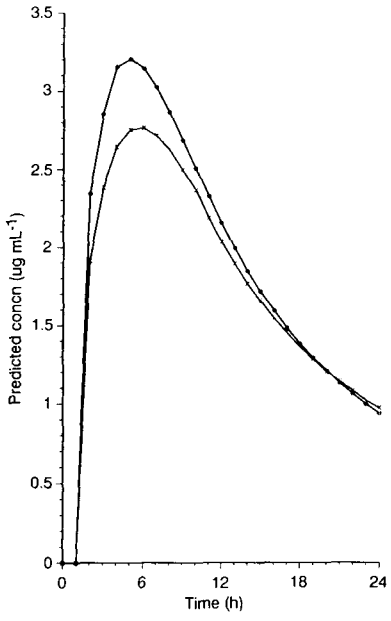

FIG. 3. Simulated plasma concentration obtained using rate of release data for Pecram (O) and Phyllocontin (×) into an acid buffer solution.

In the light of the assumptions made with this mathematical model, these extrapolations have to be treated with caution (the conditions within a British Pharmacopoeia dissolution test vessel are clearly very different to those experienced by a dosage form within the gastrointestinal tract). However, it is suggested from this work that on single dosing Pecram would obtain a higher peak plasma level at a slightly faster rate than Phyllocontin.

It may be concluded from this investigation that differences between the two formulations were detected in-vitro which may result in differing performances in-vivo. However, these differences are small and could be masked by other, larger, sources of variation experienced on in-vivo evaluation.

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Book Review

Power and Dependence: Social Audit on the Safety of Medicines
By Charles Medawar
Edited by Elaine Rassaby and Brian Guthrie
Published 1992 Social Audit Ltd, London
283 pages
ISBN 0 946448 04 3 £10.00 paperback

If you are a pharmaceutical scientist or a member of a health profession, this is an important book to read. It will not be an easy read because you will find on most pages statements or assertions which you will believe to be untrue, distorted or simple exaggerations. Consequently, the immediate temptation will be to discard the book, determined not to waste more of your time with it. That would be a mistake.

You will ignore this book at your peril. It expresses the other man's point of view. This particular author is persuasive, his book tells us how other people see the pharmaceutical industry, what others think of the regulations governing the introduction and periodic review of medicines. Eventually the book will need answering, either through better public relations or, preferably, through a more open approach by industry and the regulatory authorities.

Social Audit is an independent 'watch-dog' organization first set up in 1971, and this book comes out of a project funded for the Public Interest Research Centre by the Rowntree Charitable Trust. Charles Medawar is also a member of the advisory council of the Drug & Therapeutics Bulletin; and has been associated with patients involved in litigation with the manufacturers of the non-steroidal anti-inflammatory drug, Opren, with patients infected with HIV through contaminated blood products, and more recently the developing benzodiazepine litigation. Medawar's attitude to the pharmaceutical industry, some of its products and the various regulatory committees and procedures, is thus a consistent one.

The book comprises 15 chapters, but they are more a collection of essays than a coherent developing story. Although liberally referenced, the source material has been quoted fairly selectively, as has the interpretation placed on many of the chosen statements. Each chapter returns to the problems of sedatives, hypnotics and anxiolytics, eventually focussing on some aspect of drug-induced dependence or the benzodiazepines. It is not a scholarly treatise, its impact is almost pure journalism.

The book has important interwoven themes, and each is given some prominence. Thus, drugs cause avoidable clinical adverse effects and a substantial number of hospital beds are occupied wholly through iatrogenic disease. Too much of the information given to prescribers and other health professionals about these products is provided by the drug companies themselves, with too little data on the likely adverse effects. The pharmaceutical industry's processes of self-regulation, for example on questions of publicity and public relations, do not work; and the various regulatory committees created under the 1968 Medicines Act are clothed in secrecy. Whilst the Author identifies what he sees to be wrong, there is no real attempt to bring together a package of new regulations or procedures which would solve these problems. Perhaps the structure of the book prevents a 'chapter on strategies', but such suggestions would then possibly leave the Author open to charges of naivety. The Author's motive is

outlined at the start. He has seen so much of medicine at its best, of good drugs used with great care and understanding, that he sought to focus atention on those aspects of drug therapy which fell short of any reasonable ideals. Whilst wanting sincerely to understand the Author's concern, I was constantly thwarted by the many exaggerations or distortions which litter almost every page. I thought I would refer to just three.

