surements are made on compounds that are relatively insoluble in water, the results have little meaning unless the particle size of the administered powder is taken into account.

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Received July 24, 1967.
Accepted for publication March 31, 1968.
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Keyphrases

Trichloroethyl carbonate—toxicity
Particle size—trichloroethyl carbonate toxicity
LD_{50} value—particle size effect

Books

REVIEWS

Potential Carcinogenic Hazards from Drugs. Evaluation of Risks. UICC Monograph Series, vol. 7. Edited by Rene Truhaut. Springer-Verlag, 1 Berlin 31 (Wilmsdorf), Heidelberger Platz 3, Germany, 1967. vii + 249 pp. 16.5 × 25 cm. Price DM 68,–; U.S. $17.00.

This is the seventh volume of the monograph series sponsored by the International Union Against Cancer. It consists of a series of 24 papers presented at a symposium of the Cancer Control Commission held in Paris, November 1965.

It is quite apparent from both the formal papers and the abbreviated versions of the discussions which follow that emphasis was placed on chemical contact or ingestion as the principal etiological factor in carcinogenesis. While this orientation may be justified in a symposium dealing with drugs, it must be recognized that there are many oncologists who subscribe to the view that chemical carcinogenesis is of only minor significance in relation to the incidence of human cancer.

The initial papers in the symposium deal with the present state of methodology for evaluating the potential carcinogenicity of drugs. The statistical assessment of data from the point of view of predictability is then discussed. In view of the law prohibiting the use of carcinogenic substances as food additives, it is interesting to note the view expressed by one of the participants, Prof. I. Berenblum, that "for all practical purposes, a carcinogen is, like any other noxious substance, only harmful above a certain critical dose level." In this connection, the opinion of Prof. H. Druckrey based on his analysis of the dose–time relationships of chemical carcinogenesis, is especially pertinent. He distinguishes between the primary effect of a carcinogen at the cellular or molecular level, and the subsequent multiplication of cancer cells to the point of tumor induction. As far as the primary effect is concerned he holds to the view that "there is no indication for the existence of a subthreshold dose." Nevertheless, he recognizes that a zero tolerance for carcinogens is "not always practicable and is scientifically objectionable" and proposes as a basis for future discussion that "1% of the lowest dosage which, given daily over the whole life span to susceptible experimental animals, produces cancer only at the end of the life span, can be considered as the maximum tolerable dose for human beings."

A number of papers in this volume deal more specifically with the potential carcinogenicity of specific classes of substances such as metal-containing drugs, petroleum hydrocarbons, lactones, and hormones including progesterone. In the two reports dealing with plastics used in orthopedic or surgical practice, as well as in the discussions of these papers, the weight of evidence is in support of a physical rather than chemical explanation of the carcinogenic effect of experimental implants.

In his remarks reflecting the point of view of the pharmacologist, Professor Alastair C. Frazer emphasizes the need for discrimination and judgment in deciding when a drug should be subjected to life-span study for potential carcinogenesis, and questioned the need for identifying "extremely feeble" carcinogenic drugs intended for use over short periods in people whose life expectancy is unlikely to provide time for any effect to be induced.

This monograph is required reading for those who wish to keep up with current thought among the experts in drug safety evaluation. Although the discussions following each presentation reveal the lack of unanimity on many aspects, there is agreement that much remains to be done to get at the root of these problems from both the methodological and interpretative standpoints.

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Advances in Pharmaceutical Sciences. Vol. 2. Edited by H. S. Bean, A. H. Beckett, and J. E.