DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 70, 73, 74, 80, 81, 82, 101, 178, 201, and 701

[Docket Nos. 79N–0043 and 92N–0334]

Permanent Listing of Color Additive Lakes

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to list certain color additive lakes permanently as suitable and safe for use in food, drugs, and cosmetics. The agency is proposing to permit the use of more than one straight color in the preparation of a lake, to modify the nomenclature for lakes, and to simplify the batch certification procedure for lakes. As part of these actions, the agency is proposing to amend its regulations to require the preparation of lakes from certified batches of straight color; to provide simplified nomenclature for declaring color additives, including lakes, on cosmetic products; to require declaration of FD&C Yellow No. 5 and FD&C Yellow No. 6 on all foods and some drug products containing lakes of these straight colors; and to terminate the listing of certain straight colors as components of lakes for drug and cosmetic use and the listing of calcium salts as components of lakes for food use.

This proposed rule is intended to complete the agency's disposition of the provisional list of color additives that was established under the transitional provisions of the Color Additive Amendments of 1960 (the 1960 amendments) and to establish regulations prescribing conditions under which lakes may be prepared, labeled, and safely used in food, drugs, and cosmetics.

DATES: Written comments by June 3, 1996, except that comments regarding information collection should be submitted by April 3, 1996, but not later than May 3, 1996.

ADDRESSES: Written comments to the Dockets Management Branch (HFA–305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1–23, Rockville, MD 20857. Comments regarding information collection to the Office of Information and Regulatory Affairs, OMB, New Executive Office Building, rm. 10235, Washington, DC 20503, ATTN: Desk Officer for FDA. Process descriptions, identity information for anions in precipitants, and ingredient specifications for substrata (including rosin), and rosin samples to the Colors Technology Branch (HFS–126), Food and Drug Administration, 200 C St. SW., Washington, DC 20204.

FOR FURTHER INFORMATION CONTACT:

Regarding proposed certification procedures, including proposed paperwork requirements, and for proposed product ingredient declarations:

Julie N. Barrows, Center for Food Safety and Applied Nutrition (HFS–126), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202–205–4662.

Regarding other issues:

Arthur L. Lipman, Center for Food Safety and Applied Nutrition (HFS–217), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202–418–3073.

SUPPLEMENTARY INFORMATION:

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I. Identity, Manufacture, and Properties of Lakes

Color additives may be added to food, drugs, cosmetics, and certain medical devices for the purpose of imparting color. The three categories of color additives are: (1) ''Straight colors'' (color additives that have not been mixed or chemically reacted with any other substance); (2) lakes (color additives formed by chemically reacting a straight color with water-insoluble substances); and (3) mixtures (color additives formed by mixing a color additive with one or more other color additives or noncolored substances, without chemical reaction.)

A lake is a water-insoluble pigment composed of a water-soluble straight color strongly adsorbed onto an insoluble substratum through use of a precipitant. The regulations in part 82 (21 CFR part 82), where lakes are provisionally listed, use the term ''basic radical'' to denote a precipitant. As more fully described in section III.A.6. of this document, the agency is proposing to replace the term ''basic radical'' with the more scientifically accurate term ''precipitant.'' The proposed terminology will be used throughout the rest of this document.

The first step in manufacturing a lake is the preparation of an aqueous slurry of the substratum (e.g., alumina). This aqueous slurry is mixed with an aqueous solution of a straight color to produce a partially precipitated (or laked) product. The laking process is completed by the addition of a precipitant (e.g., aluminum chloride), which results in the production of the salt (e.g., aluminum salt) of the straight color and the adsorption of the salt onto the substratum. The resulting lake is washed, dried, and finely ground before marketing.

The literature reports several variations of the basic laking process (Refs. 1 through 5). Some substrata are synthesized in situ; i.e., the components used to prepare the substratum, rather than the preformed substratum, are added during the laking procedure. For example, alumina slurries may be prepared by precipitation of hydrated alumina from an aluminum sulfate solution with a sodium carbonate or sodium hydroxide solution. These slurries are used directly in the synthesis of lakes, without isolation of the precipitated substratum.

Some lakes are themselves prepared in situ. In this process, the chemical precursors for the straight color are mixed directly with the substratum and the precipitant during the laking procedure. The lake is produced as the

straight color is synthesized, without isolation of the straight color as a discrete batch.

The chemical association between the components of a lake may involve various types of interactions, including ionic bonds, hydrogen bonds, and van der Waals forces (Refs. 4 through 9). Lakes generally contain 10 to 40 percent by weight of the straight color. They also contain approximately 1 to 4 percent of the weight of the lake as the cationic precipitant. The remaining 56 to 89 percent, by weight, of lakes consists primarily of substrata. The color content of a lake depends on the desired color intensity and shade of the lake.

Lakes offer many technical advantages over water-soluble straight colors. The chemical bonding of the color with substrata generally promotes light and heat stability. Furthermore, because lakes are not water-soluble, the use of lakes in aqueous foods reduces color migration.

The agency's current regulations for lakes in part 82 were issued under section 203 of the Color Additive Amendments of 1960 (Pub. L. 86–618), which provided for the temporary, provisional listing of commercially established colors. The regulations provide that before a lake may be used in a food, drug, or cosmetic product, each batch of the lake must be certified by FDA. When requesting certification of a batch of a lake, the requester submits a sample from the batch to the agency for analysis. If the agency finds that the concentrations of impurities in the sample are within the levels specified, and the batch otherwise appears to comply with the applicable regulations, the agency certifies the batch by issuing the requester a certificate showing the certification lot number assigned to that batch of lake.

Lakes represent approximately 25 percent of the total poundage of color additives certified by FDA. Approximately 80 percent of the lakes certified are FD&C (food, drugs, and cosmetics) lakes and the remaining 20 percent are D&C (drugs and cosmetics) lakes. (See section II.A. of this document for an explanation of the terms ''FD&C'' and ''D&C''.)

II. Regulatory History and Current Listings of Lakes

A. Regulatory History of Lakes

Section 7 of the Food and Drugs Act of 1906 (Pub. L. 59–384) prohibited the use of poisonous or deleterious colors in confectionery and the coloring or staining of food to conceal damage or inferiority. In 1907, the agency, then part of the Department of Agriculture, issued Food Inspection Decision 76 (Ref. 10), which contains a list of seven straight colors approved for use in food. Between 1907 and 1939, the agency expanded the list of straight colors approved for use in food from 7 to 15. These colors were known as ''coal tar colors'' because they were synthesized mainly from substances obtained from coal tar. However, prior to 1939, the agency's list of acceptable colors did not include lakes of coal tar colors because such lakes were not used in food. Also, prior to 1938, the government program for batch analysis and certification of colors was voluntary.

The Federal Food, Drug, and Cosmetic Act of 1938 (21 U.S.C. 301 *et seq.* (the act)) (Pub. L. 75–717) required FDA to list coal tar colors ''harmless and suitable'' for use in foods, drugs, and cosmetics, and to certify all batches of listed colors, including lakes. The agency issued regulations under the act listing lakes for food use, as well as for drug and cosmetic use, and establishing conditions for certification of batches of lakes (4 FR 1922, May 9, 1939; 4 FR 3931, September 16, 1939; and 5 FR 1138, March 23, 1940). The agency issued the first certificate for a lake under the act on May 11, 1939 (Ref. 11).

The initial listing of lakes for food use under the act restricted their use to coloring shell eggs (egg dyeing) (5 FR 1138). In 1959, at the request of industry, the agency expanded the uses of lakes prepared from FD&C straight colors to encompass general use in foods (24 FR 3818, May 13, 1959; and 24 FR 5302, June 30, 1959).

The 1960 amendments amended the act by defining the term ''color additive'' (section 201(t) (21 U.S.C. 321(t))) for the first time and restricting the use of color additives in or on food, drugs, cosmetics, or the human body to those listed in FDA regulations. (The Medical Device Amendments of 1976 (Pub. L. 94–295) extended these restrictions to the use of color additives in certain medical devices.) As amended, the act provides that a food (section 402(c) (21 U.S.C. 342(c))), drug or device (section 501(a)(4) (21 U.S.C. 351(a)(4))), or cosmetic, other than a coal tar hair dye (section 601(e) (21 U.S.C. 361(e))), is adulterated if it is, bears, or contains an unsafe color additive. Section 721 (formerly section 706) of the amended act (21 U.S.C. 379e) provides for the listing of safe and suitable color additives for use in foods, drugs, cosmetics, and medical devices; it prohibits the listing of a color additive for a proposed use unless data establish that such use will be safe. Section 721 of the act also continues the requirement for certification of batches of color additives, with or without diluents, to determine whether each batch conforms to the purity and identity specifications in the applicable listing regulation. However, the amendments allow FDA to exempt color additives from batch certification if certification is unnecessary to protect the public health.

Section 203 of the 1960 amendments also provided for the provisional listing of color additives that were commercially established when the 1960 amendments were enacted, pending completion of scientific investigations necessary to determine their safety under the new standard established by the 1960 amendments. The purpose of section 203 was to allow the use of such color additives on an interim basis, to the extent consistent with the public health. Section 203 directed the agency to recognize as provisionally listed the following color additives: (1) Any color additive which, on the day preceding the enactment date, was listed and certifiable for any use or uses and for which a batch or batches had been certified for such use or uses prior to the enactment date; (2) any color additive which was commercially used or sold prior to the enactment date for any use or uses on any food, drug, or cosmetic, but was not required to be listed under the act; (3) synthetic beta carotene. The provisional listing was to apply only to the use or uses to which the certification applied, or for which the color additive had been commercially used or sold.

Under the authority of the 1960 amendments, in the Federal Register of October 12, 1960 (25 FR 9759), the agency provisionally listed those color additives, including lakes, covered by section 203. This listing, originally codified as 21 CFR 8.501 and later recodified as § 81.1 (21 CFR 81.1) (42 FR 15665, March 22, 1977) included many of the coal tar colors (including lakes) that had been previously listed.

In the Federal Register of December 27, 1963 (28 FR 14311), the agency determined that batch certification was unnecessary to ensure the safety of most color additives derived from plant, animal, or mineral sources, and designated these color additives as exempt from certification. However, the agency determined that batch certification was necessary to ensure the safety of most color additives, including lakes, derived principally from coal and petroleum sources, and designated those colors as subject to certification. Currently, the color additives exempt from batch certification and the permanently listed color additives

subject to batch certification are listed in parts 73 and 74 (21 CFR parts 73 and 74), respectively.

Since the establishment of the provisional list in 1960, the agency has gradually removed color additives from the list either by permanent listing or by termination of listing due to lack of interest by industry or due to safety concerns prompted by the agency's reviews. At this time, only lakes remain provisionally listed in parts 81 and 82.

After the enactment of the act in 1938, FDA established the designation ''FD&C'' to identify color additives listed for use in foods, drugs, and cosmetics; the designation ''D&C'' to identify color additives listed for general use in drugs and cosmetics, but not foods; and the designation ''Ext. D&C'' to identify color additives listed for use only in externally applied drugs and cosmetics (4 FR 1922 at 1923). These designations are still part of the names of certified color additives. However, the uses of some straight colors (and consequently also of their lakes) were restricted when they were permanently listed, based on the safety reviews conducted by the agency under the 1960 amendments. Consequently, the designations ''FD&C'' or ''D&C'' in the name of a certified color additive can no longer be relied upon to accurately describe the approved uses of the color additive.

B. Current Listings of Lakes

1. Provisional Listing and General Provisions for Lakes

Section 81.1 identifies the provisionally listed color additives. The only color additives remaining on the provisional list are lakes (§ 81.1(a), (b), and (c)).

Part 82, subpart A, prescribes the general provisions applicable to provisionally listed color additives. Section 82.3 contains definitions of terms such as ''alumina'' and ''blanc fixe.'' Section 82.5 prescribes general specifications, including specifications for levels of lead, arsenic, and heavy metals other than lead and arsenic, that are applicable to lakes listed in the other subparts of part 82. It also provides a specification for the level of soluble barium applicable to lakes listed in subpart C or D of part 82 that contain a barium salt.

2. Provisional Listing of Lakes for Use in Foods, Drugs, and Cosmetics

Part 82, subpart B, identifies the lakes that are provisionally listed for use in foods, drugs, and cosmetics. Section 82.50 prescribes the certification requirements for these lakes.

Section 82.51 specifies that lakes for use in foods, drugs, and cosmetics are made by extending, on a substratum of alumina, a salt of one of the following certified water-soluble straight colors with the cation precipitant aluminum or calcium: FD&C Blue No. 1 (§ 82.101); FD&C Blue No. 2 (§ 82.102); FD&C Green No. 3 (§ 82.203); FD&C Yellow No. 5 (§ 82.705); and FD&C Yellow No. 6 (§ 82.706). Only previously certified batches of the straight color may be used. Section 82.51 also provides specifications for soluble chlorides and sulfates and for inorganic matter insoluble in hydrochloric acid (HCl) and prescribes rules for naming the lakes that are listed for use in foods, drugs, and cosmetics.

3. Provisional Listing of Lakes for Use in Drugs and Cosmetics

Part 82, subpart C, identifies the lakes that are provisionally listed for general use in drugs and cosmetics. Section 82.1051 prescribes the certification requirements for these lakes, which may be used both in ingested and externally applied drugs and cosmetics. Externally applied drugs and cosmetics are those that are applied to the external parts of the body and not to the lips or any body surface covered by mucous membrane (§ 70.3(v) (21 CFR 70.3(v))).

