

Public inspection at the Office of the Ad-
visory Council on Environmental Educa-
tion located in Room 2025, Federal Of-
fice Building No. 5, 400 Maryland Ave-
nue, S.W., Washington, D.C.

Signed at Washington, D.C., on Aug-
ust 13, 1976.

WALTER J. BOGGS, JR.,
Director,

Office of Environmental Education.

(EPA Doc. 76-21206 Filed 8-16-76; 9:45 AM)

Food and Drug Administration

[Docket No. 76N-0154]

ORAL RESERPINE DOSAGE FORMS OF
GREATER THAN 1 MILLIGRAM STRENGTH

Opportunity for Hearing on Proposal To
Withdraw Approval of Pertinent Parts of
New Drug Applications

This notice proposes to withdraw ap-
proval of the oral reserpine drug prod-
ucts listed below. All of them contain
more than 1 milligram of reserpine per
dosage unit. Reserpine is used primarily
in the treatment of high blood pressure.
Persons wishing to request a hearing may
do so on or before September 16, 1976.

In the FEDERAL REGISTER of April 28,
1971 (36 FR 1934) (DESI 3367) reserpine
in conventional oral dosage form was
classified as effective for use in hyper-
tension and for psychiatric disorders.
The recommended dosage for use in hy-
pertension had a range of from 0.1 milli-
gram to 0.5 milligram, and the dosage for
psychiatric disorders had a range of from
0.1 milligram to 1 milligram. The notice
of April 28, 1971 did not discuss dosage
form potencies. Clinical experience has
shown that when oral doses of more than
1 milligram of reserpine are adminis-
tered, there is greater frequency and
severity of adverse effects, without com-
pensating therapeutic benefits, than
occur with doses of 1 milligram or less.
The following references support this
concept:

1. Nickerson, M., "Antihypertensive Agents and the Drug Therapy of Hypertension," The Pharmacological Basis of Therapeutics, 4th Ed., Edited by Goodman, L. S. and A. Gilman, Macmillan, New York, 1970, p. 739.
2. Jarvik, M. E., "Drugs Used in the Treatment of Psychiatric Disorders," *ibid.* pp. 172-173.
3. Silber, E. N. and L. N. Katz, "The Treatment of Hypertensive Diseases," Heart Disease, Macmillan, New York, 1975, p. 1270.
4. Vidt, D. G., "Choice of Antihypertensive Drugs for the Treatment of Hypertension, Including Hypertensive Emergencies," Cardiovascular Drug Therapy, Edited by Melmon, K. L., F. A. Davis Co., Philadelphia, 1974, p. 207.
5. Orgain, E. S. and J. C. Gunnells, "Treatment of Systemic Hypertension," The Heart, Edited by Hurst, J. W., McGraw-Hill, New York, 1974, p. 1234.

In view of this, and the availability of
reserpine products in potencies of 0.1
milligram to 1 milligram as well as other
products used for the same indications
and which have a wider margin of

safety, the Director of the Bureau of
Drugs concludes that the benefit-to-risk
considerations associated with oral dos-

age forms containing more than 1 milli-
gram of reserpine do not justify their
continued marketing.

