

installment notes or contracts, the extension of direct loans to dealers for the financing of inventory (floor planning); and acting as agent for the sale of life, accident and health insurance directly related to its extensions of credit. These activities would be conducted from an office in Carlisle, Pennsylvania, serving the surrounding area. Comments on this application must be received not later than October 28, 1983.

C. Federal Reserve Bank of Richmond (Lloyd W. Bostian, Jr., Vice President) 701 East Byrd Street, Richmond, Virginia 23261:

1. *Southern Bancorporation, Inc.*, Greenville, South Carolina (financing and insurance activities; South Carolina): To engage through its subsidiary, World Acceptance Corporation, in the activities of making extensions of credit as a licensed consumer finance lender; acting as agent for credit life and accident insurance written in connection with such extensions of credit, such activities being permissible under section 601 (A) of the Garn-St Germain Depository Institutions Act of 1982 ("Garn Act"); acting as agent for credit property insurance written solely in connection with such extensions of credit, such activities being permissible under section 601 (A) and (D) of the Garn Act. These activities would be conducted from an office in Moncks Corner, South Carolina, serving the approximate city limits of Moncks Corner and certain other parts of Berkeley County within a ten mile radius of Moncks Corner. Comments on this application must be received not later than October 27, 1983.

D. Federal Reserve Bank of St. Louis (Delmar P. Weisz, Vice President) 411 Locust Street, St. Louis, Missouri 63166:

1. *West Tennessee Bancshares, Inc.*, Bartlett, Tennessee (mortgage lending; Tennessee): To engage, through a wholly-owned subsidiary, Bartlett Mortgage, Inc., in originating and processing FHA, VA and conventional mortgage loans. These activities will be conducted from an office in Bartlett, Tennessee, serving Fayette, Shelby and Tipton Counties, Tennessee. Comments on this application must be received not later than October 24, 1983.

E. Federal Reserve Bank of Kansas City (Thomas M. Hoenig, Vice President) 925 Grand Avenue, Kansas City, Missouri 64198:

1. *Mountain States Financial Corporation, Inc.*, Albuquerque, New Mexico (mortgage banking activities; New Mexico, Colorado, Texas and Illinois): To provide mortgage servicing duties for First Federal Savings and Loan Association of Wilmette, a

nonaffiliated company, required by a contract between Federal National Mortgage Association and Evergreen Service, a previously affiliated company which was merged into First Federal Savings and Loan Association of Wilmette during 1982. These activities will take place in New Mexico, Colorado, Texas and Illinois. Comments on this application must be received not later than October 28, 1983.

Board of Governors of the Federal Reserve System, September 29, 1983.

James McAfee,

Associate Secretary of the Board.

[FR Doc. 83-27003 Filed 10-4-83; 8:45 am]

BILLING CODE 6210-01-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

Advisory Committee Meeting; Cancellation

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is cancelling the meeting of the Fertility and Maternal Health Drugs Advisory Committee scheduled for October 13 and 14, 1983. The meeting was announced by notice in the *Federal Register* of September 16, 1983 (48 FR 41649).

FOR FURTHER INFORMATION CONTACT: A. T. Gregoire, National Center for Drugs and Biologics (HFN-130), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-1869.

Dated: September 28, 1983.

William F. Randolph,

Acting Associate Commissioner for Regulatory Affairs.

[FR Doc. 83-27090 Filed 10-4-83; 8:45 am]

BILLING CODE 4100-01-M

[Docket No. 80N-0382; DESI Nos. 64, 1204, 5064, 5597, 6303, 7337, 8630, 10996, 13416, 11792 and 16109]

Human Drugs; Prescription and Over-the-Counter Drug Products Containing Phenacetin; Withdrawal of Approval of New Drug Application

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is withdrawing approval of new drug applications or parts of new drug applications that provide for drug products containing phenacetin, except for those drug

products that are the subject of a hearing request. The basis of the withdrawal is phenacetin's high potential for misuse and its unfavorable benefit-to-risk ratio when incorporated in analgesic combinations which are then subject to excessive chronic use.

EFFECTIVE DATE: November 4, 1983.

ADDRESS: Requests for an opinion of the applicability of this notice to a specific product should be identified with Docket No. 80N-0382 and directed to the Division of Drug Labeling Compliance (HFD-310), National Center for Drugs and Biologics, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD. 20857.

FOR FURTHER INFORMATION CONTACT: Herbert Gerstenzang, National Center for Drugs and Biologics (HFN-8), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-3650.

SUPPLEMENTARY INFORMATION: In a notice published in the *Federal Register* of August 10, 1982 (47 FR 34836), the Director of the National Center for Drugs and Biologics concluded that drug products containing phenacetin are not shown to be safe, proposed to withdraw approval of their new drug applications or parts of new drug applications (NDA's or ANDA's) that provide for products containing phenacetin, and offered an opportunity for a hearing on the proposal. The notice stated that most of the phenacetin-containing drug products could be reformulated to acceptable products either by deleting phenacetin from their formulations or by replacing phenacetin with another analgesic. The notice also set forth guidelines for acceptable reformulations. In addition, the Director stated his intention to publish the withdrawal of approval order for those phenacetin-containing drug products not the subject of a hearing request by October 12, 1982. This order was to take effect on August 10, 1983 and all affected drug products were to be reformulated by August 10, 1983 to continue on the market. After publication of this proposal, the agency determined that greater flexibility was needed in issuing the withdrawal order to allow for resolution of problems with the reformulation of phenacetin-containing products. Therefore, the withdrawal order was not published on October 12, 1982 and the requirement that affected products be reformulated by August 10, 1983 was not finalized. Instead, the withdrawal order is now being published with an effective date of November 4, 1983.

FK

In response to the notice of opportunity for a hearing, hearing requests were received for the drug products listed below. These requests are now under review and will be the subject of a future **Federal Register** notice. This notice does not apply to these products and their marketing may continue pending a ruling on the hearing requests.

1. Soma Compound Tablets (NDA 12-365) containing caffeine 32 milligrams (mg), carisoprodol 200 mg, and phenacetin 160 mg; Wallace Laboratories, Half Acre Rd., Cranbury, NJ 08512.

2. Soma Compound with Codeine Tablets (NDA 12-366) containing caffeine 32 mg, carisoprodol 200 mg, codeine phosphate 16 mg, and phenacetin 160 mg; Wallace Laboratories.

3. A.P.C. with Codeine Tablets (no NDA) containing aspirin 227 mg, phenacetin 162 mg, Caffeine 32 mg, and codeine phosphate in several strengths; Burroughs Wellcome Co., 3030 Cornwallis Rd., Research Triangle Park, NC 27709.

Hearing requests were not received for any other phenacetin-containing drug product listed in the August 10, 1982 notice or for any other product. The failure to file a notice of appearance and request for a hearing constitutes an election by such persons not to avail themselves of the opportunity for a hearing. Therefore, this notice withdraws approval of the new drug applications or parts of new drug below.

I. Prescription Drug Products Containing Phenacetin

A. Prescription Drug Products For Which Supplemental New Drug Applications To Delete Phenacetin From Their Formulations Were Submitted. The manufacturers of the following drug products have supplemented their new drug applications to delete phenacetin from the products. The reformulated products are now being marketed or will be marketed. This notice only withdraws approval of those parts of the following applications that provide for formulations containing phenacetin. Those parts of the applications that provide for formulations without phenacetin are not affected by this notice.

1. Those parts of NDA 17-534 that pertain to Fiorinal Tablets and Capsules containing aspirin 200 mg, butalbital 50 mg, caffeine 40 mg, and phenacetin 130 mg; Sandoz Pharmaceuticals, P.O. Box 11, Route 10, East Hanover, NJ 07936.

2. Those parts of ANDA 86-231 that pertain to A.P.C. with Butalbital

Capsules containing aspirin 200 mg, butalbital 50 mg, caffeine 40 mg, and phenacetin 130 mg; Chelsea Laboratories, Inc., 428 Doughty Blvd., Inwood, NY 11696

3. Those parts of ANDA 86-237 that pertain to A.P.C. with Butalbital Tablets containing aspirin 200 mg, butalbital 50 mg, caffeine 40 mg, and phenacetin 130 mg; Chelsea Laboratories, Inc.

4. Those parts of ANDA 86-710 that pertain to A.P.C. with Butalbital Tablets containing aspirin 200 mg, butalbital 50 mg, caffeine 40 mg, and phenacetin 130 mg; Purepac Pharmaceutical Co., 200 Elmora Ave., Elizabeth, NJ 07207.

5. Those parts of ANDA 87-048 that pertain to Butalbital with APC Tablets containing aspirin 200 mg, butalbital 50 mg, caffeine 40 mg, and phenacetin 130 mg; Generic Pharmaceutical Corp., 433 Commercial Ave., Palisades Park, NJ 07650.

6. Those parts of ANDA 87-279 that pertain to Butalbital with APC Tablets containing aspirin 200 mg, butalbital 50 mg, caffeine 40 mg, and phenacetin 130 mg; Lemmon Co., P.O. Box 30, Sellersville, PA 18960.