Section 82.1051 specifies that lakes for use in drugs and cosmetics are made by extending, on one or more listed substrata, one of the listed straight colors with one or more of the listed precipitants. The precipitant may be added either as a component of the listed straight color, or alone to form the salt of the listed straight color. The following substrata, alone or in any combination, are authorized for use in lakes for drug and cosmetic use: Alumina, blanc fixe, gloss white, clay, titanium dioxide, zinc oxide, talc, rosin, aluminum benzoate, and calcium carbonate. The regulation also lists the following cation precipitants for use in lakes for drug and cosmetic use: Sodium, potassium, aluminum, barium, calcium, strontium, and zirconium.

The regulation provides for the use of the following straight colors in producing lakes for drug and cosmetic use: FD&C Blue No. 1 (§ 82.101); FD&C Blue No. 2 (§ 82.102); FD&C Green No. 3 (§ 82.203), FD&C Red No. 4 (§ 82.304); FD&C Yellow No. 5 (§ 82.705); FD&C Yellow No. 6 (§ 82.706); D&C Blue No. 4 (§ 82.1104), D&C Green No. 5 (§ 82.1205), D&C Orange No. 5 (§ 82.1255), D&C Red No. 6 (§ 82.1306), D&C Red No. 7 (§ 82.1307), D&C Red No. 21 (§ 82.1321), D&C Red No. 22 (§ 82.1322), D&C Red No. 27 (§ 82.1327), D&C Red No. 28 (§ 82.1328), D&C Red No. 30 (§ 82.1330), D&C Red No. 33 (§ 82.1333), D&C Red No. 34 (§ 82.1334), D&C Red No. 36 (§ 82.1336), D&C Violet No. 2 (§ 82.1602), and D&C Yellow No. 10 (§ 82.1710).

The regulations for lakes of D&C Red No. 33 (§ 82.1333), D&C Red No. 36 (§ 82.1336) and FD&C Yellow No. 6 (§ 82.706) further require that lakes of these straight colors for drug and cosmetic use be prepared from previously certified batches of the straight colors. Uncertified batches of the remaining straight colors may be used to prepare lakes for drug and cosmetic use. Section 82.1051 also provides specifications for ether extracts, soluble chlorides and sulfates, and intermediates, and prescribes rules for naming lakes that are listed for drug and cosmetic use.

4. Provisional Listing of Lakes for Use in Externally Applied Drugs and Cosmetics

Part 82, subpart D, identifies the lakes that are provisionally listed for use in externally applied drugs and cosmetics. Section 82.2050 prescribes the certification requirements for these lakes.

Section 82.2051 specifies that lakes for use in externally applied drugs and cosmetics are made by extending, on one or more listed substrata, one or more of the listed precipitants, and the straight color Ext. D&C Yellow No. 7 listed in § 82.2707a. The precipitant may be added either as a component of the listed straight color, or alone to form the salt of the listed straight color.

Although Ext. D&C Yellow No. 7 is the only straight color referred to in subpart D, its lakes are not the only lakes limited to use in externally applied drugs and cosmetics. As noted above, certain straight colors that were provisionally listed for general drug and cosmetic use were restricted to use in externally applied drugs and cosmetics as part of their permanent listing. The agency also amended the provisional listings for the lakes of these straight colors to impose the same restrictions. The provisional listings of the following color additives in subparts B and C of part 82 limit the use of their lakes to externally applied drugs and cosmetics: FD&C Red No. 4 (§ 82.304); D&C Blue No. 4 (§ 82.1104), D&C Green No. 6 (§ 82.1206), D&C Orange No. 4 (§ 82.1254), D&C Orange No. 10 (§ 82.1260), D&C Orange No. 11 (§ 82.1261), D&C Red No. 17 (§ 82.1317), D&C Red No. 31 (§ 82.1331), D&C Yellow No. 7 (§ 82.1707) and D&C Yellow No. 8 (§ 82.1708).

The substrata, precipitants, and additional specifications listed in

§ 82.2051 for lakes used in externally applied drugs and cosmetics are the same as those listed in § 82.1051 for D&C lakes. Section 82.2051 also specifies that the listed names of Ext. D&C lakes are derived in the same manner as for D&C lakes.

5. Permanently Listed Lakes of FD&C Red No. 40

The color additive FD&C Red No. 40 was not included in the provisional list because FD&C Red No. 40 was not in use in 1960. In the Federal Register of April 10, 1971 (36 FR 6892), the agency published a final rule, in response to a color additive petition, permanently listing FD&C Red No. 40 for use in food and drugs. The agency later amended these regulations in response to another petition to provide for use of the lakes of FD&C Red No. 40 in food and drugs (36 FR 23553, December 10, 1971). Subsequently, in response to further petitions, the agency published final rules expanding the listing of FD&C Red No. 40 to cosmetic uses. First, in the Federal Register of August 6, 1974 (39 FR 28278), the agency published a final rule permanently listing FD&C Red No. 40 for use in dentifrices that are cosmetics. Subsequently, the agency amended these regulations to expand the use of FD&C Red No. 40 and its lakes to cosmetics generally (39 FR 44198, December 23, 1974).

The permanent listings of FD&C Red No. 40 for food, drug, and cosmetic use in §§ 74.340, 74.1340, and 74.2340, respectively, include its lakes. However, the permanent listings of these lakes cite the provisional listings for lakes in part 82 for the preparation, specifications, and labeling requirements applicable to FD&C Red No. 40 lakes. As a result, any agency action on the provisional listings for lakes will affect the permanent listings for the lakes of FD&C Red No. 40. Therefore, this proposal includes consideration of the lakes of FD&C Red No. 40.

C. The 1965 Proposal for Permanent Listing of Lakes and the 1979 Notice of Intent

In the Federal Register of May 11, 1965 (30 FR 6490), the agency proposed to list permanently certain lakes for use in foods, drugs, and cosmetics under conditions similar to their current provisional listing. However, because many straight colors were still provisionally listed and because of the need for more information on lakes, the agency, in 1979, terminated the rulemaking initiated by this proposal without taking final action (44 FR 36411, June 22, 1979).

In the same issue of the Federal Register (44 FR 36411), the agency published a notice that announced the agency's intent to repropose regulations concerning lakes (the 1979 notice of intent (NOI)). The agency also addressed the comments it had received in response to the 1965 proposal regarding the permanent listing of lakes. Three of the five comments on the 1965 proposal recommended revising the regulations to provide for the use of more than one previously certified batch of color additive in the preparation of lakes for coloring drugs and cosmetics. In the 1979 NOI, the agency stated its intention to consider this recommendation in developing a new proposal for the permanent listing of lakes. The agency also identified the following issues for the scientific review of lakes: (1) The definition and nomenclature of lakes; (2) the safety of lakes; and (3) the specifications for lakes (stability and certification methodology). The agency requested information and comments pertaining to these issues.

The agency received four comments on the 1979 NOI. These included two brief responses from manufacturers and two extensive comments from trade associations, the International Association of Color Manufacturers (IACM) (formerly the Certified Color Manufacturers' Association (CCMA)) and the Cosmetic, Toiletry, and Fragrance Association, Inc. (CTFA). The issues raised by the agency in the 1979 NOI, along with the four comments received on that notice, and the agency's responses to the comments, are discussed in the following sections. This proposal does not, however, address comments related to the straight colors that were provisionally listed in 1979 but have been denied permanent listing in subsequent rulemakings (FD&C Red No. 3 (externally applied drug and all cosmetic uses), D&C Red Nos. 8, 9, and 19, and D&C Orange No. 17).

III. Development of Proposed Actions for Lakes

A. Terminology of Lakes

The agency is proposing the following changes to the existing definitions relating to lakes.

1. Straight Color

Currently, § 70.3(j) defines the term ''straight color'' as ''a color additive listed in parts 73, 74, and 81 of this chapter, and includes lakes * * *.'' Thus, the term encompasses all listed color additives, including lakes. Current § 70.3(l) defines the term ''lake'' as ''a straight color extended on a substratum by adsorption, coprecipitation, or chemical combination that does not include any combination of ingredients made by simple mixing process.'' These two regulations, when read together, suggest that a lake may be used as a color component of another lake. This implication is inconsistent with current regulations for lakes (§§ 82.51, 82.1051, and 82.2051) and with the proposed regulations for lakes in this document, which do not allow the synthesis of a lake using another lake as a color component.

There are other instances in which the existing definition of straight color creates confusion. For example, the procedures for requesting certification of a batch of a color additive treat straight colors (§ 80.21(j)(1) (21 CFR 80.21(j)(1)) and lakes (§ 80.21(j)(2)) separately. Federal Register publications relating to color additives also commonly use the term ''straight color'' to refer to a color additive other than a lake. For example, the 1979 NOI referred to straight colors as distinct from lakes; the agency's request for information concerning the usage of FD&C Red No. 3 requested data on straight colors, lakes, and mixtures (52 FR 44485; November 19, 1987). Communications between the agency and industry also indicate that the common usage of the term ''straight color'' does not ordinarily include the term ''lake.'' To eliminate the confusion resulting from the existing definition, the agency is proposing to revise the definition for ''straight color.'' As revised, the definition would read ''The term 'straight color' means a color additive that is listed in part 73 or 74 of this chapter, but does not include color additive mixtures or lakes.''

2. Listed Color

As discussed in section III.A.1., the proposed definition of ''straight color'' would exclude lakes. Therefore, the agency is proposing a new term ''listed color'' to refer to any color additive (including a lake) listed in part 73 or 74 for any use. By definition, the term would not include mixtures, which are not themselves listed colors but rather combinations of listed colors. The agency is proposing to add the following definition at § 70.3(w): ''The term 'listed color' means a color additive listed in part 73 or 74 of this chapter and includes lakes.''

3. Mixture

Currently, § 70.3(k) defines the term ''mixture'' as ''a color additive made by mixing two or more straight colors, or one or more straight colors and one or

more diluents.'' The agency is proposing to modify this definition to replace the current reference to ''straight color'' with ''listed color'' and to clarify that a mixture does not involve a chemical reaction between its components. Proposed § 70.3(k) would read ''The term 'mixture' means a color additive made by mixing two or more listed colors, or one or more listed colors and one or more diluents, without an accompanying chemical reaction.''

4. Lake

Currently, § 70.3(l) defines the term ''lake'' as ''a straight color extended on a substratum by adsorption, coprecipitation, or chemical combination that does not include any combination of ingredients made by simple mixing process.'' As discussed in sections IV. and V. of this document, the agency is proposing to permit the preparation of a lake using more than one straight color. Proposed § 70.3(l) would read ''The term 'lake' means a color additive made by extending one or more straight colors on one or more substrata by adsorption, coprecipitation, or chemical combination, but does not include mixtures.''

5. Substratum

Currently, § 70.3(n) defines ''substratum'' as ''the substance on which the pure color in a lake is extended.'' This definition implies that it is only the pure color that is extended on the substratum. However, the data reviewed by the agency on the stability of straight colors after laking clearly demonstrate that intermediates and subsidiary colors are also extended on the substratum during the laking process. Therefore, the agency is proposing to amend the definition of substratum to read ''The term 'substratum' means the substance on which the straight color in a lake is extended.''

6. Precipitant (Basic Radical)

Although the term ''basic radical'' is not defined in the color additive regulations, §§ 82.51 and 82.1051 use ''basic radical'' to denote a substance that may be used to precipitate a lake during its manufacture. The agency believes that ''precipitant'' is a more descriptive and scientifically accurate term for such a substance. ''Precipitant'' is the term normally used in technical publications. For example, the Condensed Chemical Dictionary (12th ed., 1993) defines a lake as a pigment produced by the interaction of an ''organic dye, a precipitant, and an absorptive inorganic substrate.'' However, the same source contains no definition of ''basic radical.'' The publications of trade organizations also use the term ''precipitant'' rather than ''basic radical'' in discussions of lakes (Ref. 12). Therefore, the agency is proposing to use the term ''precipitant'' rather than the term ''basic radical'' in new §§ 74.50 and 74.1050. However, the agency is not proposing any formal definition of ''precipitant'' in § 70.3.

7. Repack

Currently, § 70.3 does not define the term ''repack.'' However, repacks are one of the four forms of color additive (in addition to straight colors, lakes, and mixtures) that are certified under the procedures in part 80. The other three forms of color additive are defined in § 70.3. Therefore, the agency tentatively concludes that a definition of repack should be added to § 70.3. Proposed § 70.3(x) would read ''The term 'repack' means all or a portion of a batch of certified color additive that has been sealed in accordance with § 70.20 and labeled in accordance with § 70.25, but has been either opened for repackaging without further processing, or relabeled for shipment or delivery, by a person other than the person to whom the certificate or acceptance of a notice claiming certification for the batch was issued.'' Under § 80.32(d), such repackaging or relabeling results in the expiration of the certificate, and the batch therefore ceases to be a certified batch. A repack may be certified under the procedures in part 80 at a lower fee than for the original batch (§ 80.10(b)). The agency notes that if a batch or portion of a batch is processed in any way, including heating, then it is not a repack and must be recertified as a new batch of color additive.