In chapter I, entitled 'Lines of descent', the Author examines the development and commercial exploitation of the benzodiazepines. On page 11, the Author states 'By the end of the 1980s, the best estimates suggested that perhaps half a million people in Britain were more or less addicted to benzodiazepines'. The journalist's technique is interesting: who says the source of this opinion was 'the best'? He softens the statement further with the words 'perhaps' and 'more or less'. Again, on page 18 of the same chapter, after an introduction to the placebo effects of drugs, the Author says: 'One cannot be precise, but perhaps a third of all drugs are now prescribed mainly for their placebo effect . . .'. On what evidence is that conclusion made . . . equally of course, what evidence is there to say the Author is wrong! In Chapter 5, entitled 'A dose of regulation', the Author examines the development of the various regulatory bodies, following upon the thalidomide disaster of 1962. Notwithstanding the Author's emboldened opening quotation from Sir Derrick Dunlop, he goes on to detail the introduction of thalidomide in the UK by the Distillers Company in 1958, records Richard Crossman's involvement both as an opposition spokesman on health and subsequently the minister behind the introduction of the 1968 Medicines Act, and concludes 'it took until the early 1970s to set up the machinery for drug control'. Not a mention of the Dunlop Committee that worked so effectively between the thalidomide episode and the implementation of the Medicines Act's provisions. Of course, any admission that the Industry had effectively self-regulated itself would have sat uneasily on other remarks inferring that the Industry was totally incapable of self-regulation.

I was annoyed by the distortions and exaggerations contained in this book and because there are aspects of the Industry's operations which do require tighter control; and the regulatory bodies could be much more open and less secretive in their activities. The Author has some good ammunition, tossed away I believe in a book of low scholarship and journalistic excesses. In the end, the Author may have served his cause less than usefully.

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Book Review

Drug Biotechnology Regulation. Scientific Basis and Practices
Edited by Yuan-yuan H. Chiu and John K. Gueriguian
Published 1991 Marcel Dekker Inc., New York
592 pages
ISBN 0 8247 8420 0, $135 (USA and Canada), $155.25 (others)

In the 1980s, medicines derived from biotechnology became a reality. This book reviews the science, technology and regulation of biotechnologically derived products. The editors are a Supervisory Chemist and a Medical Officer working in the Center for Drug Evaluation and Research of the US Food and Drug Administration. The authors are drawn from industry, academia and regulatory authorities. Many of them are based in the USA and the book tends to reflect this with an emphasis on US regulations and procedures. The compilation of US regulations of biotechnology in the food, drug and agricultural areas, provided as an appendix, will be particularly useful to those attempting to unravel this complicated and evolving area. European and Japanese interests are not forgotten. There is a chapter by Fernand Sauer of the European Commission on European regulations and a chapter on Japanese requirements.

The first part uses the successful development of such products as recombinant human insulin, human growth hormone and hepatitis B vaccine to exemplify the application of biotechnology to medicinal product development. This is backed up by extensive reference to recent literature. Subject coverage is fairly comprehensive with sections on host/expression systems, fermentation and cell culture, purification and postbiosynthesis modification, product characterization, and pre-clinical and clinical development. Further information on the introduction of genetic material into mammalian cells, on potential viral contamination and on monoclonal antibody production would have been useful. There is very little repetition even though different authors are at times covering different aspects of the same subject. Although care has obviously been given to planning the sequence of chapters, the first part of the book does not always follow a natural progression. This is, no doubt, a consequence of the difficulty in producing a cohesive whole from the many individual contributions.

The second part, on future prospects, has interesting chapters on fungi and baculovirus expression systems, the potential for gene cloning in developing new antibiotics, new approaches to vaccine production and advances towards somatic cell gene therapy.

The sections dealing with regulations and guidelines provide a useful baseline of information. It is encouraging to see the similarity in approach that already exists amongst US, European and Japanese authorities in dealing with biotechnology products. A quirk of the US system is that a product may be defined as a drug or biologic and as a result be considered by different divisions under different laws. The US Orphan Drug Act with its period of exclusivity adds another dimension to the race to the market place.

It is inevitable, with regulations and guidelines in this field being produced so rapidly, that a book can only provide a snapshot in time. The authors emphasize the need to keep abreast of regulatory developments. The chapters by industrial contributors about their experiences with the registration of medicinal products derived from biotechnology give a favourable account of the interaction between manufacturers and the regulators. Understandably, the industrial contributors concentrate on their successes. It is clear from their contributions that many changes may be made to the production process from the start of product development to the submission of a Marketing Authorization. But it is the regulators that point out the valuable lesson that care must be taken to ensure that there is good clinical data on material representative of the product to be marketed and, therefore, that some changes in production may necessitate further clinical trials.

This is an interesting book for anyone working in the drug biotechnology field. It is not a beginners text as it assumes a good basic knowledge of biotechnology. I have no doubt that I will be dipping back into it for that useful piece of information or reference that I remember seeing.

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(The views and opinions expressed are personal and do not represent those of the MCA.)