NDA No.	Name of drug	Potency	Applicant's name and address
9-111	Serpasil-tablets.....	2 and 4 mg.....	Ciba Pharmaceutical Co., Division of Ciba-Geigy Corp., 250 Morris Ave., Summit, N.J. 07901.
9-317	Reserpid tablets.....	4 mg.....	The Upjohn Co., 7171 Fortze Rd., Kalamazoo, Mich. 49002.
9-337	Rau-Sed tablets.....	2 and 4 mg.....	E. R. Seubbe, & Sons, Inc., P.O. Box 3029, Princeton, N.J. 08540.
9-374	Serdinil tablets.....	5 mg.....	El Lilly & Co., Box 618, Indianapolis, Ind. 46206.
9-381	Serpamoy tablets.....	2, 3, 4, and 5 mg.....	Parvix, Division of Grunert Drugs & Chemicals, Inc., P.O. Box 740, Englewood, N.J. 07611.
9-372	Reserpine tablets.....	2, 3, 4 mg.....	Endo-Vector Pharmaceutical Co., 2503 S. Hanley Rd., St. Louis, Mo. 63111.
9-373do.....	2, 3, 4, and 5 mg.....	U.S.M. Pharmaceutical Corp., 1 Scarsdale Rd., Tuckahoe, N.Y. 10787.
9-391	Reserpine tablets, Reserpine capsules.	2, 3, 4, and 5 mg.....	Pfizer Laboratories, Division of Charles Pfizer & Co., Inc., 235 E. 42d St., New York, N.Y. 10017.
9-326	Rauken tablets.....	2 and 4 mg.....	Lemmon Pharmaceutical Co., Sellersville, Pa. 18670.
9-323	Reserpine tablets.....	4 mg.....	American Pharmaceutical Co., P.O. Box 448, Caspale, N.J. 07035.
9-327do.....	2, 3, 4, and 5 mg.....	Richlyn Laboratories, 3725 Cantor Ave., Philadelphia, Pa. 19131.
9-320do.....	3, 4, and 5 mg.....	Kelatum Laboratories, Inc., 26 Edison St., Amityville, N.Y. 11701.
9-771	Reserpine Alkaloid tablets.	2 mg.....	Intervex Pharmaceuticals, 2023 Schuette Rd., St. Louis, Mo. 63141.
9-820	Anguil tablets.....	4 and 5 mg.....	Dunn-Wilson Co., Division Mallinckrodt Inc., 24 and Mallinckrodt Sts., St. Louis, Mo. 63117.
9-852	R-E-S tablets.....	2 mg.....	Cole Pharmaceutical Co., Inc., P.O. Box 1404, St. Louis, Mo. 63178.
10-045	Vio-Serpine tablets.....	2 and 4 mg.....	Rowen Laboratories, Inc., Baudette, Minn. 56623.

Therefore, notice is given to the hold-
ers of the new drug applications and to
all other interested persons that the Di-
rector of the Bureau of Drugs proposes
to issue an order under section 305(e)
of the Federal Food, Drug, and Cosmetic
Act (21 U.S.C. 355(e)), withdrawing ap-
proval of those parts of the new drug
applications providing for the drug
products listed above and all amend-
ments and supplements thereto on the
ground that new evidence of clinical ex-
perience, not contained in the applica-
tions or not available to him until after
the applications were approved, evalu-
ated together with the evidence avail-
able when the applications were ap-
proved, reveals that the drug products
are not shown to be safe for use under
the conditions of use upon the basis of
which the applications were approved.

In addition to the holders of the new
drug applications specifically named
above, this notice of opportunity for
hearing applies to all persons who manu-
facture or distribute a drug product
which is identical, related, or similar to
a drug product named above, as defined
in 21 CFR 310.6. It is the responsibility
of every drug manufacturer or distribu-
tor to review this notice of opportuni-
ty for hearing to determine whether it
covers any drug product he manufac-
tures or distributes. Any person may re-
quest an opinion of the applicability of
this notice to a specific drug product he
manufactures or distributes that may be
identical, related, or similar to a drug
product named in this notice by writing
to the Food and Drug Administration,
Bureau of Drugs, Division of Drug
Labeling, Compliance (HFD-310),
5600 Fishers Lane, Rockville, MD 20852.

In addition to the ground for the pro-
posed withdrawal of approval stated
above, this notice of opportunity for
hearing encompasses all issues relating
to the legal status of the drug products

subject to it (including identical, related
or similar drug products as defined in 21
CFR 310.6) e.g., any contention that any
such product is not a new drug because
it is generally recognized as safe and
effective within the meaning of section
201(p) of the act or because it is ex-
empt from part or all of the new drug
provisions of the act pursuant to the ex-
emption for products marketed prior to
June 25, 1938, contained in section 201
(p) of the act, or pursuant to section
107(c) of the Drug Amendments of 1962
or for any other reason.

In accordance with the provisions of
section 305 of the act (21 U.S.C. 355) and
the regulations promulgated thereunder
(21 CFR Parts 310, 314), the applicant
and all other persons subject to this no-
tice pursuant to 21 CFR 310.6 are hereby
given an opportunity for a hearing to
show why approval of the new drug ap-
plications should not be withdrawn and
an opportunity to raise, for administra-
tive determination, all issues relating to
the legal status of a drug product name
above and of all identical, related, or
similar drug products.

