

Grandfathered Drugs of 1938

By BENJAMIN P. LEWIS JR. and ROY V. CASTLE JR.



The Drug Regulation Reform Act of 1978, introduced into Congress on March 16, 1978, is the largest overhaul of the federal drug law since 1938, when the Food, Drug and Cosmetic Act was enacted. One of the areas of concern is a requirement for the manufacturers to submit individual monographs on all currently marketed prescription drugs.¹⁻⁴

While the Drug Regulation Reform Act was not enacted in the last session of Congress, it will undoubtedly be reintroduced in the upcoming session. The Carter administration supports an overhaul of the nation's drug laws.

Briefly, as described in the bill, a drug monograph would:

- Identify the drug entity;
- State the indications for its safe and effective use;
- Describe the types of products that may be licensed under the product;
- Prescribe standards and requirements for products to be licensed.

In addition, physician and patient labeling must be issued for products licensed under the monograph. For regulatory purposes, however, the labeling documents are not part of the monograph and may be changed without going through the procedures for amendment of a monograph.

It was not until the passage of the Food, Drug and Cosmetic Act of 1938 that a New Drug Application (NDA) was required for marketing any drug product, as the regulatory mechanism for insuring that all new drugs were cleared for safety prior to distribution. The requirement for pre-clearance for effectiveness was added by the 1962 amendment. Before 1938 there had been no legal requirement to have an NDA filed with the Food and Drug Administration (FDA) to introduce new drug products into interstate commerce.

Following enactment of the 1938 law, drugs on the market prior to that time were exempted or "grandfathered," and manufacturers were not required to file an NDA. The premise was that all pre-1938 drugs were considered safe, and if the manufacturer did not change the product formulation or indication, then an NDA was not required.

The proposed major revision in the drug law has generated an interest within FDA's Bureau of Drugs to identify all drugs in the marketplace today that were marketed before 1938. These commonly have been called the "pre-1938" or "grandfathered" drugs. The purpose of this undertaking was to estimate the number of monographs that would be generated by the pre-1938 drugs.

Benjamin P. Lewis Jr., MS, is prescription drug labeling officer and Roy V. Castle Jr., MS, is a prescription drug labeling specialist with the Bureau of Drugs, Food and Drug Administration, HFD-107, Rockville, MD 20857.

The list beginning below identifies names of prescription drugs and therapeutic chemicals on the market in 1938 and currently marketed in 1978 in which the trade name of the product has not changed in the intervening 40 years. Some of the names listed are not considered trade names by today's standards but are generic and were marketed by that name.

Some of the products listed are the subject of approved NDAs, however, for a variety of reasons. For example:

- Some products have additional dosage forms approved since 1938;

- There has been a change in formulation;

- There has been a change in an indication;

- A firm has decided to submit an NDA on its product for some reason.

The products listed may or may not require a prescription, owing to changes instituted in the original drug law, such as the Durham-Humphrey Amendment passed in 1951, which requires a prescription for drugs that cannot be used safely without adequate medical supervision. Under this amendment, drugs were divided into two classes: those that could be used safely in self-medication and sold without prescription (known as over-the-counter or OTC drugs) and those that required medi-

cal supervision and a prescription. This amendment required drug manufacturers of prescription-restricted drugs to label with the Rx legend and made it illegal to place this legend on drugs not so restricted.^{5,6}

The procedure used in retrieving the pre-1938 drugs and chemicals was as follows:

- A comparison was made between the 1977-1978 and the 1938 Red Book.^{7,8}

- The list was verified against the FDA list of currently approved but not discontinued NDAs, antibiotic application Form 5s and Abbreviated New Drug Applications (ANDAs) for the period 1938-1978 (trade name) to determine whether an NDA and ANDA were filed.^{9,10} If an NDA or ANDA was filed, this information is included in the remarks column.

- For informational purposes only, the list was then compared with the American Hospital Formulary Service (AHFS) to categorize these drugs into a therapeutic category.¹¹ Not all drugs and chemicals were assigned an AHFS number because their indications were not specific. Many package inserts and physician labeling references now include an AHFS number.

