DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[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 34636), 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 phencetin-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.

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; Wallance 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 suppiemented 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 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., Chatanooga, TN 37409.

11. NDA 11-922; Carbetapentane citrate with SPC Capsules containing caffeine 0.5 gr, carbetaphetane citrate 12.5 mg, phenacetin 1.25 gr, and salicyamide 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 iinterstate 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.A.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.

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