If an applicant or any other perso
subject to this notice pursuant to 21 CFR
310.6 elects to avail himself of the op-
portunity for a hearing, he shall file (1)
on or before September 16, 1976, a writ-
ten notice of appearance and request for
hearing, and (2) on or before October 16,
1976, the data, information, and anal-
yses on which he relies to justify a hear-
ing, as specified in 21 CFR 314.200. An
other interested person may also sub-
mit comments on this notice. The pro-
cedures and requirements governing the
notice of opportunity for hearing, the
notice of appearance and request for
hearing, a submission of data, informa-
tion, and analyses to justify a hearing,
other comments, and a grant or denial
of hearing, are contained in 21 CFR
314.200.

failure of an applicant or any person subject to this notice pursuant to 21 CFR 310.6 to file timely written appearance and request for hearing as required by 21 CFR 314.200 constitutes an election by such person not to avail himself of the opportunity for a hearing concerning the action proposed with respect to such drug product and 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 NDA 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 it 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 will enter summary judgment against the persons(s) who requests the hearing, making findings and conclusions, denying a hearing.

Submissions pursuant to this notice shall be filed in quintuplicate with the Hearing Clerk, Food and Drug Administration, Rm. 4-55, 5600 Fishers Lane, Rockville, MD 20852.

All submissions pursuant to this notice, except for data and information prohibited from public disclosure pursuant to 21 U.S.C. 331(j) or 18 U.S.C. 1905, may be seen in the office of the Hearing Clerk during working hours, Monday through Friday.

This notice is issued under the Federal Food, Drug, and Cosmetic Act (sec. 505, 52 Stat. 1052-1053, as amended (21 U.S.C. 355)), and under authority delegated to the Director of the Bureau of Drugs (21 CFR 2.121).

Dated: August 9, 1976.

CARL M. LEVENTHAL,
Acting Director, Bureau of Drugs.

(FR Doc. 76-23781 Filed 8-10-76; 8:45 am)

Office of the Secretary

OFFICE OF HUMAN DEVELOPMENT, REHABILITATION SERVICES ADMINISTRATION

Statement of Organization, Functions and Delegations of Authority

Part I of the Statement of Organization, Functions, and Delegations of Authority for the Department of Health, Education, and Welfare is hereby amended by revising Subchapter IR94, as amended, Rehabilitation Services Administration (RSA), Office of Human Development, by the reorganization of activities in RSA to fully attain the pur-

poses mandated by the Rehabilitation Act Amendments of 1974 and, the deletion of program activities from RSA concerning Developmental Disabilities which is now newly established in OHD as a separate office, the Developmental Disabilities Office. Therefore, the statement published in the Federal Register on February 7, 1975, at 40 FR 5807, is hereby deleted in its entirety and a new statement is added to read as follows:

IR94.00 Mission. Provides leadership in the planning, development, administration and coordination of RSA/OHD programs which provide services for the handicapped and severely handicapped, including disabled social security applicants and beneficiaries, the blind, and welfare recipients who are handicapped or disabled. Establishes program goals and objectives, develops standards, program policies, criteria, guidelines, and professional direction and consultation to RSA staff in the administration of RSA programs. Directs RSA regional office staff in their responsibilities to provide guidance and leadership to State, local, and voluntary organizations; conducts research and demonstration and related activities for the purpose of developing methods, procedures, and devices which could promote and advance employment for handicapped individuals; directs and promotes a training program to improve the national manpower capability to work with handicapped or severely disabled individuals; maintains relationships with Federal, State, and local organizations which serve or have an impact upon the handicapped; evaluates progress in meeting the needs of the handicapped and takes affirmative action to promote improvement. Reviews and prepares legislative proposals to enhance overall program operations, develops and directs implementation of administrative and management actions affecting agency programs and services, and coordinates its activities and programs with other OHD organizations and operating components.

IR94.10 Organization. The Rehabilitation Services Administration is under the direction of a Commissioner who reports to the Assistant Secretary for Human Development. RSA consists of the following organizational components which report to the Commissioner:

- A. Executive Office of the Commissioner
- B. Office of the Assistant Commissioner for Planning, Budget, and Information Systems
- C. Office of the Assistant Commissioner for the Blind and Visually Handicapped
- D. Office of the Assistant Commissioner for Research and Evaluation
- E. Office of the Assistant Commissioner for Training and Facility Improvement
- F. Office of the Assistant Commissioner for Special and Cooperative Programs
- G. Office of the Assistant Commissioner for State Programs

A. **Executive Office of the Commissioner (EOC).** The EOC is under the supervision and direction of The Executive Assistant Commissioner (EAC) of RSA who reports to the RSA Commissioner. Supervises and directs the staffs responsible for the following activities: Regional office operations; public affairs;

administrative services; executive correspondence; programs for the deaf and communicatively disabled populations; medical consultation support services; and committee management.

