

ular business hours, Monday through Friday.

This notice is issued pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (sec. 505, 52 Stat. 1052-53, as amended; 21 U.S.C. 355) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 2.120).

Dated: August 17, 1972.

SAM D. FINE,
Associate Commissioner
for Compliance.

[FR Doc.72-14450 Filed 8-24-72; 8:48 am]

PAREGORIC

Notice Placing Certain Paregoric and Other Opium-Containing Preparations for Veterinary Use on Prescription Dispensing Basis

An order published in the FEDERAL REGISTER of April 4, 1972 (37 F.R. 6734), provided for removal of the exemption for certain paregoric and other opium-containing preparations from the prescription dispensing requirements of section 503(b)(1)(A) of the Federal Food, Drug, and Cosmetic Act under § 165.5(a)(1) of the habit-forming drug regulations (21 CFR 165.5(a)(1)).

This action was taken based upon potential for abuse of the drug by addicts who process it into a form for intravenous administration and was based upon a consideration of a recommendation from the Bureau of Narcotics and Dangerous Drugs, Department of Justice.

Commissioner of Food and Drugs provides that, consistent with the aim of placing such drug under prescription dispensing for use in man as provided in section 503(b)(1)(A) of the act, its veterinary use should likewise be on a prescription basis under section 502(f)(1) of the act.

Therefore, paregoric and other preparations containing more than 100 milligrams of opium per 100 milliliters or per 100 grams and intended for veterinary use shall be labeled with the statement "Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian."

This notice is issued pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (secs. 502(f), 701(a), 52 Stat. 1051 and 1055; 21 U.S.C. 352(f), 371(a)) and under authority delegated to the Commissioner (21 CFR 2.120).

Dated: August 17, 1972.

SAM D. FINE,
Associate Commissioner
for Compliance.

[FR Doc.72-14451 Filed 8-24-72; 8:48 am]

[DESI 11562; Docket No. FDC-D-511; NDA 11-562]

PFIZER LABORATORIES

Carbetapentane Citrate Gel; Notice of Opportunity for Hearing on Proposal To Withdraw Approval of New-Drug Application

In an announcement (DESI 11562) published in the FEDERAL REGISTER of

July 17, 1971 (36 F.R. 13281), the Commissioner of Food and Drugs announced his conclusions pursuant to the evaluation of a report received from the National Academy of Sciences-National Research Council, Drug Efficacy Study Group on Candette Cough Jel, containing carbetapentane citrate. The announcement stated that the risks involved in its use outweigh any benefits that might be derived from such use and it is regarded as unsafe for its recommended use because inexact methods of determining dosage are potentially dangerous, particularly in the care of children, and that the Commissioner of Food and Drugs intended to initiate proceedings to withdraw approval of the new-drug application for the drug. Interested persons were invited to submit any pertinent data bearing on the proposal within 30 days following publication of the announcement. No data have been received.

Therefore, notice is given to Pfizer Laboratories Division, Pfizer, Inc., 235 East 42d Street, New York, N.Y. 10017, holder of NDA 11-562 for Candette Cough Jel and to any interested person who may be adversely affected, that the Commissioner 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 said application and all amendments and supplements thereto on the grounds that new evidence of clinical experience, not contained in the application or not available until after the application was approved, evaluated together with the evidence available when the application was approved, reveals that the drug is not shown to be safe under the conditions of use upon the basis of which the application was approved.

In accordance with the provisions of section 505 of the Act (21 U.S.C. 355) and the regulations promulgated thereunder (21 CFR Part 130), the Commissioner will give the applicant, and any interested person who would be adversely affected by an order withdrawing such approval, an opportunity for a hearing to show why approval of the new-drug application should not be withdrawn. Any related drug for human use, not the subject of an approved new-drug application, may be affected by this action.

Within 30 days after publication hereof in the FEDERAL REGISTER, such persons are required to file with the Hearing Clerk, Department of Health, Education, and Welfare, Room 6-88, 5600 Fishers Lane, Rockville, Md. 20852, a written appearance electing whether:

1. To avail themselves of the opportunity for a hearing; or
2. Not to avail themselves of the opportunity for a hearing.

If such persons elect not to avail themselves of the opportunity for a hearing, the Commissioner without further notice will enter a final order withdrawing approval of the new-drug application. Failure of such persons to file a written appearance of election within said 30 days will be construed as an election by such persons not to avail themselves of the opportunity for a hearing.

