

proposed rules

This section of the FEDERAL REGISTER contains notices to the public of the proposed issuance of rules and regulations. The purpose of these notices is to give interested persons an opportunity to participate in the rule making prior to the adoption of the final rules.

DEPARTMENT OF JUSTICE
Drug Enforcement Administration
[21 CFR Part 1308]
SCHEDULES OF CONTROLLED
SUBSTANCES

Proposed Placement of Chlordiazepoxide, Diazepam, Oxazepam, Chlorazepate, Flurazepam and Clonazepam in Schedule IV

On August 14, 1973, the Administrator of the Drug Enforcement Administration requested the Assistant Secretary for Health of the Department of Health, Education and Welfare to submit, in behalf of the Secretary of Health, Education and Welfare, a scientific and medical evaluation and recommendation that clordiazepoxide (Librium®) and diazepam (Valium®) be placed in Schedule IV of the Controlled Substances Act.

By a letter dated November 25, 1974, the Assistant Secretary for Health submitted the requested scientific and medical evaluation and recommendation concerning chlordiazepoxide and diazepam, and further submitted scientific and medical evaluations and other recommendations that oxazepam (Serax®), flurazepam (Dalmane®), and clonazepam (Clonopin®), which are other members of the benzodiazepine class of drugs, be similarly placed in Schedule IV.

In his November 25, 1974, letter, the Assistant Secretary re-submitted an earlier recommendation made by his office that chlorazepate (Tranxene®), another member of the benzodiazepine class, be placed in Schedule IV.

The recommendation and evaluation, and the supporting documentation concerning chlorazepate were originally submitted on November 1, 1972, and February 7, 1973, respectively. However, control proceedings were not commenced at that time by the Bureau of Narcotics and Dangerous Drugs (BNDD, predecessor agency to DEA), because of pending proceedings involving Librium® and Valium®. The Assistant Secretary's letter of November 25, 1974, which requests that proceedings be initiated to control all the above-listed members of the benzodiazepine class of drugs, is set out as follows:

NOVEMBER 25, 1974.

JOHN R. BARTELS, Jr.,
 Administrator,
 Drug Enforcement Administration,
 Washington, D.C.

DEAR MR. BARTELS: The Drug Enforcement Administration recommended that chlordiazepoxide (Librium) and diazepam (Valium) be controlled in Schedule IV of the Public Law 91-513 (the Controlled Substances Act) and requested in August 1973, that the De-

partment of Health, Education, and Welfare (DHEW) review the scientific and medical aspects of this proposal. This review was postponed pending the establishment of the FDA Controlled Substances Advisory Committee and a complete review of the benzodiazepine class of drugs.

This recommendation has now been reviewed by the appropriate agencies within DHEW, and the FDA Controlled Substances Advisory Committee. We have concluded that Schedule IV controls for chlordiazepoxide and diazepam are appropriate and justifiable under the provisions of the CSA.

As noted above, the review of chlordiazepoxide and diazepam was expanded to include other members of the benzodiazepine class of drugs. As a result of this evaluation we also recommend that flurazepam (Dalmane) and oxazepam (Serax), both of which are marketed drugs, be controlled in Schedule IV and reaffirm our previously forwarded recommendation for similar controls on chlorazepate (Tranxene). In addition, data on clonazepam, an unmarketed investigational drug, were evaluated. We recommend that, should the New Drug Application for clonazepam be approved, it be controlled in Schedule IV at the time of marketing.

A summary of the basis for these recommendations is enclosed. Briefly, extensive documentation of the medical and scientific aspects of the dependence liability and potential for abuse of chlordiazepoxide and diazepam was developed during the several years of hearings held on the subject of control. These documents and findings, although developed under the criteria established by the Drug Abuse Control Amendments of 1965, constitute an ample basis for support of Schedule IV controls under the Controlled Substances Act of 1970. It is our best judgment, based on analysis of presently available data, that none of the other benzodiazepines (oxazepam, chlorazepate, flurazepam and clonazepam) possess a potential for abuse and a dependence liability which is significantly different from that of chlordiazepoxide and diazepam.

The quantum of evidence delineating the dependence liability or potential for abuse (and the consequent risk to public health) differs for each benzodiazepine. For example, specific testing to determine these factors has not, to our knowledge, been performed with clonazepam.

Yet its pharmacological profile strongly suggests that these factors would be the same as those for benzodiazepines on which testing and clinical experience have demonstrated a potential for abuse and dependence.

Reasonable predictions of this type, although they can never be made with absolute certainty, are not unusual in making scientific or medical judgment. This line of thought has been the basis of our "classification" approach to the evaluation of drugs for control.