The EOC serves as the principal staff arm to the Commissioner in exercising leadership and direction for the Commissioner on matters relating to the overall administration and management of RSA. Resolves critical issues and problems concerning executive management cross-cutting RSA programs. Coordinates the activities of appropriate RSA offices in all areas of responsibility. When necessary, coordinates these responsibilities with the Office of Human Development, the Department and other organizations inside and outside Government. Provides consultation and assistance to the RSA regional offices in those areas of responsibility affecting regional office operations, which are of interest to the regions, or which require their involvement or participation.

B. **Office of Assistant Commissioner for Planning, Budget, and Information Systems (PBIS).** Provides leadership and direction, under the Commissioner, in overall program and operational planning, programs and administrative budgeting and financial services, provision of information needs, data analysis, project grants and contracts policy and technical assistance, legislation and policy development, and coordination of these activities as they interlock with other offices. Provides consultation and technical assistance to the RSA regional office staff as it relates to these activities. The Office consists of: Division of Planning and Budgeting, Division of Information Systems and Data Analysis, Legislation and Policy Development Staff, and Grants and Contracts Policy and Technical Assistance Staff.

1. **Division of Planning and Budgeting.** This Division is composed of two branches, one for planning and one for budgeting. In the area of planning, the Division provides direction and guidance to RSA in the development of plans and operational objectives to implement plans and programs for the handicapped and to be responsive to DHEW and OHD goals. Provides leadership and direction in the establishment of priority forward and short-range objectives and determines staff and other resources and responsibilities for their achievement. Works closely with Research and Evaluation, other program offices and Regional Offices to develop measurable goals and to recommend alternative plans as conditions change or goals are readjusted. Identifies trends and problems in planning and program redirection. Recommends program improvement, technical assistance and strategies to evolve new methodologies and approaches to improve the administrative management of programs for handicapped individuals. In terms of S&E and program budget matters, the Division serves as principal support arm to the Commissioner in the area of budgetary services and assistance, and maintains formal liaison with the OHD Budget Office. With technical

In the FEDERAL REGISTER of April 3, 1976 (41 FR 15029), the FDA proposed to prohibit the continued use of chloroform as an ingredient in human drug and cosmetic products because of a National Cancer Institute report that chloroform induces cancer in animals. In a companion notice published in the same issue of the FEDERAL REGISTER (41 FR 15029), FDA proposed to prohibit the use of chloroform in human food. Those proposals noted that chloroform was used as an active ingredient in drugs, as an ingredient in cosmetics, and as a component of food packaging. The drug and cosmetic final regulations were published in the FEDERAL REGISTER of June 29, 1976 (41 FR 26842).

The comments responding to the proposal to prohibit chloroform in drugs and cosmetics indicated that chloroform could become a component of a drug either directly as an added ingredient (direct ingredient) or indirectly as an incidental ingredient (indirect ingredient). The presence of chloroform as an indirect ingredient in a drug can result from its use as a solvent, an extractant, or a starting material in the manufacture of ingredients used in finished drug products or from migration to the finished product from packaging material in which it may be used. Some of the comments stated that the total removal of the small quantities of chloroform which may be present as indirect ingredients is technically impracticable.

The drug and cosmetic final regulations prohibiting chloroform as a direct ingredient did not prohibit the presence of residual chloroform in drugs and cosmetics if it is an indirect ingredient. As the Commissioner explained in the preamble to the final regulations (41 FR 26842), further information is needed before any final decision can be made about the regulation of chloroform as an indirect ingredient of drugs and cosmetics.

The National Cancer Institute (NCI) is in the process of testing various chemicals, including several halocarbons, to determine whether they are carcinogenic. The following halocarbons, as defined in this notice, are being studied by the NCI:

1,2-Dibromoethane
1,1-Dichloroethane
1,2-Dichloroethane
Hexachloroethane
1,1,2,2-Tetrachloroethane
1,1,1-Trichloroethane
1,1,2-Trichloroethane
Tetrachloroethylene
Trichloroethane
1,2-Dibromo-3-chloropropane
3-Chloropropane
Chlorobenzene
o-Dichlorobenzene
p-Dichlorobenzene
1,1-Dichloroethylene
Methylene chloride
Perchloroethylene
Benzene
trans, 1,2-Dichloroethylene

It is possible that some of these as well as other halocarbons may be shown to

be carcinogens. The Commissioner is therefore interested in the uses of the above-named halocarbons and all other halocarbons (as defined) that may be present in human food, drugs, biological products, cosmetics, animal feed, animal drugs, medical devices, and packaging for these products. He is particularly interested in information about halocarbons that might occur as impurities in or by-products of the ingredients used in the manufacture of FDA-regulated products.