The hearing contemplated by this notice will be open to the public except that any portion of the hearing that concerns a method or process the Commissioner finds entitled to protection as a trade secret will not be open to the public, unless the respondent specifies otherwise in his appearance.

If such persons elect to avail themselves of the opportunity for a hearing, they must file, within 30 days after publication of this notice in the FEDERAL REGISTER, a written appearance requesting the hearing, giving the reasons why approval of the new-drug application should not be withdrawn, together with a well organized and full factual analysis of the clinical and other investigational data they are prepared to prove in support of their opposition. A request for a hearing may not rest upon mere allegations or denials, but must set forth specific facts showing that a genuine and substantial issue of fact requires a hearing. When it clearly appears from the data in the application and from the reasons and factual analysis in the request for a hearing that no genuine and substantial issue of fact precludes the withdrawal of approval of the application, the Commissioner will enter an order on these data, making findings and conclusions on such data.

If a hearing is requested and justified by the response to this notice, the issues will be defined, a hearing examiner will be named, and he shall issue, as soon as practicable after the expiration of such 30 days, a written notice of the time and place at which the hearing will commence (35 F.R. 7250, May 8, 1970; 35 F.R. 16631, October 7, 1970).

Received requests for a hearing and/or elections not to request a hearing, may be seen in the office of the Hearing Clerk (address given above) during regular business hours, Monday through Friday.

This notice is issued pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (sec. 505, 52 Stat. 1052-53, as amended; 21 U.S.C. 355) and under the authority delegated to the Commissioner of Food and Drugs (21 CFR 2.120).

Dated: August 17, 1972.

SAM D. FINE,
Associate Commissioner
for Compliance.

[FR Doc.72-14445 Filed 8-24-72; 8:48 am]

[Docket No. FDC-D-197; NDA 5025]

PROTAMIDE

Final Order on Objections and Request for a Hearing Regarding Withdrawal of Approval of New-Drug Application

In the FEDERAL REGISTER of March 27, 1969 (34 F.R. 5753), the Food and Drug Administration announced its evaluation of a report received from the National Academy of Sciences-National Research Council, Drug Efficacy Study Group, on the preparation Protamide (colloidal solution of denatured proteolytic enzyme) Injection; Sherman Laboratories, 5031 Grandy Avenue, Detroit, Mich. 48221

(NDA 5-025; DESI 5025). The present holder of the new-drug application is Cooper Laboratories, Inc., 2900 North 17th Street, Philadelphia, Pa. 19132.

The announcement stated the conclusion of the Food and Drug Administration that there is a lack of substantial evidence of effectiveness of the drug for the indications neuritis, herpes zoster, and tabes dorsalis. The holder of the new-drug application was requested to submit, within 60 days of the date of publication of the announcement in the FEDERAL REGISTER, a supplement to its new-drug application to provide for labeling which deletes those indications for which the drug has been classified as lacking substantial evidence of effectiveness. No person or firm, including Cooper Laboratories, Inc., has submitted such a supplement.

The announcement further stated that the drug is regarded as possibly effective for the indication ophthalmic herpes zoster. The announcement allowed 6 months from the date of publication of the announcement in the FEDERAL REGISTER for the holder of the new-drug application and any person marketing the drug without approval to obtain and submit in a supplemental or original new-drug application, data to provide substantial evidence of effectiveness of the drug for use in ophthalmic herpes zoster. No supplemental or original new-drug application has been received pursuant to the announcement.

On December 22, 1969, the holder of the new-drug application was notified that the Commissioner of Food and Drugs intended to initiate proceedings to withdraw approval of the new-drug application.

A notice was thereafter published in the FEDERAL REGISTER of July 17, 1970 (35 F.R. 11535), which provided an opportunity for hearing on withdrawal of the new-drug application for Protamide (NDA 5-025). Thirty days were allowed for filing a written appearance requesting a hearing by any interested person, giving the reasons why approval of the new-drug application should not be withdrawn, together with a well organized and full factual analysis of the clinical and other investigational data they were prepared to prove in support thereof.

