number found in brackets in the hearing of this regulation. Received objections may be seen in the office of the Hearing Clerk, between 9 a.m. and 4 p.m., Monday through Friday.

Effective date: This regulation shall become effective January 13, 1978, except as to any provisions that may be stayed by the filing of proper objections. Notice of the filing of objections or lack thereof will be announced by publication in the FEDERAL REGISTER.

(Sec. 706 (b), (c), and (d), 74 Stat. 399–403 (21 U.S.C. 376 (b), (c), and (d))) and (Title II, Pub. L. 86–618; sec. 203, 74 Stat. 404–407, U.S.C. 376 note).)

Dated: December 5, 1977.

WILLIAM F. RANDOLPH,
Acting Associate Commissioner for Compliance.

[FR Doc.77-35326 Filed 12-7-77;2:28 pm]

[4110-03]

[Docket No. 77C-0383]

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

Provisional Listing of D&C Blue No. 6; Termination of Closing Date

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: This document terminates the closing date for the provisional listing, and hence the approval, of the color additive D&C Blue No. 6 for coloring drugs and cosmetics. This action is taken because of the failure to comply with the conditions for continued provisional listing of the color for use in drugs and cosmetics. Provisional listing of D&C Blue No. 6 will be continued until January 31, 1978, for its use in coloring general and ophthalmic surgical sutures only. Color additive certifications for D&C Blue No. 6 will continue to be issued for its use in sutures.

EFFECTIVE DATE: December 13, 1977.

FOR FURTHER INFORMATION CONTACT:

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

SUPPLEMENTARY INFORMATION: Section 81.1 (21 CFR 81.1) 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 D&C Blue No. 6 has been in use for many years. D&C Blue No. 6 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 regulation published in the FEDERAL REGISTER of May 9, 1939 (4 FR 1922).

Under 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. The transitional provisions of those amendments provide, however, 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, D&C Blue No. 6 was previously listed for use in 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). D&C Blue No. 6 is currently provisionally listed for use in drugs, cosmetics, and sutures with a closing date of January 31, 1981. The establishment of January 31, 1981 as the closing date for this color originated with a proposal published in the FEDERAL REGISTER of September 23, 1976 (41 FR 41860). The final regulations in response to that proposal were issued in the FEDERAL REGISTER of February 4, 1977 (42 FR 6992). The continued provisional listing of the color was conditioned on submission of final reports of chemistry data and analytical methods by August 3, 1977 and chronic toxicity feeding studies by August 4, 1980.

D&C Blue No. 6 is the subject of a petition (CAP 57) submitted 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 Hazelton Laboratories, Inc., Falls Church, Va. 22046. This petition was filed for the use of D&C Blue No. 6 for coloring ingested drugs, surgical sutures, lipsticks, and externally applied drugs and cosmetics by a notice in the FEDERAL REGISTER of November 20, 1968 (33 FR 17205). This filing notice was amended by a notice published in the FEDERAL REGISTER of March 5, 1976 (41 FR 9584) to include use of the color in area of the eye. The D&C Blue No. 6 is also the subject of petitions for coloring surgical sutures. These petitions were submitted by the Davis and Geck Division, American Cyanamid Co., Pearl River, N.Y. 10965 (CAP 6C0046); by Ethicon, Inc., Somerville, N.J. 08876 (CAP 7C0048); and by ASR Division, Cenco Medical Industries, Inc., 4150 Laclede Ave., St. Louis, Mo. 63108 (CAP 8C0054), filed by notices in the FEDERAL REGISTER of April 11, 1973 (38 FR 9176). All petitions were filed under the provisions of section 706 of the Federal Food, Drug, and Cosmetic Act, as amended by the Color Additive Amendments of 1960.

D&C Blue No. 6 is a color additive that has been subject to the requirements of batch certification as provided by section 706(c) of the act. The Commissioner has concluded that batch certification of the color would continue to be necessary if the color were to be listed. The conditions for the continued provisional listing of the color were defined in the FEDERAL REGISTER of Feburary 4, 1977 under § 81.27(c) (21 CFR 81.27(c)). Adequate analytical methods were required for the development of specifications for batch certification and the definition of purity of the color used for toxicological testing. These data and analytical methods were to be submitted to FDA by August 3, 1977.

The petitioner agreed under the requirements of § 81.27(c)(2) (21 CFR 81.27(c)(2)) to provide the information necessary for the certification and the "permanent" listing for D&C Blue No. 6. In response to the regulation, the petitioner submitted data for analytical procedures for the identification of subsidiary colors. The agency has reviewed these submissions and finds that the data are inadequate to resolve the chemistry deficiencies for the color.

The analytical methods used to determine intermediates in D&C Blue No. 6 show the presence of unidentified substances when it is extracted with methanol, *N,N*-dimethylformamide, or tergitol TMN in water, followed by examination using thin layer chromatography. Continued provisional listing of the color has been conditioned upon the submission of satisfactory methods for the determination of these unidentified substances, as well as sufficient analytical data on commercial and pharmacological samples of D&C Blue No. 6. Approximately 3 percent of the color consists of unidentified substances that are insoluble in methanol, in *N,N*-dimethylformamide, or in tergitol TMN in water; but it is uncertain whether the same or different unknowns are found by the different extraction systems.

Identification of the unknown substances continues to be necessary for listing of the color in drugs and cosmetics. The petitioners have requested that FDA consider listing of the color for use in sutures on the basis of the available data and the minimal exposure represented by sutures. The Commissioner of Food and Drugs has concluded that the data are sufficient to support listing of D&C Blue No. 6 in sutures. Published elsewhere in this issue of the FEDERAL REGISTER is a regulation listing D&C Blue No. 6 for use in sutures. The use of D&C Blue No. 6 for coloring drugs and cosmetics was provisionally listed until October 31, 1977, pending resolution of chemistry questions concerning unidentified substances. The chemistry questions are not expected to be answered in the near future. Without a satisfactory analytical procedure to compare different batches of D&C Blue No. 6, it will be impossible to certify the color.

In addition to the chemistry questions, the petitioners were also requested to conduct new chronic feeding studies with the color. The petitioners have recently advised FDA that they do not plan to conduct chronic feeding studies with the color.

ACTION

The purpose of the transitional provisions of the Color Additive Amendments of 1960, (section 203) as noted above, "is to make possible, on an interim basis for a reasonable period, through provisional listings, the use of commercially established color additives to the extent consistent with the public health, pending the completion of the scientific investigations needed as a basis for making determinations as to listing of such additives." This provisional listing of previously marketed colors was to expire on a date, also referred to as the closing date, 2½ years after the effective date of the Amendments.

Section 203 of the Amendments further provides, however, that the closing date for the provisional listing may be postponed to a later date as considered "necessary to carry out the purpose of this section, if in the Secretary's judgment such action is consistent with the objective of carrying to completion in good faith, as soon as reasonably practicable, the scientific investigations necessary for making a determination as to listing such additive, or such specified use or uses thereof, under section 706 of the basic Act."

