federal register

THURSDAY, SEPTEMBER 23, 1976

PART II:

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Food and Drug Administration

■

COLOR ADDITIVES

Title 21—Food and Drugs

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

SUBCHAPTER A—GENERAL

[Docket No. 76N-0368]

PART 8—COLOR ADDITIVES

Termination of Provisional Listing and Certification of FD&C Red No. 4 for Use in Maraschino Cherries and Ingested Drugs

The Food and Drug Administration (FDA) is cancelling all certificates and terminating the provisional listing and certification, and hence the approval, of the color additive FD&C Red No. 4 for use in maraschino cherries and ingested drugs, effective September 23, 1976. Published elsewhere in this issue of the FEDERAL REGISTER are regulations listing FD&C Red No. 4 for use in externally applied drugs and cosmetics and denying the petition for listing with respect to use in maraschino cherries and ingested drugs.

Section 8.501 (21 CFR 8.501) of the color additive regulations designates those color additives that are provisionally listed under section 203(b) of the transitional provisions of the Color Additive Amendments of 1960 (Title II, Pub. L. 86-618, 74 Stat. 404-407 (21 U.S.C. 376 note)), on an interim basis pending completion of scientific investigations needed for determinations about "permanent listing" in accordance with section 706 of the Federal Food, Drug, and Cosmetic Act (sec. 706, 74 Stat. 399-403 (21 U.S.C. 376)).

The color additive FD&C Red No. 4 has been in use in food for many years, having been originally approved for food use under its common name "Ponceau SX" through issuance on April 2, 1929 of Service and Regulatory Announcement Food and Drug (SRAFD) No. 3, Supplement No. 1, by the Food, Drug, and Insecticide Administration, Department of Agriculture. SRAFD No. 3 supplement No. 1, added FD&C Red No. 4 to the list of color additives accepted for voluntary certification. FD&C Red No. 4 was approved for drug and cosmetic use as a permitted "coal-tar" color after enactment of the Federal Food, Drug, and Cosmetic Act in 1938 by order published in the FEDERAL REGISTER of May 9, 1939 (4 FR 1922, 1936).

Under section 706 of the act, as revised by the Color Additive Amendments of 1960, a color additive may be approved only if data establish that it is safe under its permitted conditions of use. However, the transitional provisions of those amendments provide for provisional listing of color additives in use in 1960 for a period of time necessary to complete the scientific investigations needed to establish their safety. Under this procedure, FD&C Red No. 4 was provisionally listed for use in food, drugs, and cosmetics on July 12, 1960, and appeared officially on the provisional list published in the FEDERAL REGISTER of October 12, 1960 (25 FR 9759). FD&C Red No. 4 is currently provisionally listed for use in maraschino cherries, short-term ingested drugs, and externally applied drugs and cosmetics.

Concern about the safety of FD&C Red No. 4 when used in food and ingested drugs was first raised in 1964. The basis for concern about possible harm from ingesting FD&C Red No. 4 was a 7-year feeding study in which dogs were fed the color additive at levels of 2 percent and 1 percent in the diet. Adverse effects consisting of hemorrhagic papillomas in the urinary bladder detected both grossly and microscopically, and atrophy of the zona glomerulosa in the adrenals seen microscopically, were found at both feeding levels. Three of the five dogs fed at the 2 percent level died during the study after 6 months, 9 months, and 5½ years. Two of the dogs fed at the 2 percent level and all five of the dogs fed at the 1 percent level survived to the completion of the 7-year study.

On the basis of the results of this study, the provisional listing of FD&C Red No. 4 for use in food, ingested drugs, and ingested cosmetics was terminated by regulation published in the FEDERAL REGISTER of December 11, 1964 (29 FR 16983). Because no questions about the safety of FD&C Red No. 4 for external uses were raised by the feeding study, the December 11, 1964 regulation provisionally listed the color additive under the name Ext. D&C Red No. 24 for use in externally applied drugs and cosmetics.

In 1965, the National Cherry Growers and Industries Foundation and the Maraschino Cherry and Glace Fruit Association requested that FD&C Red No. 4 again be provisionally listed for limited food use in maraschino cherries. The Commissioner of Food and Drugs, in a regulation published in the FEDERAL REGISTER of August 19, 1965 (30 FR 10289), concluded that this limited use of FD&C Red No. 4 in food would present no potential for harm to the public and therefore restored the color additive to the provisional list, restricting use of the color to maraschino cherries at a level of 150 parts per million (ppm). The regulation also simultaneously revoked the provisional listing for Ext. D&C Red No. 24 and provisionally listed FD&C Red No. 4 for use in externally applied drugs and cosmetics.

In 1965, the Pharmaceutical Manufacturers Association (PMA) requested that FD&C Red No. 4 be restored to the provisional list for use in ingested drugs. The Commissioner concluded that consumption of the color additive from ingested drug use would be minimal and, by regulation published in the FEDERAL REGISTER of October 14, 1965 (30 FR 13056), amended the provisional listing for FD&C Red No. 4 to permit its use in short-term ingested drugs with specific limitations. The regulation, under § 8.503(c)(2) (21 CFR 8.503(c)(2)), permitted FD&C Red No. 4 to be used in ingested drugs provided that "the labeling does not recommend nor suggest continuous administration to patients, and the amount of FD&C Red No. 4 used is such that not more than 5 milligrams of the color additive is consumed per day if the recommended drug dosage is followed. For the purpose of this order, a recommendation or suggestion for use longer than 6 weeks shall be considered a recommendation for continuous administration."

The Commissioner's conclusions in 1965 that FD&C Red No. 4 could safely be used in maraschino cherries and short-term ingested drugs were based on the following:

1. The Division of Pharmacology of FDA had completed phase one of an FD&C Red No. 4 feeding study which had begun in October 1964. The results of that study showed no adverse effects, either grossly or microscopically, in eight young dogs fed 400 milligrams (mg) per day of FD&C Red No. 4 for 6 months.

2. In another study no significant adverse effects were detected in guinea pigs fed FD&C Red No. 4 for 6 months at the 1 percent level in the diet.

3. No adverse effects were found in rats and mice fed FD&C Red No. 4 in a 2-year study.

4. A tentative no-effect level could be extrapolated from the 7-year feeding study from the adverse reactions in the dogs fed FD&C Red No. 4 at the 1 percent dietary level as compared to the reactions in those dogs fed at the 2 percent dietary level.

5. Consumption of FD&C Red No. 4 from maraschino cherries (approximately 1 mg of the color additive per cherry) and short-term ingested drugs (5 mg per day under permitted conditions of use) would be minimal.

A color additive petition (CAP 5I1) seeking the "permanent" listing of FD&C Red No. 4 for use in maraschino cherries, short-term ingested drugs, and externally applied drugs and cosmetics was submitted to FDA on March 27, 1968 by PMA. The Toilet Goods Association, now the Cosmetic, Toiletry and Fragrance Association (CTFA), and the Certified Color Manufacturers Association (CCMA) joined the PMA as copetitioners to list FD&C Red No. 4. A notice of filing of the petition was published in the FEDERAL REGISTER of November 20, 1968 (33 FR 17205).

Submission of this petition to list FD&C Red No. 4 was deferred until 1968 to permit completion of a 2-year feeding study with dogs that had been initiated by Hazleton Laboratories, Inc., on March 18, 1965. This study was intended to establish unequivocally a no-effect level for the urinary and adrenal effects seen in the 7-year feeding study discussed above. The 58 dogs in the Hazleton study were fed FD&C Red No. 4 at levels of 0, 20, 50, and 250 milligrams/kilogram of body weight per day.

The dogs in the Hazleton study showed lesions in the urinary bladder in all groups fed FD&C Red No. 4. No dogs in the control group, however, showed lesions in the urinary bladder. While Hazleton concluded in a report received by FDA on October 7, 1969, that the lesions found were "related directly to the techniques of repeated catheterization which was required to study the level of urinary potassium" and not to the ingestion of FD&C Red No. 4, FDA pathologists who reviewed the study results concluded otherwise. In an August 23, 1972 memorandum to Dr. Charles Kokoski, Assist-

ant Director for Petitions Review, Division of Toxicology, FDA, Dr. Stuart Levin, one of the FDA reviewing pathologists, concluded:

Though Hazleton Labs has submitted a statement by several pathologists and a concurring article (Journal of the American Medical Association, 193:196, 1965) proposing that emorrhagic polyps in two low dose animals might have been caused by catheterization, the facts remain that the lesions were similar in type to those seen in uncatheterized FDA dogs (in the earlier FDA study), and such lesions were not seen in control dogs. I believe these should be considered compound-related lesions.

Review by FDA of microslides of the kidneys, urinary bladder and adrenals of all dogs in the Hazleton study also showed atrophy of the zona glomerulosa of the adrenal cortex at all feeding levels after 2 years. This response, it was concluded, was induced by ingestion of FD&C Red No. 4. Food and Drug Administration scientists ultimately concluded that an unequivocal no-effect level for FD&C Red No. 4 could not be determined from the Hazleton study and that an additional study involving dogs was necessary before a final determination could be made concerning the safety of FD&C Red No. 4. Because of the limited use of the color additive, however, the Commissioner concluded that FD&C Red No. 4 should continue to be provisionally listed pending further scientific investigations.

The Commissioner's conclusion that existing data appeared to be inadequate to establish a no-effect level in the dog for FD&C Red No. 4 was conveyed to the petitioners as early as November 25, 1969. The Commissioner's conclusion that an additional study was required to resolve the questions concerning the urinary bladder lesions before the color additive could be demonstrated to be safe as required by section 706 of the act was formally communicated to CTFA, one of the petitioners, and to Hazleton Laboratories, by letters on October 8, 1974. The need for an additional 2-year feeding study was also made known by FDA to the Inter-Industry Color Task Force, consisting of representatives of the food, drug, and cosmetic industries representing the petitioners, and at several meetings between FDA personnel and the CTFA-Color Additive Petition Committee. By letter of June 25, 1975, to Dr. John Kirschman, chairman of the Inter-Industry Color Task Force, FDA advised the sponsoring industries in detail of the reasons why a new study was needed. Most recently, separate letters to CTFA, CCMA and PMA in January and February of 1976 officially reiterated the need for an additional study.

In recent months, the commercial sponsors and some industrial users of FD&C Red No. 4 have expressed a willingness to begin the 2-year feeding study necessary to resolve the questions regarding the safety of the color additive when ingested. The Commissioner concludes, however, that this belated willingness to undertake a study to resolve the uncertainties about the safety of FD&C Red No. 4, when those uncertainties and the need for an additional study have been known to the industry sponsors for several years, is an insufficient basis to warrant continued provisional listing of the color additive. Under the transitional provisions of the Color Additive Amendments of 1960, continued provisional listing of a color additive is appropriate only when studies in progress or under evaluation are capable of demonstrating the safety of the color additive involved. There is currently no study available or underway to resolve the uncertainties about FD&C Red No. 4 and therefore it would not be proper to extend the provisional listing for FD&C Red No. 4 for at least 3 years—the time required to conduct and evaluate a 2-year feeding study and to report the findings to FDA for evaluation. The Commissioner concludes, therefore, that continued provisional listing of FD&C Red No. 4 for use in maraschino cherries and short-term ingested drugs is no longer appropriate.

The current "closing date" for continued use of FD&C Red No. 4 was postponed to September 30, 1976 by a regulation published in the FEDERAL REGISTER of January 5, 1976 (41 FR 754). That postponement was based on the assumption that a study was either underway in response to FDA's June 25, 1975 letter to Dr. Kirschman or would be undertaken soon thereafter to resolve the uncertainties about the safety of FD&C Red No. 4 when ingested. Because there are no studies in progress or under evaluation that can resolve these uncertainties, the Commissioner finds that the basis for the postponement no longer exists and hereby terminates the postponement of the closing date for the provisional listing of FD&C Red No. 4 for use in maraschino cherries and short-term ingested drugs in accordance with section 203(a)(2) of the transitional provisions of the Color Additive Amendments of 1960. Also, under section 203(d)(1)(E) of the amendments, the Commissioner concludes that the provisional listing of FD&C Red No. 4 for these uses should be terminated because such action is necessary to protect the public health, in that questions have been raised about the safety of the color additive when ingested and the available data do not permit a determination that this use is safe. Published elsewhere in this issue of the FEDERAL REGISTER is a notice denying the portion of the petition proposing to list FD&C Red No. 4 for use in maraschino cherries and ingested drugs. The safety of FD&C Red No. 4 in externally applied drugs and cosmetics has been demonstrated and a regulation listing the color additive for those uses is published elsewhere in this issue of the FEDERAL REGISTER.

All certificates heretofore issued for batches of FD&C Red No. 4 for use in maraschino cherries and ingested drugs are hereby cancelled, effective September 23, 1976. After September 23, 1976, adding FD&C Red No. 4 to any food or ingested drug will cause such product to be adulterated within the meaning of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.) and subject to regulatory action. This prohibition applies to the use of straight colors, lakes, mixtures of FD&C Red No. 4 or its lakes with other colors, and mixtures of straight colors and lakes with ingredients functioning only as diluents. The Commissioner concludes that the protection of the public health does not require the recall from the market of maraschino cherries and ingested drugs containing the color additive, or the destruction of foods or drugs in preparation to which the color additive has already been added.