A request for a hearing was submitted by Cooper Laboratories, Inc., on August 28, 1970. Thereafter, there was an extensive exchange of letters and numerous conferences were held between Cooper Laboratories, Inc., and the FDA, in which Cooper Laboratories, Inc., explored methods of establishing the effectiveness of Protamide for its labeled uses. In addition, Cooper Laboratories, Inc., has submitted to the FDA a notice of claimed investigational exemption for a new drug for a drug called Protamide which is different in composition from the Protamide subject to NDA 5-025 and this order.

The medical presentation of Cooper Laboratories, Inc., has been considered, and the Commissioner of Food and Drugs concludes that there is no genuine and

substantial issue of fact requiring a hearing and that the legal arguments offered are insubstantial, all as explained in more detail below.

I. *The drug.* Protamide Injection. This drug is a colloidal solution of denatured proteolytic enzyme provided in 1.3-cc. ampules for intramuscular injection.

II. *Recommended uses.* This product is recommended for use in treatment of neuritis, herpes zoster, and ophthalmic herpes zoster.

The recommended treatment schedule for the product varies with the use for which the product is recommended, and includes additional injections "as indicated" beyond the original course of treatment.

III. *The data to support claims of effectiveness.* In response to the notice, Cooper Laboratories, Inc., has submitted affidavits and letters from physicians and literature reprints.

A. *The affidavits.* Drs. Geiss, Foldes, Schaal, and Kessler are physicians who have used and prescribed Protamide for herpes zoster and have found it to be effective for this condition. Dr. Foldes also uses and prescribes it in treatment of tabes dorsalis, a use not recommended on the drug's labeling. Dr. McHenry is a physician who has used and prescribed Protamide in the treatment of neuritis secondary to herpes zoster, occipital neuritis, and inflammation of the sciatic nerve.

None of these affidavits relates to the labeling claim of ophthalmic herpes zoster. These opinions are based on observation of patients treated with Protamide, and compared with patients treated with other drugs available to treat herpes zoster.

None of these physicians makes any reference to any adequate and well-controlled clinical investigations having been conducted to support their opinions. Indeed, Dr. Foldes states that he believes that it is possible to conduct a study of the efficacy of Protamide and he would like to see such a study done. The only other reference to adequate and well-controlled studies in these affidavits is Dr. Kessler's statement that it is impossible to design a controlled study which could be completed in a reasonable time. None of these physicians states a controlled study cannot be done.

B. *Physicians' statements.* Sixteen testimonial statements have been submitted by 15 physicians who use Protamide in their practice to treat herpes zoster and, in a few cases, neuritis, as well as other conditions for which Protamide is not labeled, including pharyngitis, vaginitis, chickenpox, sore mouth, and pruritis.

Dr. Mason reports uniformly good results in treating ophthalmic herpes zoster with Protamide, analgesics, and antipruritics. Both Dr. Mason and Dr. Kent state that Protamide works better to relieve neuritis when administered with B-Complex and B-12. No reference is made to any adequate and well-controlled clinical investigations having been conducted to support the opinions in any of these testimonial statements.

No pre- and post-treatment clinical data for evaluation of the safety and efficacy of Protamide is presented in any of these statements. The clinical cases referred to in large numbers in the testimonials are not documented with actual patient data.

C. *Published studies.* Reprints of nine published articles have been submitted to establish that Protamide is effective: Seven by American physicians and two by foreign investigators. None of these constitute substantial evidence of efficacy.

1. Russell T. Costello, M.D., "A New Treatment For The 'Lightning Pains' Of Tabes Dorsalis," Urologic and Cutaneous Review, Vol. 51, pp. 260-263, 1947, does not relate to the conditions for which Protamide is recommended; namely, the treatment of neuritis, herpes zoster, or ophthalmic herpes zoster, but relates to tabes dorsalis, a condition for which the drug is no longer recommended in its labeling. Even if tabes dorsalis was a recommended use, this does not constitute an adequate and well-controlled clinical investigation. No controls were employed, the number of treatments varied from four to 101 injections and some of the patients were treated with a formula of the drug no longer used even in 1947 when the article was written.