Under the transitional provision of the Amendments (section 203(a)(2)), the Commissioner may "terminate a postponement of the closing date at any time if he finds that such postponement should not have been granted, or that by reason of change in circumstances the basis for such postponement no longer exists, or that there has been a failure to comply with a requirement for submission of progress reports or with other conditions attached to such postponement." Based on the available information, the Commissioner concludes that the petitioners for D&C Blue No. 6 have not successfully answered all questions concerning the unknown substances in D&C Blue No. 6, nor are they expected to do so in the near future. The Commissioner further concludes that the provisional listing of D&C Blue No. 6 for coloring drugs and cosmetics should be terminated because of the failure to comply with the conditions for continued provisional listing of submission of chemistry data and analytical methods and the conduct of new chronic feeding studies. The closing date for D&C Blue No. 6 is being continued until January 31, 1978 for its use in surgical sutures to provide time for the issuance of listing regulations for that use.

Batches of D&C Blue No. 6 will continue to be certified for coloring sutures only. All other certificates heretofore issued for batches of D&C Blue No. 6 are revoked except for use of the color in the color to any drugs or cosmetics will surgical sutures, and the addition of 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 the straight color, its lakes, and mixtures of D&C Blue No. 6 and its lakes. The Commissioner concludes that the protection of the public health does not require the recall from the market of drugs and cosmetics containing the color additive, or the destruction of drugs or cosmetics in preparations to which the color additive has already been added.

Manufacturers of new drugs and new animal drugs (including certifiable antibiotics for animal use) that contain D&C Blue No. 6 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) (21 CFR 314.8 (d)(3) and (e) or 21 CFR 514.8 (d)(3) and (e)), as appropriate. 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. The applicant shall also 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, drug and cosmetic labeling that states that the product contains "artificial color" or that specifically identifies D&C Blue No. 6 may continue to be used with the uncolored product or products containing alternative colors during the time necessary to obtain supplies of revised labeling or until December 13, 1978, 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 (HFC–20), Food and Drug Administration, Rm. 4–65, 5600 Fishers Lane, Rockville, Md. 20857.

Therefore, under the transitional provisions of the Color Additive Amendments of 1960 (Title II, Pub. L. 86–618; sec. 203, 74 Stat. 404–407 (21 U.S.C. 376 note)) and under authority delegated to the Commissioner (21 CFR 5.1), Part 81 is amended as follows:

1. In § 81.1 by revising the table entry for D&C Blue No. 6 in paragraph (b) to read as follows:

§ 81.1 Provisional lists of color additives.

* * * * *

(b) * * *

Color additive	Closing date	Restrictions
* * *	* * *	* * *
D. & C. Blue No. 6..	Jan. 31, 1978	Surgical suture use only.
* * *	* * *	* * *

2. In § 81.10 by adding new paragraph (n), to read as follows:

§ 81.10 Termination of provisional listings of color additives.

* * * * *

(n) *D&C Blue No. 6.* The Commissioner of Food and Drugs, having concluded that unresolved questions remain concerning the chemistry of unidentified minor components, hereby terminates the provisional listing of D&C Blue No. 6 for use in drugs and cosmetics.

§ 81.27 [Amended]

3. In § 81.27 *Conditions of provisional listing of additives,* by deleting the entry for D&C Blue No. 6 in pargaraphs (c) and (d).

4. In § 81.30 by adding new paragraph (o), to read as follows:

§ 81.30 Cancellation of certificates.

* * * * *

(o)(1) Certificates issued for D&C Blue No. 6 and all mixtures containing this color additive are cancelled insofar as its use in drugs and cosmetics is concerned and have no effect after December 13, 1977, and use of the color additive in the manufacture of drugs or cosmetics after this date will result in adulteration. The color will continue to be certified for use in the coloring of surgical sutures.

(2) The Commissioner finds, on the basis of the scientific evidence before him, that no action has to be taken to remove from the market drugs andcosmetics containing the color additive.

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

Because this action is final (not proposed), an economic impact evaluation is not required by Executive Order 11821 (3A CFR, 1975 Compilation, p. 203).

Effective date: This regulation shall be effective December 13, 1977.

(Sec. 203, 74 Stat. 404–407 (21 U.S.C. 376 note))

Dated: December 5, 1977.

WILLIAM F. RANDOLPH,
Acting Associate Commissioner for Compliance.

[FR Doc.77–35325 Filed 12–7–77;2:28 pm]

[4110–03]

[Docket No. 77C–0382]

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

PART 82—LISTING OF CERTIFIED PROVISIONALLY LISTED COLORS AND SPECIFICATIONS

Termination of Provisional Listing and Certification of D&C Red No. 10, D&C Red No. 11, D&C Red No. 12, and D&C Red No. 13

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: This document terminates the closing date for the provisional listing, and hence the approval, of the color additives D&C Red No. 10, D&C Red No. 11, D&C Red No. 12, and D&C Red No. 13 for coloring drugs and cosmetics. All color additive certificates for each of these colors are being cancelled. The closing date is being terminated because the color additive petition for these colors has been withdrawn, and there no longer exists a basis for their continued provisional listing. This action is effective immediately because data raise concerns about the safety of these colors. D&C Red No. 10, D&C Red No. 11, D&C Red No. 12, and D&C Red No. 13 may not be added to drugs and cosmetics after December 13, 1977.

EFFECTIVE DATE: December 13, 1977.

FOR FURTHER INFORMATION CONTACT:

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

SUPPLEMENTARY INFORMATION: Under section 706 of the act (21 U.S.C. 376), the Color Additive Amendments of 1960, a color additive may be approved only if data establish that it is safe under its intended conditions of use (sec. 706, 74 Stat. 399–403 (21 U.S.C. 376)). The transitional provisions of the Color Additive Amendments, however, "make possible, on an interim basis for a reasonable period, through provisional listing, the use of commercially established color additives to the extent consistent with the public health, pending the completion of the scientific investigations needed as a basis for making determinations as to listing of such additives." (Title II, Pub. L. 86–618; sec. 203, 74 Stat. 404–407 (21 U.S.C. 376 note).) This provisional listing of previously marketed colors was to expire on the date, also referred to as the closing date, 2½ years after the effective date of the amendments.

Section 203 of the Amendments further provides, however, that the closing date for the provisional listing can be postponed to a later date as considered "necessary to carry out the purpose of this section, if in the Secretary's judgment such action is consistent with the objective of carrying to completion in good faith, as soon as reasonably practicable, the scientific investigations necessary for making a determination as to listing such additive, or such specified use or uses thereof, under section 706 of the basic Act." Section 81.1 (21 CFR 81.1) of the color additive regulations designates those color additives that are provisionally listed.

A notice published in the FEDERAL REGISTER of August 6, 1973 (38 FR 21199) stated that a petition (CAP 5C0029) for the "permanent" listing of D&C Red No. 10, D&C Red No. 11, D&C Red No. 12, and D&C Red No. 13 had been filed by the Cosmetic, Toiletry and Fragrance Association, Inc. (CTFA), 1133 15th St. NW., Washington, D.C. 20005, %Hazleton Laboratories, Inc., P.O. Box 30, Falls Church, Va. 22046. The petition was filed pursuant to section 706 of the act.