We have learned for example from experiences with methaqualone and phenmetrazine, that drugs have been marketed with a claim that they were not abusable. Subsequently, after marketing or after restrictions on similar drugs, such as the barbiturates and amphetamines, these become subject to serious

and significant abuse. In retrospect we observed that the differences between their pharmacological profiles and those of related drugs were not as important as the similarities.

Appropriate members of FDA staff will be available to assist the Drug Enforcement Administration in evaluating aspects of this recommendation or will make available relevant information which you may need for the operational procedures at DEA. In particular, the Drug Abuse Staff of the Food and Drug Administration is in possession of several volumes of material which have been considered by the Controlled Substances Advisory Committee in making its evaluation. In order to facilitate this exchange of information FDA staff are authorized to transmit relevant materials directly to appropriate members of DEA Staff. Dr. Barrett Scovillo, Director, Division of Neuropharmacological Drug Products will act as liaison for transmittal of information.

Sincerely yours,

CHARLES C. EDWARDS, M.D.,
 Assistant Secretary for Health.

Upon receipt of this letter, the Drug Enforcement Administration undertook a review of the following: (1) Materials submitted to DEA by the Department of Health, Education and Welfare with the letter of November 25, 1974; (2) materials submitted to BNDD by the Department of Health, Education and Welfare on February 7, 1973, in support of its letter of November 1, 1972; (3) materials on file with the Food and Drug Administration, and the Drug Enforcement Administration; (4) published scientific and medical literature from the United States and other nations regarding this drug; (5) selected investigatory files compiled for law enforcement purposes by the Drug Enforcement Administration; and (6) the legislative history of the Controlled Substances Act.

Based upon the investigations and review of the Drug Enforcement Administration and upon the scientific and medical evaluations and recommendations of the Secretary of Health, Education, and Welfare, received pursuant to sections 201(a) and 201(b) of the Comprehensive Drug Abuse Prevention and Control Act of 1970 (21 U.S.C. 811(a) and 811(b)), the Administrator of the Drug Enforcement Administration finds that:

1. Based on information now available, chlordiazepoxide, diazepam, oxazepam, chlorazepate, flurazepam, and clonazepam have a low potential for abuse relative to the drugs or other substances currently listed in Schedule III.

2. Chlordiazepoxide, diazepam, oxazepam, chlorazepate, and flurazepam have a currently accepted medical use in treatment in the United States.

3. Clonazepam will, upon the approval of New Drug Application by the FDA, have a currently accepted medical use in treatment in the United States.

4. Abuse of chlordiazepoxide, diazepam, oxazepam, chlorazepate, and clonazepam may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in Schedule III.

Therefore, under the authority vested in the Attorney General by section 201(a) of the Comprehensive Drug Abuse Prevention and Control Act of 1970 (21 U.S.C. 811(a)), and delegated to the Administrator of the Drug Enforcement Administration by § 0.100 of Title 28 of the Code of Federal Regulations, the Administrator proposes that, upon approval of the New Drug Application for clonazepam by FDA, § 1308.14 of Title 21 of the Code of Federal Regulations (CFR) be amended to read:

§ 1308.14 Schedule IV.

(b) Depressants. Unless specifically excepted or unless listed in another schedule, any material, compound, mixture, or preparation which contains any quantity of the following substances, including its salts, isomers, and salts of isomers whenever the existence of such salts, isomers, and salts of isomers is possible within the specific chemical designation:

- (1) Barbitol ----- 2145
- (2) Chloral betaine ----- 2450
- (3) Chloral hydrate ----- 2465
- (4) Chlorazepate ----- 2768
- (5) Chlordiazepoxide ----- 2744
- (6) Clonazepam ----- 2737
- (7) Diazepam ----- 2765
- (8) Ethchlorvynol ----- 2540
- (9) Ethinamate ----- 2545
- (10) Flurazepam ----- 2767
- (11) Mebutamate ----- 2800
- (12) Meprobamate ----- 2820
- (13) Methohexital ----- 2264
- (14) Methyphenobarbital ----- 2250
- (15) Oxazepam ----- 2835
- (16) Paraldehyde ----- 2585
- (17) Petrichloral ----- 2591
- (18) Phenobarbital ----- 2285

All interested persons are invited to submit their comments or objections in writing regarding this proposal. The comments or objections should state with particularity the issues concerning which the person desires to be heard. Comments and objections should be submitted in quintuplicate to the Hearing Clerk, Office of the Administrative Law Judge, Drug Enforcement Administration, Department of Justice, Room 1130, 1405 Eye Street N.W., Washington, D.C. 20537, and must be received no later than March 28, 1975.

In the event that an interested party submits objections to this proposal which present reasonable grounds for this rule not to be finalized and requests a hearing in accordance with 21 CFR 1308.45, the party will be notified by registered mail that a hearing on these objections will be held as soon as the matter may be heard at the Drug Enforcement Administration, 1405 Eye Street, NW., Washington, D.C. 20537. If objections

submitted do not present such reasonable grounds, the party will be so advised by registered mail.

