

amount of time needed to process the entry.

#### COMMENTS

Comments on the proposed amendments were to have been received on or before May 4, 1978. At the request of American-flag vessel operators, a notice extending the period of time to comment until June 2, 1978, was published in the FEDERAL REGISTER on May 5, 1978 (43 FR 19417). Customs has now received a request for a further extension of time. Therefore, the period of time for comment on the proposed amendments is extended until June 30, 1978.

LEONARD LEHMAN,  
Assistant Commissioner  
Regulations and Rulings.

(FR Doc. 78-13617 Filed 5-18-78; 8:45 am)

[4110-03]

### DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Food and Drug Administration

[21 CFR Part 446]

[Docket No. 78N-0123]

#### CONCENTRATED LIQUID DOSAGE FORMS OF TETRACYCLINE

##### Proposal To Revoke Provisions for Certification

AGENCY: Food and Drug Administration.

ACTION: Proposed rule.

**SUMMARY:** This proposed rule would amend the antibiotic drug regulations by revoking provisions for certification of concentrated liquid dosage forms of tetracycline, which are labeled and formulated specifically for pediatric use. This action is being taken because new evidence reveals continued extensive prescribing of tetracycline liquid dosage forms for children from infancy to the age of 8 years despite the known adverse reactions in this age group. The new evidence supports a finding that the concentrated liquid dosage forms formulated for pediatric patients should be removed from the market.

**DATES:** Comments by July 18, 1978.

**ADDRESS:** Written comments to the Hearing Clerk (HFC-20), Food and Drug Administration, Room 4-65, 5600 Fishers Lane, Rockville, Md. 20857.

**FOR FURTHER INFORMATION CONTACT:**

Merle L. Gibson, Bureau of Drugs (HFD-140), Food and Drug Administration, Department of Health, Education, and Welfare 5600 Fishers Lane, Rockville, Md. 20857, 301-443-4310.

**SUPPLEMENTARY INFORMATION:** The tetracyclines were first intro-

duced for clinical use in 1948. Because of their broad spectrum of antimicrobial activity, drugs of this class have been used extensively since that time. Tetracyclines are currently marketed for oral use as capsules, syrups, concentrated liquids (pediatric drops), and oral suspensions. The pediatric drops, which are marketed under the certification provisions of syrups and oral suspensions, are characterized by a higher drug concentration than other oral dosage forms and are especially convenient for administering to infants and young children.

For many years the use of drugs of the tetracycline class has been known to cause adverse reactions in the fetus during the last half of pregnancy and in the infant and child through the age of 8 years. The recognized adverse reactions, which include permanent staining of the teeth (yellow, gray, brown), increase tendency to caries, enamel hypoplasia, and temporary inhibition of bone growth, are reflected in the labeling of the drugs. Despite the known adverse reactions, new evidence shows that tetracyclines continue to be used extensively in the pediatric age group. With the current availability of safer alternative antimicrobials that are as effective against the bacteria that cause most infections in young children, it is difficult to justify the continued availability of a dosage form of tetracycline that is specifically formulated for the pediatric age group.

Evidence to support this conclusion has been brought to the attention of the Commissioner of Food and Drugs from several sources:

1. At the 18th meeting of the Food and Drug Administration's (FDA) Anti-Infective Agents Advisory Committee, held on November 16, 1976, tetracycline pediatric dosage forms were discussed. The committee members, who are authorities in the fields of pediatrics, internal medicine, and pharmacology, considered new data from two studies prior to their publication from the American Academy of Pediatrics. One was a 6-month study by Ray, Wayne A., Charles F. Federspiel, and William Schaffner, "The Mal-Prescribing of Liquid Tetracycline Preparations," *American Journal of Public Health*, 67(8):762-763, August 1977, and the other was a 2-year study by the same investigators ("Prescribing of Tetracycline to Children Less than 8 Years Old," *The Journal of the American Medical Association*, 237(19):2069-2074, May 9, 1977). Both studies were conducted by the Division of Biostatistics, Department of Preventive Medicine, and the Division of Infectious Disease, Department of Medicine, Vanderbilt University School of Medicine, Nashville, Tenn., on ambulatory pediatric patients participating in the Medicaid program in Tennessee. The

6-month study surveyed 50,606 tetracycline prescriptions written for 27,888 people. Of these prescriptions 2,740 (5.4 percent) were for sirup and 95 (0.2 percent) were for pediatric drops. More than 55 percent of the prescriptions for sirup and 98 percent of the prescriptions for pediatric drops were for children under 8 years of age. Only 13.8 percent of the prescriptions for liquid tetracycline were prescribed for patients 60 years or older.