7. Those parts of NDA 10-996 that pertain to Darvon Compound 65 Capsules containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene hydrochloride 65 mg; Eli Lilly & Co., Box 618, Indianapolis, IN 46206.

8. Those parts of ANDA 80-044 that pertain to Propoxyphene Compound 65 Capsules containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene hydrochloride 65 mg; Lemmon Co.

9. Those parts of ANDA 83-968 that pertain to Propoxyphene HCl with A.P.C. Capsules containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene hydrochloride 65 mg; Mylan Pharmaceuticals, Inc., P.O. Box 4293, Morgantown, WV 26505.

10. Those parts of ANDA 84-553 that pertain to SK-65 Compound Capsules containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene hydrochloride 65 mg; Smith Kline & French Laboratories, 1500 Spring Garden St., Philadelphia, PA 19101.

11. Those parts of ANDA 85-732 that pertain to Propoxyphene Compound 65 Capsules containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene hydrochloride 65 mg; Chelsea Laboratories.

12. Those parts of NDA 10-996 that pertain to Darvon Compound Capsules containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene hydrochloride 32 mg; Eli Lilly & Co.

13. Those parts of NDA 7-337 that pertain to Percodan Tablets containing aspirin 224 mg, caffeine 32 mg, oxycodone hydrochloride 4.5 mg, oxycodone terephthalate 0.38 mg, and phenacetin 160 mg; Dupont Pharmaceuticals, 1000 Stewart Ave., Garden City, NY 11530.

14. Those parts of NDA 7-337 that pertain to Percodan-Demi Tablets containing aspirin 224 mg, caffeine 32 mg, oxycodone hydrochloride 2.25 mg, oxycodone terephthalate 0.19 mg, and phenacetin 160 mg; Dupont Pharmaceuticals.

15. Those parts of NDA 10-894 that pertain to Zactirin Compound-100 Tablets containing aspirin 227 mg, caffeine 32.4 mg, ethoheptazine citrate 100 mg, and phenacetin 162 mg; Wyeth Laboratories, Inc., P.O. Box 8299, Philadelphia, PA 19101.

16. Those parts of ANDA 87-874 that pertain to Carisoprodol Compound Tablets containing caffeine 32 mg, carisoprodol 200 mg, and phenacetin 160 mg; Danbury Pharmacal, Inc., 131 West St., Danbury, CT 06810. This product was not listed in the notice of August 10, 1982. The product was approved on January 7, 1983, with the understanding that it would be subject to the final withdrawal notice for phenacetin-containing drug products. Therefore, this product is also subject to this notice.

17. Those parts of NDA 13-416 that pertain to Norgesic Tablets containing aspirin 225 mg, caffeine 30 mg, orphenadrine citrate 25 mg, and phenacetin 160 mg; Riker Laboratories, Inc., 19901 Nordhoff St., Northridge, CA 91342.

18. Those parts of NDA 13-416 that pertain to Norgesic Forte Tablets containing aspirin 450 mg, caffeine 60 mg, orphenadrine citrate 50mg, and Phenacetin 320 mg; Riker Laboratories, Inc.

19. Those parts of NDA 16-109 that pertain to Sinubid Sustained Release Tablets containing acetaminophen 300 mg, phenacetin 300 mg, phenylpropanolamine hydrochloride 100 mg, and phenyltoloxamine citrate 66 mg; Warner-Lambert Co., 201 Tabor Rd., Morris Plains, NJ 07950.

B. Prescription Drug Products for Which Supplemental New Drug Applications To Delete Phenacetin From Their Formulations Were Not Submitted. Because the following applications have not been supplemented to delete phenacetin from their product formulations, approval of the entire applications is being withdrawn. A majority of the products are no longer marketed.

1. ANDA 85-441; APC with Butalbital Tablets containing aspirin 200 mg, butalbital 50 mg, caffeine 40 mg, and phenacetin 130 mg; Zenith Laboratories, Inc., 140 Le Grand Ave., Northvale, NJ 07647.

2. ANDA 86-162; Butalbital with APC Tablets containing aspirin 200 mg, butalbital 50 mg, caffeine 40 mg, and phenacetin 130 mg; West-Ward, Inc., 465 Industrial Way West, Eatontown, NJ 07724.

3. ANDA 86-398; Butal Compound Tablets containing aspirin 200 mg, butalbital 50 mg, caffeine 40 mg, and phenacetin 130 mg; Cord Laboratories, Inc., 2555 West Midway Blvd., Broomfield, Co 80020.

4. ANDA 86-432; Butal Compound Capsules containing aspirin 200 mg, butalbital 50 mg, caffeine 40 mg, and phenacetin 130 mg; Cord Laboratories, Inc.

5. ANDA 86-986; Lanorinal Tablets containing aspirin 200 mg, butalbital 50 mg, caffeine 40 mg, and phenacetin 130 mg; Lannett Co., Inc., 900 State Rd., Philadelphia, PA 19136.

6. ANDA 86-996; Lanorinal Capsules containing aspirin 200 mg, butalbital 50 mg, caffeine 40 mg, and phenacetin 130 mg; Lannett Co., Inc.

7. ANDA 80-882; ICN 65 Compound Capsules containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene hydrochloride 65 mg; ICN Pharmaceuticals, Inc., 5040 Lester Rd., Cincinnati, OH 45213.

8. ANDA 83-077; Propoxyphene Compound 65 Capsules containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene hydrochloride 65 mg; Zenith Laboratories, Inc.

9. ANDA 83-072; Propoxyphene Compound 65 Capsules containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene hydrochloride 65 mg; Mylan Pharmaceuticals, Inc.

10. ANDA 83-086; Dolene Compound-65 Capsules containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene hydrochloride 65 mg; Lederle Laboratories, Pearl River, NY 10965.

11. ANDA 83-101; Propoxyphene Compound 65 Capsules containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene hydrochloride 65 mg; Cord Laboratories, Inc.

12. ANDA 83-106; SK-Propoxyphene APC Capsules containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene hydrochloride 65 mg; Smith Kline & French Laboratories.

13. ANDA 83-230; Propoxyphene Compound 65 Capsules containing

aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene hydrochloride 65 mg; Park Davis, Division of Warner-Lambert Co., 201 Tabor Rd., Morris Plains, NJ 07950.

14. ANDA 83-530; Propoxyphene Compound 65 Capsules containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene hydrochloride 65 mg; Purepac Pharmaceutical Co.

15. ANDA 83-681; Propoxyphene HCl with A.P.C. Capsules containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene hydrochloride 65 mg; Richlyn Laboratories, 3725 Castor Ave., Philadelphia, PA 19124.

16. ANDA 83-701; Propoxyphene Compound 65 Capsules containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene hydrochloride 65 mg; Towne Paulsen & Co., Inc., 140 East Duarte Rd., Monrovia, CA 91016.

17. ANDA 83-737; Repro Compound 65 Capsules containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene hydrochloride 65 mg; Reid-Provident Laboratories, Inc., 640 10th St., Atlanta, GA 30318.

18. ANDA 84-190; Propoxyphene Compound 65 Capsules containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene hydrochloride 65 mg; Anabolic, Inc., 17802 Gillette Ave., Irvine, CA 92664.

19. ANDA 84-207; Propoxyphene HCl Compound 65 Capsules containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene hydrochloride 65 mg; Phillips Roxane Laboratories, Inc., 330 Oak St., Columbus, OH 43216.

20. ANDA 84-249; Propoxyphene HCl with A.P.C. Capsules containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene hydrochloride 65 mg; Abbott Laboratories, Inc., 14th & Sheridan Rd., North Chicago, IL 60064.

21. ANDA 86-488; Propoxyphene Compound 65 Capsules containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene hydrochloride 65 mg; Lemmon Co.

22. ANDA 87-142; Dolene Compound-65 Capsules containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene hydrochloride 65 mg; Lederle Laboratories.

23. NDA 16-864; Darvo Comp-N 50 Tablets containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene napsylate 50 mg; Eli Lilly & Co.

24. NDA 16-864; Darvo Comp-N 100 Tablets containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene napsylate 100 mg; Eli Lilly & Co.

25. ANDA 87-042; Carisoprodol Compound Tablets containing caffeine 32 mg, carisoprodol 200 mg, and phenacetin 160 mg; Bolar Pharmaceutical Co., Inc., 130 Lincoln St., Copiague, NY 11726.

II. Over-the-Counter (OTC) Drug Products Containing Phenacetin

Approval of the new drug applications or parts of new drug applications for the following OTC phenacetin-containing drug products is being withdrawn. A majority of these products are no longer marketed. Some have been reformulated to delete phenacetin and are now marketed based on conformance with an applicable OTC drug monograph.

1. These parts of NDA 6-412 that pertain to Decapryn S with APC containing aspirin 230 mg, caffeine 30 mg, phenacetin 150 mg, and doxylamine succinate 6 mg or 12 mg; Merrell-Dow Pharmaceuticals, Inc., P.O. Box 15260, Cincinnati, OH 45215.