2. Frank C. Combs, M.D., and Orlando Canizares, M.D., "Herpes Zoster: Its Treatment With Protamide," N.Y. St. J. of Medicine, Mar. 15, 1952, pp. 706-8. This is a report of the treatment with Protamide of 50 patients with active herpes zoster with lesions of varied distribution and degree of severity. The authors classified the results as 22 percent unsatisfactory and 78 percent excellent or satisfactory and state that no untoward reactions or evidence of toxicity were noted. This study is not an adequate and well-controlled study, even though it included six patients who were given saline placebos to which they failed to respond, since, among other reasons, there was no method of selecting patients utilized to insure that subjects were suitable for purposes of the study, subjects were not assigned in such a way as to minimize bias, and comparability of pertinent variables in test and control groups was not assured. Ten of the 50 patients had herpes zoster frontalis (which is not the ophthalmic herpes zoster for which Protamide is recommended) in whom the eyes were affected in one way or another. The regimen used varied from an injection every 6 hours to one injection every 2 or 3 days, for a total of one to 16 injections over a period of 2 to 25 days. However, there was no correlation between the numbers of injections and days of treatment.

Furthermore, there was neither an explanation of the method of observation and recording of results, nor a comparison of the results of treatment or diagnosis with a control in such a fashion as to permit a quantitative evaluation. Finally, there was no summary of the methods of analysis and evaluation.

of data derived from the study, including statistical methods.

Richard I. Smith, M.D., "Treatment of Neuritis With Protamide," *New York Medicine*, Aug. 20, 1952, pp. 16-19. One hundred twenty-five patients with various types of neuritis were treated with Protamide over a period of 6 months. The author considered 21 of the patients who had had a preceding respiratory disease or virus infection within 3 weeks of the onset of the neuritis to be "controls," but since they were also treated with Protamide they were not, in fact, controls as contemplated by 21 CFR 130.12(a)(5)(ii)(a)(4). The basic treatment was a 5-day course of 1.3 cc. (1 ampule) of Protamide injected intramuscularly daily. Where all pain was relieved, treatment was discontinued. Where some degree of pain persisted, treatment was continued for another 5 days. In two cases of facial neuritis, treatment was continued for 20 days. Eighty-four of the 104 "noncontrol" patients had complete relief of pain with five or 10 daily injections. The 21 "control" patients failed to respond to 10 or 20 daily injections. The author concluded that Protamide was a safe drug when administered intramuscularly for treatment of neuritis, but no conclusion as to the efficacy of the drug was reached.

4. H. W. Lehrer, M.D., H. G. Lehrer, M.D., and D. R. Lehrer, M.D., "Clinical Evaluation of Protamide in Sensory Nerve Root Inflammations and Allied Conditions," *Northwest Medicine*, Nov. 1955, pp. 1249-52. In this report, the authors review 109 cases of herpes zoster and 313 cases of neuritic pain that they had treated with Protamide in their practice over a 5-year period. The regimen and duration of treatment varied from patient to patient. The authors made no attempt to conduct an adequate and well-controlled investigation and do not represent their report to be one. Of all the patients treated with Protamide, only one from each group failed to respond to therapy. The authors noted that treatment soon after onset of the symptoms gave the most dramatic results. This report is a testimonial of the authors for Protamide. No cases of ophthalmic herpes zoster were reported.

5. William C. Marsh, M.D., "Treatment of Herpes Zoster With Protamide," *U.S. Armed Forces Medical J.*, 1:1045, Set., 1950. In this report, 31 cases of herpes zoster were treated with Protamide; good to excellent results were obtained in 28. No controls were used in the study on the author's premise that thousands of intramuscular injections of other drugs given to patients with herpes zoster in the past, with no appreciable benefit, would adequately serve as a control. This historical control does not comport with the historical control referred to at 21 CFR 130.12(a)(5)(ii)(a)(4)(iv) since the conditions for which Protamide is recommended have neither high or predictable mortality rates, nor are the case histories of any "controls" adequately documented with comparisons to patients or populations without treatment to provide for a quantitative

comparison between controls and the subjects of Marsh's study. Duration of treatment varied from 2 to 35 days while the number of injections varied from 3 to 22. There was no correlation between the length of treatment and the number of injections. The report states that one injection was administered daily although this conflicts with the author's tabular results. No cases of ophthalmic herpes zoster were reported.