On October 21, 1977, CTFA wrote to FDA requesting that the color additive petition for D&C Red No. 10, D&C Red No. 11, D&C Red No. 12, and D&C Red No. 13 be withdrawn without prejudice to future filing. On October 5, 1977, CTFA had advised FDA that it did not intend to conduct new chronic feeding studies with these colors as required by § 81.27 (d) (21 CFR 81.27(d)). Published elsewhere in this issue of the FEDERAL REGISTER is a notice announcing the withdrawal of the petition for D&C Red Nos. 10 through 13, while the regulations set forth below terminate the provisional listing of these four colors for use as color additives in drugs and cosmetics effective December 13, 1977, because there are no pending color additive petitions or progress reports for them as required by § 81.1. In addition, as will be discussed, the Commissioner is concerned that the continued use of these four colors in drugs and cosmetics may pose a hazard to the public health.

The colors D&C Red Nos. 10, 11, 12, and 13 have been used as color additives for many years. D&C Red Nos. 10, 11, 12, and 13 were approved for certification for drug and cosmetic use as permitted "coal-tar" colors after enactment of the Federal Food, Drug, and Cosmetic Act of 1938 by order published in the FEDERAL REGISTER of May 9, 1939 (4 FR 1922). Under the Color Additive Amendments, D&C Red No. 10, D&C Red No. 11, D&C Red No. 12, and D&C Red No. 13 were provisionally listed for use in 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). Since then, D&C Red Nos. 10, 11, 12, and 13 have been provisionally listed for use in drugs and cosmetics, with a present closing date of January 31, 1981. The establishment of January 31, 1981 as the closing date for these four colors pending submission of a final report on new chronic feeding studies originated with a proposal published in the FEDERAL REGISTER of September 23, 1976 (41 FR 41860). The final regulations in response to that proposal were issued in the FEDERAL REGISTER of February 4, 1977 (42 FR 6992).

On November 23, 1976, FDA received a comment to the proposal of September 23, 1976, which cited a reference from "Occupational and Environmental Cancers of the Urinary System," stating that according to the author, Dr. Hueper, there is reason to believe that azo dyes contain various carcinogenic amines, including β-naphthylamine. The comment objected to the listing of azo dyes. β-naphthylamine has long been known to be a carcinogen, causing bladder cancer in humans as well as test animals. Two colors, Ext. D&C Yellow No. 9 and Ext. D&C Yellow No. 10, which were synthesized from β-naphthylamine, were prohibited by FDA from use in externally applied drugs and cosmetics because of a finding that they might contain β-naphthylamine. Accordingly, the Commissioner has viewed with concern the possibility that any color additive for food, drug, or cosmetic use might contain β-naphthylamine.

β-Naphthylamine is an intermediate that is used in producing diazotized compounds for industrial use. These compounds are not, however, used in the production of color additives intended for use in food, drugs, or cosmetics. Therefore, β-naphthylamine would not be expected to be present in color additives, except as a contaminant.

Upon review of the data on each of the azo dyes, the Commissioner concluded that there were five colors that could possibly contain low levels of β-naphthylamine as impurities—four provisionally listed colors, D&C Red No. 10, D&C Red No. 11, D&C Red No. 12, and D&C Red No. 13, and a "permanently" listed color, D&C Red No. 34. These colors are synthesized from 2-amino-1-naphthalenesulfonic acid which, according to some information, might contain β-naphthylamine.

To resolve the questions raised by the comment, the Commissioner requested that the petitioner promptly provide to FDA data about the possible contamination of 2-amino-1-naphthalenesulfonic acid and each of the five colors with β-naphthylamine. In addition, FDA began some laboratory investigations of its own, including analysis of samples of each of the five colors and 2-amino-1-naphthalenesulfonic acid for the presence of β-naphthylamine. Copies of correspondence between the petitioners and FDA and memoranda of meetings and telephone conversations concerning this matter are on public display at the office of the Hearing Clerk (HFC–20), Food and Drug Administration, Room 4–65, 5600 Fishers Lane, Rockville, Md. 20857.

The liscussion and regulations stated in this document concern the Commissioner's conclusions on the provisionally listed color additives D&C Red No. 10, D&C Red No. 11, D&C Red No. 12, and D&C Red No. 13. The status of the "permanently" listed color additive D&C Red No. 34 is being considered separately and will be the subject of a future FEDERAL REGISTER document.

D&C Red No. 10 is an azo compound that is formed by the diazotization of 2-amino-1-naphthalenesulfonic acid (Tobias acid) and subsequent coupling with β-naphthol. D&C Red No. 10 is the monosodium salt of 2-(2-hydroxy-1-naphthylazo)-1-naphthalenesulfonic acid. D&C Red No. 11, D&C Red No. 12, and D&C Red No. 13 are the calcium, barium, and strontium salts, respectively, of 2-(2-hydroxy-1-naphthylazo)-1-naphthalenesulfonic acid.

The data for Tobias acid show that it contains small amounts of β-naphthylamine. The β-naphthylamine is considered to be present primarily as a result of incomplete reactions in the manufacture of Tobias acid. Tobias acid is manufactured in two steps. First, β-naphthol is sulfonated by reacting with sulfuric acid to form 2-hydroxy-1-naphthalenesulfonic acid. Second, the 2-hydroxy-1-naphthalenesulfonic acid is aminated by reacting with ammonia or ammonium bisulfite to form 2-amino-1-naphthalenesulfonic acid (Tobias acid).

The sulfonation step in the production of the Tobias acid never results in 100-percent conversion of β-naphthol to 2-hydroxy-1-naphthalenesulfonic acid. As a result, there is always some free β-naphthol present in the 2-hydroxy-1-naphthalenesulfonic acid during the subsequent amination step of the process. Because β-naphthol can be aminated to form β-naphthylamine, any β-naphthol that might be present would be expected to react during the amination step of the process for Tobias acid to produce β-naphthylamine.

Three samples of Tobias acid, one each from three color manufacturers, were analyzed by the Division of Color Technology, Food and Drug Administration. β-Naphthylamine was found in each of the three samples. In addition, analytical data on many batches of Tobias acid have been submitted by the producers, the Sherwin-Williams Co. and the American Cyanamid Co., and the data show the presence of β-naphthylamine.

The data submitted by the manufacturers show that levels of β-naphthylamine commonly detected in production lots of Tobias acid are between 100 and 500 parts per million (ppm). The current data sheets for the Tobias acid products by those two companies contain a specification of less than 0.1 percent (1,000 parts per million (ppm)) for β-naphthylamine. These levels were confirmed by FDA analyses showing levels of β-naphthylamine of 300, 400, and 1,100 ppm.

In addition, Sherwin-Williams reported that there is an apparent hydrolysis of Tobias acid to form β-napthylamine. They had extracted a solution of the sodium salt of Tobias acid with water until there was no extractable β-naphthylamine. This water solution of the Tobias acid was then permitted to stand overnight. Reanalysis of this solution on the following day disclosed 33 ppm β-naphthylamine. The firm's scientists concluded that Tobias acid dissolved in water as the sodium salt slowly hydrolyzes to form β-naphthylamine and estimated that the amount of hydrolysis was approximately 0.001 to 0.002 percent. A similar study was conducted using ethanol as the solvent. The firm's scientists concluded from this study that contact with ethanol causes Tobias acid to hydrolyze to β-naphthylamine at a greater rate.