B. Nomenclature of Lakes

The current nomenclature system for lakes is described in §§ 82.51(b), 82.1051(b) and 82.2051(b). These regulations specify that the listed name of a lake is formed from: (1) The listed name of the color from which the lake is prepared; (2) the name of the cation precipitant combined in such color; and (3) the word ''lake.'' This system of nomenclature identifies the color additive as a lake and specifies the straight-color component of the lake and the cation precipitant used to prepare the lake. However, the name of a lake does not identify the substrata used to prepare the lake. Because only one substratum (alumina) is permitted in lakes for food use, this system presents no identity problems for these lakes. However, under the current nomenclature system, lakes listed for drug and cosmetic use are not fully identified, because such lakes may contain a variety of substrata. Thus, lakes produced from a common straight color and cation, but different substrata, are identified with the same name. For example, two lakes of D&C Red No. 21, one prepared with the cation aluminum and the substratum alumina, the other with the cation aluminum and the substrata alumina and titanium dioxide, are both named ''D&C Red No. 21 Aluminum Lake.''

In the 1979 NOI, the agency described this problem with the current nomenclature system and stated its intention to modify the nomenclature system to include the substrata in the name of the lake. The agency received comments from the IACM and CTFA supporting inclusion of substrata in the name of a lake for the purpose of more accurately identifying the listed color additive. As explained above, although omitting the substratum from the name of a lake for food use presents no problems, omitting the substratum from the name of a lake restricted to drug or cosmetic use could cause confusion as to the identity of the lake. However, as the same batch of lake may be used for a food, a drug, or a cosmetic (if the lake is listed for all three uses), the agency tentatively finds that use of a single nomenclature system to identify all lakes would present the least overall confusion to users of these color additives. Use of a uniform nomenclature system for all lakes is also desirable because it avoids the necessity for manufacturers of lakes to provide different labels for packages of the same lake. Therefore, the agency is proposing that the same nomenclature system be used for all lakes.

Therefore, the agency is proposing to modify the nomenclature of lakes by requiring the inclusion of the identity of substrata in the name of a lake. The proposed nomenclature system would construct the name of a lake from the name(s) of the straight colors present in the lake (in descending order of predominance), followed by the names of the cations of the precipitants, and followed by the words ''Lake on _____ and _____'' (inserting the listed names of the substrata in descending order of predominance). For example, the name of a lake prepared by the extension of D&C Red No. 27 and D&C Orange No. 5 on alumina and titanium dioxide using aluminum chloride and calcium chloride as precipitants would be ''D&C Red No. 27 and D&C Orange No. 5 Aluminum Calcium Lake on Alumina and Titanium Dioxide.''

Currently, § 82.1051(b)(1) provides that the name of a D&C lake prepared

from an FD&C color shall be formed from the ''listed name of the color from which the lake is prepared, except that if such name contains the symbol 'FD&C' such symbol shall be changed to 'D&C'.'' For example, the name of the lake formed from FD&C Yellow No. 5, rosin, and zirconium cation is D&C Yellow No. 5 zirconium lake. The agency notes that the use of the FD&C, D&C, and Ext. D&C prefixes to designate the approved uses of colors originated in the 1939 listings of coal tar colors, including lakes (4 FR 1922) and was carried over into the provisional listing of these color additives in 1960 (25 FR 9759). The permanently listed straight colors retained the names under which they were provisionally listed, although the prefixes no longer accurately reflected the approved uses in some cases. For example, FD&C Red No. 4 is permitted for use only in externally applied drug and cosmetic products.

The agency is not proposing any action in this rulemaking to change the names of the color additives whose food, drug, or cosmetic use is no longer correctly designated by their FD&C or D&C prefix. However, the agency has tentatively decided not to continue the current system described in § 82.1051(b)(1), in which the prefix 'FD&C' is changed to 'D&C' when naming lakes for drug or cosmetic use that have been prepared from straight colors that contain the 'FD&C' prefix in their name. The agency tentatively concludes that continuation of this nomenclature provision is unnecessary to identify the approved uses of the lake and could be confusing to users of lakes. As discussed above, the designation 'D&C' does not always accurately describe the uses of the lake. Furthermore, under § 70.25, the label of the color additive must contain a declaration of the permitted uses of the lake. Finally, because the proposed procedure for certification of lakes (see section VI.B. of this document) would rely on the certificate for the straight color used to prepare the lake, the agency believes that the name of the lake should accurately identify the certified straight color on which the certification of the lake is based. For example, under the proposed certification procedure for lakes, the certificate for the straight color in the lake cited above would be for ''FD&C Yellow No. 5,'' not ''D&C Yellow No. 5.''

In the 1979 NOI, the agency also requested comments to address an inconsistency in the current system of nomenclature; namely, that certain lakes of identical composition may have different names. For example, FD&C Blue No. 1 and D&C Blue No. 4 are two separately listed straight colors that are different salt forms of the same dye. (FD&C Blue No. 1 is the disodium salt and D&C Blue No. 4 is the diammonium salt of a triphenylmethane derivative.) During the laking process the accompanying cation in the straight color is replaced by the precipitant cation. Thus, the lakes of these two straight colors, prepared from the same substrata and precipitants, are chemically identical. However, they have different names. For example, under the current nomenclature system, the aluminum lakes on alumina of these two straight colors are named ''FD&C Blue No. 1 Aluminum Lake'' and ''D&C Blue No. 4 Aluminum Lake.'' (Under the proposed system, they would be named ''FD&C Blue No. 1 Aluminum Lake on Alumina'' and ''D&C Blue No. 4 Aluminum Lake on Alumina,'' respectively.)

In its comment on the 1979 NOI, CTFA agreed with the agency's assessment of this nomenclature problem. However, the comment suggested that this and other problematic aspects of the current system of nomenclature are better viewed as problems with the general nomenclature of listed colors, not problems specific to lakes.

The agency agrees with CTFA's comment that these issues concerning the nomenclature of lakes are really issues related to the general nomenclature of listed colors. Therefore, the agency is not proposing any modifications in the nomenclature of lakes to address these issues, which are outside the scope of this rulemaking.

Under this proposal, the nomenclature proposed in this section would be used for two purposes: (1) To prescribe the listed name of the lake, because the agency is proposing to issue umbrella regulations for lakes rather than an individual regulation for each listed lake; (2) to identify the color additive on the labels of lakes that are packaged for sale to manufacturers of foods, drugs, and cosmetics to be used in coloring those products. The agency notes that lakes are also required to be declared as ingredients on the label of foods and cosmetics. Section VI.C.3. of this document describes the simplified nomenclature system that FDA is proposing for ingredient labeling of lakes on food and cosmetic labels.

TABLE 1.—CURRENT AND PROPOSED REGULATORY STATUS OF STRAIGHT COLORS USED IN LAKES

Current listings		Proposed listings	
Current regulatory status	Straight color	Proposed regulatory status	Straight color
Permanently listed: Part 74 (Subpart A—Foods, Subpart B—Drugs and Subpart C—Cosmetics).	FD&C Red No. 40	Permanently listed: Part 74 (Subpart A—Foods (§ 74.50)).	FD&C Blue No. 1, FD&C Blue No. 2, FD&C Green No. 3, FD&C Red No. 40, FD&C Yellow No. 5, FD&C Yellow No. 6.
Provisionally listed: Part 82 (Subpart B—Foods, Drugs, and Cosmetics).	FD&C Blue No. 1, FD&C Blue No. 2, FD&C Green No. 3, FD&C Yellow No. 5, FD&C Yellow No. 6, FD&C Red No. 4.	(Subpart B—Drugs (§ 74.1050) and Subpart C—Cosmetics (§ 74.2050))..	FD&C Blue No.1, FD&C Blue No. 2 (drugs only), FD&C Green No. 3, FD&C Yellow No. 5, FD&C Yellow No. 6, FD&C Red No. 4, FD&C Red No. 40, D&C Blue No. 4, D&C Orange No. 4, D&C Orange No. 5, D&C Orange No. 10, D&C Red No. 6, D&C Red No. 7, D&C Red No. 21, D&C Red No. 22, D&C Red No. 27, D&C Red No. 28, D&C Red No. 31, D&C Red No. 33, D&C Red No. 34, D&C Yellow No. 10.

TABLE 1.—CURRENT AND PROPOSED REGULATORY STATUS OF STRAIGHT COLORS USED IN LAKES—Continued

Current listings		Proposed listings	
Current regulatory status	Straight color	Proposed regulatory status	Straight color
(Subpart C—Drugs and Cosmetics).	FD&C Blue No. 1, FD&C Blue No. 2, FD&C Green No. 3, FD&C Yellow No. 5, FD&C Yellow No. 6, FD&C Red No. 4, FD&C Blue No. 4, FD&C Green No. 5, FD&C Green No. 6, FD&C Orange No. 4, FD&C Orange No. 5, FD&C Orange No. 10, FD&C Orange No. 11, FD&C Orange No. 6, FD&C Red No. 7, FD&C Red No. 17, FD&C Red No. 21, FD&C Red No. 22, FD&C Red No. 27, FD&C Red No. 28, FD&C Red No. 30, FD&C Red No. 31, FD&C Red No. 33, FD&C Red No. 34, FD&C Red No. 36, FD&C Violet No. 2, FD&C Yellow No. 7, FD&C Yellow No. 8, FD&C Yellow No. 10.	Listing Terminated (Does not form lakes).	D&C Green No. 6, D&C Red No. 17, D&C Red No. 30, D&C Red No. 36, D&C Violet No. 2.
		Listing Terminated (No batches certified):.	D&C Green No. 5, D&C Orange No. 11, D&C Yellow No. 7, D&C Yellow No. 8.
(Subpart D— Externally Applied Drugs and Cosmetics).	Ext. D&C Yellow No. 7	Listing Terminated (No confirmation of stability during laking).	Ext. D&C Yellow No. 7.

C. Issues Relating to Definition of Lakes and Termination of Certain Provisional Listings

1. Straight Colors

A summary of the current and proposed regulatory status of straight colors for use in lakes is given in Table 1.

CTFA's comments on the 1979 NOI include information on the chemical structure of the straight colors currently listed for use in lakes. Based on its evaluation of these data and other information from the published literature, the agency tentatively concludes that, to form a lake, a straight color must contain a salt-forming group (i.e., a salt, an acid, or a lactone group) as part of its chemical structure. The agency finds that the following straight colors listed in part 82 contain a salt-forming group and thus are capable of forming a lake: FD&C Red No. 4, D&C Red No. 6, D&C Red No. 7, D&C Red No. 21, D&C Red No. 22, D&C Red No. 27, D&C Red No. 28, D&C Red No. 31, D&C Red No. 33, D&C Red No. 34, FD&C Blue No. 1, FD&C Blue No. 2, D&C Blue No. 4, FD&C Green No. 3, D&C Green No. 5, D&C Orange No. 4, D&C Orange No. 5, D&C Orange No. 10, D&C Orange No. 11, FD&C Yellow No. 5, FD&C Yellow No. 6, D&C Yellow No. 7, D&C Yellow No. 8, D&C Yellow No. 10, and Ext. D&C Yellow No. 7.

However, based on the same information, the agency notes that the following five straight colors listed in part 82 do not contain a salt-forming group as part of their chemical structure and therefore cannot form lakes: D&C Red No. 17, D&C Red No. 30, D&C Red No. 36, D&C Violet No. 2, and D&C Green No. 6. CTFA's comment on the 1979 NOI also stated that D&C Green No. 6 does not form a lake. Therefore, the agency tentatively concludes that combinations of these straight colors with substrata do not meet the definition of lake in § 70.3(l). Consequently, the agency is proposing to terminate the listing of D&C Red No. 17, D&C Red No. 30, D&C Red No. 36, D&C Violet No. 2, and D&C Green No. 6 as components of lakes. This proposed action would not affect the listing of these color additives as straight colors. Under the proposal, combinations of these straight colors with substrata that are approved diluents or approved color additives would be color additive mixtures rather than lakes. Such mixtures would be exempt from certification under § 80.35(b).

