Pharmaceutical Substances: Syntheses, Patents, Applications. By Axel Kleemann, Juergen Engel, Bernhard Kutschner and Dietmar Reichert, Thieme: Stuttgart, 1999, pp 2286. DM 798. Hardback. ISBN 3-13-558403-8.

Pharmaceutical Substances: Syntheses, Patents, Applications is the revised and expended 3rd edition of *Pharmazeutische Wirkstoffe, in English*. The 2nd edition and its supplement volume were published in 1983 and 1988, respectively. *Pharmaceutical Substances (PS)* contains a collection of 2171 active pharmaceutical ingredients of interest to the pharmaceutical and chemical industry, academia and government agencies. It is available both in print and on CD-ROM (ISBN 3313115331-1). *PS* is designed to be a complete reference guide to every pharmaceutical compound of significance and an essential, first point of reference to specialists in drug chemistry and anyone involved in the synthesis and use of pharmaceuticals. The purpose of this book, according to its authors, is to establish a link between International Nonpropriety Names (INNs), structures, syntheses and production processes, patent (and literature) scenarios, medical uses and trade names of important pharmaceuticals.

The description of each compound includes the following components: Chemical structure; molecular formula; molecular weight; graphical representation of the synthetic route, including intermediates; Nomenclature: INN and other Generic Names (e.g., BAN, DCF, USAN), trivial names, synonyms, Chemical Abstract name; Trade Names; CAS Registry Number; EINES number; Anatomic Therapeutic Chemical (ATC) Code Number; medical application/therapeutic category; pharmaceutical dosage forms; toxicological data; patent numbers, origin, holder application, priority and expiry dates; bibliographical information. The book includes, in addition to the alphabetical list of drug monographs and ATC classification, four indexes: Trade Names; Intermediates; Enzymes, Microorganisms, Plants, Animal Tissue; Substance Classes. The authors decided wisely not to include newer biopharmaceuticals ("Pharmaproteins"), which are produced by recombinant DNA methods (e.g., Interferons, human Insulin, Erythropoietin). The borderline case of synthetic peptide drugs remained more or less as in the second edition and its supplement volume.

The main strength of the new edition of *PS* is inherent in the integration of the multiple components describing each pharmaceutical ingredient. An important feature of this Reference Book is the special emphasis given to patents, Trade Names and synthetic schemes. In this respect, it is complementary to the *Dictionary of Pharmacological Agents* (Chapman & Hall/CRC Press, print version published 1997, CD-ROM updated biannually). *PS* has a distinct chemical character, although its pharmacological characteristics should not be undervalued. An index on therapeutic indications will be very helpful. Has *PS* been comprehensively updated, especially with new drugs, bearing in mind that the Book was published in 1999 and the authors' Preface is dated Autumn 1998? According to the *Annual Reports in Medicinal Chemistry* (Vol. 33, 34, Academic), in 1997 and 1998, the numbers of new therapeutic chemical entities (NCEs) introduced into the world market for the first time were 39 and 27, respectively, including new biological entities (NBEs). *PS* contains 15 of the 1997 drugs and 2 of the 1998 drugs, Sibutramine hydrochloride (Meridia, Reductil) and Sildenafil (Viagra). Conspicuously missing from *PS* is the racemic drug Thalidomide, a human teratogen, which had a profound impact on the development of drugs in general and on the regulatory environment of drugs in particular. Thalidomide was originally marketed as a sedative outside the US from the 1950s until the early 1960s when it was linked with severe birth defects and withdrawn. In July, 1998, the US FDA cleared Thalidomide for marketing as a treatment for erythema nodosum leprosum (ENL), a serious inflammatory condition in patients with Hansen's disease(Leprosy),while at the same time imposing unprecedented restrictions on its distribution. Another absentee is the racemic second generation inhalation anaesthetic Desflurane. It is surprising that Quinidine and Quinine are not listed explicitly as antimalarials, but only as antiarrhythmic and as chemotherapeutic, antipyretic and stimulant, respectively, although their Quinimax combination and Quinine's ATC code, P01BC01,do appear.

The treatment of Stereochemistry, including Chirality, in *PS* should be improved. A few chiral drugs may illustrate this point.The chemical names of Quinine and Quinidine appear as (8α *9R*)-6'-methoxycinchonan-9-ol and (*9S*)-6'-methoxycinchonan-9-ol, respectively. However, Quinine and Quinidine are diastereomers with the absolute configurations (*1S,3R,4S,8R,9S*) and *1S,3R,4S,8S,9R*), respectively. The structures of the racemic drugs Omeprazole, the leading gastric proton-pump inhibitol, the bronchodilator Salbutamol (Albutamol) and the inhalation anaesthetics Enflurane and Isoflurane appear without reference to their stereogenic sulfur and carbon atoms.Both Omeprazole and Salbutamol are currently undergoing chiral switches to Esomeprazole and Levalbutamol, respectively. The authors should be complimented for introducing the acronym "wfm" whenever a drug has been withdrawn from the market. In this connection, the withdrawal from the US market in September 1997 of the antiobesity drugs REDUX (Dexfenfluramine), Pondimin(Fenfluramine), and the Fen-Phen combination, due to significant, unfavorable side-effects, has been overlooked.

In conclusion, *PS* is an excellent, indispensable source of information and reference guide of drugs. *PS* should be present in all libraries of pharmaceutical companies, departments of Medicinal Chemistry and institutes of Pharmaceutical Chemistry, colleges of Pharmacy and government agencies (including regulatory and patent agencies) involved in the design, discovery, development and evaluation of drugs, world wide. Hopefully, the electronic version of *PS* will be upgraded and published annually.

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