Data from the 2-year study showed that tetracycline was prescribed 7,046 times for 4,026 children under 8 years of age. Eighty-four percent of the prescriptions were for pediatric drops. Of the 4,026 children receiving tetracycline, 30 percent were less than 2 years of age and 55 percent were less than 4 years of age.

2. The Food and Drug Administration presented to the Advisory Committee data from the "National Prescription Audit-Therapeutic Category Report," a study conducted by IMS-America, Ltd., on new and refilled prescriptions for the liquid dosage forms of tetracyclines covering the period from January 1974 through June 1976. The audit showed that approximately 77 percent of the prescriptions for liquid dosage forms of tetracyclines were written for patients under 9 years of age. Only 3 percent of these prescriptions were written for patients over 65 years of age. All data indicate that a significant proportion of the prescriptions for liquid dosage forms are written for children and very few for other patient populations that may have difficulty taking solid dosage forms, such as the geriatric age group.

3. The Committee on Drugs of the American Academy of Pediatrics has stated in a commentary in *Pediatrics* (55:142-143, January 1975) that it is difficult to identify common pediatric infections for which an oral tetracycline would be a drug of choice. They concluded that there are few, if any, reasons for using tetracycline drugs in children less than 8 years of age.

The Anti-Infective Agents Advisory Committee considered all data presented and recommended that the Commissioner remove the concentrated liquid dosage forms of tetracycline which are for pediatric use from the market. The Committee found, however, that there is insufficient information to conclude that all oral liquid forms of tetracyclines should be removed from the market and that to recommend such an action at this time would not be in the public interest. The Committee believes that, in removing the drugs specifically formulated for use in children and by disseminating information to physicians regarding the prescribing of tetracyclines for children, the incidence of such use will be greatly reduced. The

Committee also suggested that these measures be evaluated by resurveying prescription use in 3 months to 1 year.

The Committee advised that, in conjunction with removal of the concentrated liquid, the physician labeling for all oral liquid dosage forms of tetracycline that remain on the market should be revised to strengthen the warning concerning permanent discoloration of the teeth in pediatric patients.

The Commissioner has evaluated all available data, including the recommendations of the American Academy of Pediatrics and the FDA Anti-Infective Agents Advisory Committee, and has decided that FDA will take the following actions in regard to tetracycline antibiotics:

1. Propose that the concentrated liquid forms of tetracycline antibiotics that are labeled and specifically formulated for pediatric use be removed from the market. This would be accomplished by revising §§ 446.115a and 446.166 of the regulations (21 CFR 446.115a, 446.166) to limit the amount of active ingredient permitted in syrups to 15 and 25 milligrams per milliliter (mg/ml) respectively. Currently, demeclocycline oral suspension containing 60 mg/ml of demeclocycline and oxytetracycline calcium oral suspension containing 100 mg/ml of oxytetracycline are certifiable in accordance with §§ 446.115a and 446.166, respectively. The revised regulations would no longer permit the certification of these concentrated liquids and outstanding certificates would immediately be revoked.

2. Require that the Warnings section of the physician labeling for all dosage forms of tetracyclines be revised to strengthen the warning concerning permanent discoloration of the teeth in pediatric patients.

3. Require that the Dosage and Administration section of the physician labeling for all dosage forms of tetracyclines be revised by changing the subheading "Children" to read "For children above 8 years of age."

4. Prepare and distribute an "FDA Drug Bulletin" to physicians and other health professionals which will discuss the therapeutic constraints associated with the use of tetracyclines and attempt to dissuade practitioners from prescribing the drugs for pediatric patients except in rare circumstances.