The Commissioner does not, at this time, have sufficient information about the products that contain halocarbons as direct and indirect ingredients or those halocarbons that are used as starting materials, solvents, or extractants in making finished products regulated by FDA. He also lacks adequate information about the extent to which residual amounts of halocarbons are present in finished products because of migration from packaging to finished products regulated by FDA. The Commissioner believes that many halocarbons are widely used in the manufacture of products regulated by FDA. He therefore is seeking technical data and other information about all halocarbons that could be present in FDA-regulated products to assist him in the determination of the health hazard, if it is determined that other halocarbons induce cancer. Accordingly, the Commissioner has listed several items about which he needs more information, and he requests that interested persons respond with relevant information.

The Commissioner desires to receive from any interested persons information with respect to the following matters about the use of chloroform and other halocarbons in human food, drugs, biological products, cosmetics, animal feed, animal drugs, medical devices, and packaging for these products:

1. *Direct ingredients.* The names of products containing halocarbons as a direct ingredient and the names and concentrations of the halocarbons present in these products.
2. *Indirect ingredients.* a. The names of any ingredients used in FDA-regulated products in which halocarbons are used as solvents, extractants, and starting materials.
b. The names of any products containing halocarbons as an indirect ingredient (including solvents, extractants and starting materials).
c. The names of the halocarbons present in these products as indirect ingredients (including solvents, extractants, and starting materials).
d. The concentration of halocarbons as indirect ingredients in finished FDA-regulated products.

3. *Packaging.* An identification of types of packages or packaging materials, including adhesives, for FDA-regulated products in which halocarbons are used at any stage of manufacture. The response should identify the product for which the package or packaging material is used and the residual amount of halocarbons present in the finished products

as a result of migration from the package or packaging material.

4. *Methods.* A statement of how the concentration of halocarbons as indirect ingredients, including packaging residues, in these products was determined or estimated in responding to items 2.d. and 3 above, and the methods of analysis used in detecting and verifying the concentrations of halocarbons in these products.

5. *Substitutes.* a. The names of chemicals that could be used as substitutes for halocarbons in FDA-regulated products in which halocarbons are a direct or indirect ingredient.

b. The feasibility of replacing products now containing halocarbons as direct or indirect ingredients with products that would not contain halocarbons.

c. The feasibility of removing halocarbons from products that contain them as indirect ingredients.

6. *Adverse effects.* a. Information on the carcinogenic effects of halocarbons obtained from toxicological studies published in the scientific literature.

b. Information on other effects of halocarbons obtained from toxicological studies not published in the scientific literature.

Interested persons are requested to submit relevant information by October 26, 1977 to the Hearing Clerk, Food and Drug Administration, Rm. 4-65, 56 Fishers Lane, Rockville, MD 20857. Submissions should be identified with the Hearing Clerk's docket number found in brackets in the heading of this notice. Received information may be seen in the above office between the hours of 9 a.m. and 4 p.m., Monday through Friday.

Dated: April 25, 1977.

SHERWIN GARDNER,
Acting Commissioner
of Food and Drugs

(FR Doc. 77-12230 Filed 4-28-77; 45 am)

[Docket No. 76N-0154; DESI 2357]

ORAL RESERPINE DOSAGE FORMS OF GREATER THAN 1 MILLIGRAM STRENGTH

Withdrawal of Approval of Pertinent Parts of New Drug Applications

AGENCY: Food and Drug Administration, HEW.

ACTION: Notice.

SUMMARY: This notice withdraws approval of pertinent parts of new drug applications for oral reserpine dose forms of greater than 1 milligram strength on basis of safety.

DATES: Withdrawal is effective May 9, 1977.

