



products can be complicated, arduous and expensive, often demanding technical sophistication and substantial creativity. It is not clear why the presentation of G. Zbinden, of the Institute of Toxicology, Swiss Federal Institute of Technology in Switzerland, is included in this section. In an extensive review of the theoretical and observed toxicities of biotechnology products he raises the sticky question of the "moral" (as opposed to legal) obligation that industry obtain the "scientifically relevant information necessary to safeguard research subjects and patients." It is hard to imagine who would oppose that view.

B. S. Finkle of Genentech, Inc., representing the U.S. Industrial Biotechnology Association (IBA), provides a lucid discussion, entitled "Genetically Engineered Drugs: Toxicology with a Difference," of how our limited knowledge on the biological activities of some of the endogenous human proteins provides special challenges to the toxicologist. R. E. Stoll provides the Pharmaceutical Manufacturers Association perspective, which maintains that any set of guidelines for preclinical testing of biotechnology-derived products are inappropriate at this time; his organization encourages the continued development of innovative and rational approaches to these problems.

The proceedings end with 17 pages of wide-ranging discussion, in which the contributors participate. For the reader who does not complete the book at one sitting, some of the context of this discussion is lost. However, (fortunately or unfortunately) in few instances were specific data that were presented interrogated or discussed. (Another decidedly reader-unfriendly feature of the text is that little of the volume has been set in type, with contributions appearing as originally submitted. It is not apparent to this reader that the substantial savings this provided the publisher has been passed along).

The most striking point to emerge from the discussion, and the symposium as a whole, is the extent to which consensus exists, with few exceptions, among regulatory and industrial scientists today on the major issues concerning the preclinical safety evaluation of biotechnology products. These proceedings document that consensus and the mutual resolve of both parties that we take full advantage of the opportunities biotechnology provides, while ensuring the safety

of its products through the conduct of preclinical studies that are comprehensive and scientifically defensible. The book serves to catalogue current opinion and thinking and the key issues involved in the preclinical development of these products, while providing insight as to the anatomy and role of our regulatory agencies.

THE WAIT IS WORTH IT

High Performance Liquid Chromatography in Enzymatic Analysis—Applications to the Assay of Enzymatic Activity. By Edward F. Rossomando. Pp. 253. ISBN 0-471-87959-2. \$39.95. (John Wiley and Sons, NY: 1987).

High performance liquid chromatography (HPLC) is simply an improved version of liquid chromatography, a separation method known for over 30 years. When a mixture of compounds in solution is passed through a column of a packing material, the compounds flow at different rates due to their differential affinity to the packing material, and separation occurs. This is liquid chromatography. Since a separated compound may be quantitated by its optical absorbance as it flows through a detector, HPLC is also an analytical tool. An enzyme's activity is measured by the rate of the reaction it catalyzes, usually by measuring the rate of formation of a reaction product. The higher the enzyme's activity, the more product is formed per unit time. If a reaction product has a particular color, its formation can be measured continuously in a colorimeter during the reaction. If not, it is necessary to stop the reaction at time intervals and analyze the amount of the product formed at each time point. Since the technology of HPLC has become available, it is conveniently used to analyze the product of an enzyme reaction. So, how have HPLCs been used in the analyses of compounds encountered in various enzyme catalyzed reactions?

The answer to this question is provided only after 108 pages of sometimes laborious discussion which, in essence, describes what I have stated simply in one paragraph above. The wait is nevertheless rewarded, as the next 108 pages contains a very good survey of recent examples in which HPLCs have been used to measure enzyme activities. These are conve-

As such it should be of value to scientists involved in the development of biotechnology-derived pharmaceutical products for the first time.

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niently arranged according to the physiological roles of the enzymes studied; e.g. enzymes involved in catecholamine metabolism, hydrolysis of proteins, amino acid metabolism, heme biosynthesis, purine metabolism, or oxygenations. Conditions used in the separation of respective reaction products are presented with chromatograms for each sample, giving the reader a general idea how compounds may be separated using different HPLC packing material and chromatographic conditions. The only drawback is that conditions for the enzyme reactions are not clearly stated; and the concentrations of the components of assay mixtures are not indicated. Readers who are interested in applying the example are thus forced to go back to the original reference for the detailed information. The last chapter deals with studies of multienzyme systems using HPLC. It makes an interesting read, but one wonders how useful the study of multienzyme systems will be in practical terms. As regards the first 45 percent of the book, the chapter on HPLC is well presented. Both the concepts and principles are explained with interesting analogies and many illustrations, without mathematical formulae. Other chapters in this section, however, contain rather lengthy discussions on why HPLCs are so useful in enzyme assays. These are characterized by verbosity and over-explanation of simple facts. For instance, what I described in a few sentences (above) about enzyme assay is explained in "Anatomy of an Enzyme Assay," "Classification of Enzymatic Assay Methods" and "Criteria for the Selection of an Assay Method"—over 12 pages with tables and figures.

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