other Appendices give descriptions of fluorometry and of spectrophotometry and related subjects, these however are so general that they could have been omitted from a book of standards published in 1955. Biological assays are described for the gonadotrophins, insulin and protamine zinc insulin, tubocurarine chloride and certain of the antibiotics. The test for pyrogens is arranged somewhat differently from that in the 1955 B.P. Addendum; the test is in two stages, the first with three rabbits and if this is not passed a second with five rabbits. It seems likely that the Ph.I. test is more severe than the four stage B.P. test.

The doses are not given at the foot of the monographs but, as in Volume I, in an Appendix as a table of usual and maximal metric doses. There is also a table giving the usual daily doses for children of many drugs, one column giving these for children of up to 30 months and another for older children, doses for toxic substances are usually on a weight basis. This table is likely to be useful to many who might not otherwise consult the International Pharmacopoeia. It is unfortunate that the milligram is not used in giving doses as, in spite of the increasing application of the metric system to dosage, many prescribers and pharmacists dislike long strings of noughts after a decimal point.

The Expert Committee on the International Pharmacopoeia are to be congratulated on the results of their efforts. It is however generally recognised that the major source of inspiration of the International Pharmacopoeia and its detailed planning was the late Dr. Hampshire, and the two volumes of the first edition are his monument. The Chief of the Pharmaceutical Section of the WHO, Mr. P. Blanc, who acted as secretary, and his assistant, Mr. G. R. Brown, are also entitled to our congratulations.

BOOK REVIEWS

OFFICIAL METHODS OF ANALYSIS, A.O.A.C., 1955, Eighth Edition. xvi + 1008 (including Index). Published by the Association of Official Agricultural Chemists, Washington, D.C., U.S.A. (U.S.A. $12.00; elsewhere $12.50).

The eighth edition of this work presents the Official Methods of the Association as revised during the five years since the publication of the seventh edition in 1950. "Official Methods" is well known in most analytical laboratories and it is chiefly of interest, therefore, to note the additions and alterations which have been made since 1950.

Changes have, in fact, been considerable with an expansion of about 100 pages chiefly in the sections devoted to pesticides, flavourings, drugs, extraneous materials, microchemical methods and nutritional adjuncts; chapters on spectroscopic methods and hormone drugs have also been added. Agricultural commodities are divided into six main parts: (1) soils and related materials; (2) miscellaneous materials other than foods and drugs; (3) foods; (4) drugs and cosmetics; (5) general methods; and (6) reference tables.

A substantial advance has been made towards the more rigid standardisation of methods. No longer is copper permitted as a catalyst in the Kjeldahl determination of total nitrogen; mercury or mercuric oxide alone are now allowed and other experimental details are prescribed following an extensive collaborative study.

The chapter on colouring matters has undergone fundamental revision and

the classical methods of isolation of coal-tar colours by dyeing on and stripping from wool, and identification of the colours by spot reactions have been replaced by determinations using chromatography and spectrophotometry. The microchemical chapter which in the seventh edition included only methods for micro Kjeldahl and alkoxy group determinations has been expanded by the addition of standardised methods for the elemental analysis of bromine, chlorine, carbon, hydrogen and sulphur.

The vitamin chapter has been renamed "Nutritional Adjuncts," the title being designed to recognise the potentialities of nutritionally significant factors such as amino-acids and antibiotics. The fermentation method for thiamine has no longer been included in this chapter but microbiological methods for pantothenic acid and vitamin B_{12} have been added. As a minor criticism it is a little surprising that the standard for vitamin B_{12} should consist of a weighed quantity of standard reference material; a quantitative standardisation by spectrophotometry would be more precise.

In view of the fact that collaborative trials precede the adoption of many of the Association's methods it would be most helpful if the limits of error to be expected could be given, particularly for biological and microbiological assays.

In conclusion it can be stated that the eighth edition of this work represents a considerable advance over the previous editions. "Official Methods" is an essential volume for any large analytical laboratory and it is a credit to all concerned that the book is so widely used for its methods in fields of chemistry outside those for which it is written. R. E. STUCKEY.

STATISTICS OF THERAPEUTIC TRIALS, by G. Herdan. Pp. xvi + 367 (including Index). Cleaver-Hume Press, Ltd., London, 1955. 50*s*.

