

graph (c) (5) of this section, shall be tested negative for brucellosis within 30 days prior to the date of importation into the United States.

(5) Female cattle under 18 months of age that originate in herds in which cattle were tested as described in subparagraphs (c) (1) and (2) of this section are exempted from the test requirement for brucellosis. *Provided, however,* They are accompanied by a certificate issued or endorsed by a salaried veterinarian of the Canadian Government showing that they were officially vaccinated against brucellosis as calves between the ages of 2-6 months (60-179 days old) for dairy breeds and from 2-10 months of age (60-299 days old) for beef breeds. The certificate accompanying such officially vaccinated cattle shall comply with paragraph (d) of this section except that it shall show, in lieu of the date and place of testing, the date of vaccination and the age of the animal at the time of vaccination.

(6) All cattle to be imported from Canada which originate from a brucellosis-free herd or a brucellosis-qualified for export herd shall move directly to the port of entry without contact with cattle which are not from a brucellosis-free herd or a brucellosis-qualified for export herd.

(Sec. 2, 32 Stat. 792, as amended; secs. 2, 3, 4, and 11, 76 Stat. 129, 130, 132 (21 U.S.C. 111, 134a, 134b, 134c, and 134f); 37 FR 28464, 28477; 38 FR 19141.)

These amendments impose additional restrictions on the importation of cattle from Canada. The amendments are of an emergency nature and should be placed in effect immediately in order to protect the livestock of the United States from the introduction and dissemination of disease.

Therefore, for such good cause the Department finds that notice and public comment are impracticable, unnecessary and contrary to the public interest and good cause is found for making the amendments effective less than 30 days after publication in the FEDERAL REGISTER.

Done at Washington, D.C., this 15th day of July 1977.

NOTE.—The Animal and Plant Health Inspection Service has determined that this document does not contain a major proposal requiring preparation of an Inflation Impact Statement Under Executive Order 11821 and OMB Circular A-107.

PIERRE A. CHALOUX,
Acting Deputy Administrator,
Veterinary Services.

[FR Doc.77-20933 Filed 7-21-77;8:45 am]

Title 21—Food and Drugs

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

SUBCHAPTER A—GENERAL

[Docket No. 77C-0207]

PART 73—LISTING OF COLOR ADDITIVES EXEMPT FROM CERTIFICATION

PART 81—GENERAL SPECIFICATIONS AND GENERAL RESTRICTIONS FOR PROVISIONAL COLOR ADDITIVES FOR USE IN FOODS, DRUGS, AND COSMETICS

Guanine

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: This document amends the regulations to "permanently" list guanine for use in externally applied drugs and in cosmetics generally, including drugs and cosmetics intended for use in the area of the eye. The Cosmetic, Toiletory, and Fragrance Association, Inc., filed a petition for such use: This rule will remove guanine from the provisional listing.

DATES: Effective August 22, 1977; objections by August 22, 1977.

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

FOR FURTHER INFORMATION CONTACT:

Gerard L. McCowin, Bureau of Foods (HFF-334), Food and Drug Administration, Department of Health, Education, and Welfare, 200 C St. SW., Washington, D.C. 20204, (202-472-5740).

SUPPLEMENTARY INFORMATION:

A notice published in the FEDERAL REGISTER of August 6, 1973 (38 FR 21200), stated that a petition (CAP 8C0074) for the "permanent" listing of natural pearl essence (guanine) as a color additive for use in externally applied cosmetics, including lipsticks and those for use in the area of the eye, had been filed by the Cosmetic, Toiletory, and Fragrance Association, Inc. (1133 15th Street NW., Washington, D.C. 20005), c/o Hazleton Laboratories, P.O. Box 30, Falls Church, Va. 22046. The petition was filed pursuant to section 706 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 376). A notice published in the FEDERAL REGISTER of March 5, 1976 (41 FR 9584), amended the filing of this petition to

include the additional use of natural pearl essence (guanine) in all types of cosmetics subject to ingestion. A notice published in the FEDERAL REGISTER of June 17, 1977 (42 FR 30893), amended the filing of this petition to include the additional use of guanine (pearl essence) in externally applied drugs.