The Commissioner has sent letters to all manufacturers of tetracycline class products, directing them to revise the physician labeling in the "Warnings" section and the "Dosage and Administration" section (Commissioner's conclusions 2 and 3 above) for all dosage forms of tetracyclines. These changes are to be made at the next printing of the labeling.

The Commissioner advises that if the proposal to revise §§ 446.115a and

446.166 of the regulations to limit the amount of active ingredients permitted in syrups and oral suspensions is finalized, all outstanding certificates for batches of tetracycline concentrated syrups and suspensions will be revoked on the date that revision of the regulations is effective. Manufacturers may want to consider this now as they schedule production of batches of tetracycline syrups and oral suspensions.

Within 1 year after the effective date of a final regulation, FDA will survey prescription use and manufacturing practices to determine what effect the above-described actions have had on the incidence of prescribing tetracyclines for pediatric patients.

Copies of the minutes of the Anti-Infective Agents Advisory Committee meeting, the 6-month and 2-year studies, an example of the letters to the manufacturers, current labeling for tetracyclines, the summary of data from the "National Prescription Audit-Therapeutic Category Report," and the commentary of the Committee on Drugs of the American Academy of Pediatrics are available for public inspection at the office of the Hearing Clerk, address given above, between 9 a.m. and 4 p.m., Monday through Friday.

The Commissioner has determined that this document does not contain an agency action covered by 21 CFR 25.1(b) and consideration by the agency of the need for preparing an environmental impact statement is not required.

Therefore, under the Federal Food, Drug, and Cosmetic Act (sec. 507, 59 Stat. 463, as amended (21 U.S.C. 357)) and under authority delegated to the Commissioner (21 CFR 5.1), it is proposed that §§ 446.115a and 446.166 be amended as follows:

1. In § 446.115a, by revising the second sentence of paragraph (a)(1) to read as follows:

§ 446.115a Demeclocycline oral suspension.

(a) . . . .

(1) . . . . Each milliliter contains demeclocycline equal to 15 milligrams of demeclocycline hydrochloride. . . .

. . . . .

2. In § 446.166, by revising the third sentence of paragraph (a)(1) to read as follows:

§ 446.166 Oxytetracycline calcium oral suspension.

(a) . . . .

(1) . . . . Each milliliter contains a quantity of oxytetracycline calcium equivalent to 25 milligrams of oxytetracycline. . . .

. . . . .

Interested persons may, on or before July 18, 1978, submit to the Hearing

Clerk (HFC-20), Food and Drug Administration, Room 4-65, 5600 Fishers Lane, Rockville, Md. 20857, written comments regarding this proposal. Four copies of all comments shall be submitted, except that individuals may submit single copies of comments, and shall be identified with the Hearing Clerk docket number found in brackets in the heading of this document. Received comments may be seen in the above office between the hours of 9 a.m. and 4 p.m., Monday through Friday.

NOTE.—The Food and Drug Administration has determined that this proposal will not have a major economic impact as defined by Executive Order 11821 (amended by Executive Order 11949) and (OMB Circular A-107. A copy of the economic impact assessment is on file with the Hearing Clerk, Food and Drug Administration.

Dated: May 12, 1978.

WILLIAM F. RANDOLPH,  
Acting Associate Commissioner  
for Regulatory Affairs.

[FR Doc. 78-13589 Filed 5-18-78; 3:45 am]

[4630-01]

DEPARTMENT OF THE TREASURY

Internal Revenue Service

[26 CFR Part 1]

[LR-260-74]

INCOME TAX

Deduction for Contributions to Qualified Pension Trusts

AGENCY: Internal Revenue Service, Treasury.

ACTION: Notice of proposed rulemaking.

SUMMARY: This document contains proposed regulations relating principally to the deduction limitations on contributions to defined benefit pension plans. Changes in the applicable tax law were made by the Employee Retirement Income Security Act of 1974. The regulations would provide the public with guidance needed to comply with that Act and would affect many sponsors of defined benefit plans.

DATES: Written comments and requests for public hearing must be delivered or mailed by July 18, 1978. The amendments are proposed to be effective generally for employers' taxable years beginning in 1976, but earlier (or later) in the case of some plans as provided by the Employee Retirement Income Security Act of 1974.