Manufacturers of new drugs and new animal drugs (including certifiable antibiotics for animal use) that are ingested and contain FD&C Red No. 4 may either delete the color additive or substitute a different color in accordance with the provisions of § 314.8(d)(3) and (e) or § 514.8(d)(3) and (e), as appropriate (21 CFR 314.8(d)(3) and (e), and 514.8(d)(3) and (e)). The applicant shall submit data providing the new composition and showing that the change in composition does not interfere with any assay or other control procedures used in manufacturing the drug, or that the assay and control procedures have been revised to make them adequate. Also, the applicant shall submit data available to establish the stability of the revised formulation or, if the data are too limited to support a conclusion that the drug will retain its declared potency for a reasonable marketing period, a commitment to test the stability of marketed batches at reasonable intervals, to submit the data as they become available, and to recall from the market any batch found to fall outside the approved specifications for the drug.

The Commissioner is aware that supplies of alternative color additives may be difficult to obtain immediately. Consequently, food and drug labeling stating that the product contains "artificial color" because of the prior inclusion of FD&C Red No. 4 may continue to be used with the uncolored product during the time necessary to obtain supplies of alternative color ingredients or until the current supplies of labeling are used, whichever occurs first.

The Commissioner has carefully considered the environmental effects of this action and because the action will not significantly affect the quality of the human environment, has concluded that an environmental impact statement is not required. A copy of the FDA environmental assessment, together with copies of the other documents mentioned above, are on file with the Hearing Clerk, Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20852. Because this action is final (not proposed), an inflation impact evaluation is not required by Executive Order 11821 (3A CFR, 1975 Compilation, p. 203).

Therefore, under the transitional provisions of the Color Additive Amendments of 1960 (Title II, Pub. L. 86-618, 74 Stat. 404-407 (21 U.S.C. 376 note)) and under authority delegated to the Commissioner (21 CFR 5.1) (recodi-

tion published in the FEDERAL REGISTER of June 15, 1976 (41 FR 24262)), Part 8 of Chapter I of Title 21 of the Code of Federal Regulations is amended as follows:

1. In § 8.501, the entry for FD&C Red No. 4 in the table in paragraph (a) is revised in the "Restrictions" column (reflecting in the "Closing date" column the Commissioner's extension published under Docket No. 76N-0365 elsewhere in this issue) to read as follows:

§ 8.501 Provisional lists of color additives.

(a) * * *

	Closing date		
	Food use	Drug and cosmetic use	Restrictions
F.D. & C. red No. 4 (sec. 8.4103 of this chapter):		Dec. 31, 1976, or until a new closing date is established.[1]	For coloring externally applied drugs and cosmetics.

[1] Lakes only.

2. In § 8.502, the flush paragraph appearing after paragraph (d)(3), concerning FD&C Red No. 4, is revised to read as follows:

§ 8.502 Termination of provisional listings of color additives.

(d) * * *

(3) * * *

The Commissioner of Food and Drugs has concluded that available data do not permit the establishment of a safe level of use of this color additive in food, ingested drugs and ingested cosmetics. In order to protect the public health, the Commissioner hereby terminates the provisional listing of FD&C Red No. 4 for use in food and ingested drugs. The Commissioner has previously terminated the provisional listing of FD&C Red No. 4 for use in ingested cosmetics. Section 9.63 of this chapter is retained in Part 9 to permit the use of lakes of FD&C Red No. 4 in externally applied drugs and cosmetics.

§ 8.503 [Amended]

3. In § 8.503, paragraph (c) is revoked.

4. In § 8.510, paragraph (c) is revised to read as follows.

§ 8.510 Cancellation of certificates.

(c) Certificates issued for FD&C Red No. 4 and all mixtures containing this color additive are cancelled and have no effect after September 23, 1976 insofar as food, ingested drugs, and ingested cosmetics are concerned, and use of this color additive in the manufacture of food, ingested drugs, and ingested cosmetics after this date will result in adulteration. The certificates shall continue in effect for the use of FD&C Red No. 4 in externally applied drugs and cosmetics. The Commissioner finds, on the basis of the scientific evidence before him that no action has to be taken to remove from the market food, ingested drugs and ingested cosmetics containing the color additive.

Notice and public procedure are not necessary prerequisites to the promulgation of this order because section 203 (d)(2) of Pub. L. 86-618 so provides.

Effective date: These regulations shall be effective September 23, 1976.

(Title II, Pub. L. 86-618, 74 Stat. 404-407 (21 U.S.C. 376 note).)

Dated: September 17, 1976.

SHERWIN GARDNER,
Acting Commissioner of Food and Drugs.

[FR Doc.76-27817 Filed 9-22-76;8:45 am]

[Docket No. 76N-0367]

PART 8—COLOR ADDITIVES

PART 9—COLOR CERTIFICATION

Listing of FD&C Red No. 4 for Use in Externally Applied Drugs and Cosmetics

The Food and Drug Administration (FDA) is "permanently" listing FD&C Red No. 4 for use in *externally applied* drugs and cosmetics, effective October 27, 1976. Objections to this order may be filed by adversely affected persons by October 26, 1976. Elsewhere in this issue of the FEDERAL REGISTER the Commissioner of Food and Drugs is issuing regulations terminating the provisional listing of FD&C Red No. 4 for use in maraschino cherries and ingested drugs and denying that portion of the petition seeking "permanent" listing of the color additive for those two uses.

A notice published in the FEDERAL REGISTER of November 20, 1968 (33 FR 17205) stated that a petition (CAP 61) for the "permanent" listing of FD&C Red No. 4 as a color additive for use in maraschino cherries, ingested drugs, and externally applied drugs and cosmetics had been filed by the Toilet Goods Association, Inc. (now the Cosmetic, Toiletry and Fragrance Association, 1133 15th St., NW., Washington, D.C. 20005); the Pharmaceutical Manufacturers Association (1155 15th St., NW., Washington, D.C. 20005); and the Certified Color Industry Committee (now the Certified Color Manufacturers Association, *900 17th St., NW.*, Washington, D.C. 20006), c/o Hazleton Laboratories, Inc., PO 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).

The Commissioner has evaluated the data in the petition and concludes that FD&C Red No. 4 is safe under the conditions set forth below for use in coloring externally applied drugs and cosmetics and that certification is necessary for the protection of the public health. This order "permanently" lists FD&C Red No. 4 for use in externally applied drugs and cosmetics under new §§ 8.4103 and 8.7163 (21 CFR 8.4103 and 8.7163). The provisional listing of FD&C Red No. 4 for use in externally applied drugs and cosmetics under § 8.501(a) (21 CFR 8.501(a)), which is extended to December 31, 1976 by regulation published elsewhere in this issue of the FEDERAL REGISTER under Docket No. 76N-0365, will be deleted when this order becomes effective on October 27, 1976, unless this order is stayed by the timely filing of objections, in which case the provisional listing will continue until December 31, 1976 unless terminated or extended by regulation.

This order does not list FD&C Red No. 4 for use in lakes as requested in the petition. The Commissioner notes that proposed regulations related to the use of color additives in lakes were published in the FEDERAL REGISTER of May 11, 1965 (30 FR 6490). The Commissioner advises that new proposed regulations governing the use of color additives in lakes will be published in the FEDERAL REGISTER in the near future and concludes that the listing of colors for use in lakes can best be implemented by general regulations. FD&C Red No. 4 will, therefore, continue to be approved for use in lakes for coloring externally applied drugs and cosmetics under the general provisional listing for "Lakes (FD&C)" under § 8.501(a) (21 CFR 8.501(a)).

This order establishes specifications for the certification of batches of FD&C Red No. 4 which are more restrictive than those currently prescribed under § 9.63 (21 CFR 9.63). Additionally, the identity of the color has been revised to be consistent with current chemical nomenclature. The identity nomenclature and the specifications currently prescribed in § 9.63 become obsolete upon the effective date of new § 8.4103 and § 8.7163. However, it is necessary to maintain § 9.63 to provide for the use of the color additive in lakes. Accordingly, § 9.63 is revised to reference the identity nomenclature and specifications prescribed by § 8.4103.

Therefore, under provisions of the Federal Food, Drug, and Cosmetic Act (sec. 706 (b), (c), and (d), 74 Stat. 399-403 (21 U.S.C. 376 (b), (c), (d))); under the transitional provisions of the Color Additive Amendments of 1960 (Pub. L. 86-618, Title II, 74 Stat. 404-407 (21 U.S.C. 376 note)); and under authority delegated to the Commissioner (21 CFR 5.1) (recodification published in the FEDERAL REGISTER of June 15, 1976 (41 FR 24262)), Parts 8 and 9 of Chapter I of Title 21 of the Code of Federal Regulations are amended as follows:

1. Part 8 is amended:

§ 8.501 [Amended]

a. In paragraph (a) of § 8.501 Provisional lists of color additives (as amended elsewhere in this issue of the FEDERAL REGISTER under Docket No. 76N-0365),

the entry for FD&C Red No. 4 for use in externally applied drugs and cosmetics is deleted.

b. In § 8.502, the flush paragraph appearing after paragraph (d)(3), concerning FD&C Red No. 4, is revised to read as follows:

§ 8.502 Termination of provisional listings of color additives.

(d) * * *
(3) * * *

The Commissioner of Food and Drugs has concluded that available data do not permit the establishment of a safe level of use of this color additive in food, ingested drugs and ingested cosmetics. In order to protect the public health, the Commissioner hereby terminates the provisional listing of FD&C Red No. 4 for use in food and ingested drugs. The Commissioner has previously terminated the provisional listing of FD&C Red No. 4 for use in ingested cosmetics. FD&C Red No. 4 is listed for use in externally applied drugs and cosmetics by §§ 8.4103 and 8.7163, respectively. Section 9.63 of this chapter is retained in Part 9 to permit the use of lakes of FD&C Red No. 4 in externally applied drugs and cosmetics.

c. By adding to Subpart E new § 8.4103 to read as follows:

§ 8.4103 FD&C Red No. 4.

(a) *Identity.* (1) The color additive FD&C Red No. 4 is principally the disodium salt of 3-[(2,4-dimethyl-5-sulfophenyl)azo]-4-hydroxy-1-naphthalenesulfonic acid.

(2) Color additive mixtures for use in externally applied drugs made with FD&C Red No. 4 may contain only those diluents that are suitable and that are listed in Subpart F of this part for use in color additive mixtures for coloring externally applied drugs.

(b) *Specifications.* FD&C Red No. 4 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:

Sum of volatile matter (at 135° C.) and chlorides and sulfates (calculated as sodium salts), not more than 13 percent.
Water-insoluble matter, not more than 0.2 percent.
5-Amino-2,4-dimethyl - 1 - benzenesulfonic acid, sodium salt, not more than 0.2 percent.
4-Hydroxyl-1-naphthalenesulfonic acid, sodium salt, not more than 0.2 percent.
Subsidiary colors, not more than 2 percent.
Lead (as Pb), not more than 10 parts per million.
Arsenic (as As), not more than 3 parts per million.
Mercury (as Hg), not more than 1 part per million.
Total color, not less than 87 percent.

(c) *Uses and restrictions.* FD&C Red No. 4 may be safely used in externally applied drugs in amounts consistent with good manufacturing practice.

(d) *Labeling.* The label of the color additive and any mixtures prepared therefrom intended solely or in part for coloring purposes shall conform to the requirements of § 8.32.

(e) *Certification.* All batches of FD&C Red No. 4 shall be certified in accordance with regulations in Subpart A of this part.

d. By adding to Subpart G new § 8.7163 to read as follows:

§ 8.7163 FD&C Red No. 4.

(a) *Identity and specifications.* The color additive FD&C Red No. 4 shall conform in identity and specifications to the requirements of § 8.4103(a)(1) and (b).

(b) *Uses and restrictions.* FD&C Red No. 4 may be safely used for coloring externally applied cosmetics in amounts consistent with good manufacturing practice.

(c) *Labeling.* The label of the color additive shall conform to the requirements of § 8.32.

(d) *Certification.* All batches of FD&C Red No. 4 shall be certified in accordance with regulations in Subpart A of this part.

2. Part 9 is amended by revising § 9.63 to read as follows:

§ 9.63 FD&C Red No. 4.

The color additive FD&C Red No. 4 shall conform in identity and specifications to the requirements of § 8.4103(a)(1) and (b) of this chapter. FD&C Red No. 4 is restricted to use in externally applied drugs and cosmetics.

Any person who will be adversely affected by the foregoing order may at any time on or before October 26, 1976 file with the Hearing Clerk, Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20852, 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 § 8.19 (21 CFR 8.19). 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. Five 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 above office during working hours, Monday through Friday.

This order shall become effective October 27, 1976, 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), (d), 74 Stat. 399–403 (21 U.S.C. 376 (b), (c), and (d)); Title II, Pub. L. 86–618, 74 Stat. 404–407 (21 U.S.C. 376 note).)

Dated: September 17, 1976.

SHERWIN GARDNER,
Acting Commissioner of Food and Drugs.

[FR Doc.76-27819 Filed 9-22-76;8:45 am]

[Docket No. 76N-0365]

PART 8—COLOR ADDITIVES

Termination of Provisional Listing for Color Additives

The Food and Drug Administration (FDA) is terminating the provisional listing, and hence the approval, of aluminum stearate, bentonite, calcium silicate, calcium stearate, gold, kaolin, lithium stearate, magnesium aluminum silicate, magnesium stearate, and zinc stearate for use as color additives in cosmetics, effective October 26, 1976.