2. Those parts of NDA 6-412 that pertain to Decapryn with APC containing aspirin 230 mg, caffeine 30 mg, phenacetin 150 mg, and doxylamine 6 mg or 12 mg; Merrell-Dow Pharmaceuticals, Inc.

3. Those parts of NDA 6-921 that pertain to Coricidin Tablets containing aspirin 3.5 grains (gr), caffeine 0.5 gr, chlorpheniramine maleate 2 mg, and phenacetin 2.5 gr; Schering Corp., Galloping Hill Rd., Kenilworth, NJ 07033.

4. Those parts of NDA 6-303 and 7-026 that pertain to Thephorine Tablets containing aspirin 160 mg, caffeine 15 mg, phenacetin 160 mg, and phenindamine tartrate 10 mg; Hoffman-La Roche, Inc., Roche Park, Nutley, NJ 07110.

5. Those parts of NDA 7-018 that pertain to Thenfadil Compound Tablets containing aspirin 180 mg, caffeine 15 mg, phenacetin 120 mg, and thenyldiamine maleate 6 mg; Winthrop Laboratories, 90 Park Ave., New York, NY 10016.

6. NDA 7-352; Hista-Pac Tablets containing aspirin 3.5 gr, caffeine 0.5 gr, phenacetin 2.5 gr, and pyrilamine maleate 25 mg; Hance Bros. & White Co., 442 North 12th St., Philadelphia, PA 19123.

7. NDA 7-821; Inhiston-APC Tablets containing aspirin 3.5gr, caffeine 0.5 gr, phenacetin 2.5 gr, and pheniramine maleate 10 mg; Plough, Inc., P.O. Box 377, Memphis, TN 38151.

8. NDA 8-828; Bristamine-APC containing aspirin 210 mg, caffeine 30 mg, phenacetin 150 mg, and phenyloloxamine 25 mg; Bristol Laboratories, P.O. Box 657, Syracuse, NY 13201.

9. NDA 11-292; Cardui Tablets containing pamabrom 25 mg, phenacetin 125 mg, and salicylamide 200 mg; Chattanooga Medicine Co., 1715 West 38th St., Chattanooga, TN 3709.

10. NDA 11-849; Pamprin Tablets containing pamabrom 25 mg, phenacetin 125 mg, pyrilamine maleate 12.5 mg, and salicylamide 250 mg; Chattem Chemicals, 1715 West 38th St., Chattanooga, TN 37409.

11. NDA 11-922; Carbetapentane citrate with SPC Capsules containing caffeine 0.5 gr, carbetapentane citrate 12.5 mg, phenacetin 1.25 gr, and salicylamide 3.5 gr; USV Laboratories, 1 Scarsdale Rd., Tuckahoe, NY 10707.

Any prescription or over-the-counter drug product that contains phenacetin and is not the subject of a pending hearing request is covered by this notice. Any person who wishes to determine whether a specific product is covered by this notice should write to the Division of Drug Labeling Compliance at the address given above.

The Director of the National Center for Drugs and Biologics, under the Federal Food, Drug, and Cosmetic Act (sec. 505, 52 Stat. 1052-1053 as amended (21 U.S.C. 355)) and under the authority delegated to him (21 CFR 5.82 and 47 FR 26913 published in the *Federal Register* of June 22, 1982), finds that new evidence of clinical experience, not contained in the applications or not available to the Director until after the applications were approved, evaluated, together with the evidence available when the applications were approved, shows that such drugs are not shown to be safe for use under the conditions of use upon the basis of which the applications were approved. (This finding does not apply to those products that are the subject of a pending hearing request.)

Therefore, pursuant to the foregoing finding, approval of the new drug applications listed above (except NDA's 12-365 and 12-366) or the parts of new drug applications listed above, and all amendments and supplements thereto is withdrawn effective November 4, 1983. Any drug product containing phenacetin initially introduced or initially delivered for introduction into interstate commerce after November 4, 1983, except for a drug still the subject of a hearing request, will be considered misbranded under section 502 of the act (21 U.S.C. 352) and a new drug within the meaning of section 201 (p) (21 U.S.C. 321 (p)) for which an approved new drug application under section 505 of the act (21 U.S.C. 355) and Part 314 of the regulations is required for marketing. In the absence of an approved new drug application, any such drug product

initially introduced or initially delivered for introduction into interstate commerce after November 4, 1983, will be subject to regulatory action. A recall of phenacetin-containing drug products is not warranted. The products that are the subjects of hearing requests may continue to be marketed pending a ruling on the requests.

Dated: September 22, 1983.

Harry M. Meyer, Jr.,

Director National Center for Drugs and Biologics.

[FR Doc. 83-26860 Filed 10-4-83; 8:45 am]

BILLING CODE 4160-01-M

Social Security Administration

Title II and Title XVI Research Grants; Announcement of the Availability of Grant Funds

The Commissioner of Social Security announces that applications will be accepted for research grants authorized under sections 1110 and 702 of the Social Security Act (the Act). This announcement concerns the Social Security Administration's research priority for Fiscal Year (FY) 1984.

Program Purpose

This research is intended to add to existing knowledge and to improve methods and techniques for the management, administration, and effectiveness of Social Security Administration programs.

Program Goals and Objectives

In general, the Social Security Administration (SSA) will support the following types of projects:

1. Those which examine the mental impairment criteria in the disability program, and
2. Those which examine the implications of raising the retirement age under title II of the Act.

Projects

This announcement is for the following priority research areas:

Priority Research Area—SSA—84—001

This project is intended to encourage research in the subject area of mental impairments and their relationship with functional capacity required to meet the mental demands of work. A need exists to understand better the association between mental impairments and an individual's ability to perform basic work-related activities.

The project(s) should involve an evaluation of the mental impairment concept and how one establishes the severity of a mental impairment. An

individual who is physically normal is expected to be able to perform such activities as walking, standing, lifting, carrying, pushing, pulling, reaching, and handling, without any restriction because of an impairment. An individual with a physical impairment may have limitations in one or more of these areas. There is a need to know what a normal individual can do mentally. The SSA Regulations now require considerations of such factors as ability to understand, to carry out and remember instructions, and to respond appropriately to supervision, coworkers, and work pressures in a work setting. Are there other factors which need to be considered as elements of intellectual functioning? What information is necessary to evaluate these factors and to assess the limitation of ability to perform these factors? The present process of evaluation of physical impairments under the disability programs under titles II and XVI of the Act provides for a relationship between the judgment of residual functional capacity and specific exertional levels (e.g., sedentary, light, medium work) which are considered to correlate with work. There is a need to determine what factors describing mental impairments can be used to describe the residual functional capacity and how this can be correlated with the mental demands of work. Are the factors which need to be evaluated and the limitations resulting from mental impairment different for different types of mental impairment?

Important concepts to be studied are mental impairment, severity of those impairments, and the functional capacity of the individuals relative to that impairment. In order to properly investigate these concepts and their interrelationships, a suitable population must be available for study. A grant applicant must show evidence of an agreement with one or more agencies which assess and/or treat persons with mental impairments (unless the grant applicant is such an agency) stating that the agency(ies) will encourage persons to participate in the study. Each "referral" will be voluntary and will not disadvantage the individual in any regard.

A grading structure should be developed which will assess severity of impairment and functional capacity. It will be necessary to consider what basic work-related activities are appropriate and need to be evaluated; ultimately, a prediction model should be considered which will associate mental impairments and work-related activities.

(2), (3), or (4) above. Clinical studies demonstrating substantial evidence of effectiveness will not be required, but a clinical study demonstrating that the combination product does not cause hepatic injury will be required. Such a study may not be required if it is demonstrated by clinical evidence supplied from the literature that the combination is non-toxic. In vitro dissolution rate studies are required as part of the application. In vivo demonstration of bioavailability shall be required of products which fail to achieve adequate dissolution.

This notice is issued under the Federal Food, Drug, and Cosmetic Act (secs. 502, 505, 52 Stat. 1050-1053, as amended (21 U.S.C. 352, 353)) and under the authority delegated to the Director of the National Center for Drugs and Biologics (see 21 CFR 5.70 and 47 FR 26913 published in the Federal Register of June 22, 1982).

Dated: July 1, 1982.

Harry M. Meyer, Jr.

Director, National Center for Drugs and Biologics.

(FR Doc. 82-21729 Filed 8-10-82; 2:45 am)

BILLING CODE 4160-01-M

(Docket No. 80N-0362; DESI Nos. 64, 6340, 7337, 8652, 10956, and 11792)

Prescription and Over-the-Counter Drug Products Containing Phenacetin; Opportunity for Hearing on Proposal To Withdraw Approval of New Drug Applications

AGENCY: Food and Drug Administration (FDA).

ACTION: Notice.

SUMMARY: This notice proposes to withdraw approval of new drug applications for both prescription and over-the-counter (OTC) drugs containing phenacetin due to its high potential for abuse and its unfavorable benefit-to-risk ratio when incorporated in analgesic mixtures which are then subjected to excessive chronic use. All drug products containing phenacetin are subject to this notice. Manufacturers must reformulate their products to delete phenacetin or replace it with another analgesic on or before August 10, 1983. Thereafter the marketing of any drug product containing phenacetin that is not the subject of a pending hearing request will be regarded as unlawful.