ADDRESS: Send comments and requests for a public hearing to: Commissioner of Internal Revenue, Attention: CC:LR:T, Washington, D.C. 20224.

FOR FURTHER INFORMATION CONTACT:

J. Douglas Sorensen of the Legisla-

only from the effective date of these regulations.

MANUEL D. PLOTKIN,  
*Director,*  
*Bureau of the Census.*

I concur:

RICHARD J. DAVIS,  
*Assistant Secretary,*  
*Department of the Treasury.*

(FR Doc. 78-30727 Filed 10-30-78; 8:45 am)

[6750-01-M]

Title 16—Commercial Practices

CHAPTER I—FEDERAL TRADE  
COMMISSION

(Docket No. C-2830)

PART 13—PROHIBITED TRADE PRACTICES, AND AFFIRMATIVE CORRECTIVE ACTIONS

John Hancock Mutual Life Insurance Co., et al.

AGENCY: Federal Trade Commission.  
ACTION: Final order.

SUMMARY: In settlement of alleged violations of Federal law prohibiting unfair acts and practices and unfair methods of competition, these four (4) consent orders, among other things, require four (4) Boston, Mass., insurance companies to cease interlocking directors by allowing any individual to sit on their boards who is simultaneously sitting on the board of any of the other boards or of any other competitive firms. The consent orders additionally require the companies to initiate prescribed procedures designed to eliminate interlocking directorates, and to submit detailed compliance reports to the Commission annually for a 5-year period.

DATES: Complaint and order issued September 19, 1978.

FOR FURTHER INFORMATION CONTACT:

FTC/C, Alfred F. Dougherty, Jr.,  
Washington, D.C. 20580, 202-523-3601.

SUPPLEMENTARY INFORMATION: On Tuesday, July 11, 1978, there was published in the FEDERAL REGISTER, 43 FR 29797, a proposed consent agreement with analysis in the matter of John Hancock Mutual Life Insurance Co., a corporation; Liberty Mutual Insurance Co., a corporation; New England Mutual Life Insurance Co., a corporation; and State Mutual Life Assurance Co. of America, a corporation, for the purpose of soliciting public com-

\*Copies of the complaint, and the decision and order filed with the original document.

ment. Interested parties were given sixty (60) days in which to submit comments, suggestions, or objections regarding the proposed form of order.

No comments having been received, the Commission has ordered the issuance of the complaint in the form contemplated by the agreement, made its jurisdictional findings and entered its order to cease and desist, as set forth in the proposed consent agreement, in disposition of this proceeding.

The prohibited trade practices and/or corrective actions, as codified under 16 CFR Part 13, are as follows: Subpart—Interlocking Directorates Unlawfully: § 13.1106 Interlocking directorates unlawfully.

(Sec. 6, 38 Stat. 721 (15 U.S.C. 46), interprets or applies sec. 5, 38 Stat. 719, as amended (15 U.S.C. 45); sec. 8, 38 Stat. 732; 49 Stat. 717 (15 U.S.C. 19).)

CAROL M. THOMAS,  
*Secretary.*

(FR Doc. 78-30713 Filed 10-30-78; 8:45 am)

[4810-22-M]

Title 19—Customs Duties

CHAPTER I—UNITED STATES CUSTOMS SERVICE, DEPARTMENT OF THE TREASURY

(T.D. 78-181)

PART 159—LIQUIDATION OF DUTIES

Certain Fish From Canada; Correction of Notice of Final Countervailing Duty Determination

AGENCY: U.S. Customs Service, Treasury Department.

ACTION: Correction of notice of final countervailing duty determination.

SUMMARY: This notice is to inform the public that a technical correction is being made in the notice of final countervailing duty determination regarding certain fish from Canada.

EFFECTIVE DATE: October 31, 1978.

FOR FURTHER INFORMATION CONTACT:

Charles F. Goldsmith, Economist, Office of Tariff Affairs, Department of the Treasury, 15th Street and Pennsylvania Avenue NW., Washington, D.C. 20220, telephone 202-566-2323.