2. Diluents in Color Additive Mixtures for Cosmetic and Drug Use

a. *Cosmetics.* The agency notes that its proposed action to terminate the listing of five straight colors as components of lakes would not affect the use of these straight colors in cosmetic products. Combinations of D&C Red No. 17, D&C Red No. 30, D&C Red No. 36, D&C Violet No. 2, or D&C Green No. 6 with substrata listed in § 82.1051 are color additive mixtures as defined in § 70.3(k), and the ''substrata'' used in these combinations are diluents as defined in § 70.3(m). Because no regulation limits the diluents that may be used in color additive mixtures intended for use in cosmetic products, the proposed action to terminate the listing of D&C Red No. 17, D&C Red No. 30, D&C Red No. 36, D&C Violet No. 2, and D&C Green No. 6 for use in lakes would not affect their use in cosmetics as color additive mixtures containing, as diluents, the substances now listed as substrata in § 82.1051 (alumina, blanc fixe, gloss white, clay, titanium dioxide, zinc oxide, talc, rosin, aluminum benzoate, and calcium carbonate).

b. *Drugs.* The proposed action to terminate the listing of D&C Red No. 17, D&C Red No. 30, D&C Red No. 36, D&C

Violet No. 2, and D&C Green No. 6 for use in lakes would not affect their use in drugs as color additive mixtures containing the following substrata now listed in § 82.1051: Alumina, calcium carbonate, talc, titanium dioxide, and zinc oxide. Alumina, calcium carbonate, talc, and titanium dioxide are listed in §§ 73.1010, 73.1070, 73.1550, and 73.1575, respectively, as color additives exempt from certification for use in drugs generally (ingested drugs and externally applied drugs). Therefore, combinations of these substances with D&C Red No. 17, D&C Red No. 30, D&C Red No. 36, D&C Violet No. 2, and D&C Green No. 6 are permitted as color additive mixtures under existing regulations. Zinc oxide is listed in § 73.1991 as a color additive exempt from certification for use in coloring externally applied drugs. In addition, zinc oxide is generally recognized as safe (GRAS) for use as a dietary supplement (§ 182.5991 (21 CFR 182.5991)) and as a nutrient in food (§ 182.8991 (21 CFR 182.8991)). Section 73.1001 permits the use of substances listed in § 73.1(a) as diluents in color additive mixtures for ingested drug use. In turn, § 73.1(a) permits the use of substances that are GRAS under section 201(s) of the act (21 U.S.C. 321(s)). Therefore, the agency concludes that zinc oxide may be used with D&C Red No. 17, D&C Red No. 30, D&C Red No. 36, D&C Violet No. 2, and D&C Green No. 6 either as an approved diluent in color additive mixtures for coloring ingested drugs or as a straight-color ingredient in color additive mixtures for coloring externally applied drugs.

Rosin is currently listed in § 73.1(b)(1)(i) as a diluent in color additive mixtures for use in inks for marking food supplements in tablet form, gum, and confectionery, and by reference, for use under § 73.1001(a)(2) in inks for branding pharmaceutical forms. In its review of the safety of the substrata currently listed in § 82.1051 (see section V.A.2.j. of this document), the agency determined that the ingested uses of rosin are safe. However, in this same review, the agency stated that it was aware of literature reports of dermal irritation due to rosin (Ref. 13). Recently submitted data on human skin sensitization and photoreaction to commercially available cosmetic products colored with rosin lakes (Ref. 14) establish that lakes containing rosin as a substratum are safe for externally applied drugs and cosmetics. However, the rosin present in lakes, where it is a component of an insoluble pigment, is not identical to free rosin present as a diluent in color additive mixtures. Therefore, the agency tentatively concludes that the data submitted on the safety of externally applied rosin lakes do not resolve the safety issues presented by the use of free rosin as a diluent in externally applied drug products, such as the risk of allergic contact dermatitis and occupational asthma.

Based on its safety review of rosin, the agency is proposing to amend § 73.1001 to list rosin as a diluent in color additive mixtures for ingested drug use only. However, if the agency receives information that adequately supports the safety of rosin as a diluent in color additive mixtures for use in externally applied drugs, the agency will consider listing rosin as a diluent for color additive mixtures for both ingested and externally applied drugs. Anyone interested in the listing of rosin for such use should submit information on the identity, specifications, and dermal safety of the rosin for which listing is sought.

The current regulations do not allow for the use of aluminum benzoate, blanc fixe, clay, and gloss white as diluents in color additive mixtures for drug use, because only the diluents provided for in § 73.1001 may be used in color additive mixtures for coloring drugs. However, FDA has evaluated the safety of these substances, or the materials used to make them, as part of its review of substrata in lakes for drug and cosmetic use in section V.A.2. of this document. This review included data on the ingested and dermal uses of barium sulfate (blanc fixe), kaolin (clay), benzoic acid, and benzoates. Specifically, the agency considered literature reviews of aluminum salts, barium sulfate, kaolin and bentonite (a silicate); information from the color additive petitions for use of certain aluminum lakes in eye-area cosmetics; and safety reviews of aluminum compounds, benzoic acid and benzoates, and kaolin and bentonite as food ingredients. These safety reviews were conducted by the Select Committee on GRAS Substances of the Federation of American Societies for Experimental Biology and the Joint Food and Agriculture Organization (FAO)/World Health Organization (WHO) Expert Committee on Food Additives.

Based on its review, which is discussed in section V.A.2. of this document, the agency tentatively concludes that barium sulfate (blanc fixe), aluminum benzoate, and kaolin (clay) are safe for use as diluents in color additive mixtures for drug use. Therefore, as part of its disposition of the provisional listings in part 82, the agency is proposing to amend § 73.1001 to list barium sulfate, aluminum benzoate, and kaolin as diluents that may be safely used in color additive mixtures exempt from certification that are intended for use in ingested and externally applied drugs. The agency notes that gloss white is a mixture of alumina and barium sulfate and thus would be permitted for any use in color additive mixtures for which both alumina and barium sulfate are permitted.

For the reasons discussed above, the agency tentatively concludes that the proposed action to terminate the listing of D&C Red No. 17, D&C Red No. 30, D&C Red No. 36, D&C Violet No. 2, and D&C Green No. 6 as components of lakes would not affect their use in drugs as color additive mixtures containing alumina, calcium carbonate, kaolin (clay), talc, zinc oxide, barium sulfate (blanc fixe), aluminum benzoate, titanium dioxide, gloss white, or rosin (ingested drugs only). However, the proposed termination would mean that those straight colors could no longer be used in externally applied drugs as color additive mixtures containing rosin, unless the agency receives data that establish the safety of rosin as a diluent for externally applied uses.

3. Extended Toners

In the 1979 NOI, the agency requested information to identify certain insoluble color additives, commercially described as extended toners, that are classified as lakes under part 82. The agency requested comments on the need to modify existing regulations or to promulgate new regulations to address these color additives. FDA noted its intent, in the absence of comments to the contrary, to exclude these products from the definition of lakes.

CTFA's comment on the 1979 NOI provided information that identified the composition of extended toners and of related insoluble color additives known as resinated toners, extended resinated toners, and toners. The comment requested revision of the definitions in 21 CFR 70.3 to better describe these substances. The agency has evaluated the available information and determined that the color additives described commercially as toners, resinated toners, extended toners, and extended resinated toners are not lakes. These substances are either water-insoluble straight colors or mixtures of water-insoluble straight colors with insoluble diluents. Therefore, the agency tentatively concludes that no new or modified regulations are needed to address toners, resinated toners, extended toners, and extended resinated

toners because these substances are mixtures as defined in § 70.3(k), and the ''substrata'' used in these combinations are diluents, as defined in § 70.3(m).

The proposed reclassification of toners, resinated toners, extended toners, and extended resinated toners as color additive mixtures containing as diluents the ingredients now listed as substrata in § 82.1051 would not affect their use in drugs, because, as discussed in section III.C.2. of this document, these substrata (except rosin for use in externally applied drugs) are listed as GRAS in part 182, 184, or 186 (21 CFR part 182, 184, or 186), approved as color additives for drug use in part 73, or the agency is proposing to list them in § 73.1001 as diluents in color additive mixtures for drug use. Because there is no regulation that limits the diluents that can be used in color additive mixtures for cosmetic use, the proposed reclassification of this group of color additives from lakes to color additive mixtures would not affect their use in cosmetics.

4. Requests for Listing of Additional Lake Components

CTFA's comments on the 1979 NOI included a request that FDA authorize for use in lakes the following straight colors: D&C Brown No. 1, D&C Green No. 8, and Ext. D&C Violet No. 2. These three straight colors are currently listed in part 74 for cosmetic use. In addition, D&C Green No. 8 is currently listed in part 74 for drug use. However, the agency notes that these straight colors are not listed either permanently in part 74 or provisionally in part 82 for use in preparing lakes. Therefore, the agency tentatively concludes that consideration of these straight colors for use in lakes is outside the scope of this proposal, which addresses only the provisionally listed lakes and their components. Interested persons may submit a color additive petition under § 71.1 (21 CFR 71.1) to amend the regulations to permit the use of these straight colors in lakes.

CTFA's comments on the 1979 NOI also suggested that bismuth oxychloride and mica should be listed as acceptable substrata in lakes for coloring drugs and cosmetics. IACM's comments requested the listing of titanium dioxide as a substratum for lakes for coloring foods. However, bismuth oxychloride and mica are not provisionally listed in part 82 as substrata in lakes for drug or cosmetic use, and titanium dioxide is not provisionally listed in part 82 as a substratum in lakes for food use. Therefore, the agency tentatively concludes that consideration of the requested uses of these substances as substrata in lakes is outside the scope of this rulemaking, which addresses provisionally listed lakes and their components. Interested persons may submit a color additive petition under § 71.1 to amend the regulations to permit use of these substances in lakes.

5. Definition of Lakes Versus Mixtures

CTFA's comments on the 1979 NOI noted that the straight-color component of a lake, and not the substratum, provides the coloring effect and, therefore, requested that the agency classify lakes as color additive mixtures and list permitted substrata as diluents for color additive mixtures.

As discussed in section III.C.1. of this document, the agency agrees that combinations of non-salt-forming straight colors with substrata should be classified as mixtures rather than lakes. As to salt-forming straight colors, however, the agency disagrees with CTFA's interpretation. Lakes are very different from color additive mixtures because of the chemical reaction required to produce a lake. The agency finds that, under both the current and proposed definitions of a lake, the substratum is an integral part of the lake. In a mixture, there is little if any chemical interaction between the components, which function as separate ingredients. In the preparation of a lake, however, there is a chemical reaction between the components, and the physical properties of the resulting lake are very different from those of the straight-color component (see section I. of this document). Therefore, the agency tentatively concludes that lakes are not mixtures and that substrata used to prepare a lake are not separate ingredients, but are components of the finished color additive.

6. Pre-Amendments Certification of Provisionally Listed Lakes

As discussed in section II.A. of this document, the transitional provisions of the 1960 amendments limited the provisional listing of certifiable color additives to those for which at least one batch had been certified prior to July 12, 1960, the enactment date of the 1960 amendments. In establishing the provisional list (25 FR 9759), FDA removed 32 colors from listing because the agency had never certified any batches of these colors. In preparing this document, the agency reviewed its batch certification records to confirm that each straight color, substratum, and precipitant included in the provisional listing regulations for lakes was a component of at least one batch of a lake certified between 1939 and July 12, 1960.

a. *Straight Colors.* The agency's search of color certification records between 1939 and the enactment of the 1960 amendments established that the agency did not certify any batches of lakes of D&C Orange No. 11, D&C Yellow No. 7, D&C Yellow No. 8, or D&C Green No. 5 during that time. The agency tentatively concludes that its original provisional listing of these color additives for use in lakes for drugs or cosmetics was therefore incorrect. Accordingly, the agency is proposing to terminate the provisional listings of D&C Orange No. 11, D&C Yellow No. 7, D&C Yellow No. 8, and D&C Green No. 5 as components of lakes for use in drugs or cosmetics. Any future consideration of the use of these color additives as components of lakes would be through the color additive petition process (§ 71.1).

b. *Substrata.* The agency's color certification records show that all of the substrata listed in §§ 82.51, 82.1051, and 82.2051, except calcium carbonate, have been in continuous use in lakes because certification was initiated in 1939 (Ref. 15). The agency added calcium carbonate to the list of permitted substrata in 1959 (24 FR 3818) and certified at least one batch of a lake containing this substratum for drug or cosmetic use before the enactment of the 1960 amendments.

c. *Precipitants.* Section 82.51 lists two cations (calcium and aluminum) as components of precipitants in lakes for food use. The agency certified batches of FD&C aluminum lakes before the enactment of the 1960 amendments. However, in the 1979 NOI, the agency proposed to delete calcium as a listed cation in lakes for food use because the agency had never certified any batches of FD&C calcium lakes.

Comments on the 1979 NOI from IACM and CTFA requested the agency not to take this action. However, because these comments provided no information to document agency certification of any batches of FD&C calcium lakes before the enactment of the 1960 amendments, the agency tentatively concludes that its original provisional listing of these lakes was incorrect. Therefore, the agency is proposing to terminate the provisional listing of calcium as a precipitant in the preparation of lakes for food use. Any future consideration of the use of lakes containing calcium precipitants for coloring food would be through the color additive petition process (§ 71.1).

Sections 82.1051 and 82.2051 list seven cations (sodium, potassium, aluminum, barium, calcium, strontium, and zirconium) as components of precipitants in lakes for drug or cosmetic use. The agency certified

batches of lakes containing each of these seven cations for drug or cosmetic use before the enactment of the 1960 amendments.

IV. Safety Review and Proposed Actions for Lakes for Use in Foods

A. Review of Components of Lakes for Use in Foods

The current regulation for provisionally listed lakes for use in foods (21 CFR 82.51) provides for use of the following components in such lakes: (1) Certified batches of the straight colors FD&C Blue No. 1 (21 CFR 82.101), FD&C Blue No. 2 (21 CFR 82.102), FD&C Green No. 3 (21 CFR 82.203), FD&C Yellow No. 5 (21 CFR 82.705), FD&C Yellow No. 6 (21 CFR 82.706); (2) the substratum alumina; (3) precipitants containing the cations aluminum (Al^{+3}) and calcium (Ca^{+2}). Additionally, 21 CFR 74.340 permanently lists lakes of FD&C Red No. 40 that are prepared as described in 21 CFR 82.51 and that meet the specifications and labeling requirements prescribed by § 82.51.