ADDRESSES: Requests for opinion on the applicability of this notice to a specific product should be directed to:

Division of Drug Labeling Compliance (IND-210), Bureau of Drugs, Food and Drug Administration, Department of Health, Education, and Welfare, 5030 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT:

William R. Durbin, Bureau of Drugs (HFD-32), Food and Drug Administration, Department of Health, Education, and Welfare, 5600 Fishers Lane, Rockville, MD 20857, 301-443-3650.

SUPPLEMENTARY INFORMATION: In a notice of opportunity for hearing published in the Federal Register of August 17, 1976 (41 FR 24805), the Director of the Bureau of Drugs proposed to withdraw approval of the oral reserpine drug products listed below, which contain more than 1 milligram of reserpine per dosage unit. He announced his conclusion that, although reserpine is effective for use in hypertension and for psychiatric disorders, in potencies of greater than 1 milligram there is lack of evidence of safety for those uses. In view of this, and the availability of reserpine products in potencies of 0.1 milligram to 1 milligram as well as other products used for the same indications which have a wider margin of safety, the Director concluded that the benefit-to-risk considerations associated with oral dosage forms containing more than 1 milligram of reserpine did not justify their continued marketing. No person requested a hearing.

- NDA 9-115: Serpasil tablets; 2 and 4 mg; Ciba Pharmaceutical Co., Division of Ciba-Geigy Corp., 556 Morris Ave., Summit, NJ 07901.
- NDA 9-347: Reserpoid tablets; 4 mg; The Upjohn Co., 7171 Portage Rd., Kalamazoo, MI 49002.
- NDA 9-357: Rau-Sed tablets; 2 and 4 mg; E. R. Squibb & Sons, Inc., P.O. Box 4000, Princeton, NJ 08540.
- NDA 9-376: Sundril tablets; 5 mg; Eli Lilly & Co., Box 618, Indianapolis, IN 46206.
- NDA 9-391: Serpanray tablets; 2, 3, 4, and 5 mg; Parray, Division of Ormont Drugs & Chemicals, Inc., P.O. Box 150, Englewood, NJ 07631.
- NDA 9-573: Reserpine tablets; 2, 3, 4, and 5 mg; Keith-Victor Pharmaceutical Co., 2503 S. Hanley Rd., St. Louis, MO 63114.
- NDA 9-573: Reserpine tablets; 2, 3, 4, and 5 mg; U.S.V. Pharmaceutical Corp., 1 Searsdale Rd., Tuckahoe, NY 10707.
- NDA 9-591: Reserpine tablets and capsules; 2, 3, 4, and 5 mg; Pizer Laboratories, Division of Charles Pfizer & Co., Inc., 253 E. 42d St., NY 10017.
- NDA 9-596: Raulen tablets; 2 and 4 mg; Lemmon Pharmacal Co., Sellersville, PA 18060.
- NDA 9-623: Reserpine tablets; 4 mg; American Pharmaceutical Co., P.O. Box 448, Passaic, NJ 07055.
- NDA 9-627: Reserpine tablets; 2, 3, 4, and 5 mg; Richlyn Laboratories, 3735 Castor Ave., Philadelphia, PA 19124.
- NDA 9-771: Reserpine Alkaloid tablets; 2 mg; Invorex Pharmaceuticals, 2503 Schuettez Rd., St. Louis, MO 63141.
- NDA 9-829: Anquil tablets; 4 and 5 mg; Dumas-Wilson Co., Division Mallinckrodt, Inc., 2d and Mallinckrodt Sts., St. Louis, MO 63147.
- NDA 9-882: R-E-S tablets; 2 mg; Cole Pharmaceutical Co., Inc., P.O. Box 14104, St. Louis, MO 63178.
- NDA 10-942: Tib-Serpine tablets; 2 and 4 mg; Roush Laboratories, Inc., Eudawette, MD 54923.

These parts of the above new drug applications providing for reserpine in po-

tencies of 1 milligram or less are not affected by this notice.

NDA 9-629: Ketchum Laboratories, Inc., 25 Edison St., Amherst, NY 11701; formerly Success Chemical Co., was listed in error in the August 17, 1976 notice as approval of the products had already been withdrawn on July 24, 1970 (35 FR 11029).

All identical, related, and similar drug products, as defined in 21 CFR 310.5, not the subject of an approved new drug application, are covered by the applications reviewed and are subject to this notice. Any person who wishes to determine whether a specific product is covered by this notice should write the Food and Drug Administration, Division of Drug Labeling Compliance (HFD-319), Bureau of Drugs. Neither the holders of the applications nor any other person filed a written appearance of election as provided by said notice. The failure to file such an appearance constitutes election by such persons not to avail themselves of the opportunity for a hearing.