Section 8.501 (21 CFR 8.501) of the color additive regulations designates those color additives that are provisionally listed, pursuant to section 203(b) of the transitional provisions of the Color Additive Amendments of 1960 (Title II, Pub. L. 86-618, 74 Stat. 404-407 (21 U.S.C. 376 note)), on an interim basis pending completion of scientific investigations needed for determinations as to "permanent" listing in accordance with section 706 of the Federal Food, Drug, and Cosmetic Act (sec. 706, 74 Stat. 399-403 (21 U.S.C. 376)).

A notice published in the FEDERAL REGISTER of August 6, 1973 (38 FR 21200), stated that petitions (CAP 8C0071, 8C0078, and 9C0094) for the "permanent" listing of aluminum stearate, bentonite, calcium silicate, calcium stearate, kaolin, lithium stearate, magnesium aluminum silicate, magnesium stearate, and zinc stearate had been filed by the Cosmetic, Toiletry and Fragrance Association, Inc. (CFTA), 1133 15th St., NW., Washington, DC 20005, c/o Hazleton Laboratories, Inc., P.O. Box 30, Falls Church, VA 22046. The petition was filed pursuant to section 706 of the act. Provisional listing for these nine substances has been continued pending completion of the evaluation of available data to determine whether the substances should be "permanently" listed.

On August 9, 1976, CTFA wrote to FDA requesting that the color additive petitions for these nine substances be withdrawn without prejudice to future filing. Published elsewhere in this issue of the FEDERAL REGISTER is a notice announcing the withdrawal of the petitions. The Commissioner is terminating the provisional listing of these nine substances for use as color additives in cosmetics, effective October 26, 1976, because there are no pending color additive petitions or progress reports for them as required by § 8.501.

In its letter requesting withdrawal of the petitions, CTFA stated that a survey disclosed that none of its member firms

were using any of the nine substances covered by its three petitions for coloring cosmetics, although certain of the substances are used in cosmetics for noncoloring purposes. However, CTFA advised that its survey was limited to its members' practices and did not cover those of the entire cosmetic industry. The Commissioner is not aware of any person who is currently coloring cosmetics with any of the nine substances covered by the CTFA petitions. However, because of the possibility that some cosmetic manufacturers are using one or more of the nine substances, to color their products and because there are no questions of safety regarding their use, the Commissioner is making the termination of the provisional list for the nine substances effective October 26, 1976. This 30-day period will permit both an orderly change in any cosmetic formulations that contain any of the nine substances as color additives and time for any interested person to submit a color additive petition for any of the nine substances.

Gold, the 10th substance that is the subject of this regulation, was provisionally listed for use as a color additive in cosmetics, and appeared on the so-called "Harvey list" of color additives, published in the FEDERAL REGISTER of October 8, 1974 (39 FR 36126). That notice stated that provisional listing would continue for those "Harvey list" color additives for which color additive petitions or progress reports were submitted by December 31, 1974. A progress report on gold was submitted and the closing date for the provisional listing of gold, as well as those for other provisionally listed color additives, was postponed until December 31, 1975, by regulation published in the FEDERAL REGISTER of April 4, 1975 (40 FR 15087).

No color additive petition for gold or progress report under § 8.501 was submitted by the postponed closing date, December 31, 1975. However, through inadvertence, the closing date for the provisional listing of gold was postponed along with those of the other provisionally listed color additives by regulation published in the FEDERAL REGISTER of January 5, 1976 (41 FR 754). The Commissioner is terminating the provisional listing for gold for use as a color additive in cosmetics in this regulation because no color additive petition or progress report has been submitted as required by § 8.501. Furthermore, the Commissioner is not aware of any person who is currently coloring cosmetics with gold. The termination is, however, being made effective October 26, 1976, to permit both an orderly change in any cosmetic formulations that contain gold as a color additive and time for any interested person to submit a color additive petition for gold.

After October 26, 1976, adding aluminum stearate, bentonite, calcium silicate, calcium stearate, gold, kaolin, lithium stearate, magnesium aluminum silicate, magnesium stearate, and zinc stearate to any cosmetic for use as a color additive will cause such product to be adulterated within the meaning of the Federal Food, Drug, and Cosmetic Act and subject to regulatory action. The Commissioner concludes that the protection of the public health does not require the recall from the market of cosmetics, if any, containing any of the 10 substances for use as color additives, or the destruction of products in preparation to which any of the 10 substances have already been added.

Nothing in this action precludes the Commissioner from determining that any of the 10 substances that are the subject of this regulation is in use to color cosmetics, and is, therefore, a color additive under section 706 of the act. The Commissioner expressly reserves the right in such an instance to require the prompt submission of a color additive petition for the substance, or to require that its use be terminated, or to take any other regulatory action, including court enforcement action, deemed appropriate.

In its August 9, 1976 letter withdrawing its three color additive petitions for the nine substances, CTFA requested that the use of cosmetic labeling listing any of the substances as color additives in accordance with § 701.3 (21 CFR 701.3) be permitted for 1 year so that existing stocks of labeling may be depleted. The Commissioner concludes that this request is reasonable. Consequently, cosmetic labeling listing any of the 10 substances that are the subject of this regulation as color additives, may continue to be used until current supplies are exhausted, or until September 23, 1976, whichever occurs first.

The Commissioner has reviewed this regulation pursuant to Part 6 (21 CFR Part 6) and concludes that it will not significantly affect the quality of the human environment. Because this action is final—not proposed—an inflation impact evaluation is not required by Executive Order 11821 (3A CFR, 1975 Compilation, p. 203). Copies of the documents mentioned above are on file with the Hearing Clerk, Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20852.

Therefore, under the transitional provisions accompanying the Color Additive Amendments of 1960 to the Federal Food, Drug, and Cosmetic Act (Title II, Pub. L. 86-618, 74 Stat. 404-407 (21 U.S.C. 376 note)) and under authority delegated to the Commissioner (21 CFR 5.1) (recodification published in the FEDERAL REGISTER of June 15, 1976 (41 FR 24262)), Part 8 of Chapter I of Title 21 of the Code of Federal Regulations is amended as follows:

§ 8.501 [Amended]

In paragraph (g) of § 8.501 Provisional lists of color additives, the entries for aluminum stearate, bentonite, calcium silicate, calcium stearate, gold, kaolin, lithium stearate, magnesium aluminum silicate, magnesium stearate, and zinc stearate are deleted.

Notice and public procedure are not necessary prerequisites to the promulgation of this order because section 203(d)(2) of Pub. L. 86-618 so provides.

Effective date: These regulations shall become effective October 26, 1976.

(Title II, Pub. L. 86-618, 74 Stat. 404-407 (21 U.S.C. 376 note).)

Dated: September 17, 1976.

SHERWIN GARDNER,
Acting Commissioner of Food and Drugs.

[FR Doc.76-27822 Filed 9-22-76;8:45 am]

[Docket No. 76N-0365]

PART 8—COLOR ADDITIVES

Subpart—Provisional Regulations

Postponement of Closing Dates

The Commissioner of Food and Drugs, on his own initiative, is postponing the closing date for the use of 72 provisionally listed color additives until December 31, 1976. The Commissioner is also postponing the closing date for the provisional listing of FD&C Red No. 4 for external drug and cosmetic use until December 31, 1976, or until the regulation listing the color additive for these uses, published elsewhere in this issue of the FEDERAL REGISTER, becomes effective, whichever comes first. This order becomes effective September 23, 1976.

Under Title II of the Color Additive Amendments of 1960 (sec. 203(a)(2), Pub. L. 86-618, 74 Stat. 404 (21 U.S.C. 376 note)) and under authority delegated to him (21 CFR 5.1), the Commissioner is authorized to postpone the closing date of a provisional listing of a color additive on his own initiative or upon the application of an interested person. Section 203(d)(1) of Title II requires promulgation, insofar as practical, of a current listing of color additives and the particular uses thereof deemed provisionally listed.

The current closing date, September 30, 1976, established by a regulation published in the FEDERAL REGISTER of January 5, 1976 (41 FR 754), was based upon the Commissioner's conclusion that postponement until September 30, 1976, was consistent with the objective of carrying to completion, in good faith and as soon as reasonably practicable, the scientific investigations necessary for making a determination as to listing these color additives under section 706 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 376). The Commissioner also advised that a final determination on the listing under section 706 of many of the provisionally listed color additives was expected to be completed before September 30, 1976, and that, if appropriate, further postponements of the closing date would be made for provisionally listed colors for which final determinations were not possible.

Published elsewhere in this issue of the FEDERAL REGISTER are documents:

1. Terminating the provisional listing for FD&C Red No. 4 for use in maraschino cherries and ingested drugs;

2. Listing in FD&C Red No. 4 for use in externally applied drugs and cosmetics;

3. Denying the portion of the petition to list FD&C Red No. 4 for use in maraschino cherries and ingested drugs;

4. Terminating the provisional listing of carbon black for use in food, drugs, and cosmetics;

5. Denying the petition to list carbon black for use in food, drugs, and cosmetics;

6. Terminating the provisional listing of 10 substances for use as color additives in cosmetics.

7. Also published in this issue of the FEDERAL REGISTER is a proposal to postpone further the closing date for the use of certain of these 72 provisionally listed color additives. The preamble to that proposal sets forth the Commissioner's tentative conclusions with respect to listing or provisional listing for each of these color additives and a precise timetable for accomplishing the various actions described.

Nothing in this action affects the Commissioner's authority under the transitional provisions of the Color Additive Amendments of 1960 to terminate a closing date, terminate a listing, or impose restrictions with respect to a specific color additive on the provisional list.

The postponement of the closing date until December 31, 1976, accomplished by this regulation, is necessary to provide a brief period within which to prepare orders for those colors identified in the proposal as suitable for listing and to afford the public an opportunity to comment on the actions proposed to be taken with respect to the remaining provisionally listed color additives. Because of the shortness of time until the September 30, 1976, closing date, the Commissioner concludes that notice and public procedure on this regulation are impracticable and contrary to the public interest and that good cause exists for issuing this postponement as a final order. The regulation, to be effective September 23, 1976, will permit the uninterrupted use of the affected color additives. Therefore, in accordance with 5 U.S.C. 553(b)(B), and (d) (1), and (3), this postponement is issued as a final regulation and is being made effective on September 23, 1976. A 60-day comment period is being provided on the proposed regulation related to the 72 provisionally listed color additives published elsewhere in this issue of the FEDERAL REGISTER.

Therefore, under the transitional provisions accompanying the Color Additive Amendments of 1960 to the Federal Food, Drug, and Cosmetic Act (sec. 203(a)(2), (d)(1), Title II, Pub. L. 86-618; 74 Stat. 404-405 (21 U.S.C. 376 note)) and under authority delegated to the Commissioner, (21 CFR 5.1) (recodification published in the FEDERAL REGISTER of June 15, 1976 (41 FR 24262)), Part 8 is amended as follows:

§ 8.501 [Amended]

In § 8.501 *Provisional lists of color additives*, the closing dates for the color additives listed in paragraphs (a), (b), (c), (f), and (g) are changed to read "December 31, 1976."

Effective date: This order shall become effective September 23, 1976.

(Sec. 203(a)(2), (d)(1), Pub. L. 86-618; 74 Stat. 404-405 (21 U.S.C. 376 note).)

Dated: September 17, 1976.

SHERWIN GARDNER,
Acting Commissioner of Food and Drugs.

[FR Doc.76-27823 Filed 9-22-76;8:45 am]

[Docket No. 76N-0375]

PART 8—COLOR ADDITIVES

Termination of Provisional Listing of Carbon Black

The Food and Drug Administration (FDA) is terminating the provisional listing, and hence the approval, of carbon black (all-gas channel black) for use in food, drugs, and cosmetics, effective September 23, 1976. Published elsewhere in this issue of the FEDERAL REGISTER is a notice denying the petition to "permanently" list carbon black (all-gas channel black) for use in food, drugs, and cosmetics.

Section 8.501 (21 CFR 8.501) of the color additive regulations designates those color additives that are provisionally listed under section 203(b) of the transitional provisions of the Color Additive Amendments of 1960 (Title II, Pub. L. 86-618, 74 Stat. 404-407 (21 U.S.C. 376 note)), on an interim basis pending completion of scientific investigations needed for determinations about "permanent" listing in accordance with section 706 of the Federal Food, Drug, and Cosmetic Act (sec. 706, 74 Stat. 399-403 (21 U.S.C. 376)).

The color additive carbon black (all-gas channel black) was used commercially in food, drugs, and cosmetics prior to enactment of the Color Additive Amendments of 1960. Accordingly, under section 203(b)(2) of the transitional provisions of the amendments, carbon black (all-gas channel black) was deemed provisionally listed for use in food, drugs, and cosmetics on July 12, 1960. Carbon black (all-gas channel black) appeared on the provisional list for use in food and cosmetics when that list was initially published in the FEDERAL REGISTER of October 12, 1960 (25 FR 9759). The use of carbon black (all-gas channel black) in drugs was provisionally listed when the list was first amended by notice published in the FEDERAL REGISTER of August 16, 1961 (26 FR 7578).

Under section 706 of the act, as revised by the Color Additive Amendments of 1960, a color additive may be approved only if data establish that it is safe under its permitted conditions of use. However, the transitional provisions of those amendments provide for provisional listing of color additives in use in 1960 for a period of time necessary to complete the scientific investigations needed to establish their safety. In accordance with this procedure, carbon black (all-gas channel black) has been provisionally listed since 1960 and is currently provisionally listed for use in food, drugs, and cosmetics.