SUPPLEMENTARY INFORMATION: On June 16, 1978, a notice of "Final Countervailing Duty Determination" concerning fish from Canada, T.D. 78-181, was published in the FEDERAL REGISTER (43 FR 25996). A waiver was concurrently granted.

In that final determination, a statement directing publication of the deci-

sion in the Customs Regulations was inadvertently omitted. The following paragraph should have appeared in that notice:

The table in § 159.47(f) of the Customs Regulations (19 CFR 159.47(f)) is amended by inserting after the last entry from Canada under the commodity heading "Fish," the number "78-181" in the column headed "Treasury Decision"; and in the column headed "Action," the words "Bounty declared-rate." (R.S. 251, sections 303, as amended, 624; 46 Stat. 687, 759, 88 Stat. 2049; 19 U.S.C. 66, 1303, as amended, 1624).

Consequently, this entry will immediately precede the entry for certain fish from Canada which was added as a result of T.D. 78-182.

ROBERT H. MUNDHEIM,  
*General Counsel of the Treasury.*

OCTOBER 25, 1978.

(FR Doc. 78-30724 Filed 10-30-78; 8:45 am)

[4110-03-M]

Title 21—Food and Drugs

CHAPTER I—FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

SUBCHAPTER D—DRUGS FOR HUMAN USE

(Docket No. 78N-0123)

PART 446—TETRACYCLINE ANTIBIOTIC DRUGS

Concentrated Liquid Dosage Forms of Tetracycline; Revocation of Provisions for Certification

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) amends the antibiotic drug regulations by revoking provisions for certification of concentrated liquid dosage forms of tetracycline which are labeled and formulated specifically for pediatric use. Less concentrated syrups and suspensions of tetracyclines, 25 milligrams per milliliter (mg/ml) or less, will continue to be certified because of the need for these products in certain geriatric patients, in patients who cannot swallow solid dosage forms, and in children for whom other antibiotics are not likely to be effective or are contraindicated.

EFFECTIVE DATE: January 2, 1979.

FOR FURTHER INFORMATION CONTACT:

Merle L. Gibson, Bureau of Drugs

(HFD-140). Food and Drug Administration, Department of Health, Education, and Welfare, 5600 Fishers Lane, Rockville, Md. 20857, 301-443-4310.

**SUPPLEMENTARY INFORMATION:** In the *FEDERAL REGISTER* of May 19, 1978 (43 FR 21894), the Commissioner of Food and Drugs proposed to amend the antibiotic drug regulations by revoking provisions for certification of concentrated liquid dosage forms of tetracyclines which are labeled and formulated specifically for pediatric use. This action was taken because new evidence revealed continued extensive prescribing of concentrated liquid dosage forms specifically formulated for children, from infancy to the age of 9 years, despite known adverse reactions in this age group. Interested persons were invited to submit comments by July 18, 1978. Comments were received from consumers, pharmacists, dentists, physicians, nurses, and professional associations.

The agency received comments objecting to the proposal from persons who interpreted the proposal as intending to remove all liquid dosage forms of tetracycline from the market. These comments stressed that there is a demonstrated need for liquid dosage forms of tetracycline in certain patients who are unable to ingest solid dosage forms and in those few children for whom other antibiotics are not likely to be effective or are contraindicated.

The Commissioner believes the objecting comments misunderstood the proposal, which acknowledged the need for less concentrated syrups and suspensions (25 mg/ml or less) and proposed to revoke only the provisions for certification of the concentrated liquid dosage forms that are labeled and formulated specifically for children. The Commissioner considers the final rule, which is adopted as proposed, as responsive to the objecting comments, because the less concentrated liquid dosage forms will continue to be available.

The remainder of the comments were in agreement with the proposal.

All outstanding certificates of certification or release of batches of tetracycline concentrated syrups and suspensions formulated specifically for pediatric use are revoked on the effective date of this final rule. Recall will be requested to the retail level for all products covered by these certificates. Holders of the certificates will be notified by letter of the revocations of the certificates and of the details of the recall request.