If no objections presenting reasonable grounds for a hearing on the proposal are received within the time limitations, and all interested parties waive or are deemed to waive their opportunity for the hearing or to participate in the hearing, the Administrator may, without a hearing, and, after giving consideration to written comments, issue his final order pursuant to 21 CFR 1308.48 without a hearing.

Dated: January 22, 1975.

JOHN R. BARTELS, Jr.,
Administrator,
Drug Enforcement Administration.
[FR Doc.75-2363 Filed 1-24-75;8:45 am]

DEPARTMENT OF AGRICULTURE

Animal and Plant Health Inspection Service

[9 CFR Part 113]

VIRUSES, SERUMS, TOXINS, AND ANALOGOUS PRODUCTS

Notice of Proposed Rulemaking

Notice is hereby given in accordance with the provisions contained in section 553 of Title 5, United States Code, that it is proposed to amend certain of the regulations relating to viruses, serums, toxins, and analogous products in Part 113 of Title 9, Code of Federal Regulations, issued pursuant to the provisions of the Virus-Serum-Toxin Act of March 4, 1913 (21 U.S.C. 151-158).

These proposed amendments would provide a new two stage potency test to simultaneously evaluate the Eastern and the Western fractions of Encephalomyelitis Vaccine. This new test would replace the two tests currently being used for this product. This test has been developed as a cooperative endeavor between the Veterinary Services Laboratories and the biologics industry.

It is proposed to revise § 113.127(b) to read as follows:

§ 113.127 Encephalomyelitis Vaccine, Eastern and Western, Killed Virus.

(b) Potency test. Bulk or final container samples of completed product from each serial shall be tested for potency in accordance with the two stage test provided in this paragraph. The serological interpretations required in this test shall be made for the Eastern Type fraction and the Western Type fraction independent of each other except that a serial or subserial found unsatisfactory for either fraction shall not be released.

(1) For this test, a guinea pig dose shall be one-half the amount recommended on the label for a horse and shall be administered as recommended for a horse. Each of 10 healthy guinea pigs (vaccinates) shall be injected with two guinea pig doses with an interval of 14 to 21 days between doses. Two additional guinea pigs from the same source shall be held as controls.

(2) Fourteen to 21 days after the second injection, serum samples from each

vaccinate and each control shall be tested by the plaque reduction serum neutralization test.

(3) If the control serum samples show a titer greater than 1:2 for either or both fractions, the test is inconclusive for that fraction or fractions, as the case may be, and may be repeated; *Provided*, That, if 4 or more of the vaccinate serum samples show a titer of less than 1:4 for the Eastern type fraction or less than 1:32 for the Western type fraction, the serial or subserial is unsatisfactory without further testing.

(4) If 2 or 3 of the vaccinate serum samples show a titer of less than 1:4 for the Eastern type fraction or less than 1:32 for the Western type fraction or both, the second stage may be used; *Provided*, That, if 1 or less such samples meet the titer requirements for one fraction in the first stage, such fraction need not be retested. Otherwise, the second stage shall be conducted in a manner identical to the first stage.

(5) If the second stage is used and 4 or more of the vaccinate serum samples show a titer of less than 1:4 for the Eastern type fraction or less than 1:32 for the Western type fraction, the serial or subserial is unsatisfactory.

(6) The results shall be evaluated according to the following table:

Cumulative totals			
Stage	Vaccinates	Failures for acceptance	Failures for rejection
1	10	1 or less	4 or more
2	20	3 or less	Do.

Interested parties are invited to submit written data, views, or arguments regarding the proposed regulations to Deputy Administrator, Veterinary Services, Animal and Plant Health Inspection Service, U.S. Department of Agriculture, Room 828-A, Federal Building, Hyattsville, Maryland 20782. All comments received on or before February 28, 1975, will be considered.

All written submissions made pursuant to this notice will be made available for public inspection at such times and places and in a manner convenient to the public business. (7 CFR 1.27 (b)).

Done at Washington, D.C. this 22nd day of January, 1975.

J. M. HEJL,
Deputy Administrator, Veterinary Services, Animal and Plant Health Inspection Service.

[FR Doc.75-2303 Filed 1-24-75;8:45 am]

Commodity Exchange Authority

[17 CFR Part 150]

[Hearing Docket CE-P19]

LIVE SLAUGHTER CATTLE, LIVE HOGS, AND FROZEN PORK BELLIES

Proposed Limits on Position and Daily Trading

Section 4a of the Commodity Exchange Act (7 U.S.C. 6a) directs that, for the purpose of diminishing, elim-