Free Tobias acid in these four colors would be expected to hydrolyze much in the same way as for the pure Tobias acid, as discussed above, yielding free β-naphthylamine. The specifications used in the certification of these four colors contain a limitation of "not more than 0.2 percent" for 2-amino-1-naphthalenesulfonic acid (Tobias acid). Using analytical methodology sensitive to 0.05 percent, samples of these colors submitted for certification are generally found to contain less than 0.05 percent Tobias acid (nondetectable); however, as much as 0.13 percent Tobias acid has been found in some lots. If, as suggested by scientists from Sherwin-Williams, 0.001 to 0.002 percent of this Tobias acid were to hydrolyze to yield free β-naphthylamine, as much as 0.026 ppm free β-naphthylamine might be expected to be found in these colors as a result of the hydrolysis.

Analysis for free β-naphthylamine in each of the four colors by FDA's laboratories was hampered by difficulties with the analytical methods and has not shown free β-naphthylamine. The primary difficulty is one of separating β-naphthylamine from the color.

During a meeting with representatives of the Cosmetic, Toiletry, and Fragrance Association, agency personnel were advised that American Cyanamid had reported finding 1.8 to 3.6 ppm β-naphthylamine in their technical-grade lithol red. This color is not used for drugs and cosmetics, but is used in industry, e.g., as a component of paints and printing inks. Although the exact identity of the lithol reds tested by American Cyanamid is unknown, lithol reds are generally sufficiently similar to the four colors, D&C Red Nos. 10, 11, 12, and 13, to permit a conclusion that the latter colors would also contain free β-naphthylamine. The agency received a letter of June 16, 1977, from the petitioner, transmitting the results of analysis of two laboratory batches of D&C Red No. 10. One batch was found to contain 7.0 and 5.8 ppm β-naphthylamine in duplicate analyses of the batch; no β-naphthylamine was found in the second batch.

Theoretically, free β-naphthylamine in Tobias acid would be expected to diazotize to some extent and couple with β-naphthol to form a subsidiary color. The FDA Division of Color Technology conducted experiments to determine whether any subsidiary colors formed from β-naphthylamine might be present in these four colors. Samples of the subsidiary color formed from β-naphthylamine and β-napthol were prepared by FDA chemists and used as standards for the analysis of previously certified batches of each of the four colors—D&C Red Nos. 10 through 13. These analyses revealed the presence of the subsidiary color at levels ranging from 25 to 276 ppm. The identity of the β-naphthylamine subsidiary color was confirmed by comparison with the infrared spectra, the visible spectra, and the thin-layer chromatographic R_f (retardation factor) value of authentic samples previously prepared by the Division of Color Technology, Food and Drug Administration. The presence of subsidiary colors produced from β-napthylamine raises concern about the safety of these four colors because their metabolism after ingestion or other degradation would yield free β-naphthylamine. The data for metabolism of azo dyes establish that the azo bond is broken during metabolism yielding the constituent amine.

The toxicity of β-naphthylamine is well known—it has been considered a carcinogen for many years. In its evaluation of the data on β-naphthylamine, the International Agency for Research on Cancer stated that 2-naphthylamine, another name for β-naphthylamine, is carcinogenic in the mouse, hamster, dog, and monkey. In addition, there are considerable epidemiological data that establish that β-naphthylamine is a bladder carcinogen in humans (IRAC Monographs, Vol. 4, 1974).

The Commisioner finds that the use of D&C Red No. 10, D&C Red No. 11, D&C Red No. 12, and D&C Red No. 13 as color additives could result in exposure of the consumer to β-naphthylamine. There is free β-naphthylamine at appreciable levels (up to 1,100 ppm) in the intermediate used to produce the color. There is a possibility that the intermediate Tobias acid, which can be present in the finished colors at levels as great as 2,000 ppm, may hydrolyze to form free β-naphthylamine. β-Naphthylamine was found in a laboratory sample of D&C Red No. 10. The chemistry data establish that D&C Red Nos. 10 through 13 contain a subsidiary color produced from β-naphthylamine that would be expected to yield β-naphthylamine when metabolized or degraded. The evidence of the presence of this subsidiary color supports a conclusion that each of the four colors does contain some free β-naphthylamine, particularly in view of the finding of β-naphthylamine in D&C Red No. 10.

Under the transitional provisions of the Color Additive Amendments (section 203(a)(2)), the Commissioner may "terminate the postponement of the closing date at any time if he finds that such postponement should not have been granted, or that by reason of change in circumstances the basis for such postponement no longer exists, or that there has been a failure to comply with a requirement for submission of progress reports or with other conditions attached to such postponement." In view of the petitioner's withdrawal of the petition for these four colors and its statement that it does not intend to conduct chronic feeding studies with D&C Red No. 10 through 13 as required by § 81.27 (d) as a condition of continued provi-

sional listing, the Commissioner concludes that there no longer exists a basis for the provisional listing of these four colors.

The transitional provisions of the Amendments (section 203(d)(1)(E)) "provide for the termination of a provisional listing or deemed provisional listing of a color additive or particular use thereof forthwith whenever" such action is necessary to protect the public health. On the basis of the available data, the Commissioner concludes that the colors D&C Red No. 10, D&C Red No. 11, D&C Red No. 12, and D&C Red No. 13 would be expected to contain β-naphthylamine, a known carcinogen, or to yield β-naphthylamine when ingested. Accordingly, under section 203 (d)(1)(E)) of the Amendments, the Commissioner concludes that the provisional listing of D&C Red No. 10, D&C Red No. 11, D&C Red No. 12, and D&C Red No. 13 for use in drugs and cosmetics should be terminated immediately because such action is necessary to protect the public health.

All certificates heretofore issued for batches of D&C Red No. 10, D&C Red No. 11, D&C Red No. 12, and D&C Red No. 13 are revoked, and the addition of these colors to any drugs or cosmetics after December 13, 1977, 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 the straight colors, their lakes, and mixtures of one or more of these colors: D&C Red No. 10, D&C Red No. 11, D&C Red No. 12, and D&C Red No. 13, or their lakes. The Commissioner concludes that the protection of the public health does not require the recall from the market of drugs and cosmetics containing the color additives, or the destruction of drugs or cosmetics in preparation to which the color additives have already been added.

Manufacturers of new drugs and new animal drugs (including certifiable antibiotics for animal use) that contain D&C Red No. 10, D&C Red No. 11, D&C Red No. 12, or D&C Red No. 13 may either delete the color additives or substitute a different color in accordance with the provisions of § 314.8 (d)(3) and (e) or § 514.8 (d)(3) and (e) (21 CFR 314.8 (d)(3) and (e) or 21 CFR 514.8 (d)(3) and (e)) as appropriate. 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. The applicant shall also 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 the supplies of alternative color additives may be difficult to obtain immediately. Consequently, drug and cosmetic labeling that states that the product contains "artificial color" or that specifically identifies D&C Red No. 10, D&C Red No. 11, D&C Red No. 12, or D&C Red No. 13 may continue to be used with the uncolored product or products containing alternative colors during the time necessary to obtain supplies of revised labeling or until December 13, 1978, 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 (HFC–20), Food and Drug Administration, Room 4–65, 5600 Fishers Lane, Rockville, Md. 20857.