The identity and specifications for the straight colors used in the preparation of the provisionally listed lakes for food use are provided in the regulations for the straight-color components of lakes in part 82, which are cited above. The regulations in part 82 cross-reference the permanent listings of the straight colors in part 74. As to substrata, § 82.3 defines alumina, but provides no specifications for alumina or for the materials used to prepare it in situ. Finally, with regard to precipitants, part 82 does not identify or prescribe specifications for the precipitants that may be used in the preparation of these lakes, other than specifying the cation component and providing specifications that limit the level of soluble chlorides and sulfates in the lake.

1. Straight Colors

a. *Identity.* The agency has already reviewed the identity and safety of the straight colors currently permitted as components of lakes for food use, either as part of its scientific review of provisionally listed straight colors or in response to petitions for the review of new color additives. Based on these reviews, the agency concluded that FD&C Blue No. 1, FD&C Blue No. 2, FD&C Green No. 3, FD&C Yellow No. 5, FD&C Yellow No. 6, and FD&C Red No. 40 are safe for use in foods and permanently listed these straight colors in 21 CFR part 74, subpart A. The agency is proposing to continue to permit the use of these straight colors as components of lakes for use in food, subject to the proposed requirements discussed below.

b. *Use of previously certified batches.* Currently, under § 82.51, manufacturers are required to prepare lakes for food use from previously certified batches of straight colors. This requirement was intended to ensure that the levels of intermediates, subsidiary colors, and other impurities in straight colors that are used to prepare lakes for food use are within the levels specified in the applicable regulations. Impurities in the straight color, especially the carcinogenic constituents present in some straight colors, are a primary safety concern with the use of these color additives and their lakes in food.

In the 1979 NOI, the agency requested submission of information about available methods for the determination of total (free plus bound) intermediates, as well as subsidiary colors and other impurities, and stated that without appropriate analytical methodology it might be necessary to require that all lakes be produced from certified batches of straight colors. The agency stated that there was no satisfactory analytical method to determine total intermediates in lakes. The available methods detected free intermediates but not necessarily the intermediates that, like the straight color, are bound to the substratum.

The comments on the 1979 NOI did not provide suitable methodology for the analysis of intermediates and other impurities in lakes. CTFA's comment stated that these problems could be addressed only through a time-consuming and difficult undertaking to develop satisfactory analytical methods. The comment suggested that the issue of certification methodology should be separated from that of the permanent listing of lakes, thus allowing these lakes to be permanently listed while the industry and the agency went on to address the issue of certification methodology jointly.

Section 721(b)(5)(A)(iv) of the act provides that in determining whether the proposed use of a color additive is safe, the agency must consider, among other relevant factors, the availability of any needed practicable methods of analysis for determining the identity and quantity of intermediates and other impurities contained in the color additive. If lakes are prepared from uncertified batches of straight colors, the only way to ensure that the intermediates, subsidiary colors, and other impurities derived from the straight color do not exceed the specification limits for the lake is to analyze the lake itself for those impurities. However, as indicated above, the analytical methods to accomplish this purpose are not currently available. Therefore, the agency tentatively concludes that the lack of adequate analytical methods to determine the levels of intermediates and other impurities in lakes precludes the agency from prescribing conditions of safe use for lakes prepared from uncertified batches of straight colors. Accordingly, to ensure the continued safety of lakes for food use, the agency is proposing to retain the requirement that these lakes be prepared from certified batches of straight colors. As discussed in section V.A. of this document, FDA is also proposing to require that lakes for use in drugs and cosmetics be prepared from certified batches of straight colors.

c. *Stability.* In the 1979 NOI, the agency asked for information about the chemical stability of straight colors during the laking process. The agency stated that if previously certified batches of straight colors are used in the preparation of lakes, the levels of intermediates and subsidiary colors in these lakes should be proportional to those in the original batch of the straight color. However, the agency was concerned that the laking process could cause an unstable straight color to deteriorate and, consequently, increase the levels of intermediates and subsidiary colors.

The agency requested data to confirm the stability of previously certified batches of straight colors during the laking process. The agency stated that, if such data were submitted, the agency would not require specifications for intermediates and subsidiary colors in lakes prepared from certified batches of straight colors. The agency also noted the lack of satisfactory methodology for identifying and quantifying intermediates and certain other contaminants in many lakes, but added that the lack of such methodology does not pose a problem for lakes produced from previously certified batches of colors, provided that there is no measurable degradation of the color during the laking process.

The straight colors that FDA proposes to permit as components of lakes for food use fall into the following four groups, based on chemical structure (the Color Index Structural classification (Ref. 16), as further refined by Marmion (Ref. 17)): Monoazo (FD&C Red No. 40, FD&C Yellow No. 6); pyrazolone (FD&C Yellow No. 5); triphenylmethane (FD&C Blue No. 1, FD&C Green No. 3); and indigoid (FD&C Blue No. 2). The FD&C lakes of these straight colors made up about 80 percent of the total poundage of lakes certified in fiscal year 1995 (FY–95) (Ref. 18). FD&C lakes of three

straight colors (FD&C Yellow No. 5, FD&C Yellow No. 6, and FD&C Red No. 40) made up about 90 percent of the FD&C lakes certified in FY–95. Lakes of FD&C Blue No. 1 and FD&C Blue No. 2 made up the remaining 10 percent. No batches of FD&C Green No. 3 lakes were certified in FY–95. Because lakes of monoazo and pyrazolone dyes make up such a high proportion of lakes certified, the agency is particularly concerned about possible degradation of FD&C lakes of these dyes.

CTFA submitted data (Ref. 19) to confirm the stability during laking on alumina of three straight colors (FD&C Blue No. 1, FD&C Red No. 40, and FD&C Yellow No. 5) that represent three of the four structural groups. The data presented a comparison of the high performance liquid chromatography (HPLC) evaluations of each of five samples of FD&C Red No. 40, FD&C Yellow No. 5, and FD&C Blue No. 1 with the corresponding lake made from each sample. FDA has evaluated the data submitted by CTFA. A quantitative comparison of the levels of intermediates and subsidiary colors present in the straight color and the corresponding lake confirmed that the levels of intermediates and subsidiary colors in the lakes (after adjustment for the percent straight color in the lake) did not differ significantly from those in the corresponding straight colors (Ref. 20).

The agency also conducted a brief study on the stability of FD&C Blue No. 2 during the laking process (Ref. 21). This study presented a comparison of the HPLC evaluations of a sample of a certified batch of FD&C Blue No. 2 and a sample of a certified batch of the aluminum lake prepared from this batch. A quantitative comparison of the levels of intermediates and subsidiary colors present in the straight color and the corresponding lake confirmed that the levels of intermediates and subsidiary colors in the lake (after adjustment for the percent straight color in the lake) did not differ significantly from those in the corresponding straight color.

The data evaluated by the agency provide evidence that lakes of the straight colors FD&C Yellow No. 5, FD&C Red No. 40, FD&C Blue No. 1, and FD&C Blue No. 2 can be produced without significant degradation of the straight color. When produced under conditions of current good manufacturing practice (CGMP), these lakes meet the specifications for intermediates and subsidiary colors in the straight color, after adjustment for total color content of the lake. Although data have not been submitted for all of the straight colors FDA proposes to permit as components of lakes for food use, the remaining such straight colors (FD&C Green No. 3 and FD&C Yellow No. 6) have chemical structures that are similar to other straight colors (FD&C Blue No. 1 and FD&C Red No. 40, respectively) discussed above. The stability of FD&C Yellow No. 6 aluminum lake, which makes up over 25 percent of the total poundage of FD&C lakes certified in FY–95, is also supported by published studies. In these studies, the FD&C Yellow No. 6 aluminum lake showed greater thermal stability than did FD&C Red No. 40 aluminum lake (Ref. 22), and the straight color FD&C Yellow No. 6 was as stable as the straight color FD&C Red No. 40 under the pH conditions studied, showing no appreciable change over a week's exposure (Ref. 17). The agency tentatively finds that because of the similarity of chemical structure, the data available for the lakes of FD&C Blue No. 1 and FD&C Red No. 40 are adequate to confirm the stability of FD&C Green No. 3 and FD&C Yellow No. 6, respectively, during the manufacture of lakes in accordance with CGMP. In addition, the published data on FD&C Yellow No. 6 and its aluminum lake provide corroborative evidence for the stability of this straight color during the laking process when conducted under conditions consistent with CGMP.

Based on its previous evaluations of the safety of the straight colors that FDA proposes to permit as components of lakes for food use and on the scientific evidence that lakes of these straight colors can be produced under conditions consistent with CGMP without significant degradation of the straight color, the agency now tentatively concludes that certified batches of FD&C Blue No. 1, FD&C Blue No. 2, FD&C Green No. 3, FD&C Yellow No. 5, FD&C Yellow No. 6, and FD&C Red No. 40 are safe for use as components of lakes for food use that are prepared under conditions of CGMP. Therefore, the agency is proposing to permit certified batches of these straight colors as components of lakes for food use in § 74.50.

The agency is not, however, proposing to establish any definition of CGMP for the preparation of lakes for food use. FDA recognizes that CGMP for laking will vary with the straight color used, may include a variety of combinations of conditions, and may change over time with the introduction of new combinations of conditions. The agency's regulatory goal is to protect the public health by assuring that laking is conducted in a manner such that no significant degradation of the straight color occurs, not to prescribe the details of industry practice. Safety issues relating to the use of CGMP in preparing lakes are discussed further in sections IV.B.5 and IV.C. of this document.

d. *Use of more than one straight color in a lake.* The agency also tentatively concludes that the current prohibition on the use of more than one straight color in a lake is unnecessary. This prohibition was instituted as part of the original listing of lakes as certified colors in 1939 (4 FR 1922, 4 FR 3931, and 5 FR 1138). At that time, the regulations did not require that lakes be prepared from previously certified batches of straight color, and the only food use for which lakes were listed was for dyeing eggs in the shell. The requirement that lakes for food use be prepared from previously certified batches of straight color was initiated in 1959, when the regulations were amended to permit, for the first time, the use of certain lakes in foods generally (24 FR 3818 and 24 FR 5302). The agency now tentatively concludes that, because of the proposed requirement that certified batches of straight colors be used in preparing all lakes, the evidence for the stability of straight colors during the laking process, and the proposed certification requirement for lakes (discussed in section IV.C. of this document), the prohibition against the use of more than one straight color to make a lake is unnecessary. Therefore, the agency is proposing to permit the preparation of a lake from certified batches of more than one straight color.

2. Substratum—Alumina

Alumina is the only substratum provisionally listed for lakes for food use. Section 82.3(g) defines alumina as ''a suspension in water of precipitated aluminum hydroxide'' but prescribes no quality requirements for alumina substratum. This definition covers both preformed (precipitated and dried) alumina that is subsequently suspended in water and alumina that is prepared in situ, without subsequent recovery and drying.

As noted in section I. of this document, alumina may be prepared in situ from aluminum sulfate and sodium hydroxide or sodium carbonate during the manufacture of lakes. Aluminum sulfate is GRAS for food use (§ 182.1125) and is subject to the specifications in the Food Chemicals Codex 2d. ed. (1972) (§ 170.30(h)(1) (21 CFR 170.30(h)(1))). Sodium carbonate and sodium hydroxide are affirmed as GRAS for food use (§§ 184.1742 and 184.1763, respectively) and are required

to meet the specifications in the Food Chemicals Codex, 3d. ed. (1981).

In addition, § 73.1010 lists alumina (dried aluminum hydroxide) as a color additive for use in drugs and provides identity and specifications for alumina as a color additive. The agency tentatively concludes that, although the listed use of alumina (dried aluminum hydroxide) is for coloring drug products, alumina that meets the identity and quality requirements in § 73.1010 (a)(1) and (b) is safe as a substratum for lakes for food use (Ref. 13).

The agency has evaluated the available data relating to the safety of aluminum salts. These data included literature reviews, information from a color additive petition for use of several aluminum lakes on alumina in eye-area cosmetics, and safety reviews of aluminum compounds (including aluminum salts) as food ingredients by the Select Committee on GRAS Substances of the Federation of American Societies for Experimental Biology and the Joint FAO/WHO Expert Committee of Food Additives. Based on this evaluation, the agency tentatively concludes that alumina conforming to the identity and quality requirements set forth in § 73.1010 (a)(1) and (b) (Refs. 13, 23, and 24) is safe for use as a substratum in lakes for food use. The agency also tentatively concludes that alumina prepared from aluminum sulfate and sodium carbonate or sodium hydroxide that meet the requirements for these compounds in the Food Chemicals Codex 2d ed. (1971) (aluminum sulfate) or 3d ed. (1981) (sodium carbonate and sodium hydroxide) is safe as a component of lakes for food use.

3. Precipitants

a. *Aluminum cation (Al^{+3}).* In its safety review of alumina (see section IV.A.2. of this document), the agency evaluated the safety of the use of the aluminum salts (salts containing the aluminum cation (Al^{+3})). Based on this safety review, the agency tentatively concluded that the use of alumina as a substratum in lakes is safe. Based on the same data, the agency also tentatively concludes that the use of the aluminum cation as a component of precipitants used in the preparation of lakes for food use is safe (Ref. 13, 23, and 24). Aluminum cation is added as a precipitant with an accompanying anion. If an aluminum salt is added as a precipitant, the anion is added as part of the salt. Alternatively, if aluminum oxide or hydroxide is used as a precipitant, the anion is added as an acid to ensure the solubility of the aluminum cation to function as a precipitant. The anions that the agency proposes to permit for use in lakes are discussed in section IV.A.3.c. of this document.

