# Introduction

## INFORMATION SOURCES USED

A variety of sources were used to identify the patent associated with particular commercial products and to serve as a source of process information. These include the following:

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|---|---|
| Merck Index: | followed by a citation of the entry number in the Tenth (1983) Edition.[1] |
| DFU: | The periodical publication, *Drugs of the Future,*[2] published in Spain. |
| DOT: | The periodical publication, *Drugs of Today,*[3] also published in Spain. |
| Kleeman & Engel: | The encyclopedic German work, *Pharmazeutische Werkstoffe,*[4] second revised edition published in 1982. |
| OCDS: | The 3-volume reference series on the *Organic Chemistry of Drug Synthesis.*[5] |

In addition, sources of pharmacological data and comparative information on trade names used in various countries were obtained from:

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|---|---|
| REM: | The latest edition of *Remington's Pharmaceutical Sciences.*[6] |
| | The nonproprietary name index published by Paul de Haen.[7] |
| I.N.: | The biannual Swiss publication, *Index Nominum.*[8] |
| PDR: | The guide to commercially available U.S. drugs, the *Physicians' Desk Reference.*[9] |

Finally, earlier books by this author were drawn on to provide information for some entries. These include:

The *Pharmaceutical Manufacturing Encyclopedia,* first edition.[10]

A book entitled, *Manufacturing Processes for New Pharmaceuticals.*[11] This book attempted to review processes for manufacturing drugs still in the developmental stage—those which had attained generic name status but not trade name status in most cases. Many of these have since fallen by the wayside.

The *Veterinary Drug Manufacturing Encyclopedia.*[12] The present volume deals only in "people drugs" as did its predecessor volume[10] but some drugs find application in both areas.

It should be emphasized again that this is simply a guide to manufacturing processes. Under each generic named product a "Therapeutic Function" is indicated. However, the reader is referred to the *Merck Index*[1] and to *Remington*[6] as well as to *Drugs of the Future,*[2] *Drugs of Today,*[3] and the *Physicians' Desk Reference (PDR)*[9] for more information on the material, its properties, its therapeutic use and its side effects. The chemist who is interested in synthesis routes is referred to Lednicer and Mitscher[5] as well as to Kleeman & Engel[4] for more information on routes to these products and to products having similar structures.

## SALES RANKINGS OF U.S. DRUGS

In the preparation of the first edition of this volume, contact was made with IMS, Inc. of Ambler, Pa., a well-known source of international statistics. With their help, a list was prepared of the 100 top products based on U.S. sales volume in 1976; that list is given in Table 1.

**Table 1: The Top 100 Generic Pharmaceuticals in the U.S. in 1976**

(1) Diazepam
(2) Methyldopa
(3) Hydrochlorothiazide
(4) Acetaminophen
(5) Amitriptyline
(6) Cephalexin
(7) Ibuprofen
(8) Cephalothin
(9) Furosemide
(10) Norethindrone
(11) Indomethacin
(12) Gentamicin Sulfate
(13) Chlordiazepoxide
(14) Thoridazine
(15) Norgestrel
(16) Propranolol
(17) Estrogenic Substances, Conjugated
(18) Ampicillin Trihydrate
(19) Spironolactone
(20) Amoxicillin
(21) Triamterene
(22) Penicillin V
(23) Isosorbide Dinitrate
(24) Chlorpropamide
(25) Chlorthalidone
(26) Allopurinol
(27) Cefazolin Sodium
(28) Hydralazine
(29) Doxepin
(30) Clidinium Bromide
(31) Doxycycline
(32) Erythromycin Estolate
(33) Papaverine
(34) Hydroxyzine Pamoate
(35) Flurazepam
(36) Tolbutamide
(37) Methylprednisolone Sodium Succinate
(38) Clofibrate
(39) Ethynodiol Diacetate
(40) Insulin Isophane
(41) Phenylpropanolamine
(42) Diphenoxylate
(43) Prochlorperazine
(44) Isoxsuprine
(45) Clorazepate
(46) Diphenyl Hydantoin (Phenytoin)
(47) Haloperidol
(48) Dihydroergocornine
(49) Chlorothiazide
(50) Trifluoperazine
(51) Doxorubicin
(52) Propoxyphene
(53) Nitrofurantoin
(54) Trimethoprim
(55) Betamethasone Valerate
(56) Pseudoephedrine
(57) Diethylpropion
(58) Meclizine
(59) Ampicillin Anhydrous
(60) Pentazocine Lactate
(61) Tetracycline
(62) Procainamide
(63) Imipramine
(64) Chlorpromazine
(65) Triamcinolone Acetonide
(66) Dipyridamole
(67) Clindamycin Phosphate
(68) Miconazole Nitrate
(69) Chlorpheniramine Maleate
(70) Theophylline
(71) Naproxen
(72) Kanamycin Sulfate
(73) Pentaerythritol Tetranitrate
(74) Meperidine
(75) Neomycin Sulfate
(76) Oxazepam
(77) Guaiacol Glyceryl Ether
(78) Oxymetazoline
(79) Tolazamide
(80) Insulin Zinc Suspension
(81) Metronidazole
(82) Phentermine Resin
(83) Erythromycin Stearate
(84) Phenobarbital
(85) Povidone-Iodine
(86) Quinidine Gluconate
(87) Hydroflumethiazide
(88) Imipramine Pamoate
(89) Methyl Phenidate
(90) Nitroglycerin
(91) Albumin, Normal Human Serum
(92) Cyclandelate
(93) Dicyclomine
(94) Enflurane
(95) Erythromycin Ethyl Succinate
(96) Minocycline
(97) Carbendicillin Disodium
(98) Hydroxyzine
(99) Tobramycin Sulfate
(100) Meprobamate