6. Arthur G. Baker, M.D., "Use of Protamide In Treatment of Herpes Zoster," *The Pennsylvania Medical Journal*, May, 1960, Vol. 63, pp. 697-8. Thirty-four patients with herpes zoster were treated with Protamide while 10 "control" patients with herpes zoster were treated with Vitamin B₁₂. Protamide injections were administered intramuscularly at 12 to 24 hour intervals on the first two days and thereafter one injection daily on an alternating day basis depending on the severity of symptoms. The duration of treatment varied from 5 to 16 days; 1,000 micrograms of Vitamin B₁₂ were administered daily for 1 to 2 weeks. No other medications were used with either drug, except for some sedation in a few patients. Good to excellent results were stated to have been obtained in 94 percent of the patients treated with Protamide while the results obtained with Vitamin B₁₂ were reported as unsatisfactory. This study is not well controlled since the size of the control group is statistically inadequate and there is no raw data provided upon which a comparison of the test and control groups can be made. No cases of ophthalmic herpes zoster were reported.

7. Gordon W. Xander, M.D., "The Problem of Post-Herpetic Neuralgia," *Western Medicine*, Sept. 1960, pp. 14-15. Dr. Xander's report covers his observations of 60 cases of herpes zoster. One injection of Protamide was administered daily for 3 days and on alternate days for the next 5 to 7 days. In most cases, treatment did not exceed 10 injections. No correlation was drawn between the number of injections and the length of treatment. No cases of herpes zoster ophthalmic were reported. No reference was made to any adequate and well-controlled studies having been conducted by Dr. Xander or anyone else on the efficacy of Protamide in the treatment of herpes zoster.

8. C. A. P. Boundy and J. A. C. Bamford, "Treatment of Herpes Zoster With Protamide," *The Medical Journal of Australia*, Mar. 30, 1968, pp. 528-531. This is a report of a well-controlled study conducted over a period of 4 years with the cooperation of Sherman Laboratories (Cooper Laboratories, Inc.) to measure the effect, if any, of Protamide on the severity of pain which is characteristic of herpes zoster and to investigate its effect on postherpetic pain. The authors stated that the conclusions stated in the articles by Marsh, Lehrer, Xander, Combs, Baker, and Smith, cited above, were simply testimonials for Protamide.

Boundy and Bamford's study included 138 patients suffering from herpes zoster.

Sixty-eight were treated with Protamide while 69 were treated with a placebo supplied by Sherman Laboratories (Cooper Laboratories, Inc.). The size of this study appears to be acceptable from a statistical point of view. The authors concluded that "there were no distinguishable differences between the effects of the dummy and of 'Protamide'". They further concluded that the only value of Protamide in treating herpes zoster is its placebo effect. Finally they summarize their study: "There is as yet no specific treatment for herpes zoster which has been proven successful. 'Protamide' has been used extensively over the last 20 years, but in spite of the claims of the makers, there is no evidence of its therapeutic value." None of the patients treated suffered from ophthalmic herpes zoster.

9. G. S. Sforzolini, M.D., "The Treatment of Ophthalmic Herpes Zoster With Protamide," *A.M.A. Archives of Ophthalmology*, Sept. 1959, pp. 381-385. The author, an Italian doctor, reports on his experiences with the use of Protamide in 15 patients with ophthalmic herpes zoster. He concluded that Protamide proved to be of unquestionable value for treatment of ophthalmic herpes as the pain was alleviated and the lesions favorably influenced. Moreover, he found that severity of complications such as keratitis and conjunctivitis were reduced. The author found that there was no significant relationship between the degree of response obtained and the promptness of treatment after the onset of the disease. He concluded that "Different hypotheses have been advanced to explain the mechanism of action of the drug (Protamide), but none of these is based on an element of certainty." There were no controls used in treating his patients. The article is substantially a testimonial for Protamide.