Therefore, under the transitional provisions of the Color Additive Amendments of 1960 (Title II, Pub. L. 86–618, sec. 203, 74 Stat. 404–407 (21 U.S.C. 376 note)) and under authority delegated to the Commissioner (21 CFR 5.1), Parts 81 and 82 are amended as follows:

1. Part 81 is amended:

§ 81.1 [Amended]

a. In § 81.1 *Provisional lists of color additives,* in paragraph (b), by deleting the table entries for D&C Red No. 10, D&C Red No. 11, D&C Red No. 12, and D&C Red No. 13.

b. In § 81.10 by adding new paragraph (h), to read as follows:

§ 81.10 Termination of provisional listing of color additives.

* * * * *

(h) *D&C Red Nos. 10, 11, 12, and 13.* The petition for these color additives was withdrawn so that there no longer exists a basis for their continued provisional listing. In addition, the Commissioner has learned of the possible contamination of D&C Red No. 10, D&C Red No. 11, D&C Red No. 12, and D&C Red No. 13 with β-naphthylamine. The Commissioner concludes that these colors cannot be produced with any reasonable assurance that they will not contain β-naphthylamine as an impurity or not yield β-naphthylamine from the metabolism of subsidiary colors present in them. β-Naphthylamine is a known carcinogen; therefore, there is no scientific evidence that will support a safe tolerance for these colors in drugs or cosmetics. The Commissioner of Food and Drugs, upon withdrawal of the petition for their use and in order to protect the public health, hereby terminates the provisional listing of D&C Red No. 10, D&C Red No. 11, D&C Red No. 12, and D&C Red No. 13 for use in drugs and cosmetics, effective December 13, 1977.

§ 81.25 [Amended]

c. In § 81.25 *Temporary tolerances,* paragraph (a) is amended by deleting the table entries for D&C Red No. 10, D&C Red No. 11, D&C Red No. 12, and D&C Red No. 13; and paragraph (b)(1) is amended by deleting the tabular entry for D&C Red No. 12.

§ 81.27 [Amended]

d. In § 81.27 *Conditions of provisional listing,* paragraph (d) is amended by deleting the entries for D&C Red No. 10, D&C Red No. 11, D&C Red No. 12, and D&C Red No. 13 from the introductory text.

e. In § 81.30, by adding new paragraph (k) to read as follows:

§ 81.30 Cancellation of certificates.

* * * * *

(k) (1) Certificates issued for D&C Red No. 10, D&C Red No. 11, D&C Red No. 12, and D&C Red No. 13, their lakes and all mixtures containing these color additives or their lakes are cancelled and have no effect after December 13, 1977, and use of these color additives in the manufacture of drugs or cosmetics after this date will result in adulteration.

(2) The Commissioner finds, on the basis of the scientific evidence before him, that no action has to be taken to remove from the market, drug and cosmetic products containing the color additives.

2. Part 82 is amended:

§ 82.1310 [Revoked]

a. By revoking § 82.1310 *D&C Red No. 10.*

§ 82.1311 [Revoked]

b. By revoking § 82.1311 *D&C Red No. 11.*

§ 82.1312 [Revoked]

c. By revoking § 82.1312 *D&C Red No. 12.*

§ 82.1313 [Revoked]

d. By revoking § 82.1313 *D&C Red No. 13.*

Notice and public procedure are not necessary prerequisities to the promulgation of these regulations because section 203(d)(2) of Pub. L. 86–618 so provides.

NOTE.—Because this action is final (not proposed), an economic impact evaluation is not required under Executive Orders 11821 and 11949 and OMB Circular A–107.

Effective date. These regulations shall be effective on December 13, 1977.

(Sec. 203, 74 Stat. 404–407 (21 U.S.C. 376 note).)

Dated: December 5, 1977.

WILLIAM F. RANDOLPH,
Acting Associate Commissioner for Compliance.

[FR Doc.77–35324 Filed 12–7–77;2:28 pm]

[4110–03]

[Docket No. 77C–0384]

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

PART 82—LISTING OF CERTIFIED PROVISIONALLY LISTED COLORS AND SPECIFICATIONS

Provisional Listing of Ext. D&C Yellow No. 1; Termination of Closing Date

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: This document terminates the closing date for the provisional listing, and hence the approval, of the color additive Ext. D&C Yellow No. 1 for use in externally applied drugs and cosmetics. All color additive certificates for this color are being cancelled. The closing date is being terminated because the color additive contains 4-aminobiphenyl, a known carcinogen. Ext. D&C Yellow No. 1 may not be used in externally applied drugs and cosmetics after December 13, 1977.

DATE: Effective December 13, 1977.

FOR FURTHER INFORMATION CONTACT:

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

SUPPLEMENTARY INFORMATION: The Color Additive Amendments of 1960 provide that a color additive may be approved only if data establish that it is safe under its permitted conditions of use. 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)) provides, however, for provisional listing of color additives in use in 1960 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)). Section 81.1 (21 CFR 81.1) of the color additive regulations designates those colors that are provisionally listed.

The color additive Ext. D&C Yellow No. 1 has been in use for many years, having been listed for use in externally applied drugs and cosmetics as a permitted "coal-tar" color after enactment of the FEDERAL REGISTER of May 9, 1939 (4 FR 1922). Ext. D&C Yellow No. 1 was provisionally listed for use in externally applied 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). Ext. D&C Yellow No. 1 is currently provisionally listed under § 81.1 (c) (21 CFR 81.1(c)) for use in externally applied drugs and cosmetics with a closing date of October 31, 1977. The establishment of October 31, 1977, as the closing date for this color originated with a proposal published in the FEDERAL REGISTER of September 23, 1976 (41 FR 41860). The final regulations in response to that proposal were issued in the FEDERAL REGISTER of February 4, 1977 (42 FR 6992).

On November 23, 1976, the FDA received a letter that cited a reference from "Occupational and Environmental Cancers of the Urinary System," stating that according to the author, Dr. Hueper, there is reason to believe that azo dyes contain various carcinogenic amines, including 4-aminobiphenyl. This letter had been filed as a comment in response to the September 23, 1976, proposal concerning the extension of the closing date for the provisionally listed color additives. The comment objected to the listing of azo dyes.

Upon review of the data, the Commissioner of Food and Drugs concluded that Ext. D&C Yellow No. 1 could possibly contain low levels of 4-aminobiphenyl and benzidine as impurities. The synthesis of the color utilizes the chemical intermediate, diphenylamine, which might contain free 4-aminobiphenyl as a result of the manufacturing process of the intermediate. In addition to the likelihood of free 4-aminobiphenyl being present in the color additive, there is also the possibility of chemical formation of another carcinogen, benzidine. The chemically active 4-aminobiphenyl would be expected to react with diazotized metanilic acid yielding a product that could subsequently decompose to release benzidine.

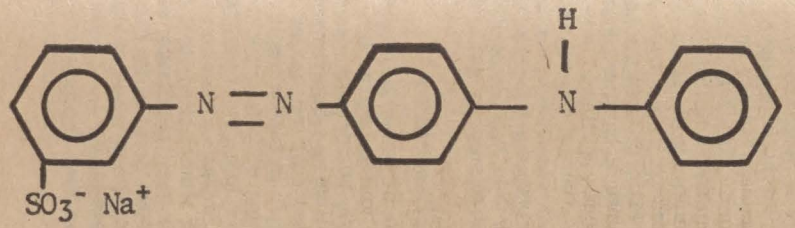
To resolve the questions raised by the comment, the Commissioner requested that the petitioner promptly provide to FDA data about the possible contamination of the intermediate diphenylamine with 4-aminobiphenyl and the possible formation of benzidine. In addition, FDA requested information from the manufacturer of diphenylamine relative to the presence of 4-aminobiphenyl in the product.