Carbon black is defined in the "Encyclopedia of Industrial Chemical Analysis" as "the generic term for a wide variety of finely divided carbonaceous pigments produced by the pyrolysis of hydrocarbon gases or oils" (Schubert Ford, and Lyon, "Analysis of Carbon Black," in "Encyclopedia of Industrial Chemical Analysis" 8:174-243 (1969)). There are five basic types of carbon black that are classified according to the source of raw materials or method of manufacture: impingement or channel carbons, lamp black, thermal blacks, acetylene blacks, and furnace carbons (ibid.). Of these five types, only the impingement or channel carbon, and more specifically, that type produced by using all natural gas, has been provisionally listed for use in food, drugs, and cosmetics. The other four types of carbon blacks, including those that are made by the impingement or channel process using natural gas that is oil-enriched, have never been and are not now provisionally listed.

Concern about the safety of carbon black (all-gas channel black) in food, drugs, and cosmetics stems from the possibility that extractable polynuclear aromatic hydrocarbons (PNA's) may be present in the color. The PNA's, which are also referred to as polycyclic aromatic hydrocarbons, comprise a large family of chemicals where two to seven benzene rings have fused in an angular arrangement to form the PNA molecule. The particular PNA's that have raised the greatest concern are those containing three to six benzene rings in their molecular structure. Some of these particular PNA's, such as 3,4-benzpyrene and 1,2-benzanthracene, have been demonstrated to be carcinogens. Analysis of furnace blacks has disclosed the presence of 3,4-benzpyrene and 1,2-benzanthracene.

As explained more fully below in this preamble, carbon black produced by the channel process using all natural gas appears least likely of the carbon blacks to contain extractable PNA's, and toxicity studies on this compound have not disclosed any adverse effects. The Commissioner cannot reasonably conclude, however, that use of carbon black (all-gas channel black) is safe unless there are adequate data available to establish that the color additive contains no extractable PNA's. In addition, the Commissioner cannot "permanently" list carbon black (all-gas channel black) in the absence of data that permit establishment of specifications, i.e., precise physical and chemical properties of the color additive, to differentiate all-gas channel black from furnace carbons, lampblack, thermal blacks, acetylene blacks, and channel blacks manufactured with oil-enriched natural gas.

The petitioners have previously been advised by FDA that such data would be required for "permanent" listing. The petitioners were also advised that the color additive would, even if "permanently" listed, be subject to batch certification by FDA. Because samples of the carbon black (all-gas channel black) used in the various toxicological tests to

blish the safety of the color were not available for current analysis, the specifications for certification were to include physical and chemical properties of commercially available carbon black (all-gas channel black) that would differentiate it from the other types of carbon blacks and thus assure that the color certified was identical to the color tested, as well as a requirement that no extractable PNA's be measurable using an analytical method of suitable sensitivity.

In general, PNA's appear to be present in carbon blacks as a byproduct of the manufacturing process and are probably formed during combustion (H. L. Falk and P. E. Steiner, "The Identification of Aromatic Polycyclic Hydrocarbons in Carbon Blacks," Cancer Research, 12:40–43, 1952). Studies on carbon blacks have indicated that PNA's are not formed during the manufacture of the color additive unless the temperature of pyrolysis, i.e., the subjection of organic compounds to very high temperatures in atmospheres deficient in oxygen, reaches 1100° C. In a review of the available data on carbon blacks submitted with the color additive petition for the listing of carbon black (all-gas channel black) (CAP 9C0092), Jack L. Radomski, M.D., Professor of Pharmacology, University of Miami, School of Medicine, Coral Gables, Florida, noted that carbon black (all-gas channel black) appears to be free of PNA's and speculated that this might be attributable to the fact that pyrolysis temperatures do not routinely exceed 1100° C during the production of the color additive.

The sensitivity of the analytical methods used in the studies upon which Dr. Radomski relied is not known; therefore, it cannot be determined whether the methods employed were sufficiently precise to conclude with reasonable certainty that extractable PNA's are not in fact present in the commercially available color additive. Based upon their review of the data submitted with the petition and other pertinent data, FDA scientists have concluded that the analytical methods employed in the available studies probably were not capable of detecting extractable PNA's much below 100 parts per million (ppm). The Commissioner has previously concluded, in a regulation published in the FEDERAL REGISTER of September 23, 1974 (39 FR 34188) establishing safe conditions of use for the food additive citric acid obtained from *Candida lipolytica* under § 121.1259 (21 CFR 121.1259), that an analytical method must be sufficiently sensitive to detect extractable PNA's to a level of 2 parts per billion (ppb). The Commissioner is not aware of a reliable method for detecting extractable PNA's in carbon black (all-gas channel black) that is sensitive to a level of 2 ppb and, as described below, persistent efforts to obtain this required method from the petitioners have been unavailing.

The agency's conclusions that existing data are inadequate to establish specifications for carbon black (all-gas channel black) and that an appropriately sensitive anlytical method to detect PNA's is needed have been known since shortly after the first color additive petition for carbon black was submitted on November 8, 1963. The first petition (CAP 9), submitted to FDA by Carl A. Nau, M.D., Medical Center, University of Oklahoma, Oklahoma City, Oklahoma, was rejected for filing because it lacked, inter alia, (1) chemistry data adequate to establish specifications for the color additive and (2) adequate information about the nature of the volatiles present. Dr. Nau withdrew his petition in a letter dated July 11, 1966.

Subsequent to the withdrawal of Dr. Nau's petition, FDA received letters from H. Kohnstanm & Co. and from the Toilet Goods Association stating their intention to conduct the studies necessary to support "permanent" listing for carbon black (all-gas channel black) for use in food, drugs, and cosmetics. Thereafter, the types of data required on carbon black were discussed at meetings between FDA and the Toilet Goods Association. On April 25, 1969, a color additive petition (CAP 9C0092) was submitted by the Toilet Goods Association (now the Cosmetic, Toiletry and Fragrance Association, Inc., 1133 15th St. NW., Washington, D.C. 20005), the Pharmaceutical Manufacturers Association (1155 15th St. NW., Washington, D.C. 20005) and the National Confectioners Association of the U.S., Inc. (1225 19th St. NW., Washington, D.C. 20036), c/o Hazleton Laboratories, Inc., P.O. Box 30, Falls Church, Va. 22046, seeking the "permanent" listing and certification of carbon black (all-gas channel black) for use in food, drugs, and cosmetics.

The Commissioner's conclusion that the Toilet Goods Association petition was inadequate because it did not contain details concerning the manufacturing process and methods of analysis for the color additive was conveyed to the petitioners as early as May 7, 1969. The petitioners were also asked during a conference with FDA on February 10, 1970, to submit information to the agency concerning the specifications for carbon black (all-gas channel black). Again, FDA advised the petitioners of the need for additional data by letter of December 7, 1973. The Commissioner has repeatedly sought from the petitioners data adequate to establish specifications for carbon black (all-gas channel black) that would permit him to conclude with reasonable certainty that the commercially available carbon black (all-gas channel black) had been manufactured from all-natural gas using the impingement or channel process, data demonstrating the absence of PNA's in benzene extraction of carbon black (all-gas channel black) using an analytical method sensitive to 2 ppb, and specifications for permissible levels of lead and arsenic.

As noted, data adequate to resolve the Commissioner's concerns about the safety of carbon black (all-gas channel black) have not been provided to FDA, and it does appear likely that they will soon be forthcoming. The Commissioner concludes therefore that continued provisional listing for carbon black (all-gas channel black) for use in food, drugs, and cosmetics is no longer appropriate.

The current closing date for continued use of carbon black (all-gas channel black) was postponed to September 30, 1976 by a regulation published in the FEDERAL REGISTER of January 5, 1976 (41 FR 754). That postponement was based on the assumption that scientific investigations in progress would soon provide the data necessary to establish specifications for the color additive and that an analytical method to detect extractable PNA's sensitive to 2 ppb would be developed. Because it has now become clear that the necessary data are not available and will not soon be forthcoming, the Commissioner finds that the basis for the postponement no longer exists and hereby terminates the postponement of the closing date for the provisional listing of carbon black (all-gas channel black) for use in food, drugs, and cosmetics in accordance with section 203(a)(2) of the transitional provisions of the Color Additive Amendments of 1960. Also, under section 203(d)(1)(E) of the amendments, the Commissioner concludes that the provisional listing of carbon black (all-gas channel black) should be terminated because such action is necessary to protect the public health, in that questions have been raised about the safety of the color additive and the available data do not permit a determination of safety. Published elsewhere in this issue of the FEDERAL REGISTER is a notice denying the petition proposing to list "permanently" carbon black (all-gas channel black) for use in food, drugs, and cosmetics.

The provisional listing of carbon black (all-gas channel black) is hereby terminated, effective September 23, 1976. After September 23, 1976, adding carbon black (all-gas channel black) to any food, drug, or cosmetic will cause such product to be adulterated within the meaning of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.) and subject to regulatory action. This prohibition applies to the use of carbon black, mixtures of carbon black with other colors or their lakes, and such mixtures with ingredients functioning only as diluents. The Commissioner concludes that the protection of the public health does not require the recall from the market of food, drugs, and cosmetics containing the color additive, or the destruction of products in preparation, to which the color additive has already been added.

This action applies to externally applied products as well as to those intended for ingestion, and to pet food and animal feed as well as to human food.

Manufacturers of new drugs and new animal drugs, including certifiable antibiotics for animal use, containing carbon black (all-gas channel black) may either delete the color additive or substitute a different color in accordance with the provisions of § 314.8(d)(3) and (e) or § 514.8(d)(3) and (e), as appropriate (21 CFR 314.8(d)(3) and (e), 514.8(d)(3) and (e)). The applicant shall submit data providing the new composition and showing that the change in composi-

tion does not interfere with any assay or other control procedures used in manufacturing the drug, or that the assay and other control procedures have been revised to make them adequate. Also, the applicant shall submit data available to establish the stability of the revised formulation, or if the data are too limited to support a conclusion that the drug will retain its declared potency for a reasonable marketing period, a commitment to test the stability of marketed batches at reasonable intervals, to submit the data from such tests as they become available, and to recall from the market any batch found to fall outside the approved specifications for the drug.

The Commissioner is aware that supplies of alternative color additives may be difficult to obtain immediately. Consequently, food and drug labeling stating that the product contains "artificial color" because of the prior inclusion of carbon black (all-gas channel black) may continue to be used with the uncolored product during the time necessary to obtain supplies of alternative color ingredients or until the current supplies of labeling are used, whichever occurs first.

Carbon black (all-gas channel black) is the subject of food additive regulations in Subpart F of Part 121 (21 CFR Part 121) for its use in food-contact articles as a colorant (e.g., in paragraph (b)(3)(xxvi) of § 121.2514 Resinous and polymeric coatings) and as a filler (e.g., in paragraph (c)(4)(v) of § 121.2562 Rubber articles intended for repeated use). These uses generally were supported by data showing an absence of migration of the carbon black from the food-contact surface to food. The Commissioner has not considered these uses of carbon black as part of this action but rather intends to include them as part of a planned review of the available data for the regulated food additives.

The Federation of American Societies for Experimental Biology (FASEB) will soon be reviewing the available literature concerning the use of carbon in the processing of food as part of the ongoing review of substances that are generally recognized as safe (GRAS). Included in this review will be substances such as charcoal or activated charcoal whose use in food has been considered GRAS. The GRAS review of carbon may also involve certain applications of carbon black (all-gas channel black). The Commissioner has not considered the use of carbon for uses other than coloring as part of this action. Instead, he concludes that action on the various uses of carbon that are to be reviewed by FASEB as part of the GRAS review should await the receipt of the final reports of their evaluation.

The Commissioner has carefully considered the environmental effects of this action and, because the action will not significantly affect the quality of the human environment, has concluded that an environmental impact statement is not required. A copy of the FDA environmental assessment, together with copies of the other documents mentioned above, are on file with the Hearing Clerk, Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, Md. 20852. Because this action is final (not proposed), an inflation impact evaluation is not required by Executive Order 11821 (3A CFR, 1975 Compilation, p. 203).

Therefore, under the transitional provisions of the Color Additive Amendments of 1960 (Title II, Pub. L. 86-618, 74 Stat. 404-407 (21 U.S.C. 376 note)) and under authority delegated to the Commissioner (21 CFR 5.1) (recodification published in the FEDERAL REGISTER of June 15, 1976 (41 FR 24262)), Part 8 of Chapter I of Title 21 of the Code of Federal Regulations is amended as follows:

§ 8.501 [Amended]

1. In § 8.501 *Provisional lists of color additives:*

a. Paragraph (e) is revoked and reserved.

b. In paragraphs (f) and (g), the entry for carbon black (prepared by the "impingement" or "channel" process) is deleted.

2. In § 8.502, new paragraph (g) is added to read as follows:

§ 8.502 Termination of provisional listing of color additives.

* * * * * *

(g) *Carbon black (prepared by the "impingement" or "channel" process).* The Commissioner of Food and Drugs, in order to protect the public health, hereby terminates the provisional listing of carbon black (prepared by the "impingement" or "channel" process) for use in food, drugs, and cosmetics.

Notice and public procedure are not necessary prerequisites to the promulgation of this order because section 203 (d)(2) of Pub. L. 86-618 so provides.

Effective date. These regulations shall be effective September 23, 1976.