DATES: Hearing requests due on or before September 9, 1982.

ADDRESSES: Communications in response to this notice should be identified with Docket No. 80N-0382, directed to the attention of the appropriate office named below, and

addressed to the Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

Supplements to full new drug applications (identify with NDA number): Division of Neuropharmacological Drug Products (HFD-120), Rm. 10B-34 (or Division of Surgical-Dental Drug Products (HFD-160), Rm. 18B-03, National Center for Drugs and Biologics.

Supplements to abbreviated new drug applications (identify with ANDA number): Division of Generic Drug Monographs (HFD-530), National Center for Drugs and Biologics.

Requests for Hearing (identify with Docket Number appearing in the heading of this notice): Dockets Management Branch (HFA-505), Rm. 4-52.

Requests for guidelines or information on conducting dissolution tests and bioavailability studies: Division of Biopharmaceutics (HFD-520), National Center for Drugs and Biologics.

Questions about phenacetin substitutes and whether a reformulated product is identical, similar, or related to a drug product evaluated by the Drug Efficacy Study Implementation (DESI) review: Division of Drug Labeling Compliance (HFD-510), National Center for Drugs and Biologics, Rm. 9B-29 (301-443-3750).

FOR FURTHER INFORMATION CONTACT: Herbert Gerstanzang, National Center for Drugs and Biologics (HFD-52), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857; 301-443-3650.

SUPPLEMENTARY INFORMATION:

Background

Phenacetin, an ingredient in prescription and OTC drug products, has been widely used as an analgesic for over 90 years. It is usually used in combination with other analgesic ingredients; it is virtually never used as a single-ingredient drug product. Analgesic mixtures containing phenacetin when used chronically and excessively can result in severe and irreversible toxic effects. Phenacetin's history of abuse from its misuse and prolonged use led FDA in 1964 to require a warning statement in the labeling of all phenacetin-containing preparations. See 21 CFR 201.309.

In 1977, the FDA Advisory Review Panel on Over-the-Counter Internal Analgesic and Antirheumatic Products classified phenacetin as not safe for OTC use as an analgesic because of the high potential for abuse, the high potential for harm to the kidneys from

phenacetin-containing mixtures, and the possibility of hemolytic anemia and methemoglobinemia resulting from abuse. In arriving at its conclusions regarding the safety of phenacetin, the Panel considered documented evidence showing:

1. That the central nervous system effects of phenacetin appear to be a major factor in the chronic abuse of combinations containing this drug. Several authors of the medical literature reviewed noted the habituation potential of phenacetin-containing combinations.

2. An association between excessive chronic ingestion of phenacetin-containing analgesics and life-threatening urinary tract and kidney disease (renal papillary necrosis, nonobstructive interstitial nephritis, calcification), and cancer of the kidney and bladder.

A thorough review of the literature on the relationship between phenacetin and severe renal disease was made by the Panel and submitted for outside statistical evaluation. Numerous experts appeared before the Panel. In addition, the Panel collected new information from a variety of sources including kidney dialysis centers and regulatory agencies of other countries. The Panel report states in part at 42 FR 35425:

"In the opinion of the Panel, the evidence relating phenacetin to severe renal disease now derives from a world body of published reports so numerous and varied in design that the possibility of coincidental association is negligible and requires that phenacetin be removed from the OTC drug market.

"There is a view set forth in material submitted to the Panel that phenacetin should not be singled out as the causative agent in analgesic combination products because other agents in analgesic combinations, such as aspirin or acetaminophen, have been shown to produce kidney damage when used alone in man and animals, whereas phenacetin alone has rarely been shown to produce kidney damage in man The Panel does not agree with this argument because there are now thousands of reported cases of kidney disease associated with the use of phenacetin-containing mixtures, while there are probably no more than ten well-documented cases of analgesic-induced kidney disease in the world literature that can be definitively associated with abuse of all other single agent products or combination analgesic products not involving phenacetin, even though these products are extensively used throughout the world. The Panel has discussed the adverse effects of,

aspirin on the kidney elsewhere in this document.

"From the point of view of safety of phenacetin, whether it causes kidney disease itself, augments effects of other active ingredients or increases the use of other nephrotoxic agents, it is the Panel's opinion that prolonged excessive ingestion of any common analgesic product containing phenacetin will significantly increase the probability of serious kidney disease and premature death. These levels and duration of ingestion, far exceeding label directions for use of such analgesic mixtures, are indicative of a serious potential for abuse problem that the Panel believes is associated with CNS effects of phenacetin and other components of such mixtures. This is especially true for powder formulations.

"Phenacetin is virtually never used as a single agent in the U.S. or any other country. It is almost always commercially available and used only in combinations containing other analgesic compounds. Obviously, since the actual use of phenacetin as a single entity is rare, it could not be expected that renal disease resulting from its use alone would occur or be reported. It should be noted though that at least one case allegedly involving only phenacetin has been reported. Although epidemiological or experimental studies on the effects of phenacetin alone in producing renal disease in man are not available or feasible, several other types of evidence indicate the major involvement of phenacetin in analgesic-induced renal disease.

"In several major industrialized countries, where kidney disease induced by analgesic abuse has been a problem, many analgesic mixtures have been involved. Phenacetin has been the common denominator of analgesic products responsible for the problem. In the U.S., available data also indicate that phenacetin-containing products are involved in almost all reported cases of analgesic-induced kidney disease.

"In addition to phenacetin being involved qualitatively as the common denominator, data from several countries show similar quantitative relationships between the dose of phenacetin required to produce a given degree of kidney injury or incidence of kidney disease, irrespective of the dose of other agents involved.

"Retrospective case control studies indicate that total doses of 2 to 4 kg phenacetin over a period of about 10 years would result in approximately a 70 percent probability of renal papillary necrosis. The probability of death due to kidney failure in patients with degeneration of the part of the kidney

affected by phenacetin is about 30 to 40 percent. This incidence appears to be similar for all mixtures of phenacetin regardless of whether they contain aspirin, antipyrine, or caffeine.

"Several different types of studies consistently suggest temporal and dose relationships between phenacetin ingestion and renal dysfunction. In the opinion of the Panel, and consulting reviewers, studies following changes in renal function in the same individual or groups of individuals when phenacetin is removed, replaced, or readministered provide strong evidence for a direct causal effect. Followup studies in countries after complete removal of phenacetin from nonprescription use have shown a decrease in the incidence of kidney damage associated with analgesic abuse as will be discussed later in this document. This not only supports the assumption of causality but also the conclusion that removal from OTC drug status would be beneficial. Data collected from kidney dialysis units in the U.S. and previous autopsy studies suggest the incidence of analgesic-induced kidney disease to be significantly high to warrant the Panel's action to recommend restriction of this drug from the OTC drug market.

"The Panel further believes that these data provide the same early warning indications seen in other countries just before analgesic-induced kidney disease was diagnosed as a major public health problem. The 'lag time' between several initial diagnoses of analgesic-induced kidney disease and the realization that in fact the problem was widespread is what most concerns the Panel. While there are not large numbers of cases of analgesic-induced kidney disease being presently reported in the U.S., the Panel believes that if the medical community were aware of this problem and looked for this type of kidney disease, the incidence of analgesic-induced kidney disease would in fact be found to be a major public health problem in the U.S."

More detailed examination and documentation of the data supporting these Panel conclusions are contained in the Panel's report and proposed monograph for OTC Internal Analgesic, Antipyretic and Antirheumatic Products (Ref. 1) published in the Federal Register of July 8, 1977 (42 FR 35346) on pages 35424-35434.

The central nervous system effects of phenacetin in combination products have been further reported in recent years in experimental studies (Ref. 41) and in historical surveys (Refs. 42, 43) where both in the United States and in Europe phenacetin-containing combination products have been used for nonanalgesic indications.

Although attempts have been made to define the prevalence of analgesic abuse, it has been impossible so far to arrive at a generalized assessment. Real differences exist in the prevalence between countries and between different sections of individual countries, e.g., the United States and Australia (Refs. 42 through 46). The public health problems are primarily those secondary to chronic ingestion and although analgesic abuse leads to multiorgan dysfunction, it is primarily the renal disease that is of public health importance. It is estimated that in some areas of the United States "20 percent of patients with interstitial nephropathy had ingested large quantities of analgesic mixtures and that this consumption appeared to be the primary cause of their renal disease" (Ref. 45).

The adverse effects of chronic high doses of phenacetin-containing analgesic combination products discussed above and in the OTC Panel report have also been documented in recent medical literature (Refs. 41 through 45, 47 through 49). While experimental data from animal studies (Ref. 44) suggest that aspirin is more potent than phenacetin in producing renal papillary necrosis in animals, when the drugs are taken together the incidence of renal lesions is greater than with aspirin alone. Analgesic nephropathy is rare in humans who have abused aspirin alone, presumably because of the lesser toxic propensities of aspirin in man and less potential for abuse of the single ingredient. Although analgesic nephropathy occurs in patients with rheumatoid arthritis, the incidence is not high, and in almost all reported series has been limited to those patients who have taken combination analgesics containing phenacetin and not to those patients who have taken large quantities of aspirin alone (Ref. 46). Kincaid-Smith (Ref. 42) states that dosage may account for the fact that patients with rheumatoid arthritis who take aspirin for prolonged periods do not have a high incidence of analgesic nephropathy. That is, although they take large amounts of aspirin by conventional standards, the amounts are often less than those taken by analgesic abusers. Kincaid-Smith further states that when serious analgesic nephropathy is found in patients with rheumatoid arthritis they have almost always abused drug combinations.