The Commissioner continued the provisional listing for Ext. D&C Yellow No. 1 because the short period of time required to resolve this question did not present a hazard to the public health. The Commissioner had noted that if data became available, either from investigation by FDA or from the petitioner, verifying that 4-aminobiphenyl or benzidine is present in the color additive, action would be taken to protect the public health.

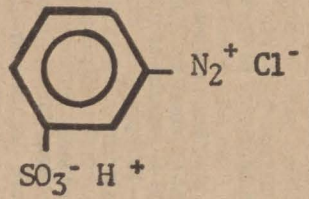
CHEMISTRY

The color Ext. D&C Yellow No. 1 is an azo compound that is formed by the diazotization of metanilic acid and the subsequent coupling with diphenylamine. The chemical structures for the color, its intermediates, and the possible contaminants are as follows:

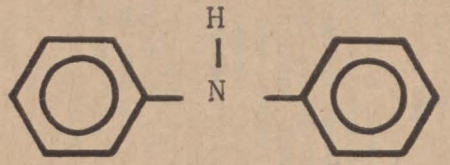
Ext. D&C Yellow No. 1



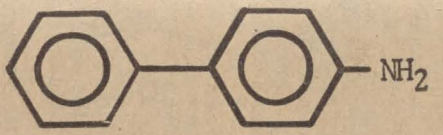
Diazotized Metanilic Acid



Diphenylamine

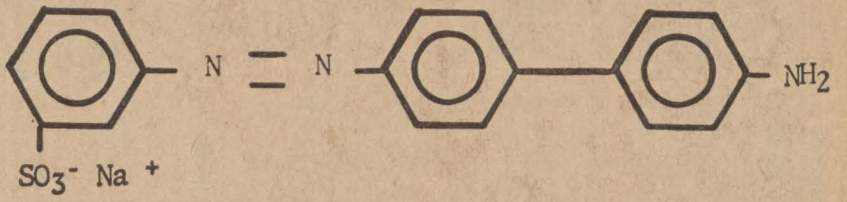


4-Aminobiphenyl (4-ABP)



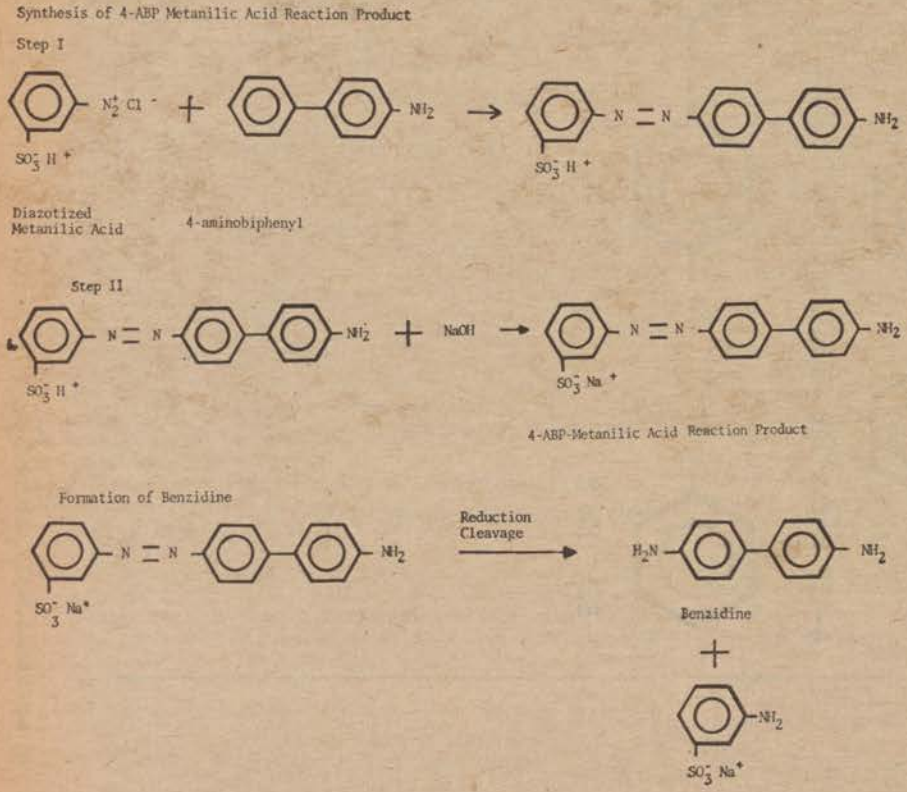
Benzidine
(4,4'-Diaminobiphenyl)

4-ABP-Metanilic Acid Reaction Product



The data provided for diphenylamine by the manufacturer show that it contains small amounts of 4-aminobiphenyl. The 4-aminobiphenyl is considered to be present primarily as a result of the manufacturing process for diphenylamine. The chemical formation of the carcinogenic byproduct is not currently understood, and literature references on its formation are therefore not available.

The chemical interaction of 4-aminobiphenyl (4-ABP) with diazotized metanilic acid leads to the formation of a possible reaction product that can decompose to release an additional carcinogen, benzidine. The chemical reactions that are involved may be depicted as follows:



Analytical data on typical production batches of diphenylamine have been submitted by a producer, the American Cyanimid Co., which show the presence of 4-aminobiphenyl in each of the sampled batches. The data indicated that levels of 4-aminobiphenyl commonly detected in production lots of diphenylamine are between 23 and 48 parts per million (ppm). In addition, current data sheets for diphenylamine produced by this company contain a specification of less than 0.01 percent (100 ppm) for 4-aminobiphenyl.

The producer could not explain the chemistry that would result in the formation of 4-aminobiphenyl in the manufacture of diphenylamine. During a meeting with representatives of the Cosmetic, Toiletry, and Fragrance Association, agency personnel were advised that there is currently no available source of diphenylamine that would not contain 4-aminobiphenyl as a contaminant. Recently, the petitioner has submitted analytical data that confirmed the presence of 4-aminobiphenyl in the finished color additive by sensitive analytical methods.

The presence of 4-ABP could lead to certain chemical reactions involving 4-aminobiphenyl producing a reaction product that can degrade to form an additional carcinogen, benzidine, in the finished color and/or product. During the manufacturing process a chemical reaction of 4-aminobiphenyl with diazotized metanilic acid can be predicted that would produce a 4-aminobiphenyl-diazotized metanilic reaction product. Subsequent conditions may be encountered that cause breakage of the azo bond in the reaction product and the release of the carcinogen benzidine. The probability for free benzidine in the color or its formation from additional chemical action on the reaction product is supported by information showing that free 4-aminobiphenyl is present at appreciable levels (up to 100 ppm) in the intermediate diphenylamine used to produce the color and the confirmed presence of 4-aminobiphenyl in the finished color. The chemical reactions for the formation of benzidine were depicted in the previous section. Analysis for free benzidine and/or the reaction product by existing analytical methods has not shown that the chemicals are present in the color. However, from the strong presumptive evirence cited above it appears that with more sensitive validated analytical methods, benzidine and/or its precursor compound would be found in the color.