The agency is not proposing to establish quality requirements for precipitants used in the preparation of lakes for food use. The agency recognizes that a variety of precipitant ingredients can be used to produce the aluminum cation that functions as a precipitant in lakes for food use. Furthermore, the agency does not anticipate that the use of precipitant ingredients that form the aluminum cation, under conditions consistent with CGMP, would introduce contaminants that require limitation by specifications for the precipitant ingredients. Precipitants are used at low levels (a small percentage of the total batch weight) and, by virtue of their function in the laking process, are always water-soluble cations. Because lakes are washed when prepared in accordance with CGMP, the agency anticipates that only low levels of water-soluble contaminants will remain in the finished lake. The only possible concern would be the presence of heavy metals deriving from contaminants in the precipitants. To address this potential problem, as discussed below, the proposed specifications for lakes will limit the levels of heavy metal contaminants permitted in the end product. Therefore, the agency tentatively concludes that quality requirements for the ingredients used to form precipitants in lakes for food use are unnecessary.

b. *Calcium cation (Ca^{+2}).* As discussed in section III.C.6.c. of this document, the agency is proposing to terminate the listing of calcium as a cation in lakes for food use because calcium lakes were not used in food in 1960 and thus should not have been provisionally listed. Any future consideration of the use of calcium lakes for coloring foods would be through the color additive petition process (§ 71.1).

c. *Accompanying anions.* The use of the aluminum cation in preparation of lakes results in the formation of chloride or sulfate anions. Chloride and sulfate are components of many food ingredients that the agency has listed or affirmed as GRAS for general food use (for example: Aluminum sulfate, § 182.1125; calcium sulfate, § 184.1230; table salt (sodium chloride), § 182.1(a); potassium chloride, § 184.1622). In the safety reviews conducted as part of the GRAS rulemakings for these ingredients, the agency found that ingestion of chloride and sulfate (in the presence of the accompanying cation) was safe at levels that vastly exceed possible levels of exposure to these anions as components of lakes. Therefore, the agency tentatively concludes that the presence of these anions in lakes for food use is safe when CGMP is observed (Ref. 13).

B. Specifications for Lakes for Use in Foods

1. Intermediates and Other Impurities Derived From Straight Colors

A typical straight color contains, in addition to the primary color component, intermediates and subsidiary colors. Intermediates are unreacted starting materials used to synthesize the primary color. Subsidiary colors are colored by-products of the synthesis of the primary color. As discussed in section IV.A.1.b. of this document, the agency is proposing to require that lakes be prepared from certified batches of straight color. The regulations for straight colors contain specifications that limit the levels of intermediates and subsidiary colors that may be present in the straight color. In this proposal, the agency has also tentatively concluded that the straight colors in lakes for food use do not degrade significantly during preparation of the lakes under conditions consistent with CGMP. Therefore, the agency tentatively concludes that the specifications for intermediates and subsidiary colors in straight colors are sufficient to ensure the safety of lakes prepared from certified batches of straight colors and that separate specifications for intermediates and subsidiary colors in lakes are unnecessary.

2. Heavy Metals

The current specifications for lakes for food use (§ 82.5) establish limits of 10 ppm lead, 1.4 ppm arsenic, and ''not more than trace'' levels of total heavy metals (other than lead and arsenic). In the 1979 NOI, the agency proposed adding a specification for mercury in lakes. The agency tentatively finds that the manufacturing processes for lakes use metal salts that are sources of potential contamination by heavy metals; moreover, in its certification of lakes, the agency has rejected batches because of the presence of heavy metals, including lead. Therefore, the agency tentatively concludes that specifications to limit the levels of lead, arsenic, and mercury in lakes are necessary to ensure their safe use in food. As a result of its safety reviews of the straight colors used in food, the agency established limits of not more than 10 parts per million

(ppm) lead, 3 ppm arsenic, and 1 ppm mercury in the specifications for most color additives permanently listed for food use in parts 73 and 74. The agency tentatively concludes that such specifications are also sufficient to ensure the safety of lakes.

FDA is unaware of any heavy metals, other than lead, arsenic, and mercury, that have a significant level of toxicity and that would be expected to occur in lakes. Therefore, the agency tentatively concludes that a general heavy metal specification is unnecessary to ensure the safety of lakes for food use.

One comment received in response to the 1979 NOI suggested that a limitation on iron be included in the specifications for lakes for food use. Iron salts may be present in lakes as contaminants inadvertently introduced during the manufacturing process. For example, a batch of lake prepared using rusted equipment or water with a high iron content may contain iron salts.

The agency has evaluated the safety of iron salts as a contaminant in lakes to determine whether their presence would present a sufficient safety hazard to warrant inclusion of a specification for iron. The agency notes that iron is an essential mineral, and that iron and many of its salts are affirmed as GRAS in part 184 for use as nutrients in food (for example, elemental iron, § 184.1375; ferric ammonium citrate, § 184.1296; ferric chloride, § 184.1297; ferric sulfate, § 184.1307; ferrous carbonate, § 184.1307b; ferrous sulfate, § 184.1315). However, the agency also notes that high levels of iron consumption can be toxic, especially for certain subpopulations. (See, e.g., 59 FR 51030, October 6, 1994).

Lakes are generally used at low levels (typically less than 0.05 percent) in foods, except for some low-consumption food items such as candy and candy coatings, colored sugar and frostings, dietary supplements, seasonings, flavorings, and chewing gum (Ref. 25). Therefore, consumption of iron due to its presence in lakes as a contaminant would be low. Under these circumstances, the agency finds no evidence of a safety hazard from exposure to iron as a contaminant in lakes for food use. Therefore, the agency tentatively concludes that a specification to limit the level of iron is unnecessary to ensure the safety of lakes for food use. Moreover, the agency notes that the conditions and practices that lead to the presence of iron salts as a contaminant in a batch of lake are addressed by the proposed requirement that lakes be prepared in accordance with CGMP (see section IV.B.5. of this document).

3. Soluble Chlorides and Sulfates

Current § 82.51 contains a specification that limits the content of the soluble chloride and sulfate anions in lakes for food use. The agency finds that the washing of the lake during the manufacturing process removes most of these water-soluble anions. Furthermore, as discussed above in section IV.A.3.c. of this document, the agency found in safety reviews conducted as part of several GRAS rulemakings that soluble chloride and sulfate anions are safe in foods at levels considerably greater than those found in lakes (Ref. 13). Therefore, the agency tentatively concludes that a specification to limit the levels of soluble chlorides and sulfates is unnecessary to ensure the safety of lakes prepared in conformity with CGMP for food use.

4. Inorganic Material Insoluble in HCl

Current § 82.51 contains specifications that limit the content of inorganic material insoluble in HCl in lakes. This specification was intended to ensure that the lake was prepared in accordance with CGMP and that no foreign material was inadvertently added during the laking process. However, agency certification records for lakes for food use in the past 20 years show that only one batch of lake has been denied certification based on this specification. Even without the specification for inorganic material insoluble in HCl, this batch of lake would not have met the requirements in this proposal because the alumina used as a substratum would not have met the applicable quality requirements. Furthermore, the agency is proposing to include in the specifications for lakes a provision to require that lakes be prepared in accordance with CGMP. Therefore, the agency tentatively concludes that a specification for material insoluble in HCl is unnecessary for lakes that meet the other proposed requirements for lakes, and such a specification is not included in this proposal.

5. Other Impurities and Contaminants

The agency has tentatively concluded above that specifications to limit the level of total heavy metals (except lead, arsenic, and mercury), soluble chlorides and sulfates, and material insoluble in HCl are unnecessary to ensure the safety of lakes for food use as long as a general provision is included in the specifications for lakes to ensure that they are prepared in conformity with CGMP. The identity requirements and specifications in color additive regulations include impurities that are expected to occur at significant levels in a color additive that has been prepared in accordance with CGMP. In its certification of color additives, FDA has occasionally denied certification for batches of color additives due to the presence of significant levels of impurities for which the listing regulation contains no specifications. In a few instances, these impurities could be linked to improper storage of the color additive or to cross-contamination from insufficiently cleaned processing equipment. In most cases, the source of the impurity was unknown. Based on the agency's experience in certifying thousands of batches of color additives annually, corroborated by the agency's analyses of reference standards (reference batches of color additives) used in toxicological studies of various straight colors as part of the safety reviews of these color additives, FDA believes that the impurities in the rejected batches would not have been present had the color additives been manufactured under conditions consistent with CGMP.

As noted above in section IV.A.1.c. of this document, it is important that lakes be prepared in accordance with CGMP to ensure that the straight color does not degrade during preparation of the lake. Manufacturing conditions must be controlled so that levels of uncolored components in the straight color, including the carcinogenic constituents in certain monoazo and pyrazolone straight colors, do not increase during preparation or handling of the lake. CGMP includes use of proper temperatures, especially during drying, to avoid affecting the composition of the lake, and sufficient washing of the lake to remove water-soluble impurities. For example, the agency recently rejected a batch of a monoazo straight color because the batch exceeded the specifications for certain carcinogenic constituents. Subsequent discussions with the manufacturer revealed that the batch had been previously certified, but had failed to meet the manufacturer's microbiological specifications and had been reprocessed (redried). After redrying, the batch no longer met the specification for trace-level carcinogenic constituents. The agency notes, however, that because of their chemical properties, such carcinogenic constituents are unlikely to be incorporated into lakes to the same extent as into straight colors, and sufficient washing of the lake could significantly decrease the levels of these constituents.

To ensure the safety of lakes for use in foods, FDA is proposing to continue

the requirement in existing § 82.5 that lakes shall be free from impurities other than those named in the specifications, to the extent that such impurities may be avoided by CGMP. However, the agency is not proposing to define specific conditions that would constitute CGMP in the preparation of lakes. The agency recognizes that appropriate manufacturing conditions may differ for the preparation of different lakes and, in fact, may change over time. Furthermore, even the preparation of a single lake that meets the requirements of part 74 may be accomplished using different conditions of manufacture. The agency wants to retain the current flexibility in preparation of lakes for food use, but maintain the assurance that there will be no significant degradation of the straight color during preparation of the lake and that the resulting lake will be otherwise in compliance with the requirements of part 74. To accomplish this objective, the agency is not proposing to define any specific conditions of CGMP; however, in its review of notices claiming certification for batches of lake, the agency is proposing to use the accountability of the straight color in the lake, calculated as described below, as an indicator of the use of CGMP in the preparation of the lake.

Under the current certification procedure for FD&C lakes, the agency can monitor both the use of certified batches of straight color in lakes for food use and indicators for the use of CGMP in the preparation or repack of a batch of lake. In a request for certification for a batch of lake, the firm must declare the certified lot number and the poundage from that lot for the straight color that is added to prepare the lake. The agency can determine a poundage accountability of the batches of straight colors that are used to prepare FD&C lakes. This accountability ensures that no more straight color is used in FD&C lakes than has been certified. For example, a firm that owns a 100-pound batch of straight color cannot credibly claim to use 1,000 pounds from that batch to make lakes.

From the information in the request for certification and from analysis of the sample submitted with the request, the agency determines the total color accountability for each batch of lake (the amount of total color that was added to the batch of lake compared to the total color of the resulting batch). This accountability for total color is an indicator for the use of CGMP in the preparation or repack of a batch of lake. In its determination of accountability of the straight color in lakes for food use, the agency calculates a theoretical range for the expected total color content of a lake based on the minimum total color permitted in the listing regulation for the straight color, the maximum total color possible for the straight color (100 percent), the weight of straight color used to prepare the lake, and the weight of the lake. For example, for a 100-pound batch of FD&C Yellow No. 5 aluminum lake on alumina that was prepared from 25 pounds of FD&C Yellow No. 5, the theoretical range for the expected total color content of the lake would be from 21.8 percent to 25 percent. This theoretical range allows for variations in total color resulting from factors that normally occur during the manufacture of a lake, such as incomplete laking of the color and bleeding of the color during washing.

The agency is requesting comments on the usefulness of total color accountability as an indicator of the use of CGMP in the preparation and repacking of batches of lake.

C. Certification Requirement

The agency has evaluated the necessity, in the interest of public health, for the certification of lakes prepared from certified batches of straight color. The agency tentatively concludes that continued batch certification of lakes is necessary to protect the public health. The agency bases this tentative conclusion on two safety issues: The need to ensure the safety of the components (straight colors, precipitants, and substrata) used to prepare a lake; and the need to ensure that lakes are prepared and repacked under conditions of CGMP to prevent degradation of the straight color.

The agency's traditional means for postmarket assurance of product safety is the collection and analysis of a sample. However, as discussed in section IV.A.1.b. of this document, suitable analytical methodology is not available to identify and quantify all potentially harmful impurities that may be present in lakes. Therefore, the agency tentatively concludes that the premarket controls afforded by the certification requirement are necessary to allow FDA to verify that the conditions for safe use of lakes are being met. Therefore, the agency is proposing to list lakes in part 74 as color additives subject to certification.