The Director of the Bureau of Drugs, under the Federal Food Drug, and Cosmetic Act (sec. 505, 52 Stat. 1053, as amended (21 U.S.C. 355)), and under authority delegated to him (21 CFR 5.82) (recodification published in the Federal Register of March 22, 1977 (42 FR 13553)), finds that new evidence, not contained in the applications or not available until after the applications were approved, evaluated together with the evidence available when the applications were approved, reveals that the drug products are not shown to be safe for use under the conditions of use upon the basis of which the applications were approved.

Therefore, pursuant to the foregoing finding, approval of those parts of the new drug applications providing for the drug products listed above and all amendments and supplements applying thereto is withdrawn effective ~~May 9, 1977~~ ^{May 9, 1977}.

Shipment in interstate commerce of the above listed products or of any identical, related, or similar product, not the subject of an approved new drug application, will then be unlawful.

Dated: April 19, 1977.

J. RICHARD CROUT,
Director, Bureau of Drugs.

[FR Doc. 77-12301 Filed 4-29-77; 9:45 am]

[Docket No. 77N-3147]

PHENFORMIN

Public Hearing

AGENCY: Food and Drug Administration

ACTION: Notice of public hearing.

SUMMARY: The Commissioner of Food and Drugs announces that a public hearing will be held on May 10, 1977 to receive information and views from interested persons on the issue of whether phenformin, as currently marketed, constitutes such a serious hazard that in light of the delay anticipated in the administrative proceedings to withdraw

approval of the new drug application for the compound, the Secretary of Health, Education, and Welfare should be advised by the Food and Drug Administration (FDA) to invoke the "imminent hazard" clause of section 505(e) of the Federal Food, Drug, and Cosmetic Act (the act) to remove the drug from the market immediately.

DATES: The public hearing will be held on May 10, 1977 at 9 a.m. A written notice of participation must be filed by May 10, 1977.

ADDRESSES: Written notice of participation should be sent to the Hearings Clerk (HFC-20), Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT:

Julian A. Santangelo, Bureau of Drugs (HFD-130), Food and Drug Administration, Department of Health, Education, and Welfare, 5600 Fishers Lane, Rockville, MD 20857, 301-443-3499

SUPPLEMENTARY INFORMATION:

On April 22, 1977, the Secretary of Health, Education, and Welfare received a petition from the Health Research Group, Washington, D.C., that he immediately suspend approval of the new drug applications for phenformin under section 505(e) of the act on the ground that the continued marketing of a drug represents an imminent hazard to the public health. The petitioner cites as the reasons for this request the fact that phenformin can produce a fatal reaction known as lactic acidosis in some patients, that the number of cases of lactic acidosis reported to FDA is continued to increase in the past months, and that continued use of a drug will result in additional deaths and therefore constitutes an imminent hazard.

The Secretary has asked FDA to advise him promptly on the action he should be taken in response to the petition. The Commissioner has, in turn, decided to solicit public comment whether the imminent hazard provision of the law can and properly should be invoked in this case before preparing advice to the Secretary. A decision to invoke this provision of the law would result in immediate withdrawal of a drug from the market, with resulting impact on the diabetic patients taking the drug, their physicians, the involved manufacturers. The Commissioner believes that these and other interested parties should have an opportunity to comment to the agency on the petition before a final recommendation to the Secretary is formulated. Accordingly, a public hearing will be held on expedited basis before the Director of the Bureau of Drugs to provide an opportunity for such comment. The Commissioner emphasizes that the duty for the hearing is whether the Commission to the Secretary that invokes in this case the imminent hazard provision of section 505(e) of the act.

I. Phenformin is an oral hypoglycemic drug used in the treatment of patients

26468

[Docket No. 78N-3154]

**ORAL RESERPINE DOSAGE FORMS OF
GREATER THAN 1 MILLIGRAM STRENGTH**

**Withdrawal of Approval of Pertinent Parts
of New Drug Applications**

Correction

In FR Doc. 77-12301 appearing at page 21844 in the issue of Friday, April 29, 1977, on page 21845 in the second column, the third full paragraph, the date in the last line should read "May 9, 1977".

FEDERAL REGISTER, VOL. 42, NO. 100—TUESDAY, MAY 24, 1977