(Title II, Pub. L. 86-618, 74 Stat. 404-407 (21 U.S.C. 376 note).)

Dated: September 17, 1976.

SHERWIN GARDNER,
Acting Commissioner of Food and Drugs.

[FR Doc.76-27824 Filed 9-22-76;8:45 am]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Food and Drug Administration

[21 CFR Part 8]

[Docket No. 76N-0366]

PROVISIONALLY LISTED COLOR ADDITIVES

Proposed Postponement of Closing Dates

The Commissioner of Food and Drugs, on its own initiative, is proposing to postpone the closing date for the use of certain provisionally listed color additives beyond December 31, 1976. The postponement would be conditioned on the undertaking of appropriate scientific investigations and the submission of data to the Food and Drug Administration (FDA) on a prescribed schedule. Interested persons have until November 22, 1976, to submit comments.

Under Title II of the Color Additive Amendments of 1960 (sec. 203(a)(2), Pub. L. 86-618, 74 Stat. 404 (21 U.S.C. 376 note)) and under authority delegated to him, the Commissioner is authorized to postpone the closing date of a provisional listing of a color additive on his own initiative or upon the application of an interested person. Section 203(d)(1) of Title II requires promulgation, insofar as practicable, of a current listing of color additives and the particular uses thereof deemed provisionally listed.

The closing date, September 30, 1976, was established by a regulation published in the FEDERAL REGISTER of January 5, 1976 (41 FR 754) for 84 provisionally listed color additives based upon the Commissioner's conclusion that the postponement was consistent with the objective of carrying to completion, in good faith and as soon as reasonably practicable, the scientific investigations necessary for making a determination as to listing these color additives under section 706 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 376). In the proposal to postpone the closing dates, published in the FEDERAL REGISTER of November 14, 1975 (40 FR 53039), the Commissioner also advised that a final determination on the "permanent" listing under section 706 of the act of many of the provisionally listed color additives was expected to be completed before September 30, 1976. The Commissioner also stated that, if appropriate, further postponements would be made for individual color additives for which final determinations were not possible.

The Commissioner has postponed the closing date for the provisional listing of 72 color additives until December 31, 1976, by regulation published elsewhere in this issue of the FEDERAL REGISTER, effective September 23, 1976. The brief postponement is necessary to allow time for public comment on this proposal, to prepare notices "permanently" listing 20 of the provisionally listed color additives and to provide for the uninterrupted use of the remaining color additives.

In accordance with the Commissioner's stated intention to make final determinations for many of the provisionally listed color additives before September 30, 1976, the FDA Bureau of Foods has reviewed each of the petitions to list the 84 provisionally listed color additives and other pertinent data. This review involved evaluation of 64 color additive petitions seeking "permanent" listing for 83 provisionally listed color additives. The 64 color additive petitions were reviewed in accordance with the criteria for "permanent" listing set forth in section 706(b)(5)(A) of the act. In particular, the Bureau of Foods reviewed available toxicity, chemistry and usage data and reexamined previous evaluations of these data to determine if safe conditions of use for the color additives could be established for purposes of "permanent" listing under section 706 of the act. The review also involved examination of correspondence and memoranda of meetings to assure that, in each instance in which a color additive petition has previously been found to contain inadequate or insufficient data or in which additional data or studies were required to resolve uncertainties about the safety of the color, the petitioners had been apprised of the deficiencies or uncertainties. Copies of the correspondence and memoranda of meetings between FDA and the petitioners and their representatives, advising them of the need for additional data or studies, are on file with the Hearing Clerk, Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20852.

Final determinations have been made on 12 of the 84 provisionally listed color additives on the basis of the Bureau of Foods' review of the petitions seeking "permanent" listing for them. The 12 colors and the action taken with respect to each are as follows:

1. *FD&C Red No. 4.* The provisional listing for FD&C Red No. 4 for use in maraschino cherries and ingested drugs is terminated by regulation published elsewhere in this issue of the FEDERAL REGISTER, effective September 23, 1976. Also published elsewhere in this issue of the FEDERAL REGISTER are a notice denying the portion of the petition seeking "permanent" listing of FD&C Red No. 4 for use in maraschino cherries and ingested drugs and a regulation "permanently" listing the color additive for use in externally applied drugs and cosmetics.

2. *Carbon black (all-gas channel black).* The provisional listing for carbon black (all-gas channel black) for use in food, drugs, and cosmetics is terminated by regulation published elsewhere in this issue of the FEDERAL REGISTER, effective September 23, 1976. Also published in this issue of the FEDERAL REGISTER is a notice denying the petition to list "permanently" carbon black (all-gas channel black) for use in food, drugs, and cosmetics.

3. Aluminum stearate, bentonite, calcium silicate, calcium stearate, gold, kaolin, lithium stearate, magnesium aluminum silicate, magnesium stearate, and zinc stearate. The provisional listing fort hese 10 substances for use as color additives in cosmetics is terminated by regulation published elsewhere in this issue of the FEDERAL REGISTER, effective October 26, 1976. Also published elsewhere in this issue of the FEDERAL REGISTER is a notice announcing the withdrawal of the color additive petitions seeking to list "permanently" all of these substances except gold. No color additive petition or progress report had been submitted on gold, the 84th provisionally listed color additive, as required by § 8.501 of the color additive regulations (21 CFR 8.501).

The remaining 72 color additives on the provisional list have been grouped into th following 5 categories based on the review of the individual petitions seeking their "permanent" listing:

A. Color additives for which safe conditions of use can be established and for which "permanent" listing is appropriate;

B. Color additives that require additional short-term eye area studies;

C. Color additives that require additional short-term toxicity studies;

D. Color additives that require additional chemistry data to establish safe conditions of use;

E. Color additives that require new chronic toxicity studies.

The available data on 20 of these 72 provisionally listed color additives are adequate to support final determinations of safety and regulations "permanently" listing the color additives are being prepared. The Commissioner anticipates that these regulations will be issued before December 31, 1976. The remaining 52 provisionally listed color additives cannot be "permanently" listed at this time because the available data are inadequate to make final determinations. The Commissioner concludes, however, that there are no significant questions of safety regarding any of these 52 color additives, and that continued provisional listing for them presents no risk to the public health.

Most (49) of these 52 color additives are provisionally listed for use only in drugs and/or cosmetics. Three—FD&C Yellow No. 6, FD&C Green No. 3 and FD&C Blue No. 2—are provisionally listed for use in food as well. Additionally, 7 of these 52 colors—FD&C Yellow No. 5, FD&C Red No. 3, FD&C Blue No. 1, annatto, caramel, carmine and carotene—are "permanently" listed for use in food and ingested drugs.

Under the transitional provisions of the Color Additive Amendments of 1960, however, continued provisional listing of a color additive is appropriate only when studies in progress or under evaluation are capable of demonstrating the safety of the color additives involved. The Commissioner proposes, therefore, to condition further postponement of the closing dates for the use of these 52 provisionally listed color additives on compliance with specific requirements to be contained in a new § 8.505 of the color additive regulations. Section 8.505 would explicitly set forth the type of additional studies that must be conducted and data that must be submitted to FDA to demonstrate the safety of the color additives involved. The type and extent of the

studies and data required are based on the recent Bureau of Foods' review of the 64 individual color additive petitions. The majority of the 52 provisionally listed color additives involved require only a single type of data, e.g., short-term eye area studies, or short-term toxicity studies, or additional chemistry data or chronic toxicity studies. In several instances described below, however, more than one type of data or study are required.

Proposed § 8.505 would require that each of the petitioners agree in writing within 30 days of the effective date of the regulation to undertake the scientific investigations necessary to permit FDA to make final determinations on the color additives, and that the petitioners or other interested persons undertake those scientific investigations, file progress reports with FDA, and submit the final results within fixed time periods prescribed in the regulation. Additionally, the petitioners would be required to notify FDA immediately of any findings that indicate a potential for a color additive to cause adverse effects. Failure of the petitioners for any additive to comply with the requirements contained in § 8.505 would result in immediate termination of the provisional listing of the color additive. New § 8.505 would also establish closing dates for each of the categories of color additives listed above by which the provisional listing would be terminated, except in extraordinary circumstances.

The proposed provision for postponement in extraordinary circumstances of the closing dates beyond those in § 8.505 is included in anticipation of the possibility, although unlikely, that unforeseeable and unavoidable occurrences or situations may make compliance with § 8.505 extremely impracticable, if not virtually impossible, and which would therefore require in fairness that the provisional listing be further postponed. A request for further postponement on the grounds of "extraordinary circumstances" would have to be submitted in writing and state in detail the basis for the request. The Commissioner does not anticipate that "extraordinary circumstances" will occur and therefore fully expects that no color additive will be provisionally listed after December 31, 1980, the proposed closing date for those color additives for which new chronic toxicity studies are being required.

The requirements of proposed § 8.505 are set forth in detail in the following discussion of the five categories of provisionally listed color additives.

A. Color additives for which safe conditions of use can be established and for which "permanent" listing is appropriate: The Commissioner concludes, based on the Bureau of Foods' review, that the safety of 20 of the 72 provisionally listed color additives has been demonstrated. There are no adverse effects associated with the use of any of these 20 color additives under the conditions of use in the petition; the chemistry and usage data are adequate for "permanent" listing. The 20 color additives to be "permanently" listed and their uses are as follows:

1. D&C Green No. 8 (externally applied drugs and cosmetics).
2. D&C Yellow No. 7 (externally applied drugs and cosmetics).
3. D&C Yellow No. 8 (externally applied drugs and cosmetics).
4. D&C Yellow No. 11 (externally applied drugs and cosmetics).
5. D&C Red No. 17 (externally applied drugs and cosmetics).
6. D&C Red No. 31 (externally applied drugs and cosmetics).
7. D&C Red No. 34 (externally applied drugs and cosmetics).
8. D&C Violet No. 2 (externally applied drugs and cosmetics).
9. D&C Brown No. 1 (externally applied cosmetics).
10. Ext. D&C Yellow No. 7 (externally applied drugs and cosmetics).
11. Ext. D&C Violet No. 2 (externally applied drugs and cosmetics).
12. D&C Blue No. 4 (externally applied drugs and cosmetics).
13. Azulene (externally applied cosmetics).
14. Iron oxides (all cosmetics including use in areas of the eye).
15. Manganese violet (all cosmetics including use in area of the eye).
16. Ultramarine blue (externally applied cosmetics including use in area of the eye).
17. Ultramarine green (externally applied cosmetics including use in area of the eye).
18. Ultramarine pink (externally applied cosmetics including use in area of the eye).
19. Ultramarine red (externally applied cosmetics including use in area of the eye).
20. Ultramarine violet (externally applied cosmetics including use in area of the eye).

Notices "permanently" listing these 20 color additives are currently being prepared; the Commissioner expects that they will be published in the FEDERAL REGISTER before the December 31, 1976 closing date. The provisional listing for these color additives will be terminated when the "permanent" listing becomes effective, unless any regulation is stayed by the filing of valid objections, in which case the provisional listing for that color would continue.

B. Color additives that require additional short-term eye area studies: Color additive petitions for 14 of the 72 provisionally listed color additives seek "permanent" listing for use in cosmetics, including cosmetics intended for use in the area of the eye. "Permanent" listing for all types of cosmetic use, i.e., ingested, external, and area of the eye, is sought for the following 10 provisionally listed color additives:

1. Annatto.
2. Bismuth oxychloride.
3. Bronze powder.
4. Caramel.
5. Carmine.
6. Carotene.
7. Copper, metallic powder.
8. Mica.
9. Guanine (pearl essence).
10. Zinc oxide.

"Permanent" listing for external and area of the eye use only is sought for the following four provisionally listed color additives:

1. Aluminum powder.
2. Chromium hydroxide green.
3. Chromium oxide greens.
4. Ferric ferrocyanide.

Of the 14 color additives listed ab 7 appeared on the so-called "Har list" published in the FEDERAL REGIS of October 8, 1974 (39 FR 3612 aluminum powder, annatto, bismuth o chloride, caramel, carotene, cop powder, and zinc oxide. Petitions for t 7 "Harvey list" colors and the remaini 7 color additives and other pertin data have been reviewed and are ac quate to establish the safety of 8 of t 10 provisionally listed colors for whi "permanent" listing for external and i gested cosmetic use is sought and for t 4 provisionally listed color additives f which permanent listing for extern cosmetic use only is sought. The da are inadequate, however, to "perma ently" list any of the 14 colors for co metic use in the area of the eye becau each of the color additive petitions f thi se 14 color additives lacks results fro a short-term eye area study with rabbi in which the color additive is repeated instilled into the eye for 4 weeks. Th studies involving repeated instillatic into the eye will provide an added mea ure of assurance that each of the col additives may be used safely in cosmeti for use in the area of the eye.

The petitioners for these 14 color ac ditives were advised by FDA on July 3 1969 that short-term eye area studie involving repeated instillation of th color into the eyes of test animals woul be required before final determination could be made on "permanent" listin Considerable discussion thereafter en sued between FDA and the petitioner concerning the format and conduct of th eye area studies. The petitioners subsequently prepared a protocol, conducte pilot toxicological studies, and submitted the results to FDA. The results of th pilot studies were evaluated by FDA anc the petitioners were advised to initiate the eye area studies on each of the 14 color additives. Eye area studies on these 14 color additives are either underway or have been contracted for and will begin very shortly.