In addition to carcinogens, the Commissioner is concerned about the unresolved chemistry deficiencies for Ext. D&C Yellow No. 1. Ext. D&C Yellow No. 1 is a color additive that has been subject to the requirements of batch certification as provided by section 706(c) of the act. The Commissioner has concluded that batch certification of the color would continue to be necessary if the color were listed. Under the regulation published in the FEDERAL REGISTER of February 4, 1977, the petitioner agreed to the requirement of developing adequate analytical procedures for the identification of subsidiary colors that are formed during the synthesis of the color additive. The identification of these compounds is necessary for definition of the purity of the color used for toxicological testing and, therefore, is necessary for the development of specifications for subsequent batch certification. The regulation required that adequate chemistry data and validated analytical methods be submitted to FDA by August 3, 1977. The continued provisional listing of the color was conditioned upon the satisfactory completion of these regulation requirements.

The commissioner has reviewed the petitioner's submissions and concludes that the chemistry data and analytical methods submitted by the petitioner are inadequate to support the certification and the "permanent" listing for Ext. D&C Yellow No. 1 as required by the February 4, 1977, regulations. Adequate analytical methods have not been developed that would allow the satisfactory identification of subsidiary colors found in association with the color additive. The purpose of certification is to detect differences in batches of colors from those tested toxicologically or from the normal analytical findings of batches submitted for certification. Without adequate chemistry data to permit identification of the subsidary colors, there can be no means for determining whether differences are present in the composition of batches of the color submitted for certification.

CARCINOGENICITY

The carcinogenic potential of both 4-aminobiphenyl and benzidine has been well documented. Historically, 4-aminobiphenyl (also named 4-biphenylamine; xenylamine) was first recognized as a human carcinogen in 1954 when 19 cases of bladder tumors were found in workers of the rubber industry ("ACS Monograph 173, Chemical Carcinogens," pp. 465–466). Other studies cited 53 cases in an industrial-exposed population of 315 men. Experimental proof of its carcinogenicity was confirmed with dog experiments in 1952 and 1954.

Benzidine has been recognized as not

only carcinogenic to men in the chemical industry, but it is also carcinogenic in certain animal species ("ACS Monograph 173, Chemical Carcinogens," pp. 392–393). Benzidine, also named 4,4'-diaminobiphenyl, is carcinogenic in dogs, rats, mice, and hamsters.

As stated above, the concern over the safety of Ext. D&C Yellow No. 1 is related to its contamination with 4-aminobiphenyl and/or a possible subsidiary reaction product of 4-aminobiphenyl and diazotized metanilic acid that would yield benzidine under certain conditions. The carcinogen 4-aminobiphenyl has been detected in batches of diphenylamine, and the Commissioner is unaware of any means of purification that would be adequate for its removal from this essential intermediate chemical used in the production of the color. The Commissioner states that the evidence is sufficient to lead to the conclusion that Ext. D&C Yellow No. 1 does contain 4-aminobiphenyl and/or a product that could lead to the formation of benzidine.

PETITIONS

Ext. Yellow No. 1 is the subject of a petition (CAP 7C0056) submitted by the Procter & Gamble Co., Toilet Goods Division, 6000 Center Hill Road, Cincinnati, Ohio 45224. This petition was filed by a notice in the FEDERAL REGISTER of August 6, 1973 (38 FR 21200) under the provisions of section 706 of the act, as amended by the Color Additive Amendments of 1960. The petition for Ext. D&C Yellow No. 1 seeks listing for use in externally applied drugs and cosmetics.

ACTION

The purpose of the transitional provisions of the Color Additive Amendments of 1960 (section 203) as noted above, "is to make possible, on an interim basis for a reasonable period, through provisional listings, the use of commercially established color additives to the extent consistent with the public health, pending the completion of the scientific investigations needed as a basis for making determinations as to listing of such additives * * *." This provisional listing of previously marketed colors was to expire on the date, also referred to as the closing date, 2½ years after the effective date of the amendments.

Section 203 of the Amendments further provides, however, that the closing date for the provisional listing may be postponed to a later date as considered "necessary to carry out the purpose of this section, if in the Secretary's judgment such action is consistent with the objective of carrying to completion in good faith, as soon as reasonably practicable, the scientific investigations necessary for making a determination as to listing such additive, or such specified use or uses thereof, under section 706 of the basic Act."

Under the transitional provisions of the Amendments (section 203(d)(1)(E)), the Commissioner may "provide for the termination of a provisional listing (or deemed provisional listing) of a color additive or particular use thereof forthwith whenever in his judgment such action is necessary to protect the public health." On the basis of the available data, the Commissioner concludes that the color Ext. D&C Yellow No. 1 contains 4-aminobiphenyl and may yield benzidine, both known carcinogens. The presence of 4-aminobiphenyl raises serious questions about the safety of the color under conditions of use. The "Delaney Clause" of the Color Additive Amendments of 1960 (21 U.S.C. 376(b)(5)(B)(ii)) has been interpreted by some persons, however, as permitting the use of a color additive, though potentially carcinogenic when ingested, for external use if there are no data demonstrating it to be carcinogenic when so used. The petitioner has suggested use in bar soap as a condition of use that would be safe. Although the potential for 4-aminobiphenyl to induce cancer has been established in part through review of incidents of industrial exposure, which clearly would have involved dermal contact, there are no definitive animal studies establishing it as a carcinogen when applied externally. In any case, because 4-aminobiphenyl is recognized by experts in carcinogenesis as a potent human carcinogen, prudence would dictate that no color additive be approved for any use if it may be concluded that it will contain or yield 4-aminobiphenyl, even though there are no definitive data showing a hazard from the external use of such a color. Accordingly, under section 203(d)(1)(E) of the Amendments, the Commissioner concludes that the provisional listing of Ext. D&C Yellow No. 1 for use in externally applied drugs and cosmetics should be terminated because such action is necessary to protect the public health.

Under the transitional provisions of the Amendments (section 203(a)(2), the Commissioner may "terminate a postponement of the closing date at any time if he finds * * * that there has been a failure to comply with a requirement for submission of progress reports or with other conditions attached to such postponement." The Commissioner finds that the petitioner for Ext. D&C Yellow No. 1 has failed to comply with conditions established for continued provisional listing. Accordingly, under section 203(a)(2) of the Amendments, the Commissioner concludes that the provisional listing of Ext. D&C Yellow No. 1 for use in externally applied drugs and cosmetics should be terminated for this failure to comply with a condition of provisional listing.

The Commissioner also finds that the presence of 4-aminobiphenyl and the apparent inability to resolve the chemistry questions in a timely fashion prevent him from granting the petition requesting the listing of Ext. D&C Yellow No. 1 (CAP 7C0056). Published elsewhere in this issue of the FEDERAL REGISTER is a notice denying the petition proposing to list the color for use in externally applied drugs and cosmetics.