This order "permanently" lists guanine for use in externally applied drugs and in cosmetics generally, including those for use in the area of the eye, under new § 73.1329 (21 CFR 73.1329) for drug use and new § 73.2329 (21 CFR 73.2329) for cosmetic use. The provisional listing of guanine (pearl essence) for use in cosmetics under § 81.1(g) (21 CFR 81.1(g)), which was extended to August 30, 1977, by regulation published in the FEDERAL REGISTER of July 1, 1977 (42 FR 33724), is being deleted because it will become obsolete when this order becomes effective on August 22, 1977, unless this order is stayed by the timely filing of objections.

The Commissioner, having evaluated the data in the petition and other relevant material, concludes that guanine is safe under the conditions set forth below for use in coloring cosmetics generally and in externally applied drugs, including cosmetics and drugs for use in the area of the eye, and that certification is not necessary for the protection of the public health.

The original filing notice for the petition identified the color additive as "natural pearl essence," although the color additive is provisionally listed as "guanine (pearl essence)." The Commissioner, in evaluating the data for this color additive concludes that both the term "natural pearl essence" and the parenthetical expression "(pearl essence)" are inappropriate for identifying this color additive because they are ambiguous and do not reflect the true nature of the color. The Commissioner further concludes that the name "guanine" would be more appropriate nomenclature, and he identifies the color by that name in the order set forth below.

Therefore, under the Federal Food, Drug, and Cosmetic Act (sec. 706 (b), (c), and (d), 74 Stat. 399-403 (21 U.S.C. 376 (b), (c), and (d))) and the transitional provisions of the Color Additive Amendments of 1960 (Title II, Pub. L. 86-618, sec. 203, 74 Stat. 404-407 (21 U.S.C. 376 note)) and under authority delegated to the Commissioner (21 CFR 5.1), Parts 73 and 81 are amended as follows:

1. Part 73 is amended:

a. By adding new § 73.1329 to Subpart B, to read as follows:

§ 73.1329 Guanine.

(a) *Identity.* (1) The color additive guanine is the crystalline material obtained from fish scales and consists principally of the two purines, guanine and hypoxanthine. The guanine content will vary from 75 to 97 percent, and the hypoxanthine will vary from 3 to 25 percent, depending on the particular fish and tissue from which the crystals are derived.

(2) Color additive mixtures for drug use made with guanine may contain only those diluents listed in this subpart as safe and suitable for use in color additive mixtures for coloring externally applied drugs.

(b) *Specifications.* The color additive guanine shall conform to the following specifications and shall be free from impurities other than those named to the extent that such other impurities may be avoided by good manufacturing practice:

Guanine, not less than 75 percent.
Hypoxanthine, not more than 25 percent.
Ash (ignition at 800° C), not more than 2 percent.
Lead (as Pb), not more than 20 parts per million.
Arsenic (as As), not more than 3 parts per million.
Assay, not less than 96 percent total purines.
Mercury (as Hg), not more than 1 part per million.

(c) *Uses and restrictions.* Guanine is safe for use in coloring externally applied drugs, including those intended for use in the area of the eye, in amounts consistent with good manufacturing practice.

(d) *Labeling.* The color additive and any mixture prepared therefrom intended solely or in part for coloring purposes shall bear, in addition to any information required by law, labeling in accordance with § 70.25 of this chapter.

(e) *Exemption from certification.* Certification of this color additive is not necessary for the protection of the public health, and therefore, batches thereof are exempt from certification pursuant to section 706(c) of the act.

b. By adding new § 73.2329 to Subpart C, to read as follows:

§ 73.2329 Guanine.

(a) *Identity and specifications.* (1) The color additive guanine shall conform in identity and specifications to the requirements of § 73.1329 (a) (1) and (b).

(2) Color additive mixtures of guanine may contain the following diluents:

(i) For coloring cosmetics generally, only those diluents listed under § 73.1001 (a) (1);

(ii) For coloring externally applied cosmetics, only those diluents listed in § 73.1001 (b) and, in addition, nitrocellulose.