The Commissioner proposes to postpone the closing dates for the provisional listing of these 14 color additives until July 1, 1977, to provide sufficient time for the petitioners to complete the eye area studies, conduct the pathology work in the rabbits, analyze and write up the results, and submit them to FDA for review. This brief period would also include time for FDA to evaluate the results and to prepare regulations either "permanently" listing the colors or terminating the provisional listing for use in the area of the eye, based on the results of studies.

Proposed § 8.505(a) would require that each of the petitioners advise FDA in writing of the status of the eye area studies within 30 days after the effective date of the final regulation, and that they complete the studies and submit the results to FDA within 45 days after the effective date of the final regulation. The Commissioner is of the opinion that these short periods of time to comply with proposed § 8.505(a) are reasonable because the petitioners have advised

FDA that the eye area studies are underway or will soon begin. New § 8.505 would also require that the petitioners notify FDA immediately of any findings that indicate a potential for any color additive to cause adverse effects. Failure to submit the status letter within 30 days or to submit the final results within 45 days or to provide immediate notification of findings indicating a potential for a color additive to cause adverse effects would result in immediate termination of the provisional listing for the color additive for use in the area of the eye. The Commissioner would, in any event, terminate the provisional listing and "permanently" list the colors or deny the petitions for these 14 colors for eye area use and "permanently" list them for other uses supported by available data by July 1, 1977, unless extraordinary circumstances were shown.

As discussed below in this preamble, caramel also requires a chronic study to determine if it causes chronic adverse effects, including carcinogenicity when externally applied, and a short-term toxicity study. The closing date for caramel would be postponed under proposed § 8.505(d) until December 31, 1980, only if the petitioner complies with § 8.505(a) and (b).

The Commissioner concludes that the continued provisional listing of these 14 color additives under their intended conditions of use until July 1, 1977, does not present a hazard to the public health.

C. Color additives that require additional short-term toxicity studies: Of the 72 provisionally listed color additives, bismuth citrate, bismuth oxychloride, caramel, and lead acetate cannot be "permanently" listed at this time because short-term toxicity studies are needed to provide additional assurance that their use is safe. Bismuth citrate and lead acetate, which are petitioned for use to color hair, require short-term absorption studies because earlier studies suggest a potential for percutaneous absorption. The required short-term absorption studies involve administration of the product containing the color additive to the hair for 90 days under conditions of use. During and at the completion of the period of administration of the product, urine and blood tests would be conducted to determine of the color additive has been absorbed through the skin into the body systems.

An absorption study on bismuth citrate at a level of 0.25 percent of the product has been completed and suggests that there may be absorption. Accordingly, an additional absorption study is necessary at the 0.5 percent use concentration because the petition seeks a "permanent" listing for use at that higher concentration. In addition, a 90-day study with rabbits, as described below, is required for bismuth citrate because of the possibility of absorption and the absence of data concerning the distribution of absorbed bismuth in the body.

Bismuth oxychloride and caramel, 2 of the 21 color additives that appeared on the so-called "Harvey list" in the October 8, 1974 FEDERAL REGISTER, require short-term skin studies with rabbits to support their use in externally applied cosmetics. These studies involve application of the color to the intact and abraded skin of rabbits for 90 days. Color additive petitions for these two colors were submitted in response to the October 8, 1974 notice and the colors were provisionally listed thereafter while the petitions and other data were evaluated. Review of the petitions and other data on bismuth oxychloride and caramel disclosed the need for additional skin studies because data were lacking to establish that the colors were safe for use in externally applied cosmetics. As noted above, bismuth oxychloride and caramel require short-term eye area studies. As explained below in this preamble, caramel also requires a chronic study to determine if it causes chronic adverse effects, including carcinogenicity, upon external application.

Proposed § 8.505(b) would postpone the closing date for bismuth citrate, bismuth oxychloride, caramel and lead acetate until September 30, 1977. These postponements would be conditioned on the written agreement by each of the petitioners within 30 days after this regulation becomes effective, to undertake the required studies needed to provide assurance that use of the color additives is safe for purposes of "permanent" listing. New § 8.505(b) would also require that the results of the absorption studies and the results of subchronic studies be submitted to FDA within 180 days after this regulation becomes effective, and that the petitioners notify FDA immediately of any findings that indicate a potential for any of the color additives to cause adverse effects. Failure to comply with any of the requirements contained in § 8.505(b) would result in immediate termination of the provisional listing for the color additive.

After submission of the study results, FDA will promptly review them and, if they are adequate to establish safe conditions of use, the color additives would be permanently listed. If the data are inadequate, the provisional listings would be terminated. The Commissioner would, in any event, make final determinations on each of the colors and terminate their provisional listing by September 30, 1977, unless extraordinary circumstances were shown. The closing date for caramel would be December 31, 1980, if the conditions of § 8.505 (a) and (b) are met.

The Commissioner concludes that continued provisional listing of these four colors until September 30, 1977, does not present a hazard to the public health.

D. Color additives that require additional chemistry data to establish safe conditions of use: Of the 72 provisionally listed color additives, 15 cannot be "permanently" listed at this time because complete chemistry data are lacking to establish specifications for them. The 15 colors and their provisionally listed uses are:

1. D&C Orange No. 4 (externally applied drugs and cosmetics)
2. D&C Orange No. 5 (drugs and cosmetics)
3. D&C Orange No. 11 (externally applied drugs and cosmetics)
4. Ext. D&C Green No. 1 (externally applied drugs and cosmetics)
5. Ext. D&C Yellow No. 1 (externally applied drugs and cosmetics)
6. FD&C Yellow No. 6 (food, drugs and cosmetics)
7. D&C Yellow No. 10 (drugs and cosmetics)
8. D&C Red No. 6 (drugs and cosmetics)
9. D&C Red No. 7 (drugs and cosmetics)
10. D&C Red No. 27 (drugs and cosmetics)
11. D&C Red No. 28 (drugs and cosmetics)
12. D&C Red No. 30 (drugs, cosmetics, and surgical sutures)
13. D&C Blue No. 6 (drugs, cosmetics, and surgical sutures)
14. Logwood (sutures)
15. Graphite (externally applied cosmetics including use in area of the eye)

The chemistry data lacking on these 15 colors consist of sufficiently precise analytical methods and other information to enable FDA to identify and define the color additives more accurately than currently available data permit. Detailed specifications and precise analytical methods are required to certify batches of each color additive as equivalent to the batches of each color additive used in conducting animal studies to establish the safety of the color.

The closing date for the provisional listing for use of these 15 colors would be postponed until September 30, 1977, under proposed § 8.505(c), which would condition the postponement on the written agreement by each petitioner, within 30 days after this regulation becomes effective, to undertake to develop and submit to FDA the necessary chemistry data and analytical methods required to establish specifications for each color additive and to certify batches of each color additive where certification is necessary. Proposed § 8.505(c) would also require that the chemistry data and analytical methods be submitted to FDA within 210 days after the regulation becomes effective and that FDA be notified immediately of findings that indicate a potential for any of the color additives to cause adverse effects. Failure to comply with the requirements contained in § 8.505(c) would result in immediate termination of the provisional listing for the color additive involved.

Personnel of the FDA Bureau of Foods will be available to clarify the type of data and analytical methods required and to consult with the petitioners, if necessary. The chemistry data and analytical methods for each color will be promptly reviewed by FDA after their submission and, if the data and analytical methods are adequate to establish specifications, the Commissioner would publish a notice in the FEDERAL REGISTER "permanently" listing the color additives that do not require chronic toxicity studies. If the data and methods are inadequate for any color, the provisional listing would be terminated. The Commissioner would, in any event, terminate the provisional listing and "permanently" list, or deny the petition, for each of these 15 colors by September 30, 1977, except as noted below, unless extraordinary circumstances were shown.

Nine of the fifteen color additives also require new chronic toxicity studies: D&C Orange No. 5, FD&C Yellow No. 6, D&C Yellow No. 10, D&C Red No. 6, D&C Red No. 7, D&C Red No. 27, D&C Red

No. 28, D&C Red No. 30, and D&C Blue No. 6. The closing date for each of these colors would be postponed under proposed § 8.505(d) until December 31, 1980, to permit completion of the chronic toxicity studies, but only if the chemistry data and analytical methods are supplied in accordance with § 8.505(c).

The Commissioner concludes that continued provisional listing of these 15 color additives under their intended conditions of use until September 30, 1977, does not present a hazard to the public health.

E. Color additives that require new chronic toxicity studies: Of the 72 provisionally listed color additives, 31 cannot be "permanently" listed because the available toxicity data—though suggestive of no adverse effects—are derived from studies that do not meet contemporary standards generally accepted within the scientific community as minimum requirements for the design and conduct of toxicological studies to establish safety.

These color additives and their provisionally listed uses are as follows:

1. FD&C Yellow No. 5 (cosmetics and externally applied drugs)
2. FD&C Yellow No. 6 (food, drugs and cosmetics)
3. D&C Yellow No. 10 (drugs and cosmetics)
4. FD&C Red No. 3 (cosmetics and externally applied drugs)
5. D&C Red No. 6 (drugs and cosmetics)
6. D&C Red No. 7 (drugs and cosmetics)
7. D&C Red No. 8 (drugs and cosmetics)
8. D&C Red No. 9 (drugs and cosmetics)
9. D&C Red No. 10 (drugs and cosmetics)
10. D&C Red No. 11 (drugs and cosmetics)
11. D&C Red No. 12 (drugs and cosmetics)
12. D&C Red No. 13 (drugs and cosmetics)
13. D&C Red No. 19 (drugs and cosmetics)
14. D&C Red No. 21 (drugs and cosmetics)
15. D&C Red No. 22 (drugs and cosmetics)
16. D&C Red No. 27 (drugs and cosmetics)
17. D&C Red No. 28 (drugs and cosmetics)
18. D&C Red No. 30 (drugs, cosmetics, and surgical sutures).
19. D&C Red No. 33 (drugs and cosmetics)
20. D&C Red No. 36 (drugs and cosmetics)
21. D&C Red No. 37 (drugs and cosmetics)
22. FD&C Green No. 3 (food, drugs and cosmetics)
23. D&C Green No. 5 (drugs and cosmetics)
24. D&C Green No. 6 (drugs and cosmetics)
25. FD&C Blue No. 1 (cosmetics and externally applied drugs)
26. FD&C Blue No. 2 (food and ingested drugs)
27. D&C Blue No. 6 (drugs, cosmetics, and surgical sutures)
28. D&C Orange No. 5 (drugs and cosmetics)
29. D&C Orange No. 10 (drugs and cosmetics)
30. D&C Orange No. 17 (drugs and cosmetics)
31. Caramel (cosmetics)

The chronic toxicity studies to establish the safety of these color additives were conducted during the 1950's and 1060's by laboratories under contract with the various petitioners and, in some instances, by FDA itself. Review of these studies by the Bureau of Foods disclosed that, when judged by contemporary standards for toxicological studies, the studies conducted to support the petitions to "permanently" list the 31 color additives were deficient in the basic respects discussed below. Memoranda summarizing these evaluations are on file with the Hearing Clerk, Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, Md. 20852.

The available studies do not show any adverse effects associated with use of any of the 31 color additives under their intended conditions of use. However, the deficiencies in the studies make it impossible for the Commissioner currently to conclude that the color additives are safe for purposes of "permanent" listing under section 706 of the act. Additional chronic toxicity feeding studies and, in the case of caramel, a 2-year mouse skin painting study are required to provide data to permit final determinations to be made on listing these color additives. Final determinations cannot be made in the absence of such new data because to do so would require that the Commissioner ignore the substantial advances made in testing color and food additives since the presently available studies were conducted. The Commissioner advises that because of such improvements in test methodology, FDA is also reviewing the data that supported the approval of many food additives and "permanently" listed color additives and is contemplating a "cyclic" review of those substances and may, in the future, require new studies to be conducted on them.

Although not all of the studies on the 31 color additives are deficient in each of the respects listed in the following paragraphs, the deficiencies in the studies for each color additive are significant enough to make a final determination impossible at this time and to warrant new chronic studies. The available studies on these 31 color additives are deficient in the following respects:

1. Many of the studies were conducted using groups of animals, i.e., control and those fed the color additive, that are too small to permit conclusions to be drawn today on the chronic toxicity or carcinogenic potential of the color. The small number of animals used does not, in and of itself, cause this result, but when considered together with the other deficiencies in this listing, does do so. By and large, the studies 25 animals in each group; today FDA recommends using at least 50 animals per group.

2. In a number of the studies, the number of animals surviving to a meaningful age was inadequate to permit conclusions to be drawn today on the chronic toxicity or carcinogenic potential of the color additives tested.

3. In a number of the studies, an insufficient number of animals was reviewed histologically.

4. In a number of the studies, an insufficient number of tissues was examined in those animals selected for pathology.

5. In a number of the studies, lesians or tumors detected under gross examination were not examined microscopically.

The inadequacies of the available studies are attributable to the dynamic and ever-improving scientific techniques for testing various types of substances. They are not, at least in most instances, the result of inherent defects in the studies or failure to conduct them competently. Studies conducted in accordance with current standards will provide results that are more useful and reliable in evaluating chronic toxicity and the carcinogenic potential of the test substance than those studies conducted over a decade ago. The Commissioner concludes that new chronic toxicity studies on these 31 provisionally listed color additives must be conducted to provide data that are essential for current determinations about their safety.