It has also been suggested by Natta et al. (Ref. 44) that removal of phenacetin from combination analgesics does not lower the incidence of analgesic nephropathy. This is based on a study in Australia of two consecutive groups of

patients who had exclusively abused either a product containing aspirin, phenacetin, and caffeine or a product containing aspirin, salicylamide, and caffeine. The authors concluded that the absence of phenacetin from this one product over an eight-year period did not appear to influence the frequency of renal insufficiency in patients. However, the pattern of drug ingestion in these patients was not validated in any manner other than by patient history, and the free availability of phenacetin in other OTC products throughout the period of the study raises issues of validity of these findings. This is in contrast to the experience in Canada, Denmark, and Sweden (Refs. 43, 46, 50) where removal of phenacetin from all combination analgesic products has resulted in a significant decline in analgesic nephropathy as measured by sensitive indices (Refs. 47, 49). There appear to be true differences between analgesic nephropathy as it occurs in Australia and as it occurs in other countries. Evidence of this is Australia's high frequency (25 percent) of end stage renal disease associated with analgesic nephropathy compared to 3.1 percent in Europe. This difference was also noted and discussed by the OTC Panel (Ref. 1).

Due to FDA's increasing concern about the toxicity of phenacetin, the agency requested its Peripheral and CNS Drugs Advisory Committee to evaluate the data on the safety and effectiveness of phenacetin in prescription analgesic combination products. At its meeting of February 13-14, 1978, the Committee concluded that a statement on the association of phenacetin with renal damage should be required in the labeling of such products, but the committee did not recommend that phenacetin be removed from the prescription drug market. On November 20, 1978, FDA wrote to NDA holders for prescription products that contained phenacetin, asking them to add a boxed warning statement to the labeling highlighting the association of large doses of phenacetin for long periods with severe kidney disease and with cancer of the kidney, and to add a statement to the Warnings section concerning kidney disease associated with phenacetin. Many firms have already revised their labeling to include these warnings. Since August 7, 1964, warning statements on the hazards of long-term use of phenacetin have been required in the labeling of phenacetin-containing products under 21 CFR 201.209.

Although the evidence linking abuse of analgesics to cancer of the kidney was not reviewed by the Peripheral and

CNS Drugs Advisory Committee in 1978, several reports implicating long-term use of phenacetin-containing products with cancer of the kidney and urinary bladder were reviewed by both the OTC Panel (Ref. 1) and FDA (Refs. 21 through 40). FDA later reviewed additional medical literature, notably the 1978 Bengtsson report (Ref. 40) which states that over 100 cases of uro-epithelial cancers have been reported in users of phenacetin-containing analgesics. In 1980, the first epidemiologic study of analgesic nephropathy and transitional cell carcinoma of the urinary tract was reported from the United States by Gonwa et al. (Ref. 51). The findings here were consistent with the previous epidemiologic studies from Europe and implicate analgesic abuse, particularly of phenacetin, as being carcinogenic.

The Director of the National Center for Drugs and Biologics has reevaluated the conclusions of the Advisory Review Panel on Over-the-Counter Internal Analgesic and Antirheumatic Products, the Peripheral and CNS Drugs Advisory Committee, and the evidence available to the agency as discussed above and concludes that because the high potential for abuse of phenacetin-containing products may lead to excessive ingestion, producing a clinical syndrome characterized by serious kidney disease and premature death, the risks from use of such combination drug products outweigh any benefit and therefore they cannot be considered safe. The medical literature (Ref. 44) also reports that this clinical syndrome is characterized by gastrointestinal symptoms with peptic ulcerations in 35 percent of patients, anemia in 50-90 percent, hypertension in 15-70 percent, ischemic heart disease in 35 percent, pigmentation, psychiatric disorders, and possible effects on pregnancy. Although phenacetin is not unique in its ability to cause nephropathy, its central nervous system properties make it likely that analgesic combination products containing phenacetin will be abused. Because of the availability of other safe and effective analgesics both for prescription and OTC use, consumers would not be deprived of useful analgesic products.

Proposed Action

The Food and Drug Administration is charged with assuring that drugs are safe and effective for their intended use. The statutory framework anticipates that new information on the safety of marketed drugs may require that FDA withdraw certain drug products from the market or cause certain ingredients to be deleted from drug products, or prescribe changes in their labeling to

reveal limitations on use, or to warn of previously unanticipated hazards. See 21 U.S.C. 352 and 355. In accordance with the Federal Food, Drug, and Cosmetic Act, the Director is now proposing to withdraw approval of all new drug applications for products containing phenacetin. However, the agency has determined that most of its products that contain phenacetin can be reformulated adequately by either deleting phenacetin or by replacing it with another analgesic whose safety and effectiveness is well established, thereby permitting reformulation to safe and effective products without the need to conduct safety and effectiveness studies. Therefore, these products as reformulated may continue to be available to consumers without marketing disruption. Many products that contained phenacetin have already been reformulated; several manufacturers have expressed a desire to reformulate their products and are awaiting FDA guidelines. In many other countries phenacetin has already been removed from the market without causing problems for consumers or manufacturers.

This notice applies not only to the particular phenacetin-containing drug products listed below, but also to any phenacetin-containing drug product that is the subject of a new drug application (NDA) approved either before or after the Drug Amendments of 1962 and to any other drug products containing phenacetin, whether or not they are the subject of approved NDA's. OTC drug products containing phenacetin previously deferred to the OTC review (37 FR 9464) are no longer deferred and are subject to this notice. Therefore, OTC drug products containing phenacetin will not be subject to the OTC rule making procedure set forth in § 330.10 (21 CFR 330.10).

I. Prescription Drug Products Containing Phenacetin.

A. The following products contain aspirin 200 mg, butalbital 50 mg, caffeine 40 mg, and phenacetin 130 mg.

1. NDA 17-534: Fiorinal Tablets and Capsules; Sandoz Pharmaceuticals, P. O. Box 11, Route 10, E. Hanover, NJ 07930.
2. ANDA 85-441: APC with Butalbit Tablets; Zenith Laboratories, Inc., 140 Grand Ave., Northvale, NJ 07647.
3. ANDA 86-162: Butalbital with APC Tablets; West-Ward, Inc., 465 Industrial Way West, Eastontown, NJ 07724.
4. ANDA 86-231: A.P.C. with Butalbital Capsules; Chelsea Laboratories, Inc., 428 Doughty Blvd., Inwood, NY 11596.