(b) *Uses and restrictions.* The color additive guanine may be safely used in cosmetics generally, including cosmetics intended for use in the area of the eye, in amounts consistent with good manufacturing practice.

(c) *Labeling requirements.* The color additive and any mixtures prepared therefrom intended solely or in part for coloring purposes shall bear, in addition

to any other information required by law, labeling in accordance with the provisions of § 70.25 of this chapter.

(d) *Exemption from certification.* Certification of this color additive is not necessary for the protection of the public health, and therefore, batches thereof are exempt from certification pursuant to section 706(c) of the act.

§ 81.1 [Amended]

2. In § 81.1 *Provisional lists of color additives* by amending paragraph (g) by deleting the listing for "Guanine (pearl essence)."

Any person who will be adversely affected by the foregoing order may at any time on or before August 22, 1977, file with the Hearing Clerk (HFC-20), Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, Md. 20857, written objections thereto. Objections shall show wherein the person filing will be adversely affected by the order, specify with particularity the provisions of the order deemed objectionable, and state the grounds for the objections. Objections shall be filed in accordance with the requirements of § 71.30 (21 CFR 71.30). If a hearing is requested, the objections shall state the issues for the hearing, shall be supported by grounds factually and legally sufficient to justify the relief sought, and shall include a detailed description and analysis of the factual information intended to be presented in support of the objections in the event that a hearing is held. Four copies of all documents shall be filed and should be identified with the Hearing Clerk docket number found in brackets in the heading of this order. Received objections may be seen in the Hearing Clerk's office, between 9 a.m. and 4 p.m., Monday through Friday.

Effective date: August 22, 1977, except as to any provisions that may be stayed by the filing of proper objections. Notice of the filing of objections or lack thereof will be announced by publication in the FEDERAL REGISTER.

(Sec. 706 (b), (c), and (d), 74 Stat. 399-403 (21 U.S.C. 376 (b), (c), and (d)); sec. 203, 74 Stat. 404-407 (21 U.S.C. note).)

Dated: July 14, 1977.

WILLIAM F. RANDOLPH,
Acting Associate Commissioner
for Compliance.

[FR Doc. 77-20783 Filed 7-21-77; 8:45 am]

[Docket No. 77C-0210]

PART 73—LISTING OF COLOR ADDITIVES EXEMPT FROM CERTIFICATION

PART 81—GENERAL SPECIFICATIONS AND GENERAL RESTRICTIONS FOR PROVISIONAL COLOR ADDITIVES FOR USE IN FOODS, DRUGS, AND COSMETICS

Zinc Oxide

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: This document "permanently" lists zinc oxide for use in ex-

ternally applied drugs and in cosmetics generally, including those intended for use in the area of the eye. The Cosmetic, Toiletry, and Fragrance Association, Inc., filed a petition for such use. The color additive will be removed from the provisional listing.

DATES: Effective August 22, 1977; objections by August 22, 1977.

ADDRESS: Written objection: Hearing Clerk (HFC-20), Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, Md. 20857.

FOR FURTHER INFORMATION CONTACT:

Gerald L. McCowin, Bureau of Foods (HFF-334), Department of Health, Education, and Welfare, 200 C Street SW., Washington, D.C. 20204, (202-472-5740).

SUPPLEMENTARY INFORMATION: The Commissioner of Food and Drugs, having evaluated the data in a petition (CAP 6C0122) filed by the Cosmetic, Toiletry, and Fragrance Association, Inc. (1133 15th Street NW., Washington, D.C. 20005), and other relevant material, concludes that zinc oxide is safe and suitable for use, under the conditions prescribed in the regulations, in coloring externally applied drugs and in coloring cosmetics generally, including drugs and cosmetics intended for use in the area of the eye, and that certification is not necessary for the protection of the public health. This order "permanently" lists zinc oxide for use in externally applied drugs under new § 73.1991 (21 CFR 73.1991) and also "permanently" lists zinc oxide for use in cosmetics generally, including those for use in the area of the eye, under new § 73.2991 (21 CFR 73.2991).