Three of the thirty-one color additives for which new chronic studies are required—FD&C Red No. 3, D&C Red No. 33, and D&C Orange No. 10—may also require new reproduction studies. Reproduction studies on these three colors have recently been evaluated by FDA and, although no adverse effects were seen, questions have been raised because the procedures prescribed in the protocol for randomly selecting the animals were not followed precisely. The Bureau of Foods has met on several occasions with the petitioners in recent months to determine whether the deviation from the protocol affected the validity of the results of the studies. The petitioners will soon submit data to support their view that the studies are valid ones. The Commissioner concludes that the petitioners should be provided this brief period to submit data in support of their view because the study results were negative. The Commissioner anticipates that FDA will soon resolve the questions regarding the reproduction studies on these three colors. When the questions are resolved, a notice will be published in the FEDERAL REGISTER announcing the resolution. Section 8.505 will be amended if new reproduction studies on these three colors are required.

Caramel, one of the color additives that appeared on the so-called "Harvey list," requires a chronic skin painting study to evaluate its potential for causing chronic adverse effects and carcinogenicity when used in products intended for external application. A single color additive petition for caramel and six other "Harvey list" color additives was submitted in December 1975. In January 1976, FDA rejected the petition by letter and indicated that separate petitions for the seven color additives were necessary. A color additive petition for caramel was submitted on February 27, 1976. The 2-year mouse skin painting study to be required for caramel will provide assurance that the color additive is safe for external use.

The Commissioner proposes to postpone the closing date for the 31 provisionally listed color additives that require new chronic toxicity studies until December 31, 1980. This 4-year period is necessary to plan, conduct and evaluate the chronic toxicity studies that would be required by proposed § 8.505(d). The provisional listing would be continued for the 4 years based on the Commissioner's conclusion that continued use of the 31 color additives under their intended conditions of use presents no hazard to the public health. New § 8.505(d) would condition the postponement on the written agreement by each of the petitioners, within 30 days after the regulation becomes effective, to conduct the required studies. New § 8.505(d) would also require that protocols for the con-

duct of the studies be submitted to FDA for review and acceptance or rejection within 60 days after § 8.505 becomes effective. Personnel from the Bureau of Foods will be available to consult with the various petitioners concerning the design of protocols and will promptly review the protocols and advise the petitioners in writing whether they are acceptable or, if not, what modifications are necessary. All protocols will be placed on file with the Hearing Clerk, Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, Md. 20852.

New § 8.505(d) would also require that the petitioners submit to FDA semiannual progress reports on the studies and notify FDA immediately of any findings that indicate a potential for any of the color additives to cause adverse effects. Reports of the results of the studies would be required to submitted to FDA within 42 months after this regulation becomes effective. After promptly reviewing the results, FDA would, by December 31, 1980, publish regulations either "permanently" listing individual color additives or terminating the provisional listing if "permanent" listing is inappropriate. Failure to submit the written agreement within 30 days, or the protocol within 60 days, or the semiannual reports, or to notify FDA immediately of potential adverse effects, or to submit the final report of the results within 42 months would result in immediate termination of the provisional listing for the color additive involved. The Commissioner would, in any event, terminate the provisional listing for these 31 color additives by December 31, 1980, unless extraordinary circumstances were shown justifying further postponement.

The Commissioner concludes that continued provisional listing of these 31 color additives under their intended conditions of use until December 31, 1980, does not present a hazard to the public health. The closing date for color additives subject to paragraphs (b) and (c) as well as (d) of § 8.505 would be postponed until December 31, 1980, only if the requirements of paragraphs (b) and (c) are met.

The Commissioner advises that FDA is currently evaluating the data that formed the basis for the "permanent" listing of color additives in previous years. It is anticipated that many of the past decisions to list "permanently" color additives were based on data derived from studies that suffer from the same deficiencies as those described above. In that event, the Commissioner will consider what action is appropriate to update those data, including conditioning continued "permanent" listing on the undertaking, over a period of time, of studies of the sort that the Commissioner proposes to require for 31 of the 72 provisionally listed color additives. Should the Commissioner conclude that those data need updating, the Commissioner will take appropriate action. One of the alternatives the Commissioner would seriously consider is publishing regulations proposing a cyclic review of "permanently" listed color additives.

Three of the color additives that require new chronic studies—FD&C Blue No. 1, FD&C Red No. 3, and FD&C Yellow No. 5—were "permanently" listed for food and ingested drug use by regulations published in the FEDERAL REGISTER of May 8, 1969 (34 FR 7445, 7446, 7447). The three colors were not, however, "permanently" listed for ingested cosmetic use. The Commissioner recognizes that use of these three colors in food and ingested drugs is more substantial than their use in ingested cosmetics. The Commissioner is of the opinion, nonetheless, that it is appropriate to condition the continued provisional listing for the three colors on the undertaking of new chronic studies. It is likely that new chronic studies on the three colors would be required as part of the contemplated cyclic review of the "permanently" listed color additives. New chronic studies will, therefore, not only support continued provisional listing of these three colors for use in ingested cosmetics, but also generate data appropriate for use in a review of other uses. It will thus be in the interest of all persons who use the three colors to have new chronic studies conducted at this time.

Nothing in this proposed action affects the Commissioner's authority under the transitional provisions of the Color Additive Amendments of 1960 to terminate a closing date, terminate a listing, or impose restrictions with respect to any color additive on the provisional list.

The Commissioner has carefully considered the environmental effects of the proposed regulation and, because the proposed action will not significantly affect the quality of the human environment, has concluded that an environmental impact statement is not required. The Commissioner has also carefully considered the inflation impact of the proposed regulation as required by Executive Order 11821, OMB Circular A-107, and the Guidelines issued by the Department of Health, Education, and Welfare, and no major inflation impact has been found. Copies of the FDA environmental and inflation impact assessments are on file with the Hearing Clerk, Food and Drug Administration.

Accordingly, the Commissioner is proposing to add a new sentence to the introductory text and change the closing dates listed in paragraphs (a), (b), (c), (f) and (g) of § 8.501, and to establish a new § 8.505.

Therefore, under the transitional provisions of the Color Additive Amendments of 1960 (Title II, Pub. L. 86-618, 74 Stat. 404-407 (21 U.S.C. 376 note)) and under authority delegated to him (21 CFR 5.1) (recodification published in the FEDERAL REGISTER of June 15, 1976 (41 FR 24262)) the Commissioner proposes that Part 8 of Subchapter A of Title 21 of the Code of Federal Regulations be amended as follows:

1. By amending § 8.501 by revising the introductory text and the tables in paragraphs (a), (b), (c), (f) and (g) to read as follows:

§ 8.501 Provisional lists of color additives.

The Commissioner of Food and Drugs finds that the following lists of color additives are provisionally listed under section 203(b) of the Color Additive Amendments of 1960 (sec. 203(b), 74 Stat. 405 (21 U.S.C. 376 note)). Except for color additives for which petitions have been filed, progress reports are required by January 1, 1968, and at 6-month intervals thereafter. Specifications for color additives listed in paragraphs (a), (b), and (c) of this section appear in the respective designated sections. The listing of color additives in this section is not to be construed as a listing for surgical suture use unless color additive petitions have been submitted for such use or the Commissioner has been notified of studies underway to establish the safety of the color additive for such use. The color additives listed in paragraphs (a), (b), and (c) of this section may not be used in products which are intended to be used in the area of the eye. The color additives listed in paragraphs (a), (b), (c), (f), and (g) of this section are provisionally listed until the closing dates set forth therein, conditioned on compliance with the applicable requirements of paragraphs (a), (b), (c), and (d) of § 8.505.

(a) * * *

	Closing date		Restrictions
	Food use	Drug and cosmetic use	
F.D. & C. green No. 3 (sec. 9.23 of this chapter)	Dec. 31, 1980	Dec. 31, 1980	
F.D. & C. yellow No. 5 (sec. 8.275 of this chapter)	do.[1]	do.	
F.D. & C. yellow No. 6 (sec. 9.41 of this chapter)	do.	do.	
F.D. & C. red No. 3 (sec. 8.242 of this chapter)	do.[1]	do.	
F.D. & C. blue No. 1 (sec. 8.206 of this chapter)	do.[1]	do.	
F.D. & C. blue No. 2 (sec. 8.4027 of this chapter)	do.	do.	Food and ingested drugs.
Lakes (F.D. & C.) (sec. 9.100 of this chapter)			

[1] Lakes only.

(b) * * *

	Closing date	Restrictions
D. & C. green No. 6 (sec. 8.1060 of this chapter)	Dec. 31, 1980	
D. & C. green No. 8 (sec. 8.1070 (a) and (b) of this chapter)	do	
D. & C. yellow No. 10 (sec. 8.1130 of this chapter)	do	
D. & C. red No. 6 (sec. 8.1151 of this chapter)	do	
D. & C. red No. 7 (sec. 8.1152 of this chapter)	do	
D. & C. red No. 8 (sec 8.1153 of this chapter)	do	Sec. 8.508.
D. & C. red No. 9 (sec. 8.1154 of this chapter)	do	Do.
D. & C. red No. 10 (sec. 8.1155 of this chapter)	do	Do.
D. & C. red No. 11 (sec. 8.1156 of this chapter)	do	Do.
D. & C. red No. 12 (sec. 8.1157 of this chapter)	do	Do.
D. & C. red No. 13 (sec. 8.1158 of this chapter)	do	Do.
D. & C. red No. 19 (sec. 8.1164 of this chapter)	do	Do.
D. & C. red No. 21 (sec. 8.1166 of this chapter)	do	
D. & C. red No. 22 (sec. 8.1167 of this chapter)	do	
D. & C. red No. 27 (sec. 8.1172 of this chapter)	Dec. 31, 1980	
D. & C. red No. 28 (sec. 8.1173 of this chapter)	do	
D. & C. red No. 30 (sec. 8.1175 of this chapter)	do	
D. & C. red No. 33 (sec. 8.1178 of this chapter)	do	Sec. 8.508.
D. & C. red No. 36 (sec. 8.1181 of this chapter)	do	Do.
D. & C. red No. 37 (sec. 8.1182 of this chapter)	do	Do.
D. & C. orange No. 4 (sec. 8.1201 of this chapter)	Sept. 30, 1977	External use only.
D. & C. orange No. 5 (sec. 8.1202 of this chapter)	Dec. 31, 1980	Sec. 8.508.
D. & C. orange No. 10 (sec. 8.1207 of this chapter)	do	
D. & C. orange No. 11 (sec. 8.1208 of this chapter)	Sept. 30, 1977	
D. & C. orange No. 17 (sec. 8.1214 of this chapter)	Dec. 31, 1980	Do.
D. & C. blue No. 6 (sec. 8.1242 of this chapter)	do	
Lakes (D. & C.) (sec. 8.1250 of this chapter)		

(c) * * *

	Closing date	Restrictions
Ext. D. & C. yellow No. 1 (sec. 8.1301 of this chapter)	Sept. 30, 1977	
Ext. D. & C. green No. 1 (sec. 8.1400 of this chapter)	do	
Lakes (ext. D. & C.) (sec. 8.1440 of this chapter)		

(f) * * *

	Closing date	Restrictions
Logwood	Sept. 30, 1977	Surgical suture use only.

(g) * * *

Color additive	Closing date	Restrictions
Aluminum powder	July 1, 1977	None.
Annatto	do	Do.
Bismuth citrate	Sept. 30, 1977	For use as a color component in hair dye.
Bismuth oxychloride	do	None.
Bronze powder	July 1, 1977	Do.
Caramel	Dec. 31, 1980	Do.
Carmine	July 1, 1977	Do.
Carotene	do	Do.
Chromium hydroxide green	do	Do.
Chromium oxide greens	do	Do.
Copper, metallic powder	do	Do.
Ferric ferrocyanide (iron blue)	do	Do.
Graphite	Sept. 30, 1977	None.
Guanine (pearl essence)	July 1, 1977	Do.
Lead acetate	Sept. 30, 1977	For use as a color component in hair dye.
Mica	July 1, 1977	Do.
Zinc oxide	do	Do.

2. By adding new § 8.505 to read as follows:

§ 8.505 Conditions of provisional listing.

The closing dates for the use of the color additives provisionally listed in § 8.501 are postponed until the dates established in that section conditioned on compliance with the requirements of paragraphs (a), (b), (c), and (d) of this section, where applicable. The closing dates will not be postponed beyond the dates in § 8.501 unless extraordinary circumstances are shown. Requests for further postponement based on extraordinary circumstances shall be submitted in writing and state in detail the basis for the request. If the requirements of paragraphs (a), (b), (c), and (d) of this section are not complied with, the provisional listing for the color additive(s) involved will be terminated immediately.

(a) The closing date for the following 14 color additives is postponed until July 1, 1977, while 4-week eye area studies in the rabbit are conducted and evaluated, and subject to compliance with the requirements of this paragraph: Aluminum powder, annatto, bismuth oxychloride, bronze powder, caramel, carmine, carotene, chromium hydroxide green, chromium oxide greens, copper (metallic powder), ferric ferrocyanide, guanine (pearl essence), mica, and zinc oxide.

(1) Each of the petitioners for the 14 color additives listed in paragraph (a) of this section shall agree in writing by (30 days after effective date of final regulation) to undertake the eye area studies.

(2) A full written report of the results of the studies shall be submitted to the Division of Food and Color Additives, Food and Drug Administration, 200 C St. SW., Washington, DC 20204, by (45 days after effective date of final regulation).

(3) The petitioners shall immediately notify the Division of Food and Color Additives of any findings that indicate a potential for the color additive to cause adverse effects.