The listing is divided into two sections: drugs and therapeutic chem-

icals. This is not an all-inclusive list, and not to be considered a final resource. The purpose of publishing it at this time is to solicit from readers any additional listing of the pre-1938 drugs. The author welcomes any comments by readers. □

References

1. Califano, J. A., Jr.: Drug Regulation Reform Act of 1978, The Administration Proposal, Secretary of Health, Education and Welfare, Washington, DC, 1978.
2. Dickinson, J.: Public Monographs: The Center-piece of the New Drug Bill, *Pharm. Technol.* 37 (May) 1978.
3. H.R. 11611, A Bill, 95th Congress, 2nd Session, Drug Regulation Reform Act of 1978.
4. S.2755, *Congressional Record, Senate*, March 16, 1978, pp. 5-3873-S-3903.
5. *Journal of Public Law*, Vol. 13:1, Emory University Law School, Atlanta, GA, 1964, p. 214.
6. A Brief Legislative History of the Food, Drug and Cosmetic Act, Committee on Interstate and Foreign Commerce, U.S. House of Representatives, Subcommittee on Public Health and Environment, 93rd Congress, 2nd Session, Committee Print No. 14, U.S. Government Printing Office, Washington, DC, 1974.
7. Red Book 1977, Drug Topics, Medical Economics Company, Oradell, NJ.
8. *Druggists Circular, Red Book Price List Section*, 88th Revision, Vol. LXXXII, No. 5, New York, NY (May) 1938.
9. *Druggists Circular, Red Book Price List Section*, 89th Revision, Vol. LXXXII, No. 11, New York, NY (Nov.) 1938.
10. Approved Drug Products, Availability of Interim List, Food and Drug Administration, *Fed. Regist.* 43:127, 28557 (June 30) 1978. (Available as PB 281 349/AS from National Technical Information Service, Springfield, VA 22161.)
11. American Hospital Formulary Service, American Society of Hospital Pharmacists, Washington, DC, 1978.

Proprietary Products Manufactured in 1938 and Currently Manufactured in 1978

I. Drugs

Name of Drug	Manufacturer 1938	Manufacturer 1977-1978	AHFS* Category	Current NDA Status**	Name of Drug	Manufacturer 1938	Manufacturer 1977-1978	AHFS* Category	Current NDA Status**
Adrenalin	Parke-Davis	Parke-Davis	12:12, 52:24, 52:32		Ben-caine B-B	Ulmer	Ulmer	52:16, 64:08	
Algie	Prague	Unimed			Benzedrine	Smith Kline & French	Smith Kline & French	28:20	N17017—spanule
Alurate	Roche	Roche	28:24		Berocca	Roche	Roche	88:28	N83900—tablet
Aminophylline	Searle	Searle	40:28, 86:00	numerous NDAs	Betalin S	Lilly	Lilly	88:08	N00240—elixir
Amyl nitrite	Calco	Burroughs-Wellcome	24:12		Bromural	Knoll; Merck	Knoll	92:00	N80853—injectable only
Amytal	Lilly	Lilly	28:24		Butisol	McNeil	McNeil	28:24	
Anabolin	Harrower	Alto	88:08		Butisol Sodium	McNeil	McNeil	28:24	N06793—tablet
Anthralin	Abbott	Dermik	84:28		Butyn Sulfate	Abbott	Abbott	52:16	
Aphrodes	Rex	Rex							
A.P.L.	Ayerst	Ayerst	68:18	N17055	Caffeine sodium benzoate	Various	Various	28:20	
Apasmon	Norgine	Kretschmar			Calcidrine	Abbott	Abbott	48:00	
Atabrine	Winthrop	Winthrop	08:08, 10:00	N15052—injectable only	Calciphen	Rorer	O'Neal, Jones & Feldman		
Atrobarb # 1, 2, 3	Jenkins	Jenkins			Calcium chloride solution ampules	Various	Various	68:24	
Auralgan	Doho	Ayerst			Calcium gluconate 10 percent ampules	Various	Various	68:24	
Barbidonna	Van Pelt & Brown	Mallinckrodt			Calcium Levulinate ampules	Crookes	Corvit	68:24	
Belbarb	Haskell	Arnar-Stone			Calpholac Carbazone	Nestles Lilly	Century Lilly	8:04	
Belbarb #2	Haskell	Arnar-Stone							
Belladene	Sandoz	Sandoz							
Bellafoline	Sandoz	Sandoz	12:08						
Bellergal	Sandoz	Dorsey							