The provisional listing of zinc oxide for use in cosmetics under § 81.1(g) (21 CFR 81.1(g)) will be deleted when this order becomes effective on August 22, 1977, unless this order is stayed by the timely filing of objections.

Therefore, under the Federal Food, Drug, and Cosmetic Act (sec. 706 (b), (c), and (d), 74 Stat. 399-403, as amended (21 U.S.C. 376 (b), (c), and (d))) and the transitional provisions of the Color Additive Amendments of 1960 (Title II, Pub. L. 86-618, sec. 203, 74 Stat. 404-407 (21 U.S.C. 376 note)), and under authority delegated to the Commissioner (21 CFR 5.1), Parts 73 and 81 are amended as follows:

1. By amending Part 73:

a. By adding new § 73.1991 to Subpart B, to read as follows:

§ 73.1991 Zinc oxide.

(a) *Identity.* (1) The color additive zinc oxide is a white or yellow-white amorphous powder manufactured by the French process (described as the indirect process whereby zinc metal isolated from the zinc-containing ore is vaporized and then oxidized). It is principally composed of Zn.

(2) Color additive mixtures for drug use made with zinc oxide may contain only those diluents listed in this subpart as safe and suitable in color additive

mixtures for coloring externally applied drugs.

(b) *Specifications.* Zinc oxide shall conform to the following specifications and shall be free from impurities other than those named to the extent that such impurities may be avoided by good manufacturing practice:

Zinc oxide (as ZnO), not less than 99 percent.

Loss on ignition at 800° C, not more than 1 percent.

Cadmium (as Cd), not more than 15 parts per million.

Mercury (as Hg), not more than 1 part per million.

Arsenic (as As), not more than 3 parts per million.

Lead (as Pb), not more than 20 parts per million.

(c) *Uses and restriction.* The color additive zinc oxide may be safely used for coloring externally applied drugs, including those used in the area of the eye, in amounts consistent with good manufacturing practice.

(d) *Labeling.* The color additive and any mixtures prepared therefrom intended solely or in part for coloring purposes shall bear, in addition to any information required by law, labeling in accordance with the provisions of § 70.25 of this chapter.

(e) *Exemption from certification.* Certification of this color additive is not necessary for the protection of the public health, and therefore batches thereof are exempt from certification pursuant to section 706(c) of the act.

b. By adding new § 73.2991 to Subpart C, to read as follows:

§ 73.2991 Zinc oxide.

(a) *Identity and specifications.* The color additive zinc oxide shall conform in identity and specifications to the requirements of § 73.1991 (a) (1) and (b).

(b) *Use and restrictions.* Zinc oxide may be safely used in cosmetics, including cosmetics intended for use in the area of the eye, in amounts consistent with good manufacturing practice.

(c) *Labeling.* The color additive and any mixture prepared therefrom intended solely or in part for coloring purposes shall bear, in addition to any information required by law, labeling in accordance with § 70.25 of this chapter.

(d) *Exemption from certification.* Certification of this color additive is not necessary for the protection of the public health, and therefore batches thereof are exempt from certification pursuant to section 706(c) of the act.

§ 81.1 [Amended]

2. Part 81 is amended in § 81.1 *Provisional lists of color additives*, by deleting the entry for "Zinc oxide" in paragraph (g).

Any person who will be adversely affected by the foregoing order may at any time on or before August 22, 1977, file with the Hearing Clerk (HFC-20), Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, Md. 20857, written objections thereto. Objections shall show wherein the person filing will be

adversely affected by the order, specify with particularity the provisions of the order deemed objectionable, and state the grounds for the objections. Objections shall be filed in accordance with the requirements of § 71.30 (21 CFR 71.30). If a hearing is requested, the objections shall state the issues for the hearing, shall be supported by grounds factually and legally sufficient to justify the relief sought, and shall include a detailed description and analysis of the factual information intended to be presented in support of the objections in the event that a hearing is held. Four copies of all documents shall be filed and should be identified with the Hearing Clerk docket number found in the heading of this order. Received objections may be seen in the Hearing Clerk's office during working hours, Monday through Friday.