This data courtesy of IMS, Inc.; interpreted by M. Sittig.

The top four items on the list each had sales over $100 million; by coincidence the cutoff point at the end of the 100 top generic products was at the $10 million sales level; the total sales of the 100 products listed was about $3 billion. Of this total, some $600 million was in antiinfective products (penicillins, antibiotics, sulfa drugs, etc.), some $500 million in tranquilizers and some $400 million in cardiovascular drugs. These three categories represented half the dollar total of the top 100 drugs sold in the U.S. Other major drug market areas are in antiarthritic drugs and antiulcer drugs.

Now, for this second edition, an attempt was made to list the top prescription drugs in the U.S. as of 1985–some ten years later than the earlier tabulation. This new listing was done by the author based on his interpretation of the sales list by trade name in the magazine *American Druggist* for February 1986; it gives approximate rank by generic product as of the date of manuscript preparation in 1986. See Table 2.

**Table 2: The Top 100 Generic Pharmaceuticals in the U.S. in 1985**

(1) Hydrochlorothiazide
(2) Triamterene
(3) Propranolol
(4) Digoxin
(5) Norethindrone
(6) Ethinyl Estradiol
(7) Diazepam
(8) Acetaminophen
(9) Amoxicillin
(10) Cimetidine
(11) Furosemide
(12) Propoxyphene
(13) Ibuprofen
(14) Estrogens, Conjugated
(15) Atenolol
(16) Cephalexin
(17) Norgestrel
(18) Methyldopa
(19) Levothyroxine
(20) Metoprolol
(21) Theophylline
(22) Alprazolam
(23) Potassium Chloride
(24) Phenytoin
(25) Lorazepam
(26) Naproxen
(27) Erythromycin Ethyl Succinate
(28) Miconazole Nitrate
(29) Nifedipine
(30) Piroxicam
(31) Ranitidine
(32) Timolol Maleate
(33) Prazosin Hydrochloride
(34) Cefaclor
(35) Chlorpropamide
(36) Mestranol
(37) Flurazepam
(38) Indomethacin
(39) Penicillin V
(40) Chlorazepate
(41) Triazolam
(42) Diltiazem
(43) Clonidine Hydrochloride
(44) Albuterol
(45) Erythromycin
(46) Levonorgestrel
(47) Nadolol
(48) Sulindac
(49) Metaproterenol
(50) Ethynodiol Diacetate
(51) Temazepam
(52) Diphenhydramine
(53) Captopril
(54) Dipyridamole
(55) Nitroglycerin
(56) Isosorbide Dinitrate
(57) Polymyxin B
(58) Neomycin
(59) Bacitracin
(60) Amiloride
(61) Butalbital
(62) Liothyronine
(63) Cyclobenzaprine
(64) Oxycodone
(65) Warfarin Sodium
(66) Guaifenesin
(67) Phenylpropanolamine
(68) Methoxyprogesterone Acetate
(69) Nicotine Polacrilex
(70) Allopurinol
(71) Phenobarbital
(72) Doxepin
(73) Metoclopramide
(74) Chlorthalidone
(75) Aspirin
(76) Erythromycin Stearate
(77) Haloperidol
(78) Trimethoprim
(79) Sulfamethoxazole
(80) Tetracycline
(81) Clotrimazole
(82) Amitriptyline
(83) Perphenazine
(84) Ampicillin
(85) Tolazamide
(86) Diflunisal
(87) Nitrofurantoin
(88) Thoridazine
(89) Promethazine
(90) Fluocinonide
(91) Carbamazepine
(92) Terbutaline
(93) Trazodone
(94) Betamethasone Valerate
(95) Hydrocodone Bitartrate
(96) Fenoprofen
(97) Hydroxyzine
(98) Tolmetin Sodium
(99) Meclizine
(100) Acyclovir

## TRENDS IN PATENT EXPIRATION

It has been estimated that patents on the top 100 drugs in the U.S. market will expire in the period between 1973 and 1990.

This will help to lead to a situation where generically-designated drugs are expected to account for 40% of the prescription drug market by 1990.

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