Name of Drug	Manufacturer 1938	Manufacturer 1977-1978	AHFS* Category	Current NDA Status**	Name of Drug	Manufacturer 1938	Manufacturer 1977-1978	AHFS* Category	Current NDA Status**
Carbromal	Calco; Upjohn; Bluline	Bluline; Freeman	28:12	N01592—tablets N01177—tablets	Ketochol	Searle	Searle		
Cenolate	Abbott	Abbott			Lextron	Lilly	Lilly	20:04.04	
Cerose	Wyeth	Ives	48:00		Lipo-lutin	Parke-Davis	Parke-Davis	68:32	
Cheracol	Upjohn	Upjohn	4:00, 48:00		Liver extract	Lederle; Lilly; Parke-Davis; Valentine	Lederle; Lilly; Parke-Davis; Valentine	20:04.08	
Choline Chloride	Merck	Baker; City Chemical			Luminal	Winthrop	Winthrop	28:12, 28:24	
Calcichine	Abbott	Abbott	92:00		Luminal sodium	Winthrop	Winthrop	28:12, 28:24	
Congo red	Kirk	Harvey; Consolidated Midland	36:08		Magnesium sulfate	Various	Various	28:12, 56:12	
Copavin	Lilly	Lilly	28:08, 86:00, 48:00		Mebaral	Winthrop	Winthrop	28:12, 28:24	
Coramine	Ciba	Ciba	28:20		Mecholyl	Merck	Baker	12:04	
Corec	Roth Labs	Econo-Rx			Methenamine	Abbott	Various	8:36	
Cosanyl	Parke-Davis	Parke-Davis	48:00		Methylene blue	Abbott; Breaon; Calco; Endo	Various	8:36	
Decholin Sodium	Riedel de Haen	Dome	56:16		Metrazol	Knoll	Knoll	28:20	
Diacin	Diacin Labs	Danal Labs			Metycaine	Lilly	Lilly	54:21, 72:00	
Digifortis	Parke-Davis	Parke-Davis	24:04		Myochrysin	Merck Sharpe & Dohme	Merck Sharpe & Dohme	60:00	
Digiglusin	Lilly	Lilly	24:04		Naftalan	Sciencs; Donner	Hark		
Digitalis	Various	Various	24:04		Nembutal	Abbott	Abbott	28:24	N83244—syrup
Digoxin	Burroughs-Wellcome	Burroughs-Wellcome	24:04	N83391—injectable only	Nep- Synephrine	Sterns	Winthrop	12:12, 52:24, 52:32	
Dihydro- tachysterol	Winthrop	Phillips Roxane	68:24		Nitroglycerin	Abbott	Various	24:12	
Dilantin	Parke-Davis	Parke-Davis	28:12	N84349—capsules N85762—suspension	Novocain	Winthrop	Winthrop	72:00	
Dilaudid	Knoll; Merck	Knoll	28:08		Nupercaine	Ciba	Ciba	52:16, 84:08, 72:00	
Dionin	Merck	Merck			Ocin	Knoll; Merck	Knoll	86:00	N06420—injectable
Donnatal	Robins	Robins	12:08		Oreton	Schering	Schering	68:08	
Emeracol	Upjohn	Upjohn	48:00		Organidin	Wampole	Wallace	48:00	
Emetine hydrochloride	Various	Various	8:04		Orolgasic	Bluline	Bluline	84:00	
Empirin Compound #2 and #3	Burroughs-Wellcome	Burroughs-Wellcome	52:32		Quabain	Merck	Lilly	24:04	
Ephedrine hydrochloride alkaloid sulfate	Various	Various	12:12		Oxoids	Professional	Lemmon		
Ephedrine and Amytal	Lilly	Lilly			Pancreatic hormone	Grant	Amfre-Grant		
Ephedrine and Nembutal	Abbott	Abbott			Pantopon	Roche	Roche	28:08	
Ephedrine and phenobarbital	Massengill	Various			Papaverine	Roche	Various	86:00	
Epinephrine	Various	Various	52:24		Parathyroid	Squibb	Lilly	68:24	
Epragen	Lilly	Lilly			Pentobarbital sodium	Lilly	Lilly	28:24	N02368—capsules N03962—injectable N84569—capsules
Ergostrate H	Lilly	Lilly	76:00		Pentothal Sodium	Abbott	Abbott	28:24	N11679—rectal
Eschatin	Parke-Davis	Parke-Davis	52:08, 68:04		Phenacaine hydrochloride	Werner	Muro		
Estrolin	Lakeside	Laser			Phenacetin	Winthrop	Various	28:08	
Estrone	Ayerst; Lilly	Various	68:16	N04823—injectable	Phenobarbital	Squibb	Various	28:12, 28:24	
Ethobral	Wyeth	Wyeth			Phenol	Hynson	Hynson	36:40	
Ethyl Chloride	Amaco	Various	84:08		phthalin	Westcott & Dunning	Westcott & Dunning		
Eurexol	Knoll	Knoll	84:28		Piperazine	Winthrop	Various	8:08	N09437—syrup; N80671; N80774; N80963; N83756; N80681—tablet; N80874—tablet N13508—tablet
Extralin	Lilly	Lilly	20:04.08		Pitocin	Parke-Davis	Parke-Davis	76:00	
Follutin	Squibb	Squibb	68:18	N17056—injectable	Pitressin	Parke-Davis	Parke-Davis	68:28	
Gluco-calcium	Lilly	Lilly			Podophyllin	Abbott; Lilly	Robinson	84:28	
Glypectol	Schiffellin	International Chemical			Pontocaine	Winthrop	Winthrop	52:16, 72:00	
Gold sodium thiosulfate	Abbott; Merck; Searle	Harvey			Potassium sulfocyanate	Winthrop	Baker; Mallinckrodt		
Gomenol	Bard	Various			Procaine hydrochloride	Abbott; Merck; Squibb	Various	72:00	Numerous NDAs
Gynergen	Sandoz	Sandoz	12:16		Progesterone	Breaon	Various	68:32	N17338—injectable
Hexaler	Riedel	Webeon	8:36		Proluton	Schering	Schering	68:32	
Histamine phosphate	Parke-Davis; Breaon	Various	36:64	N03862—injectable N02854—injectable N80697—injectable	Prostigmin	Roche	Roche	12:04	N00654—solution N02449—injectable
Indigo carmine	Hynson, Westcott & Dunning	Various	36:40		Prnicodeine	Lilly	Lilly	36:56	
Iron cacodylate	Various	Various	20:04.04		Pyridium	Merck	Warner-Chilcott	8:36	
Ithyphen	Strauss	Universal			Rectocaine	Kirk	Moore Kirk		
Ivyol	Merck; Sharpe & Dohme	Merck; Sharpe & Dohme	84:36		Reton	Roche-Renand	Tri-State		