Effective date: August 22, 1977, except any provisions that may be stayed by the filing of proper objections. Notice of the filing of objections or lack thereof will be announced by publication in the FEDERAL REGISTER.

(Sec. 706 (b), (c), and (d), 74 Stat. 399-403 as amended (21 U.S.C. 376 (b), (c), and (d)); sec. 203, 74 Stat. 404-407 (21 U.S.C. 376 note).)

Dated: July 14, 1977.

WILLIAM F. RANDOLPH,
Acting Associate Commissioner
for Compliance.

[FR Doc. 77-20782 Filed 7-21-77; 8:45 am]

SUBCHAPTER D—DRUGS FOR HUMAN USE

[Docket No. 76N-0028]

PART 310—NEW DRUGS

Requirements for Inhalation Anesthetic Drug Products: Studies for Carcinogenic and Teratogenic Potential

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: This document requires animal studies and reports to the Food and Drug Administration (FDA) on the potential of inhalation anesthetic drug products to cause cancer and fetal abnormalities. The regulation, based on concern expressed in the medical literature and on findings in personnel exposed while administering these drugs, requires all holders of approved new drug applications (NDA's) and abbreviated new drug applications (ANDA's) for halogenated inhalation anesthetic drug products to conduct appropriate animal studies and to submit reports on the studies to FDA. Also, all NDA's and ANDA's for nonhalogenated and new halogenated inhalation anesthetic drug products approved on or after August 22, 1977, must contain the results of such studies.

DATES: Effective August 22, 1977. Workshop: December 5, 1977. Notification of intent to participate in workshop: October 20, 1977. Submission of preliminary study protocols: September 20, 1977. Submission of final protocols: February 13, 1978.

FOR FURTHER INFORMATION CONTACT:

Michael C. McGrane, Bureau of Drugs (HFD-30), Food and Drug Administration, Department of Health, Education, and Welfare, 5600 Fishers Lane, Rockville, MD 20857, 301-443-5220.

FOR NOTIFICATION OF INTENT TO PARTICIPATE IN THE WORKSHOP AND SUBMISSION OF INITIAL AND FINAL PROTOCOLS CONTACT:

I. David Wolfson, Bureau of Drugs (HFD-160), Food and Drug Administration, Department of Health, Education, and Welfare, 5600 Fishers Lane, Rockville, MD 20857, 301-443-3500.

SUPPLEMENTARY INFORMATION:

In a proposal published in the FEDERAL REGISTER of April 8, 1976 (41 FR 14888), the Commissioner of Food and Drugs proposed to require that holders of NDA's and ANDA's for halogenated inhalation anesthetic drug products and applicants for pending and future NDA's and ANDA's for all nonhalogenated and new halogenated inhalation anesthetic drug products conduct studies in animals to determine the carcinogenic potential and effects on reproduction, including the teratogenic potential, of their drug products and submit reports on the studies to FDA. Interested persons were given 60 days to submit comments on the proposal.

Eleven comments were received on the proposal: six from manufacturers of halogenated inhalation anesthetic drug products, three from professors of anesthesiology, one from an association of medical-gas manufacturers, and one from a government agency. A summary of the comments and the Commissioner's conclusions regarding them are as follows:

1. One comment objected to the proposal on the grounds that section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)) does not authorize FDA to require NDA holders to conduct studies on their drug products after their NDA's have been approved. The comment observed that section 505(j) of the act provides that NDA holders may be required to maintain records and make reports concerning data and information "received or otherwise obtained by such applicant with respect to such drugs * * *." It was the position of the comment that section 505(j) of the act only authorizes FDA to require the submission of records and reports obtained by the NDA holder in the normal conduct of its business and that it does not represent authority under which the agency can require that studies be conducted on drugs to generate records that will then be subject to the reporting requirements of that section.

The Commissioner concludes that this comment too narrowly construes the applicable statutory scheme. Section 505(j) of the act expressly authorizes FDA to monitor the marketing of a drug subject to an approved NDA to provide a basis for subsequently determining whether that approval should be withdrawn under section 505(e) of the act (21 U.S.C. 355