Therefore, under the Federal Food, Drug, and Cosmetic Act (sec. 507, 59 Stat. 463, as amended (21 U.S.C. 357)) and under authority delegated to the

Commissioner (21 CFR 5.1), Part 446 is amended as follows:

1. In § 446.115a, the second sentence of paragraph (a)(1) is revised to read as follows:

§ 446.115a Demeclocycline oral suspension.

(a) . . . .

(1) . . . . Each milliliter contains demeclocycline equivalent to 15 milligrams of demeclocycline hydrochloride. . . .

2. In § 446.166, the third sentence of paragraph (a)(1) is revised to read as follows:

§ 446.166 Oxytetracycline calcium oral suspension.

(a) . . . .

(1) . . . . Each milliliter contains a quantity of oxytetracycline calcium equivalent to 25 milligrams of oxytetracycline. . . .

*Effective date.* This regulation is effective January 2, 1979.

(Sec. 507, 59 Stat. 463, as amended (21 U.S.C. 357))

Dated: October 24, 1978.

WILLIAM F. RANDOLPH,  
Acting Associate Commissioner  
for Regulatory Affairs.  
(FR Doc. 78-30516 Filed 10-30-78; 8:45 am)

[4410-01-M]

Title 28—Judicial Administration

CHAPTER I—DEPARTMENT OF JUSTICE

(Criminal Division Directive No. 2)

PART 0—ORGANIZATION OF THE DEPARTMENT OF JUSTICE

Subpart Y—Authority To Compromise and Close Civil Claims and Responsibility for Judgments, Fines, Penalties, and Forfeitures.

APPENDIX TO SUBPART Y—REDELEGATIONS OF AUTHORITY TO U.S. ATTORNEYS, DEPUTY ASSISTANT ATTORNEYS GENERAL, AND SECTION CHIEFS IN CRIMINAL DIVISION CASES

AGENCY: Department of Justice.

ACTION: Final rule.

**SUMMARY:** This Criminal Division Directive supersedes Criminal Division Directive No. 1, regarding redelegation of the Assistant Attorney General's authority with respect to compromise of civil penalties and forfeitures and

closing of civil claims. This directive lodges settlement authority in U.S. attorneys in cases falling within certain monetary limitations and redelegates the remainder of the Assistant Attorney General's authority to Deputy Assistant Attorneys General and to Section Chiefs.

EFFECTIVE DATE: October 31, 1978.

FOR FURTHER INFORMATION CONTACT:

Donald B. Nicholson, attorney, Government Regulations and Labor Section, Criminal Division, Department of Justice, Washington, D.C. 20530, 202-739-2694.

By virtue of the authority vested in me by part 0 of title 28 of the Code of Federal Regulations as amended, particularly §§ 0.160, 0.162, 0.164, and 0.168, it is hereby ordered that Criminal Division Directive No. 1 (29 FR 7383, June 6, 1964) is deleted and is superseded by the following:

(a) Each U.S. attorney is authorized to accept or reject offers in compromise of claims in behalf of the United States in all cases in which the difference between the gross amount of the original claim (or the forfeiture value of the merchandise claimed) and the proposed settlement does not exceed \$60,000, and of claims against the United States in all cases, or in administrative actions to settle, in which the amount of the proposed settlement does not exceed \$60,000, and to close (other than by compromise or by entry of judgment) civil claims asserted by the United States in all cases in which the gross amount of the original claim or the forfeiture value of the merchandise claimed does not exceed \$60,000 except:

(1) when, for any reason, the compromise or closing of a particular claim, as a practical matter, will control or adversely influence the disposition of other claims which, when added to the claim in question, total more than the respective amounts designated above, or

(2) when the U.S. attorney is of the opinion that because of a question of law or policy presented, or for any other reason, the matter should receive the personnel attention of the Assistant Attorney General.

(b) Notwithstanding the provisions of this Directive, the Assistant Attorney General of the Criminal Division may delegate to U.S. attorneys authority to compromise or close other cases, including those involving amounts greater than as set forth in paragraph (a) above, and up to the maximum limit of his authority, where the circumstances warrant such delegation.

(c) All other authority delegated to me by §§ 0.160, 0.162, and 0.164 of title 28 of the Code of Federal Regulations not falling within the limitations of