(b) The closing date for bismuth citrate, bismuth oxychloride, caramel, and lead acetate is postponed until September 30, 1977, while short-term studies are conducted and evaluated, and subject to compliance with the requirements of this paragraph.

(1) The petitioners for the four color additives listed in paragraph (b) of this section shall agree in writing by (30 days after effective date of final regulation) to undertake the short-term studies on the color additives.

(2) A full written report on the absorption studies for bismuth citrate and lead acetate and a full written report on the subchronic studies for bismuth citrate, bismuth oxychloride, and caramel shall be submitted to the Division of Food and Color Additives, Food and Drug Administration, 200 C St. SW., Washington, DC 20204, by (180 days after effective date of final regulation).

(3) The petitioners shall immediately notify the Division of Food and Color Additives of any findings that indicate a potential for the color additive to cause adverse effects.

(c) The closing date for the following 15 color additives is postponed until September 30, 1977, while chemistry data and analytical methods to establish specifications for them are developed and evaluated and subject to compliance with the requirements of this paragraph: FD&C Yellow No. 6, D&C Yellow No. 10, D&C Red No. 6, D&C Red No. 7, D&C Red No. 27, D&C Red No. 28, D&C Red No. 30, D&C Orange No. 4, D&C Orange No. 5, D&C Orange No. 11, D&C Blue No. 6, Ext. D&C Yellow No. 1, Ext. D&C Green No. 1, graphite, and logwood.

(1) Each of the petitioners for the 15 color additives listed in paragraph (c) of this section shall agree in writing by (30 days after effective date of final regulation) to undertake to develop the necessary chemistry data and analytical methods for the color additives.

(2) The required chemistry data and analytical methods shall be submitted to the Division of Food and Color Additives, Food and Drug Administration, 200 C St. SW., Washington, DC 20204, by (180 days after effective date of final regulation).

(3) The petitioners shall immediately notify the Division of Food and Color Additives of any findings that indicate a potential for the color additive to cause adverse effects.

(d) The closing date for the following 31 color additives is postponed until December 31, 1980, while chronic toxicity feeding studies and in the case of caramel, a 2-year mouse skin painting study, are conducted and evalated, and subject to compliance with the requirements of this paragraph: FD&C Yellow No. 5, FD&C Yellow No. 6, D&C Yellow No. 10, FD&C Red No. 3, D&C Red No. 6, D&C Red No. 7, D&C Red No. 8, D&C Red No. 9, D&C Red No. 10, D&C Red No. 11, D&C Red No. 12, D&C Red No. 13, D&C Red No. 19, D&C Red No. 21, D&C Red No. 22, D&C Red No. 27, D&C Red No. 28, D&C Red No. 30, D&C Red No. 33, D&C Red No. 36, D&C Red No. 37, FD&C Green No. 3, D&C Green No. 5, D&C Green No. 6, FD&C Blue No. 1, FD&C Blue No. 2, D&C Blue No. 6, D&C Orange No. 5, D&C Orange No. 10, D&C Orange No. 1, and caramel.

(1) Each of the petitioners for the 31 color additives listed in paragraph (d) of this section shall agree in writing by (30 days after effective date of final regulation) to undertake the required studies on the color additives.

(2) Each of the petitioners shall submit a protocol for the conduct of the studies to the Division of Food and Color Additives, Food and Drug Administration, 200 C St. SW., Washington, DC 20204, for review, and acceptance or rejection, by (60 days after effective date of final regulation).

(3) A full report of the studies conducted on the color additives shall be submitted to the Division of Food and Color Additives by (42 months after effective date of final regulation).

(4) The petitioners shall immediately notify the Division of Food and Color Additives of any findings that indicate potential for the color additive to cause adverse effects.

Interested persons may, on or before November 22, 1976, submit to the Hearing Clerk, Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20852, written comments (preferably in quintuplicate and identified with the Hearing Clerk docket number found in brackets in the heading of this document) regarding this proposal. Received comments may be seen in the above office during working hours, Monday through Friday.

Dated: September 17, 1976.

SHERWIN GARDNER,
Acting Commissioner of Food and Drugs.

[FR Doc.76-27825 Filed 9-22-76;8:45 am]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Food and Drug Administration

[Docket No. 76C-0369]

COLOR ADDITIVES

Denial of Petition for Listing of FD&C Red No. 4 for Use in Maraschino Cherries and Ingested Drugs

The Food and Drug Administration (FDA) is denying the portion of a petition to list "permanently" FD&C Red No. 4 as a color additive that seeks listing for use in maraschino cherries and ingested drugs because evidence is lacking that the color is safe for those uses. Objections to this order may be filed by adversely affected persons by October 26, 1976. Published elsewhere in this issue of the FEDERAL REGISTER are regulations terminating the provisional listing of FD&C Red No. 4 for use in maraschino cherries and ingested drugs and "permanently" listing FD&C Red No. 4 for use in externally applied drugs and cosmetics.

A notice published in the FEDERAL REGISTER of November 20, 1968 (33 FR 17205) stated that a petition (CAP 61) for the "permanent" listing of FD&C Red No. 4 as a color additive for use in maraschino cherries, ingested drugs, and externally applied drugs and cosmetics had been filed by The Toilet Goods Association, Inc. (now the Cosmetic, Toilery, and Fragrance Association, 1133 15th St., NW., Washington, DC 20005); the Pharmaceutical Manufacturers Association (1155 15th St., NW., Washington, DC 20005); and the Certified Color Industry Committee (now the Certified Color Manufacturers Association, 900 17th St., NW., Washington, DC 20006) c/o Hazleton Laboratories, Inc., PO 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).

Results from chronic dog feeding studies with FD&C Red No. 4 have raised questions about the safety of the color additive when ingested. These studies and other available data bearing on the safety of FD&C Red No. 4 are discussed in detail in the preamble to the regulation published elsewhere in this issue of the FEDERAL REGISTER terminating the provisional listing of the color for use in maraschino cherries and ingested drugs. The available data do not permit establishment of a no-effect level for FD&C Red No. 4 in the dog, and a safe level for human ingestion cannot, therefore, be established. Furthermore, chronic feeding studies on FD&C Red No. 4 in rats and mice conducted by FDA in the early 1960's to determine whether the color additive is a carcinogen have recently been reevaluated and found to be inadequate by contemporary standards for such studies. The Commissioner concludes that without chronic feeding studies that meet contemporary standards, for purposes of "permanent" listing under section 706 of the act (21 U.S.C. 376) there are insufficient data to permit a determination about the safety of the use of FD&C Red No. 4 when ingested.

The Commissioner has fully considered the data submitted in support of the petition and other pertinent data related to the use of FD&C Red No. 4 in maraschino cherries and ingested drugs and conoludes that the data before him do not establish that ingested use of FD&C Red No. 4 will be safe. The portion of the petition seeking listing for use in maraschino cherries and ingested drugs is therefore denied.

Any person who will be adversely affected by the foregoing order may at any time on or before October 26, 1976, file with the Hearing Clerk, Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20852, 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 § 8.19 (21 CFR 8.19). 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. Five 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 above office during working hours, Monday through Friday.

This notice is issued under provisions of the Federal Food, Drug, and Cosmetic Act (secs. 701, 706, 52 Stat. 1055–1056, 74 Stat. 399–403 (21 U.S.C. 371, 376)) and under authority delegated to the Commissioner (21 CFR 5.1) (recodification published in the FEDERAL REGISTER June 15, 1976 (41 FR 24262)).

Dated: September 17, 1976.

SHERWIN GARDNER,
Acting Commissioner of Food and Drugs.

[FR Doc.76-27818 Filed 9-22-76;8:45 am]

[Docket No. 76C-0376]

COLOR ADDITIVES

Denial of Petition for Permanent Listing of Carbon Black

The Food and Drug Administration (FDA) is denying a petition to list carbon black (all-gas channel black) as a color additive for use in food, drugs, and cosmetics because the available data are insufficient to establish safe conditions of use for the color additive. Objections to this order may be filed by adversely affected persons by October 26, 1976. Published elsewhere in this issue of the FEDERAL REGISTER is a regulation terminating the provisional listing of carbon black for use in food, drugs, and cosmetics.

A notice published in the FEDERAL REGISTER of July 24, 1973 (38 FR 19851), stated that a petition (CAP 9C0092) had been filed for the "permanent" listing of carbon black (all-gas channel black) as a color additive for use in food, drugs, and cosmetics, including cosmetics for application in the area of the eye, by the Cosmetic, Toiletry and Fragrance Association, Inc. (CTFA), the National Confectioners Association (NCA), and the Pharmaceutical Manufacturers Association (PMA), c/o Hazleton Laboratories, Inc., P O Box 30, Falls Church, VA 22246. The petition was filed pursuant to section 706 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 376).

Of the five basic types of carbon black, only carbon black produced with natural gas using the impingement or channel process has been provisionally listed under § 8.501 (21 CFR 8.501). The petition to use carbon black for use with food drugs, and cosmetics seeks listing only for "all-gas channel black." Carbon black (all-gas channel black) cannot be "permanently" listed without data adequate to establish specifications for the color. These specifications are necessary to enable FDA to certify batches of carbon black as being the type produced with natural gas using the impingement or channel process. Without adequate data to establish specifications and to certify batches of carbon black as "all-gas channel black," there is no assurance that the carbon black being used is the type covered by the petition and for which toxicity data have been submitted to and reviewed by FDA. The Commissioner concludes that safe conditions of use cannot be established without adequate specifications for carbon black (all-gas channel black).

Furthermore, carbon black, including all-gas channel black, may contain low levels of polynuclear aromatics (PNA's), some of which are known carcinogens. All-gas channel black is the least likely of the carbon blacks to contain PNA's, but there is no analytical method currently available that is sufficiently sensitive to detect extractable PNA's at low levels. The Commissioner concludes that safe conditions of use for carbon black (all-gas channel black) cannot be established without an appropriately sensitive analytical method for detecting extractable PNA's.

The questions regarding the specifications for carbon black (all-gas channel black) and the Commissioner's unsuccessful efforts to obtain the necessary additional data to resolve the questions from the petitioners are discussed in detail in the preamble to the regulation published elsewhere in this issue of the FEDERAL REGISTER terminating the provisional listing for carbon black.

The Commissioner has fully considered the data submitted in support of the petition and other pertinent data related to the use of carbon black (all-gas channel black) and concludes that the data before him are insufficient to establish safe conditions of use for the color additive. The petition to list carbon black

(all-gas channel black) is therefore denied.

Any person who will be adversely affected by the foregoing order may at any time on or before October 26, 1976, file with the Hearing Clerk, Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20852, 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 § 8.19 (21 CFR 8.19). 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. Five copies of all documents shall be filed and should be identified with the Hearing Clerk docket number found in brackets in the hearing of this order. Received objections may be seen in the above office during working hours, Monday through Friday.

This notice is issued under provisions of the Federal Food, Drug, and Cosmetic Act (secs. 701, 706, 52 Stat. 1055-1056, 74 Stat. 399-403 (21 U.S.C. 371, 376)) and under authority delegated to the Commissioner (21 CFR 5.1) (recodification published in the FEDERAL REGISTER of June 15, 1976 (41 FR 24262)).

Dated: September 17, 1976.

SHERWIN GARDNER,
Acting Commissioner of Food and Drugs.

[FR Doc.76-27820 Filed 9-22-76;8:45 am]

[Docket No. 76C-0363]

COSMETIC, TOILETRY AND FRAGRANCE ASSOCIATION

Withdrawal of Color Additive Petitions

The Food and Drug Administration (FDA) is announcing the withdrawal without prejudice of three petitions to "permanently" list aluminum stearate, benfonite, calcium silicate, calcium stearate, kaolin, lithium stearate, magnesium aluminum silicate, magnesium stearate, and zinc stearate for use as color additives in cosmetics. Published elsewhere in this issue of the FEDERAL REGISTER is a regulation terminating the provisional listing of those nine substances and a tenth, gold, for use as color additives in cosmetics.

A notice published in the FEDERAL REGISTER of August 6, 1973 (38 FR 21200), stated that petitions (CAP 8C-0071, 8C0078, and 9C0094) for the "permanent" listing of aluminum stearate, bentonite, calcium silicate, calcium stearate, caolin, lithium stearate, magnesium aluminum silicate, magnesium stearate, and zinc stearate had been filed by the Cosmetic, Toiletry and Fragrance Association, Inc. (CTFA), 1133 15th St., NW., Washington, DC 20005, c/o Hazleton Laboratories, Inc., P.O. Box 30, Falls Church, VA 22046.

The petitions were filed pursuant to section 706 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 376). On August 9, 1976, CTFA wrote to FDA requesting that the color additive petitions for the nine substances be withdrawn without prejudice to future filing.

Therefore, in accordance with § 8.8(c) of the color additive regulations (21 CFR 8.8(c)); under the Federal Food, Drug, and Cosmetic Act (sec. 706(d), 74 Stat. 402 (21 U.S.C. 376(d))); and under authority delegated to the Commissioner (21 CFR 5.1) (recodification published in the FEDERAL REGISTER of June 15, 1976 (41 FR 24262)), notice is given that color additive petitions 8C0071, 8C0078, and 9C0094 have been withdrawn without prejudice to future filing.

Dated: September 17, 1976.

SHERWIN GARDNER,
Acting Commissioner of Food and Drugs.

[FR Doc.76-27821 Filed 9-22-76;8:45 am]