This elegantly produced book is written to help people who are concerned with therapeutic trials and who find mathematics distasteful. Explanations of mathematical processes are avoided and emphasis is placed on a clinical approach. Most of the chapters deal with trials in specific diseases. The acute diseases which are particularly considered are the pneumonias, poliomyelitis, scarlet fever, diphtheria, typhoid fever and pneumococcal meningitis, and the chronic ones are cancer, tuberculosis of the lung, rheumatoid arthritis, congestive heart failure, hypertension, diabetes and nephritis. It is a little difficult to see why this list was selected. It omits some very widespread disorders, such as peptic ulceration, schizophrenia and the common cold, in which properly designed therapeutic trials are urgently needed to separate effective treatments from useless ones. On the other hand, the diseases included are sometimes rather similar to each other and sometimes extraordinarily indefinite (e.g., cancer), and unlikely always to be amenable to the same kind of therapeutic trial. This sort of difficulty seems to arise from trying to avoid general treatment of the logic and mathematics of therapeutic trials, and distinctly limits the usefulness of this book.

Once general principles are discarded in favour of a series of examples, there is no end to the material which must be brought in, and there is always uncertainty whether a new situation may not arise which will not be filled by any of the available examples. It may also be questioned whether anyone who does not understand the principles which underlie therapeutic trials can safely decide which example it is appropriate to follow in a given instance. Even as a set of recipes this book therefore has limitations: as a reasoned guide to procedure it is quite bewildering.

It must also be admitted that the style of writing is rather ponderous and

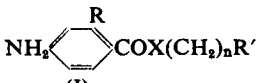
sentences such as this are common. "The therapeutic comparison between the disease behaviour in the control and the trial group is necessarily restricted to that of one or the other nosographic criterion which has been chosen for observation by the investigator because he considered it representative of the disease." The author is also inconsistent in his use of abbreviations (e.g., the tangent of an angle is referred to as tg. on p. 169 and tang on p. 355, and it is difficult to see why the orthodox symbol tan is avoided) and not always accurate in his references (e.g., to Burns, for Burn, on p. 255 and p. 349). The non-mathematical should be warned that in spite of the clinical approach, they will not be spared much algebra and an occasional and perhaps unnecessary flavour of trigonometry. MILES WEATHERALL.

(ABSTRACTS *continued from p.* 219).

both acetylcholine and histamine was noted in a few cases during the phase of recovery of the action of acetylcholine and histamine on repeated changing of the bath fluid after an earlier observation of the action in the presence of rauwolfia extract. A. H. B.

Riboflavine Excretion Technique, Reliability in Determining Availability of Coated Tablets. D. G. Chapman and J. A. Campbell. (*Canad. J. Biochem. Physiol.*, 1955, **33**, 753.) Determination of the urinary excretion of riboflavine in human volunteers is a valid and reliable procedure for determining the physiological availability of coated tablets. Eight volunteers receiving a normal diet were given 1, 3 and 5 mg. amounts of riboflavine. Excretion was the same whether these amounts were given as single or divided doses. With doses of 1, 3, 5, 7·5 and 10 mg. there was a linear relationship between the excretion and the dose, but the response line did not pass through the origin. In calculating the availability of riboflavine from a tablet, a curve for each subject should be referred to and there is a suggestion of a slope difference between subjects. G. F. S.

Thiocaine and Related Compounds, Alkoxy Analogues of, Corneal Anaesthetic Activity and Toxicity. F. P. Luduena and J. O. Hoppe. (*J. Amer. pharm. Ass., Sci. Ed.*, 1955, **44**, 393.) Procaine and a series of its derivatives of the general formula (I) below were tested for anæsthetic activity on the rabbit cornea. The concentration required to produce anæsthesia lasting for 5 minutes was calculated and compared with the concentration of cocaine required to produce the same effect. The LD50 of each substance was determined in mice and compared with that of cocaine. Replacement of the oxygen atom (X) in procaine by S resulted in a sixfold increase in activity and toxicity. In the sulphur analogue (thiocaine), introduction of a 2-propoxy group at R produced a 130-fold increase in activity with a 13-fold increase in toxicity. In this series (where X = S) activity increased with the length of the 2-alkoxy side chain, the 2-hexyloxy derivative being particularly active. Toxicity increased with the length of side-chain, but to a lesser extent. In the procaine series (X = 0), activity and toxicity also increased with the length of the 2-alkoxy group. A moderate increase in activity was obtained by substituting a methylpiperidyl group for the diethylamino group in the thiocaine series. The ratio of activity to toxicity (taking cocaine as 1) varied from 0·16 for thiocaine to 8·3 for its 2-hexyloxy derivative. All the compounds except procaine, thiocaine and 2-ethoxyprocaine were more active than cocaine, and all the 2-alkoxy derivatives of thiocaine were more active than cinchocaine. G. B.



(I)

X=O or S