Name of Drug	Manufacturer 1938	Manufacturer 1977-1978	AHFS* Category	Current NDA Status**	Name of Drug	Manufacturer 1938	Manufacturer 1977-1978	AHFS* Category	Current NDA Status**
Salyrgan-theophylline	Winthrop	Winthrop			Testosterone propionate	ProMedico	Various	68:08	N0188—injectable; N80254; N80262; N80276; N80678; N80741; N80742; N80743; N83303
Sarapin	High	High		N07392—injectable	Theamin and Amytal	Lilly	Lilly	86:00	
Seconal	Lilly	Lilly	28:24		Theelin	Parke-Davis	Parke-Davis	86:16	N03977—injectable
Serenium	Squibb	Squibb	8:36	Theobromin with phenobarbital	Premoj Upjohn	Paramount	40:25		
Siderol	Wyeth	Doral		Thiamine hydrochloride injectable	Abbott; Lederle; National; Squibb	Invenzy; Jenkins; Robimson; West-ward	86:08	Numerous NDAs	
Skiodan	Winthrop	Winthrop		Thyroid	Various	Various	68:36		
Sodium cacodylate	Various	Various		Thyroxin	Squibb	Various	68:36		
Sodium thiosulphate	Various	Various		Thyroxine	Roche	Various	68:36		
Somnos	Merck Sharpe & Dohme	Merck Sharpe & Dohme	28:24	Trilax	Barksdale	Drug Industries			
Strontium bromide	Breon; Endo; Kirk	Various	28:12	Tuberculin	Winthrop	Lederle; Lilly	36:84		
Strychnine	Houde Wallace	Baker; Humco		Urolax	High	Century			
Sulfanilamide	Baker	Baker							