Certification will allow the agency to confirm, before a lake is marketed, that only safe and suitable components have been used to prepare it; that any batches of straight color used in the lake were previously certified; and that the straight-color component of the lake has not degraded during manufacture or repacking. The agency tentatively concludes, however, that not all aspects of the current batch certification procedure are necessary to accomplish these objectives, and is proposing a simplified procedure for certifying batches of lakes. This proposed procedure is discussed in section VI.B. of this document.

The agency is specifically requesting, as comments on this proposal, comments on the usefulness of its proposed certification procedure for the intended purpose of protecting the public health.

D. Provisions of Proposed § 74.50 Lakes for Use in Foods

The agency is proposing new § 74.50 to list lakes permanently for use in foods as color additives subject to certification. Section 74.50(a)(1), (a)(2), and (a)(3) would designate the components permitted for use in lakes for coloring food. These paragraphs would authorize the use of certified batches of one or more of the straight colors FD&C Blue No. 1, FD&C Blue No. 2, FD&C Green No. 3, FD&C Yellow No. 5, FD&C Yellow No. 6, and FD&C Red No. 40; the substratum alumina that either conforms to the requirements for alumina under § 73.1010(a)(1) and (b), or is a suspension in water of precipitated aluminum hydroxide prepared from aluminum sulfate that meets the requirements of the Food Chemicals Codex 2d ed. (1972) and sodium carbonate or sodium hydroxide that meets the requirements of the Food Chemicals Codex 3d ed. (1981); and precipitants that form the aluminum cation (Al^{+3}) and the anion chloride (Cl^{-1}) or sulfate (SO_4^{-2}).

Proposed § 74.50(a)(4) would provide that only diluents that are permitted in mixtures of straight colors for food use may be used in color additive mixtures containing lakes for such use.

Proposed § 74.50(b) would prescribe the following specifications for lakes for food use: Lead (not more than 10 ppm), arsenic (not more than 3 ppm), mercury (not more than 1 ppm). It would also state that lakes shall be free from impurities other than those named in the specifications, to the extent that such impurities may be avoided by CGMP.

Proposed § 74.50(c)(1) would permit the use of lakes in foods generally, except in foods subject to a standard of identity that does not authorize such use. The proviso relating to standardized foods would clarify that authorization for use of lakes in this regulation does not take precedence over any restrictions on color additive use in a food standard regulation.

Currently, all the straight colors authorized for use in lakes for food use are approved for the same food uses. Because this may not always be the case, however, proposed § 74.50(c)(2) would restrict the use of a lake manufactured from more than one straight color to those uses common to all of the straight colors in the lake.

Proposed § 74.50(d) would identify each lake made as prescribed in § 74.50(a) as a listed color and would prescribe the formation of its listed name from the names of the certified straight colors present in the lake (in descending order of predominance), followed by the name of the cation of the precipitant (aluminum) and followed by the words ''lake on alumina.'' The anion component of the precipitant would not be included in the name of the lake because this anion is removed during processing under conditions of CGMP and is not a component of the final lake.

Proposed § 74.50(e)(1) would require that the label of the lake and of any mixtures prepared from it for coloring purposes conform to the requirements of § 70.25. Proposed § 74.50(e)(2) would require that the label of food products that contain a lake declare the presence of the lake in accordance with § 101.22(k) (21 CFR 101.22(k)). Proposed § 74.50(e)(3) would require that butter, cheese, and ice cream that contain a lake of FD&C Yellow No. 5 or FD&C Yellow No. 6 be labeled in accordance with § 101.22(k)(1). These proposed labeling provisions are discussed more fully in sections VI.C.2. and VI.C.3. of this document.

Proposed § 74.50(f) would require that all batches of lakes be certified in accordance with proposed regulations in part 80.

V. Safety Review and Proposed Actions for Lakes for Use in Drugs and Cosmetics

A. Review of Components of Lakes for Use in Drugs and Cosmetics

The current provisional listing regulations for lakes for use in drugs and cosmetics generally (§ 82.1051) and for use in external drugs and cosmetics only (§ 82.2051) provide for use of the following components: (1) The straight colors FD&C Blue No. 1 (§ 82.101), FD&C Blue No. 2 (§ 82.102), FD&C Green No. 3 (§ 82.203), FD&C Yellow No. 5 (§ 82.705), FD&C Yellow No. 6 (§ 82.706), D&C Blue No. 4 (§ 82.1104), D&C Green No. 5 (§ 82.1205), D&C Green No. 6 (§ 82.1206), D&C Orange No. 4 (§ 82.1254), D&C Orange No. 5 (§ 82.1255), D&C Orange No. 10 (§ 82.1260), D&C Orange No. 11 (§ 82.1261), FD&C Red No. 4 (§ 82.304), D&C Red No. 6 (§ 82.1306), D&C Red No. 7 (§ 82.1307), D&C Red No. 17 (§ 82.1317), D&C Red No. 21 (§ 82.1321), D&C Red No. 22 (§ 82.1322), D&C Red No. 27 (§ 82.1327), D&C Red No. 28 (§ 82.1328), D&C Red No. 30 (§ 82.1330), D&C Red No. 31 (§ 82.1331), D&C Red No. 33 (§ 82.1333), D&C Red No. 34 (§ 82.1334), D&C Red No. 36 (§ 82.1336), D&C Violet No. 2 (§ 82.1602), D&C Yellow No. 7 (§ 82.1707), D&C Yellow No. 8 (§ 82.1708), D&C Yellow No. 10 (§ 82.1710), and Ext. D&C Yellow No. 7 (§ 82.2707a); (2) the substrata alumina, blanc fixe, gloss white, clay, titanium dioxide, zinc oxide, talc, rosin, aluminum benzoate, and calcium carbonate; (3) precipitants containing the cations sodium (Na^{+1}), potassium (K^{+1}), aluminum (Al^{+3}), barium (Ba^{+2}), calcium (Ca^{+2}), strontium (Sr^{+2}), and zirconium (Zr^{+4}). Additionally, the lakes of FD&C Red No. 40 prepared with the substrata and precipitants listed above are permanently listed in §§ 74.1340 and 74.2340.

The identity and specifications for the straight colors used to prepare lakes are provided in the regulations cited above and generally cross-reference the requirements of the permanent listing for the straight color in part 74. As to substrata, § 82.3 defines three of the substrata used in lakes (alumina, blanc fixe, gloss white), but provides no specifications for the materials to be used. Part 82 does not identify or prescribe specifications for other substrata (clay, titanium dioxide, zinc oxide, talc, rosin, aluminum benzoate, and calcium carbonate) for lakes for drug or cosmetic use, or for the precipitants to be used in the preparation of these lakes.

1. Straight Colors

a. *Identity and uses.* As discussed in sections III.C.1. and III.C.6.a. of this document, the agency has tentatively concluded that several of the straight colors currently listed for use in lakes for coloring drugs and cosmetics either do not form lakes (D&C Red No. 17, D&C Red No. 30, D&C Red No. 36, D&C Violet No. 2, and D&C Green No. 6) or were not present in any batch of lake certified for drug or cosmetic use before the enactment of the 1960 amendments (D&C Orange No. 11, D&C Yellow No. 7, D&C Yellow No. 8, and D&C Green No. 5). The proposed termination of the provisional listing of these straight colors for use in lakes would mean that lakes of these straight colors would no longer be permitted for coloring drugs and cosmetics. (See Table 1 in section III.C. of this document for a summary of the current and proposed regulatory status of straight colors addressed in this rulemaking.)

The agency has already reviewed the identity and safety of the remaining straight colors currently permitted as components of lakes for coloring drugs and cosmetics, either as part of its scientific review of provisionally listed straight colors or in response to petitions for the review of new color additives (§ 71.1). On the basis of these reviews, the agency concluded that these straight colors are safe for use in drugs and cosmetics and issued regulations in part 74 permanently listing them for such uses. The agency is proposing to continue to permit the use of these straight colors as components of lakes for use in drugs and cosmetics, subject to the exceptions and proposed requirements discussed below.

In the Federal Register of September 30, 1975 (40 FR 44812), the agency restricted the provisional listing of FD&C Blue No. 2 to uses in foods and ingested drugs, the uses for which a petition had been filed for the permanent listing of the color additive. In the Federal Register of February 4, 1983 (48 FR 5252), the agency published a final rule permanently listing FD&C Blue No. 2 for use in food (§ 74.102) and ingested drugs (§ 74.1102). However, the provisional listing for the lake of FD&C Blue No. 2 (§ 82.102) was not amended accordingly. Therefore, despite the lack of a listing in part 74 authorizing the use of FD&C Blue No. 2 in cosmetics, the provisional listing regulations still permit the use of lakes of FD&C Blue No. 2 in cosmetics. Proposed § 74.2050 would correct this inconsistency by excluding FD&C Blue No. 2 from the straight colors permitted as components of lakes for cosmetic use.

The lakes of D&C Red No. 34 are provisionally listed in part 82 for use in drugs and cosmetics without any restrictions. However, the straight color is listed in part 74 for external drug and external cosmetic uses only (§§ 74.1334 and 74.2334), based on the agency's safety evaluation of the straight color. The proposed permanent listings for lakes for drug and cosmetic use (§§ 74.1050 and 74.2050) would correct this inconsistency by limiting the use of a lake to the use(s) permitted for the straight-color component(s) of the lake. Thus, under the proposed regulations, any lake containing D&C Red No. 34 would be allowed for use only in externally applied drugs and externally applied cosmetics.

b. *Use of previously certified batches.* Currently, under §§ 82.1051 and 82.2051, manufacturers may use uncertified batches of straight colors to

prepare most lakes for drug and cosmetic use. The resulting lake is then subject to batch certification. The exceptions are the lakes of D&C Red No. 33 (§ 82.1333), D&C Red No. 36 (§ 82.1336), and FD&C Yellow No. 6 (§ 82.706), which must be prepared from previously certified batches of the straight color. (As discussed in section III.C.1. of this document, the agency is proposing to terminate the listing of D&C Red No. 36 as a straight-color component of a lake for drug or cosmetic use because it does not contain a salt-forming group.)

For the reasons discussed in section IV.A.1.b. of this document, the agency tentatively concludes that the lack of adequate analytical methods to determine levels of intermediates and other impurities in lakes prepared from uncertified batches of straight colors precludes the agency from prescribing conditions of safe use for lakes prepared from uncertified batches of straight colors. Accordingly, the agency is proposing to require that lakes for use in drugs and cosmetics, including externally applied drugs and cosmetics, be prepared from certified batches of straight colors.

As discussed above, under current regulations the lakes of many D&C straight colors are prepared from uncertified batches of the straight colors. However, lakes of D&C Red Nos. 6, 7, 31, and 34 are commonly produced in situ (a process described in section I. of this document). In FY–95 (Ref. 18), lakes of these straight colors represented about 55 percent of the total quantity of D&C lakes certified. The agency recognizes that its proposal to require the use of certified batches of straight color to prepare lakes for coloring drugs and cosmetics would, in effect, prohibit use of the in situ process for preparing lakes. However, as noted above, the reason for this proposed requirement is that the safety of lakes prepared from uncertified batches of straight color (including lakes prepared in situ) has not been demonstrated. Specifically, the agency is not aware of the existence of any methods that may be used to demonstrate that lakes produced by the in situ process meet the specifications for impurities, including carcinogenic constituents (e.g., para-toluidine in D&C Red Nos. 6 and 7), in the listing regulation for the straight color. Because FDA has the responsibility to ensure that color additives in foods, drugs, and cosmetics are safe for their intended uses, the fact that no methods that allow the safety of lakes produced in situ to be demonstrated appear to be available leads the agency to propose that use of the in situ method be discontinued. FDA recognizes, however, that the potential costs associated with this proposed action may be considerable, and therefore solicits proven methodology for analysis of the lake for the impurities specified in the listing regulation for the straight color. If such information is received in response to this proposal, the need to prohibit the use of lakes prepared by the in situ process will be obviated.

c. *Stability.* The straight colors that FDA proposes to permit as components of lakes for drug or cosmetic use fall into the following eight groups, based on chemical structure (Refs. 16 and 17): Triphenylmethane (FD&C Blue No. 1, FD&C Green No. 3, D&C Blue No. 4); pyrazolone (FD&C Yellow No. 5); monoazo (FD&C Red No. 4, FD&C Red No. 40, FD&C Yellow No. 6, D&C Orange No. 4, D&C Red No. 6, D&C Red No. 7, D&C Red No. 31, D&C Red No. 33, and D&C Red No. 34); indigoid (FD&C Blue No. 2); fluoran (D&C Orange No. 5, D&C Orange No. 10, D&C Red No. 21, and D&C Red No. 27); xanthene (D&C Red No. 22 and FD&C Red No. 28); quinoline (D&C Yellow No. 10), and nitro (Ext. D&C Yellow No. 7). In FY–95, D&C lakes accounted for approximately 20 percent of the total poundage of lakes certified (Ref. 18). Of the D&C lakes certified in FY–95, approximately 55 percent were lakes of the monoazo dyes (primarily lakes of D&C Red Nos. 6 and 7), about 20 percent were lakes of the fluoran and xanthene dyes (primarily lakes of D&C Red Nos. 21 and 27), and about 15 percent were lakes of quinoline dye (D&C Yellow No. 10). No batches of lakes of the nitro dye (Ext. D&C Yellow No. 7) were certified in FY–95.