5. ANDA 36-237: A.P.C. with Butalbital Tablets: Chesea Laboratories, Inc.
6. ANDA 86-398: Butal Compound Tablet: Cord Laboratories, Inc., 2555 West Midway Blvd., Broomfield, CO 80020.
7. ANDA 86-432: Butal Compound Capsule: Cord Laboratories, Inc.
8. ANDA 36-710: A.P.C. with Butalbital Tablets: Purepac Pharmaceutical Co., 200 Elmora Ave., Elizabeth, NJ 07207.
9. ANDA 86-366: Lanorinal Tablets: Lannett Co., Inc., 900 State Rd., Philadelphia, PA 19136.
10. ANDA 86-996: Lanorinal Capsules: Lannett Co., Inc.
11. ANDA 87-048: Butalbital with APC Tablets: Generic Pharmaceutical Corp., 433 Commercial Ave., Passaic Pk., NJ 07650.
12. ANDA 87-279: Butalbital with APC Tablets: Premo Pharmaceutical Laboratories, Inc., 111 Leaning St., South Hackensack, NJ 07606.
- B. The following products contain aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene hydrochloride 65 mg.
1. NDA 10-996: Darvon Compound 65 Capsules: Eli Lilly & Co., Box 618, Indianapolis, IN 46206.
2. ANDA 80-044: Propoxyphene Compound 65 Capsules: Federal Pharmacal, Inc., P.O. Box Q, Kingshill St., St. Croix, VI 00850.
3. ANDA 80-382: ICN 65 Compound Capsules: ICN Pharmaceuticals, Inc., 5040 Lester Rd., Cincinnati, OH 45213.
4. ANDA 83-077: Propoxyphene Compound 65 Capsules: Zenith Laboratories, Inc.
5. ANDA 33-072: Propoxyphene Compound 65 Capsules: Mylan Pharmaceuticals, Inc., P.O. Box 4293, Morgantown, WV 26505.
6. ANDA 83-086: Dolene Compound-65 Capsules: Lederle Laboratories, Pearl River, NY 10955.
7. ANDA 83-101: Propoxyphene Compound 65 Capsules: Cord Laboratories.
8. ANDA 83-106: SK-Propoxyphene APC Capsules: Smith Kline & French Laboratories, 1500 Spring Garden St., Philadelphia, PA 19101.
9. ANDA 83-230: Propoxyphene Compound 65 Capsules: Parke Davis, Division of Warner-Lambert Co., 201 Tabor Rd., Morris Plains, NJ 07950.
10. ANDA 83-530: Propoxyphene Compound 65 Capsules: Purepac Pharmaceutical Co.
11. ANDA 83-681: Propoxyphene HCl with A.P.C. Capsules: Richlyn Laboratories, 3725 Castor Ave., Philadelphia, PA 19124.
12. ANDA 83-701: Propoxyphene Compound 65 Capsules: Towne Paulsen & Co., Inc., 140 E. Duarte Rd., Monrovia, CA 91016.
13. ANDA 33-737: Repro Compound 65 Capsules: Reid-Provident Laboratories, Inc., 640 10th St., Atlanta, GA 30318.
14. ANDA 33-368: Propoxyphene HCl with A.P.C. Capsules: Mylan Pharmaceuticals, Inc.
15. ANDA 34-190: Propoxyphene Compound 65 Capsules: Anabanc, Inc., 17802 Gillette Ave., Irvine, CA 92664.
16. ANDA 34-207: Propoxyphene HCl Compound 65 Capsules: Philips Roxane Laboratories, Inc., 330 Oak St., Columbus, OH 43216.
17. ANDA 34-249: Propoxyphene HCl with A.P.C. Capsules: Abbott Laboratories, Inc., 14th & Sheridan Rd., N. Chicago, IL 60664.
18. ANDA 34-353: SK-35 Compound Capsules: Smith Kline & French Laboratories.
19. ANDA 35-732: Propoxyphene Compound 65 Capsules: Chesea Laboratories.
20. ANDA 36-488: Propoxyphene Compound 65 Capsules: Premo Pharmaceutical Laboratories, Inc.
21. ANDA 37-142: Dolene Compound-65 Capsules: Lederle Laboratories.
- C. NDA 10-996: Darvon Compound Capsules containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene hydrochloride 65 mg; Eli Lilly & Co.
- D. NDA 16-364: Darvo Comp-N 50 Tablets containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene napsylate 60 mg; Eli Lilly & Co.
- E. NDA 16-364: Darvo Comp-N 100 Tablets containing aspirin 227 mg, caffeine 32.4 mg, phenacetin 162 mg, and propoxyphene napsylate 100 mg; Eli Lilly & Co.
- F. NDA 7-337: Percodan Tablets containing aspirin 224 mg, caffeine 32 mg, oxycodone hydrochloride 4.3 mg, oxycodone terephthalate 0.33 mg, and phenacetin 160 mg; Endo Laboratories, Inc., 1000 Stewart Ave., Garden City, NJ 11530.
- G. NDA 7-337: Percodan-Demi Tablets containing aspirin 224 mg, caffeine 32 mg, oxycodone hydrochloride 2.25 mg, oxycodone terephthalate 0.19 mg, and phenacetin 160 mg; Endo Laboratories, Inc.
- H. NDA 10-394: Zactirin Compound-100 Tablets containing aspirin 227 mg, caffeine 32.4 mg, ethoneptazine citrate 100 mg, and phenacetin 162 mg; Wyeth Laboratories, Inc., P.O. Box 8299, Philadelphia, PA 19101.
- I. NDA 11-536: Kryl Tablets containing ascorbic acid 100 mg, aspirin 230 mg, isothipendyl hydrochloride 4 mg, phenacetin 160 mg, and phenylephrine hydrochloride 5 mg; Ayerst Laboratories, 685 Third Ave., New York, NY 10017.
- J. NDA 12-365: Soma Compound Tablets containing caffeine 32 mg, carisoprodol 200 mg, and phenacetin 160 mg; Wallace Laboratories, Half Acre Rd., Cranbury, NJ 08512.
- K. ANDA 37-042: Carisoprodol Compound Tablets containing caffeine 32 mg, carisoprodol 200 mg, and phenacetin 160 mg; Solar Pharmaceutical Co., Inc., 130 Lincoln St., Copiague, NY 11723.
- L. NDA 12-365: Soma Compound with Codeine Tablets containing caffeine 32 mg, carisoprodol 200 mg, codeine phosphate 16 mg, and phenacetin 160 mg; Wallace Laboratories.
- M. NDA 13-416: Norgesic Tablets containing aspirin 225 mg, caffeine 30 mg, orphenadrine citrate 25 mg, and phenacetin 160 mg; Riker Laboratories, Inc., 19901 Northchiff St., Northridge, CA 91324.
- N. NDA 13-416: Norgesic Forte Tablets containing aspirin 430 mg, caffeine 60 mg, orphenadrine citrate 50 mg, and phenacetin 320 mg; Riker Laboratories, Inc.
- O. NDA 16-109: Sinubid Sustained Release Tablets containing acetaminophen 300 mg, phenacetin 300 mg, phenylpropranolamine hydrochloride 100 mg, and phenytoloxamine citrate 66 mg; Warner-Lambert Co., 201 Tabor Rd., Morris Plains, NJ 07950.
- II. OTC Drug Products Containing Phenacetin (some of these products have been discontinued and are not being marketed.)
- A. That part of NDA 6-412 pertaining to Decapryn S with APC containing aspirin 230 mg, caffeine 30 mg, phenacetin 150 mg, and doxylamine succinate 6 mg or 12 mg; Merrell-Dow Pharmaceutical Inc., P.O. Box 15260, Cincinnati, OH 45215.
- B. That part of NDA 6-412 pertaining to Decapryn with APC containing aspirin 230 mg, caffeine 30 mg, phenacetin 150 mg, and doxylamine 6 mg or 12 mg; Merrell-Dow Pharmaceuticals Inc.
- C. That part of NDA 6-921 pertaining to Coricidin Tablets containing aspirin 3.5 gr, caffeine 0.5 gr, chlorpheniramine maleate 2 mg, and phenacetin 2.5 gr; Schering Corp., Calloping Hill Rd., Kenilworth, NJ 07033.
- D. Those parts of NDA 6-303 and 7-026 pertaining to Thephorine Tablets containing aspirin 160 mg, caffeine 15 mg, phenacetin 160 mg, and phenindamine tartrate 10 mg; Hoffmann-LaRoche, Inc., Roche Park, Nutley, NJ 07110.

E. That part of NDA 7-718 pertaining to Thenfacil Compound Tablets containing aspirin 100 mg, caffeine 15 mg, phenacetin 120 mg, and thenyidiamine maleate 5 mg; Winthrop Laboratories, 90 Park Ave., New York, NY 10016.

F. NDA 7-352: Hista-Pac Tablets containing aspirin 3.5 gr, caffeine 0.5 gr, phenacetin 2.5 gr, and pyrimidine maleate 25 mg; Hanco Bros. & White Co., 442 North 12th St., Philadelphia, PA 19123.

G. NDA 7-312: Inhiston-APC Tablets containing aspirin 3.5 gr, caffeine 0.5 gr, phenacetin 2.5 gr, and piperazine maleate 10 mg; Plough, Inc., P.O. Box 377, Memphis, TN 38151.

H. NDA 8-528: Bristamine-APC containing aspirin 210 mg, caffeine 30 mg, phenacetin 150 mg, and phenyltoloxamine 25 mg; Bristol Laboratories, P.O. Box 557, Syracuse, NY 13201.

I. NDA 11-292: Cardui Tablets containing pamabrom 25 mg, phenacetin 125 mg, and salicylamide 200 mg; Chattanooga Medicine Co., 1715 West 38th St., Chattanooga, TN 37409.

J. NDA 11-349: Pamprin Tablets containing pamabrom 25 mg, phenacetin 125 mg, pyrimidine maleate 12.5 mg, and salicylamide 250 mg; Chattem Chemicals, 1715 West 38th St., Chattanooga, TN 37409.

K. NDA 11-922: Carbetapentane Citrate with SPC Capsules containing caffeine 0.5 gr, carbetapentane citrate 12.5 mg, phenacetin 1.25 gr, and salicylamide 3.5 gr. USV Laboratories, 1 Scarsdale Rd., Tuckahoe, NY 10707.

Accordingly, all drug products that contain phenacetin are regarded as new drugs (21 U.S.C. 321(p)) and are subject to the requirements of this notice.

Opportunity for Hearing

Therefore, notice is given to the holders of the new drug applications for products containing phenacetin and to all other interested persons that the Director of the National Center for Drugs and Biologics proposes to issue an order under section 505(e) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(e)), withdrawing approval of the new drug applications (or if indicated above, those parts of the applications providing for the drug products listed above) and all amendments and supplements thereto because new evidence of clinical experience, not contained in such applications or not available to the Director until after such applications were approved, evaluated together with the evidence available to the Director when the applications were approved, shows that such drugs are not shown to be safe for use under the

conditions of use on the basis of which the applications were approved.

This notice of opportunity for hearing applies not only to new drug application holders (named above), but to all persons who manufacture or distribute a drug product, whether prescription or over-the-counter, that contains phenacetin. It is the responsibility of every drug manufacturer or distributor to review this notice of opportunity for hearing to determine whether it covers a drug product that the person manufactures or distributes. Such person may request an opinion of the applicability of this notice to a specific drug product by writing to the Division of Drug Labeling Compliance (address given above).