All certificates heretofore issued for batches of Ext. D&C Yellow No. 1 are revoked, and the addition of this color to any drugs or cosmetics after December 13, 1977, 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 the straight color, its lake, and mixtures of this color or its lake. The Commissioner concludes that the protection of the public health does not require the recall from the market of drugs and cosmetics containing the color additive, or the destruction of drugs or cosmetics 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 contain Ext. D&C Yellow No. 1 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) (21 CFR 314.8 (d)(3) and (e) or 21 CFR 514.8 (d)(3) and (e)), as appropriate. The applicant shall also 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. In addition, 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 identity, quality, purity, and strength 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, drug and cosmetic labeling that states that the product contains "artificial color" because of the presence of Ext. D&C Yellow No. 1 or that specifically identifies Ext. D&C Yellow No. 1 may continue to be used with the uncolored product or products containing alternative colors during the time necessary to obtain supplies of revised labeling or until December 13, 1978, whichever occurs first.

The Commissioner has carefully considered the enivronmental effects of this action, and because the action will not significantly affect the quality of the human environment, has concluded that an enivronmental 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 (HFC–20, Food and Drug Administration, Room 4–65, 5600 Fishers Lane, Rockville, Md. 20857.

Therefore, under the transitional provisions of the Color Additive Amendments of 1960 (Title II, Pub. L. 86–618; sec. 203, 74 Stat. 404–407 (21 U.S.C. 376 note)) and under authority dele-

gated to the Commissioner (21 CFR 5.1), Parts 81 and 82 are amended as follows:

1. Part 81 is amended:

§ 81.1 [Amended]

a. In § 81.1 *Provisional lists of color additives,* in paragraph (c), by deleting the table entry for Ext. D&C Yellow No. 1.

b. In § 81.18 by adding new paragraph (i), to read as follows:

§ 81.10 Termination of provisional listing of color additives.

* * * * *

(i) *Ext. D&C Yellow No. 1.* The Commissioner has learned of the contamination of Ext. D&C Yellow No. 1 with 4-aminobiphenyl. The Commissioner concludes that this color cannot be produced with any reasonable assurance that it will not contain 4-aminobiphenyl as an impurity or not yield benzidine from the decomposition of a subsidiary reaction product that might be present in the color. 4-aminobiphenyl and benzidine are known carcinogens; therefore, there is no scientific evidence that will support a safe tolerance for these colors in drugs or cosmetics. In addition, insufficient data have been submitted to permit establishment of appropriate specifications for the batch certification of the color. The Commissioner of Food and Drugs, in order to protect the public health, hereby terminates the provisional listing of Ext. D&C Yellow No. 1 for use in externally applied drugs and cosmetics, effective December 13, 1977.

* * * * *

c. In § 81.30 by adding new paragraph (l), to read as follows:

§ 81.30 Cancellation of certificates.

* * * * *

(l) (1) Certificates issued for Ext. D&C Yellow No. 1 and all mixtures containing this color additive are cancelled and have no effect after December 13, 1977, and use of this color additive in the manufacture of drugs or cosmetics after this date will result in adulteration.

(2) The Commissioner finds, on the basis of the scientific evidence before him, that no action has to be taken to remove from the market drugs and cosmetics containing the color additive.

§ 82.2701a [Revoked]

2. Part 82 is amended by revoking § 82.2701a *Ext. D&C Yellow No. 1.*

Notice and public procedure are not necessary prerequisites to the promulgation of these regulations because section 203(d)(2) of Pub. L. 86-618 so provides. Because this action is final (not proposed), an economic evaluation is not required by Executive Order 11821 (3A CFR, 1975 Compilation, p. 203).

Effective date. These regulations shall be effective December 13, 1977.

(Sec. 203, 74 Stat. 404-407 (21 U.S.C. 376 note).)

Dated: December 5, 1977.

WILLIAM F. RANDOLPH,
Acting Associate Commissioner for Compliance.

[FR Doc.77-35321 Filed 12-7-77;2:28 pm]

[4310-70]

Title 36—Parks, Forests, and Public Property

CHAPTER I—NATIONAL PARK SERVICE, DEPARTMENT OF THE INTERIOR

PART 7—SPECIAL REGULATIONS, AREAS OF THE NATIONAL PARK SYSTEM

Fire Island National Seashore, New York; Vehicle Use Regulations

AGENCY: National Park Service, Interior.

ACTION: Final rule.

SUMMARY: This amendment prescribes the routes within Fire Island National Seashore on which the off-road operation of motor vehicles is permitted. It also revises the current regulations pertaining to permits for vehicles used on these routes by establishing clear standards for the issuance of these permits. Revised restrictions on the travel which will be allowed by vehicles under permit are also included in the regulations.

DATES: This amendment shall become effective on January 1, 1978.

FOR FURTHER INFORMATION CONTACT:

Richard W. Marks, Superintendent, Fire Island National Seashore, telephone 516-289-4810.

SUPPLEMENTARY INFORMATION: On July 12, 1977, the National Park Service published a notice of proposed rulemaking for amended vehicle use regulations for Fire Island National Seashore (42 FR 35859). These proposed regulations were intended to provide a greater degree of control over vehicle use within the Seashore, use which has increased greatly in recent years, despite existing regulations.

A period of 30 days after publication of the proposed regulations was originally provided for public comment. This period was later extended for an additional 30 days in order to allow for additional participation in the rulemaking process.

In all, 87 written comments were received during the 60 days provided, with 9 additional comments arriving after this period. Of this total of 96 comments, 68 were generally in favor of the regulations, while 28 opposed them.

All comments received were carefully analyzed, particularly those that included specific suggestions for changes in the regulations. From these suggestions and from further study of the proposal, it was determined that a number of changes to the regulations should be made. These changes are primarily clarifications and are not expected to have significant effects on the application of the regulations.

CHANGES MADE

The following is a discussion of the changes which have been made, other than minor editorial revisions.

Definition of residents. On the basis of comments received and further study of the situation, it was determined that the definition of the term "residents" contained in subparagraph (a)(1)(viii) of the proposed regulations was inadequate. This has been rectified in the final regulation by tightly defining those who will be considered "year-round residents" and who, therefore, have travel needs which are different from other categories of users. A definition of "part-time residents" has also been supplied in order to identify those persons who are domiciled on the island but who, because they do not reside there year-round, must meet additional requirements in order to qualify for a permit.

Route descriptions. The description of the route known as the "Burma Road," found in subparagraph (a)(2)(iv), was expanded to indicate that it may be used by fire and law enforcement vehicles, as well as public utility vehicles. This description was also changed to more accurately identify the route as being an intermittent one.

Alternative transportation. Subparagraph (a)(3)(iii), which deals with the location of transportation terminals which will be considered to determine available alternative transportation, has been modified by deleting the requirement for a planked or surfaced pathway between the terminal and the island point of origin or destination. This was found to be necessary to avoid situations in which a location very close to a terminal would have to be considered as not providing alternative transportation, when the only requirement lacking would be a very short length of pathway.

Permit issuance standards. A clarifying change was made in the language of subparagraph (a)(6), which states criteria which will be considered in issuing permits. In the proposal, one criterion had been stated to be "the existence of other permits issued to the applicant." This was felt to be unclear as to the time being referred to. Therefore, this phrase has been changed to speak of "the present or past issuance of other permits to the applicant." This more correctly states the relationship of an applicant's permit status to the decision as to whether or not a permit will be issued. In this same subparagraph, language has been added to make it clear that limitations on numbers of permits will also be a consideration.

Vehicle size limitations. The proposed restriction on vehicle capacity, in (a)(7)