II. Therapeutic Chemicals

Name of Chemical	AHFS* Category	Current NDA Status**	Name of Chemical	AHFS* Category	Current NDA Status**	Name of Chemical	AHFS* Category	Current NDA Status**
Acetanilid			Iodoform			Potassium thiocyanate		NDA—tablets
Acetophenetidin	28:08	Now phenacetin	Iron, peptonized			Procaine hydrochloride	72:00	Numerous NDAs
Alcohol, absolute	28:08, 36:36		Lithium carbonate	28:16,12	NDA—tablets, capsules	Quinidine sulfate	24:04	Numerous NDAs
Apomorphine hydrochloride	56:20		Magnesium carbonate (heavy)	56:04		Resorcinol	84:28	
Atropine	12:08, 52:24		Magnesium hydroxide		NDA—liquids	Silver nitrate	52:04,12, 84:12, 84:28	
Atropine sulfate	12:08, 52:24	NDA—tablets, injections, ophthalmics	Magnesium oxide (light)	56:04	NDA—tablets	Sodium acetate		
Barbital			Mercury, ammoniated	84:04,16		Sodium acid phosphate	40:04	
Barbital sodium			Methylene blue	8:36		Sodium bicarbonate solution	40:08, 96:04	
Belladonna leaves, powdered	12:08		Morphine sulfate	28:04	Injectable, tablets	Sodium chloride solution	40:12, 40:36	Numerous NDAs
Benzocaine	56:16, 84:08		Nux vomica			Sodium fluoride	92:00	
Bismuth subsalicylate solution	8:28		Opium	28:08, 56:08		Sodium hydroxide		
Calomel			Pancreatin	56:16		Sodium iodide	36:08	
Cantharides			Papain	44:00	NDA—tablets	Sodium nucleate		
Chloral hydrate	28:24		Paraldehyde	28:24		Sodium phosphate	56:12	
Chloroform			Pilocarpine alkaloid	52:20		Sodium salicylate	28:08	
Cocaine hydrochloride	52:16		Pilocarpine hydrobromide	32:20		Sodium succinate		NDA—injection
Codaine phosphate	28:08, 48:00		Pilocarpine hydrochloride	52:20	Ophthalmics	Theobromine		
Codaine sulfate	28:08, 48:00	NDA—tablets, injections	Pilocarpine nitrate	52:20		Theophylline	86:00	NDA—elixir
Dextrosa	40:20	I.V. plastic bags	Pilocarpine salicylate	52:20		Thymol		
Eserine sulfate	12:04, 52:30		Pilocarpine sulfate	52:20		Tin metal		
Fluorescein	52:36		Potassium acetate injection	40:12		Tin oxide		
Guaiacol			Potassium bromide	28:12		Urea	40:28, 84:16	NDA—injection
Hexamethylenamine (methenamine)	8:36		Potassium chloride	28:12		Yohimbine hydrochloride		
Homatropine hydrobromide	12:08, 52:24		Potassium chloride solution	40:12	Numerous NDAs	Zinc chloride	52:28	
Hyoscine (scopolamine)	12:08, 52:24		Potassium iodide solution	48:00		Zinc peroxide	84:04,16	
Hyoscyamine hydrobromide	12:08		Potassium permanganate	84:04,16		Zinc sulfate	52:04,12	
Hyoscyamine sulfate	12:08		Potassium phosphate	40:12		Zinc sulfocarbolate (zinc phenolsulfonate)		

*AHFS: American Hospital Formulary Service published by the American Society of Hospital Pharmacists.

**Since 1938, manufacturers of drugs/therapeutic chemicals have submitted to the FDA New Drug Applications (NDAs) for the same or different dosage forms.