In accordance with section 505 of the act (21 U.S.C. 355) and the regulations promulgated under it (21 CFR Parts 310, 314), the applicants and all other persons subject to this notice including drug manufacturers of over-the-counter products containing phenacetin are hereby given an opportunity for a hearing to show why approval of the new drug applications should not be withdrawn and an opportunity to raise, for administrative determination, all issues relating to the legal status of drug products containing phenacetin.

An applicant or any other person subject to this notice who decides to seek a hearing, shall file (1) on or before September 9, 1982, a written notice of appearance and request for hearing, and (2) on or before October 12, 1982, the data, information, and analyses relied on to justify a hearing, as specified in 21 CFR 314.200. Any other interested person may also submit comments on this notice. The procedures and requirements governing this notice of opportunity for hearing, a notice of appearance and request for hearing, submission of data, information, and analyses to justify a hearing, submission of other comments, and the granting or denial of hearing, are contained in 21 CFR 314.200.

The failure of an applicant or any other person subject to this notice to file a timely written appearance and request for hearing as required by 21 CFR 314.200 constitutes an election by the person not to make use of the opportunity for a hearing concerning the action proposed with respect to the product and constitutes a waiver of any contentions concerning the legal status of any such drug product. Any such drug product may not thereafter lawfully be marketed, and the Food and Drug Administration will initiate appropriate regulatory action to remove such drug products from the market. Any new drug product marketed without an approved

new drug application is subject to regulatory action at any time.

A request for a hearing may not rest upon mere allegations or denials, but must set forth specific facts showing that there is a genuine and substantial issue of fact that requires a hearing. If conclusively appears from the face of the data, information, and factual analyses in the request for the hearing that there is no genuine and substantial issue of fact which precludes the withdrawal of approval of the application, or when a request for hearing is not made in the required format or with the required analyses, the Commissioner of Food and Drugs will enter summary judgment against the person(s) who requests the hearing, making findings and conclusions, denying a hearing. See 21 CFR 314.200(f).

All submissions under this notice must be filed in four copies. Such submissions, except for data and information prohibited from public disclosure under 21 U.S.C. 301(j) or 13 U.S.C. 1906, may be seen in the office of the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Guidelines for Reformulation

The Director has determined that many phenacetin-containing combination products currently being marketed can be reformulated by deleting phenacetin or by replacing phenacetin with another analgesic. Manufacturers will be given until August 10, 1983, to reformulate their products. Reformulation of an OTC drug product containing phenacetin must be in accord with the provisions of any applicable OTC drug final monograph. Before an applicable OTC drug final monograph is published, manufacturers of such OTC drug products may reformulate either by deleting phenacetin or by replacing phenacetin with other analgesic ingredients, provided the following conditions are met. The reformulation does not result in a product containing combination of ingredients not previously marketed in this country; or it does not result in a product containing: (1) an active ingredient limited to prescription use on or after May 11, 1972, or (2) an active ingredient present at a dosage level higher than that available in any OTC drug product on December 4, 1975, and unless the ingredient and/or dosage level (single unit or total daily dosage) is classified in a proposed or tentative final monograph in Category I.

Phenacetin-containing prescription drug products that are the subject of a

approved full or abbreviated new drug application may be reformulated without prior FDA approval by either deleting phenacetin or replacing phenacetin with another analgesic ingredient as follows: (1) Because the data establishing the safety and effectiveness of the analgesics aspirin and acetaminophen are well-known, phenacetin in combination products containing one of these analgesics should be replaced on a milligram-for-milligram basis with aspirin or acetaminophen, whichever analgesic ingredient is already in the product. (2) If both of the above analgesics are in a product, then either one or both of the analgesics present can be used to replace the phenacetin on a milligram-for-milligram basis (i.e., the total milligram amount of the analgesics added must be equal to the milligram amount of phenacetin deleted). Clinical studies demonstrating the safety and effectiveness of the reformulated product are not required. If reformulated as above these products may be marketed before FDA approves a supplemental application, according to the procedure provided by 21 CFR 314.8 (d) and (e).

A manufacturer may not reformulate a phenacetin-containing prescription drug product that is the subject of an approved full or abbreviated new drug application by substituting for phenacetin another analgesic ingredient not now in the drug product unless a supplemental application is first approved. Clinical studies will not be required for a reformulated product in which either aspirin or acetaminophen is substituted for phenacetin, except when acetaminophen is substituted for phenacetin and the product contains a known or potential inducer of hepatic enzymes; then a liver toxicity study will be required. An applicant may not be required to conduct such a study if it is demonstrated by clinical evidence supplied from the literature that the combination is non-toxic. For the prescription drug products listed in this notice, the only products of which the agency is aware that would require such evidence on liver toxicity (because they do not already contain aspirin or acetaminophen which can be increased to replace phenacetin) are products containing carisoprodol. If the phenacetin ingredient in carisoprodol-containing products is replaced with acetaminophen, then supplements to full new drug applications or full new drug applications will be required.

Reformulation of a product that is now the subject of an approved ANDA by substituting for phenacetin an

analgesic other than aspirin or acetaminophen will require a full approved NDA if FDA has not made a determination that an ANDA is acceptable. Because the Director is allowing manufactures 1 year in which to reformulate their products, early submission of a supplement or full new drug application requiring premarketing approval will provide a better opportunity for the applicant to obtain approval of the reformulated product in time to avoid interruption in its marketing.

Products that are subject to the drug efficacy study (DESI) program will continue to be subject to the requirements and conditions of the DESI program when the products are reformulated to delete phenacetin or to replace it with another analgesic. Reformulation of a phenacetin-containing prescription drug product subject to DESI for which a final effectiveness determination has been made must be in accordance with the applicable DESI notice. For example butalbital-analgesic combination products containing phenacetin are subject to DESI 64 which appears elsewhere in this issue of the Federal Register. A number of phenacetin-containing products also are in that part of the DESI program for which a final effectiveness determination has not yet been made. The Director advises that reformulation in accord with this notice will not alter any interim classifications of these drug products as less-than-effective.

Any phenacetin-containing prescription drug product that is not the subject of an approved NDA may be reformulated in accord with the same requirements as set forth for a prescription product that is the subject of an NDA. However, the reformulated product may result in a product that requires an approved NDA or ANDA prior to marketing. Inquiries as to the new drug status of a product should be sent to the Division of Drug Labeling Compliance (address given above).

The supplemental new drug applications, abbreviated new drug applications, or full new drug applications submitted for reformulated drug products as required by this notice are to include in vitro dissolution rate studies with the methods provided for in the guidelines on conducting dissolution tests and bioavailability studies, which are available from the Division of Biopharmaceutics at the address given above. In vivo demonstration of bioavailability shall be required of all products which fail to achieve adequate dissolution.

Any change in the formulation of a drug product required by this notice is subject to the requirements of 21 CFR 207.30 (drug listing amendment).

The Director intends to publish a notice withdrawing approval of those parts of the new drug applications that provide for products containing phenacetin, except for those products that are the subject of a hearing request, by October 12, 1982. The effective date of the withdrawal notice will be August 10, 1983. Therefore, any drug product containing phenacetin initially introduced or initially delivered for introduction into interstate commerce after August 10, 1983, except for a drug still the subject of a hearing request, will be considered misbranded under section 502 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 352) and a new drug within the meaning of section 201(p) for which an approved new drug application under section 505 of the act (21 U.S.C. 355) and Part 314 of the regulations is required for marketing. In the absence of an approved new drug application, any such drug product initially introduced or initially delivered for introduction into interstate commerce after August 10, 1983 will be subject to regulatory action. The agency concludes that although phenacetin poses an unfavorable benefit-to-risk ratio when incorporated into analgesic mixtures, a recall of phenacetin products is not warranted. Further, many firms have already reformulated their products and the agency expects that many other firms will reformulate their products as a result of the publication of this notice.

References

1. "Establishment of a Monograph for OTC Internal Analgesic, Antipyretic and Antirheumatic Products." Federal Register, July 8, 1977, pp. 35424-35434.
2. "Summary of the Report of the Advisory Review Panel on OTC Internal Analgesic, Antipyretic, and Anorectic Products." Food and Drug Administration, 1977, pp. 64-67.
3. Minutes of the Peripheral and CNS Drugs Advisory Committee Meeting, February 10-14, 1978.
4. Hultengren, N., C. Lagergren, and A. Ljungqvist, "Carcinoma of the Renal Pelvis in Renal Papillary Necrosis." *Acta Chir Scandinavica*, 130:314-320, 1965.
5. Bengtsson, U., L. Angervall, H. Ekman and L. Lehmann, "Transitional Cell Tumors of the Renal Pelvis in Analgesic Abusers." *Scandinavian Journal of Urology and Nephrology*, 2:145-150, 1968.
6. Angervall, L., U. Bengtsson, C. G. Zetterlund and M. Zsombor, "Renal Pelvic Carcinoma in a Swedish District with Abuse of a Phenacetin-Containing Drug." *British Journal of Urology*, 41:401-405, 1969.