These studies are not adequate and, with the exception of the Boundy study, are not well controlled in accordance with the criteria set forth at 21 CFR 130.12(a)(5). No plan or protocol for any of the studies, or the report of the results of the effectiveness of Protamide in any of the studies, with the exception of the Boundy study, provide adequate assurance that the subjects were always suitable for the purposes of the study, or that the subjects were assigned to test groups in such a way as to minimize bias, or that comparability of pertinent variables in test and control groups were assured. Furthermore, these studies do not adequately explain the methods of observation of subjects and recording of results, and, with the exception of the Boundy study, fail to adequately provide a comparison of the results of treatment or diagnosis with a control in such a fashion as to permit quantitative evaluation. No controls were used in the Smith, Lehrers, Sforzolini, or Xander studies. The historical "controls" in the Marsh paper, the saline placebo "controls" in the Combs study, and the Vitamin B₁₂ "controls" in the Baker study do not constitute proper controls for reasons pointed out above. Finally, the sum-

maries of the methods of analysis and evaluation of data derived from the studies, including appropriate statistical methods, especially in the Lehrers, Baker, and Xander studies, are inadequate. The most that can be said for these studies is that they are clinical impressions. The one well-controlled study submitted, the Boundy study, shows Protamide to be ineffective in the treatment of herpes zoster.

IV. Legal objections. The Commissioner has authority to establish criteria for adequate and well-controlled clinical investigations necessary to demonstrate effectiveness of drug products on the market and may condition holding of an evidentiary hearing on a showing by Cooper Laboratories, Inc., that reasonable grounds exist therefor. ("Ciba-Geigy Corp. v. Richardson," 446 F. 2d 468 (C.A. 2, 1971); "Pfizer, Inc. v. Richardson," 434 F. 2d 536 (C.A. 2, 1970); "Pharmaceutical Manufacturers Assn. v. Richardson," 318 F. Supp. 301 (D. Del., 1970)). Thus, the objections of Cooper Laboratories, Inc., on these grounds are unfounded.

Since Cooper Laboratories, Inc., has submitted no adequate and well-controlled clinical studies establishing the effectiveness of Protamide for its recommended uses, no hearing on the withdrawal of the NDA of Protamide is justified as no genuine issue exists as to the material question of the effectiveness of Protamide for its recommended uses (21 CFR 130.12(a)(5)(ii), 130.14(b), and 130.27(b)(3); "Ciba-Geigy Corp. v. Richardson, supra; Upjohn Co. v. Finch," 422 F. 2d 944 (C.A. 6, 1970)).

The contentions of Cooper Laboratories, Inc., that Protamide is no longer a new drug because the drug was generally recognized as safe for its intended purposes and is sold for the same purposes for which it was sold on October 9, 1962, and is thereby protected by the grandfather provisions of the 1962 drug amendments, are likewise unfounded. A drug subject to an NDA prior to October 9, 1962, does not qualify for an exemption from the new-drug provisions of the Act under the grandfather provisions of the 1962 Drug Amendments. "USV Pharmaceutical Corp. v. Richardson," No. 71-1596 (C.A. 4, 1972). Moreover, the fact that Sherman Laboratories received a letter dated June 14, 1955, from the Food and Drug Administration to the effect that Protamide was no longer considered a new drug is irrelevant, as all such informal and formal opinions have been revoked by 21 CFR 130.39.

Finally, Cooper Laboratories, Inc., has submitted an affidavit from its executive vice president stating that it has discontinued all direct sales promotions of Protamide and virtually curtailed all advertising of the drug but that in spite of this, sales have advanced measurably and the volume of sales of the drug has stabilized. Such facts, however, standing alone, do not meet the standards of substantial evidence required by 21 U.S.C. 355(d). "Upjohn Co. v. Richardson, supra," 446 F. 2d at 951-54.

V. Findings. The Commissioner, based on the review of the medical documentation offered to support the claims of efficacy for Protamide in the treatment of neuritis, herpes zoster, and ophthalmic herpes zoster, finds that Cooper Laboratories, Inc., has failed to present substantial evidence of effectiveness for this product. No objection or documentation were presented by any other firms and, in accordance with the provisions of 21 CFR 130.15, this failure is construed as an election by any other firm not to avail itself of the opportunity for the hearing.