7. Johansson, S., L. Angervail, U. Bengtsson, and L. Waniqvist. "Uroepithelial Tumors of the Renal Pelvis Associated with Abuse of Phenacetin-Containing Analgesics." *Cancer*. 33:743-753, 1974.
8. Hoybye, G. and O. E. Nielson. "Renal Pelvic Carcinoma in Phenacetin Abusers." *Scandinavian Journal of Urology and Nephrology*, 5:190-192, 1971.
9. Liu, T., G. W. Smith, and I. T. Rankin. "Renal Pelvic Tumour Associated with Analgesic Abuse." *Canadian Medical Association Journal*, 107:770-771, 1972.
10. Hoybye, G. and O. E. Nielson. "Renal Pelvic Carcinoma in Phenacetin Abusers," *ibid* pp. 241-246.
11. Taylor, J. S. "Carcinoma of the Urinary Tract and Analgesic Abuse." *Medical Journal of Australia*, 1:407-409, 1972.
12. Mannion, R. A. and D. Susmano. "Phenacetin Abuse Causing Bladder Tumor." *Journal of Urology*, 106:692, 1971.
13. Murray, T. and M. Goldberg. "Analgesic Abuse and Renal Disease." *Annual Review of Medicine*, 26:537-550, 1975.
14. Goldberg, M. and T. G. Murray. "Analgesic-Associated Nephropathy." *New England Journal of Medicine*, 299:716-717, 1978.
15. Anonymous. "The Analgesic Powder." *The Medical Journal of Australia*, 2:689-690, 1971.
16. Murray, R. M., G. C. Timbury, and A. L. Linton. "Analgesic Abuse in Psychiatric Patients." *Lancet*, 1:1303-1305, 1970.
17. Hutchinson, H. E., J. M. Jackson, and P. Cassidy. "Phenacetin-Induced Haemolytic Anaemia." *Lancet*, 2:1022-1024, 1962.
18. Lorenzen, I. and M. Schwartz. "Phenacetin-Induced Haemolysis in Patients with Chronic Nephritis and Phenacetin Abuse." *Acta Medica Scandinavica*, 168:461-466, 1960.
19. Cumming, R. L. C. and A. Pollock. "Drug Induced Suiaphaemoglobinaemia and Heinz Body Anaemia in Pregnancy with Involvement of the Foetus." *Scottish Medical Journal*, 12:320-322, 1967.
20. Gault, M. H., et al. "Snyndrome Associated with the Abuse of Analgesics." *Annals of Internal Medicine*, 38:306-325, 1968.
21. Armstrong, B., A. Garrod, and R. Doll. "A Retrospective Study of Renal Cancer with Special Reference to Coffee and Animal Protein Consumption." *British Journal of Cancer*, 33:127-130, 1976.
22. Mahony, J. F. et al. "Analgesic Abuse, Renal Parenchymal Disease and Carcinoma of the Kidney or Ureter." *Australian and New Zealand Journal of Medicine*, 7:463-469, 1977.
23. Bengtsson, U., et al. "Phenacetin Abuse and Renal Pelvic Carcinoma." *International Journal of Clinical Pharmacology*, 12:290-294, 1975.
24. Bock, K. D. and J. Hogrefe. "Analgetika-Abusus und Maligne Tumoren der Ableitenden Harnwege." *Munichener Medizinische Wochenschrift*, 114:645-652, 1972.
25. Olafsson, O., K. R. Gudmundsson, and A. Brekkan. "Migraine, Gastritis and Renal Papillary Necrosis." *Acta Medica Scandinavica*, 179:121-128, 1966.
26. Cuatrecasas, P. "Phenacetin Studies" (letter), *Science*, 203:3-7, 1979.
27. Johansson, S. and L. Angervail (letter), *Science*, 204:120, 1979.
28. Tomatis, L. "Carcinogenicity of Phenacetin" (letter), *Science*, 204:129-130, 1979.
29. Macklin, A. W., R. M. Welch, and P. Cuatrecasas. "Drug Safety: Phenacetin" (letter), *Science*, 205:144-146, 1979.
30. Vauzou, J. B. and C. M. King. "Phenacetin Studies" (letter), *Science*, 206:637-639, 1979.
31. Macklin, A. W., and R. M. Welch. "Phenacetin Safety" (letter), *Science*, 207:129-132, 1980.
32. IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Man, 13:141-155, 1977.
33. Tomatis, L., et al. "Evaluation of the Carcinogenicity of Chemicals: A Review of the Monograph Program of the International Agency for Research on Cancer." *Cancer Research*, 38:377-385, 1978.
34. Woodard, G., et al. "Phenacetin: Long-Term Studies in Rats and Dogs." (abstract), *Toxicology and Applied Pharmacology*, 7:503, 1965.
35. "Bioassay of a Mixture of Aspirin, Phenacetin, and Caffeine for Possible Carcinogenicity." National Cancer Institute Carcinogenesis Technical Report Series No. 67, DHEW Publication No. (NIH) 78-1317, U.S. Government Printing Office, Washington, 1978, pp. 55.
36. Johansson, S. and L. Angervail. "Urothelial Hyperplasia of the Renal Papillae in Female Sprague-Dawley Rats Induced by Long Term Feeding of Phenacetin." *Acta Pathologica et Microbiologica Scandinavica Section A*, 84:353-354, 1975.
37. Johansson, S. and L. Angervail. "Urothelial Changes of the Renal Papillae in Sprague-Dawley Rats Induced by Long Term Feeding of Phenacetin." *ibid.*, pp. 375-383.
38. Isaka, H., et al. "Tumors of Sprague-Dawley Rats Induced by Long Term Feeding of Phenacetin." *Gann*, 70:29-36, 1979.
39. Smith, R. L. and J. A. Timbreth. "Factors Affecting the Metabolism of Phenacetin." *Xenobiotica*, 4:489-501, 1974.
40. Bengtsson, U., S. Johansson, and L. Angervail. "Malignancies of the Urinary Tract and Their Relation to Analgesic Abuse." *Kidney International*, 13:107-113, 1978.
41. World Health Organization, Dunne, J. F., letter of September 10, 1980 to J. R. Crout with attachment "Reports on Individual Drugs."
42. Kincaid-Smith, P. "Analgesic Abuse and the Kidney." *Kidney International*, 17:250-250, 1973.
43. Murray, R. "Genesis of Analgesic Nephropathy in the United Kingdom." *Kidney International*, 13:50-57, 1973.
44. Nanna, R., et al. "Analgesic Nephropathy: Etiology, Clinical Syndrome, and Clinicopathologic Correlations in Australia." *Kidney International*, 13:79-92, 1973.
45. Murray, T. G. and M. Goldberg. "Analgesic-associated Nephropathy in the U.S.A.: Epidemiologic, Clinical and Pathogenetic Features." *Kidney International*, 13:64-71, 1973.
46. Cove-Smith, J. R. and M. S. Knapp. "Analgesic Nephropathy: An Important Cause of Chronic Renal Failure." *Quarterly Journal of Medicine*, 185:49-69, January 1978.
47. Gloor, F. J. "Changing Concepts in Pathogenesis and Morbidity of Analgesic Nephropathy As Seen in Europe." *Kidney International*, 13:27-40, 1978.
48. Gault, M. H. and D. R. Wilson. "Analgesic Nephropathy in Canada: Clinical Syndrome, Management, and Outcome." *Kidney International*, 13:58-62, 1978.
49. Kincaid-Smith, P. "Analgesic Nephropathy." *Kidney International*, 13:1-3, 1978.
50. Burry, A. "Pathology of Analgesic Nephropathy: Australian Experience." *Kidney International*, 13:34-40, 1978.
51. Gonwa, T. A., et al. "Analgesic-Associated Nephropathy and Transitional Cell Carcinoma of the Urinary Tract." *Annals of Internal Medicine*, 93:249-252, 1980.
52. Minutes of August 2, 1979 meeting between Burroughs Wellcome Co. and FDA.
53. Crout, J. R. letter to P. Cuatrecasas, May 29, 1980.

Reprints of the above references have been placed on file with the Dockets Management Branch (address given above) and may be seen between 9 a.m. and 4 p.m., Monday through Friday.

This notice is issued under the Federal Food, Drug, and Cosmetic Act (sec. 305, 52 Stat. 1052-1053, as amended (21 U.S.C. 355)) and under the authority delegated to the Director of the National Center for Drugs and Biologics (see 21 CFR 5.82 and 47 FR 26913 published in the Federal Register of June 22, 1982).

Dated: July 1, 1982.

Harry M. Meyer, Jr.,

Director, National Center for Drugs and Biologics.

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BILLING CODE 4160-01-4

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Statement of Organization, Functions, and Delegations of Authority; Food and Drug Administration

Part H, Chapter HF (Food and Drug Administration) of the Statement of Organization, Functions, and Delegations of Authority for the Department of Health and Human Services (35 FR 3485-92, February 25, 1970, as amended to pertinent part at FR 16417-19, April 19, 1973) is amended to reflect the consolidation of the Office of Public Affairs and the Office of Legislative Affairs into a new Office of Legislation and Information. This reorganization will provide a single release point for FDA information to Congress and the media thereby ensuring better coordination between