The Commissioner further finds that the approval of the new-drug application heretofore approved for Protamide (NDA 5-025) should be withdrawn on the basis of a lack of substantial evidence of effectiveness.

Therefore, pursuant to the provisions of the Federal Food, Drug, and Cosmetic Act (secs. 505, 701, 52 Stat. 1052-1053, 1055-1056, as amended, and 76 Stat. 781-785, as amended; 21 U.S.C. 355, 371), and under authority delegated to the Commissioner (21 CFR 2.120), notice is given that the approval of the new-drug application for Protamide (NDA 5-025) is withdrawn. The withdrawal will become effective 30 days after the date of publication of this order in the FEDERAL REGISTER to allow time for recall of all outstanding stocks of Protamide.

(Secs. 505, 701, 52 Stat. 1052-1053, 1055-1056, as amended, and 76 Stat. 781-785, as amended; 21 U.S.C. 355, 371)

Dated: August 16, 1972.

SAM D. FINE,
Associate Commissioner
for Compliance.

[FR Doc.72-14452 Filed 8-24-72; 8:48 am]

[Docket No. FDC-D-505; NADA No. 10-184V]

UPJOHN CO.

Biosol; Notice of Withdrawal of Approval of New Animal Drug Application

In the FEDERAL REGISTER of August 21, 1970 (35 F.R. 13403, DESI 10-184V), the Commissioner of Food and Drugs announced the conclusions of the Food and Drug Administration following evaluation of a report received from the National Academy of Sciences—National Research Council, Drug Efficacy Study Group, on Biosol; NADA (new animal drug application) No. 10-184V; marketed by the Upjohn Co., Kalamazoo, Mich. 49001.

The Upjohn Co. advised the Commissioner that the above-named product is no longer marketed.

Based on the grounds set forth in said announcement and the firm's statement, the Commissioner concludes that the new animal drug application for the above-named product should be withdrawn. Therefore, pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (sec. 512, 82 Stat. 343-51; 21 U.S.C. 360b) and under the authority delegated to the Commissioner (21 CFR 2.120), ap-

proval of NADA No. 10-184V including all amendments and supplements thereto, is hereby withdrawn effective on the date of publication of this document.

Dated: August 17, 1972.

SAM D. FINE,
Associate Commissioner
for Compliance.

[FR Doc.72-14449 Filed 8-24-72; 8:48 am]

DEPARTMENT OF HOUSING AND URBAN DEVELOPMENT

Office of Assistant Secretary for
Housing Management

[Docket No. D-72-197]

DIRECTOR, OFFICE OF LOAN MANAGEMENT

Redelegation of Authority and Assignment of Functions

The redelegation of authority and assignment of functions to the Director, Office of Loan Management, et al., published at 35 F.R. 4019, March 3, 1970, and amended at 36 F.R. 14164, July 30, 1971; 36 F.R. 17373, August 28, 1971; and 37 F.R. 11195, June 3, 1972, is further amended by adding a new paragraph 15 to section A to read as follows:

15. To execute the functions, powers, and duties authorized by Executive Order 10657 of February 14, 1956 (21 F.R. 1063, Feb. 16, 1956), as amended by Executive Order 10734 of October 1957 (22 F.R. 8275, Oct. 22, 1957), Executive Order 11105 of April 18, 1963 (28 F.R. 3909, Apr. 20, 1963), with respect to servicing mortgages on certain properties at the Atomic Energy Commission communities of Oak Ridge, Tenn., Richland, Wash., and Los Alamos, N. Mex., pursuant to the Atomic Energy Community Act of 1955, as amended (42 U.S.C. 2301), except the Secretary's power to make the finding required under section 51 of the Act (42 U.S.C. 2341).

(Secretary's delegation of authority, 36 F.R. 5005, Mar. 16, 1971)

Effective date. This amendment is effective as of August 22, 1972.

NORMAN V. WATSON,
Assistant Secretary
for Housing Management.

[FR Doc.72-14509 Filed 8-24-72; 8:53 am]

DEPARTMENT OF TRANSPORTATION

Federal Highway Administration

[Notice 72-13]

MINIMUM AGE OF DRIVERS

Waiver for Drivers Engaged in Disaster Relief

The purpose of this notice is to announce that the Director of the Bureau