Section IV.A.1.c. of this document sets forth the agency's evaluation of data confirming the stability of certain straight colors in the triphenylmethane, pyrazolone, monoazo and indigoid classes during the laking process. This information includes data received from CTFA in response to the 1979 NOI (Ref. 19), data generated by FDA (Ref. 21), and published studies (Refs. 17 and 22). In addition to these data, the agency received a preliminary stability study for two additional lakes prepared from monoazo dyes (FD&C Red No. 4 and D&C Orange No. 4) (Ref. 26). The study, which was conducted by a color additive manufacturer, compared the levels of total color, uncombined intermediates, and subsidiary color in a certified batch of each straight color to the levels of these materials in an aluminum lake prepared from the batch. The study found no evidence that the straight color degraded during manufacture of the lake.

Based on its evaluation of all these data, the agency tentatively concludes that when prepared in accordance with CGMP,straight colors in the monoazo, triphenylmethane, pyrazolone, and indigoid classes do not degrade significantly during preparation of lakes for use in drugs or cosmetics.

The agency received no studies evaluating the stability of the straight colors in the fluoran, xanthene, quinoline, or nitro groups during the laking process. However, the agency has reviewed certification records for batches of lakes made from straight colors in the fluoran, xanthene (Ref. 27), and quinoline (Ref. 28) classes. The agency has not certified a batch of lake of Ext. D&C Yellow No. 7 since 1975; therefore, no recent certification data are available for lakes of Ext. D&C Yellow No. 7.

The lakes of straight colors in the fluoran, xanthene, and quinoline groups are not required to be prepared from certified batches of straight color. Nevertheless, for lakes of the quinoline dye, D&C Yellow No. 10, the agency determined that one manufacturer used certified lots of D&C Yellow No. 10 to prepare the lake. The agency evaluated certification reports for the 36 such batches of D&C Yellow No. 10 lake that were certified in FY–95. The agency compared the levels, adjusted for total color content of the lake, of one intermediate (24 batches) and one subsidiary color (36 batches) in the batches certified to the levels permitted for these impurities in the straight color. The agency also determined total color accountability for all 36 batches. As discussed in section IV.B.5. of this document, the total color accountability was determined by comparing the actual total color content of each batch of lake with the range of estimated total color content for the same batch. The actual total color content of the batch of lake was determined during certification of the batch. The range of expected total color content of the lake was determined from the amount (weight) of straight color in the batch, multiplied by the range of expected total color content of the batch of straight color (as a percentage), and divided by the weight of the batch of lake. The lower limit of the range of expected total color content of the straight color was the minimum total color permitted by the applicable specification in the listing regulation for the straight color. The upper limit of the range was assumed to be 100 percent.

All but one of the batches contained levels of the intermediate and subsidiary color that, adjusted for total color content of the lake, were within the limit set by the specification for the

straight color. These data show that it is technologically feasible to prepare lakes of D&C Yellow No. 10 from certified batches of straight color without significant increases in impurities derived from the straight color. Over 40 percent of the batches had a total color content within the theoretical range of expected color content. The data showed that, after an adjustment for the total color content of the lake, the levels of sulfonated quinaldines, which are presumptive products of decomposition, remained within the specification limit for the straight color. Therefore, the agency tentatively finds that the data are adequate to conclude that there is no significant degradation of D&C Yellow No. 10 during laking under conditions of CGMP.

The agency also evaluated FY–95 certification reports for lakes of the fluoran and xanthene straight colors. These lakes were all prepared from uncertified batches of straight color. To make its evaluation as accurate as possible, the agency compared levels (adjusted for total color content of the lake) of impurities found in the lakes to the maximum levels permitted for the same impurities in certified batches of straight color. The agency combined the data from the fluoran and xanthene classes of lakes because, during the laking process, the lactone group in the xanthene dyes is converted to the corresponding salt. Therefore, lakes of straight colors from the xanthene class are structurally identical to the lakes of comparable straight colors from the fluoran class.

The agency evaluated the certification reports from the 104 batches of lakes of the fluoran and xanthene straight colors that had been certified in FY–95, including 16 reports for lakes of the xanthene straight colors D&C Red No. 22 (3 batches) and D&C Red No. 28 (13 batches) and 88 reports for lakes of the fluoran straight colors D&C Orange No. 5 (4 batches), D&C Red No. 21 (23 batches), and D&C Red No. 27 (61 batches). The agency compared the levels (adjusted for total color content of the lake) of three intermediates (55 batches) and one subsidiary color (104 batches) in these batches to the levels of these impurities permitted by the specifications in the listing regulation for the straight color. The agency also determined the total color accountability for 104 batches. (The theoretical range of expected total color content for these batches of lakes was determined in the same manner as described above for batches of D&C Yellow No. 10 lakes.) All but four of the batches contained levels of the intermediates and subsidiary color that, after adjusting for the total color content of the batch, met the specifications for the straight color. These data show that it is technologically feasible to prepare lakes of the fluoran and xanthene straight colors without significant degradation of the straight color. Over 60 percent of the batches had a total color content that was within the theoretical range of expected color content. The analyses showed that, after adjustment for the total color content of the lake, levels of the subsidiary colors tribromofluoresceins (D&C Red Nos. 21 and 22) and the lower halogenated fluoresceins (D&C Red Nos. 27 and 28), which are prime indicators of possible dehalogenation (a decomposition reaction) of the parent compound, remained within the applicable specifications for the straight color. Therefore, the agency tentatively finds that the data are adequate to conclude that no significant degradation of these straight colors occurs during preparation of lakes under conditions consistent with CGMP.

The agency tentatively concludes that the available information provides sufficient evidence for the stability of the straight-color component of lakes prepared from colors in the monoazo, pyrazolone, triphenylmethane, indigoid, fluoran, xanthene, and quinoline classes. Although the agency has not evaluated data for all of the straight colors that FDA is proposing to approve as components of lakes for drug and cosmetic use, the agency tentatively concludes that the available information is adequate to conclude that there is no significant degradation of straight colors in these classes during the preparation of lakes in accordance with CGMP.

The agency has no data on the stability of the nitro straight color, Ext. D&C Yellow No. 7, during the laking process. No lakes of this straight color were certified in FY–95; the last batch of this lake was certified by the agency in 1975. Based on the absence of data concerning the stability of Ext. D&C Yellow No. 7 during the laking process, the agency tentatively concludes that it has insufficient data to ensure the safety of lakes prepared with Ext. D&C Yellow No. 7. Therefore, the agency is not proposing to permit the use of Ext. D&C Yellow No. 7 as a component of lakes for drug or cosmetic use. Consequently, the proposed termination of the provisional listings of lakes (see section VI.A.2. of this document) would remove the listing for lakes of Ext. D&C Yellow No. 7. Anyone interested in the permanent listing of lakes of Ext. D&C Yellow No. 7 should submit, as a comment on this proposal, data showing the stability of Ext. D&C Yellow No. 7 during the laking process. If data on the stability of Ext. D&C Yellow No. 7 lakes are received as a comment on this proposal, the agency will consider permanently listing the lakes of Ext. D&C Yellow No. 7 in the final rule.

The agency has also considered the safety evaluations for the straight colors discussed above. Based on these safety evaluations and the data showing the stability of straight colors when the laking process is conducted in accordance with CGMP, the agency tentatively concludes that, when lakes are prepared under conditions of CGMP, the certified batches of straight colors listed in proposed §§ 74.1051 and 74.2051 are safe for use in lakes for the same drug and cosmetic uses as part 74 allows for the straight colors. Therefore, the agency is proposing to permit certified batches of these straight colors as components of lakes for drug or cosmetic use.

As discussed in section IV.A.1.c. of this document, the agency is not proposing to establish a definition of CGMP for the preparation of lakes. Rather, FDA is proposing to permit any manufacturing method that ensures that straight colors do not significantly degrade during laking.

d. *Use of more than one straight color in a lake.* For the reasons discussed in section IV.A.1.d. of this document, the agency is also proposing to permit the preparation of a lake from certified batches of more than one straight color.

2. Substrata

a. *Regulatory approach.* The agency is proposing to include the following in its permanent listing regulations for lakes for drug and cosmetic use as substrata permitted for preparing such lakes: alumina, barium sulfate, kaolin, titanium dioxide, zinc oxide, talc, aluminum benzoate, calcium carbonate, and rosin. In addition, gloss white will also be permitted, although not explicitly listed in the regulations, because FDA is proposing to allow combinations of substrata. Thus, all of the substrata currently permitted as components of lakes for drug and cosmetic use under §§ 82.1051 and 82.2051, the provisional listing regulations, will continue to be permitted under the proposed regulations.

Ordinarily, the agency establishes identity and specification requirements for the color additive, rather than for the components used to make the color additive. However, because of the unique characteristics of lakes, the agency is proposing to regulate them under a broadly based, flexible system that permits the use, in drug and

cosmetic products, of lakes that may contain a variety of components at varying levels. As noted above in section V.A.1.b. of this document, the agency is proposing to establish quality requirements (identity and specifications) for the straight-color components of lakes by requiring the use of certified batches of straight colors to prepare lakes. To ensure the safety of lakes prepared with the substrata listed above, and at the same time to permit manufacturers the continued flexibility to prepare lakes using any one or mixtures of these substrata at varying levels, the agency is proposing to establish quality requirements (identity and specifications) for these substrata or their components. In this way, the agency can ensure the safety of substrata used to prepare lakes without setting rigid specifications for the finished lake to limit impurities in substrata, which may be present at varying levels in a lake, and without requiring analysis of the lake itself for these impurities.

b. *Alumina.* In section IV.A.2. of this document, the agency reviewed the identity and safety of alumina, and tentatively concluded that alumina is safe as a substratum in lakes for food use. Furthermore, alumina is listed in § 73.1010 as a color additive for use in drugs generally at levels consistent with CGMP. Based on its review of the use of alumina as a substratum in lakes for food use and on the listing of alumina as a color additive safe for general use in drugs, the agency tentatively concludes that alumina is also safe for use as a substratum in lakes for drug and cosmetic use, provided that it either conforms to the identity and specification requirements in § 73.1010 (a)(1) and (b), or is a suspension in water of precipitated aluminum hydroxide prepared from aluminum sulfate and sodium carbonate or sodium hydroxide that meet the requirements of Food Chemicals Codex 2d ed. (1972) (aluminum sulfate) or Food Chemicals Codex 3d ed. (1981) (sodium carbonate and sodium hydroxide).

c. *Barium sulfate (blanc fixe).* Section 82.3(h) defines blanc fixe as ''a suspension in water of precipitated barium sulfate.'' The definition provides no quality requirements for blanc fixe as a substratum. This definition covers both preformed barium sulfate that is subsequently suspended in water and barium sulfate that is prepared in situ, without subsequent recovery and drying.

The United States Pharmacopeia 23d ed. (1990) (USP) defines barium sulfate as ''$BaSO_4$ 233.39; sulfuric acid, barium salt (1:1); Barium sulfate (1:1) [7727–43–7]'' and provides specifications. The act recognizes the USP as an official drug compendium whose specifications are applicable to drug uses of substances listed therein (21 U.S.C. 321(g)(1)(a) and 351(b)). Although the USP specifications for barium sulfate and other compounds discussed below that are recognized by the USP are not directly applicable for purposes of this proposal, the agency tentatively concludes that the USP specifications for these compounds when used as drugs are also appropriate for these compounds when they are used as substrata for lakes to color drugs.

The agency has approved barium sulfate for use in adhesives (§ 175.105) and as a colorant for food-contact use (§§ 178.3297 (21 CFR 178.3297) and 176.170(b)(2)). As part of the current rulemaking, the agency also evaluated data relating to the safety of ingested and dermal uses of barium sulfate, and found no reports in the scientific literature of adverse effects resulting from topical use of barium sulfate. Moreover, scientific data establish that barium sulfate is highly insoluble. For example, the CRC Handbook of Chemistry and Physics (59th ed., 1978) reports that precipitated blanc fixe ($BaSO_4$) has a solubility in water of 0.246 milligram (mg)/100 gram (g) at 26 °C and 0.4113 mg/100g at 100 °C and 60 mg/100g in 3 percent HCl. Consequently, its absorption and toxicity are low. However, to provide further assurance of safety, the agency is proposing to retain the current specification for soluble barium of not more than 0.05 percent in lakes that contain a barium salt (§ 82.5(b)(3)). The agency tentatively concludes that barium sulfate that meets the requirements of the USP is safe for use as a substratum in lakes for drug and cosmetic use (Ref. 13).

The definition in § 82.3(h) for blanc fixe and the definition in § 82.3(i) for gloss white (a suspension in water of co-precipitated aluminum hydroxide and barium sulfate) suggest that barium sulfate may be prepared in situ either alone or with alumina during the manufacture of lakes. The International Pharmacopoeia 3d ed. (1979) describes the preparation of barium sulfate suspension by mixing barium chloride solution, sulfate-free ethanol, and potassium sulfate solution. The WHO's Specifications for Reagents Mentioned in the International Pharmacopoeia (1963) describes barium chloride and potassium sulfate and provides specifications for each. However, the agency has no information to confirm that the International Pharmacopeia method and the identity and specifications for barium chloride in the WHO publication represent CGMP for preparing barium sulfate in situ as substrata for lakes for drug or cosmetic use. Therefore, the agency requests comments on appropriate methodology for the in situ preparation of barium sulfate as a substratum, and on identity requirements and specifications for reagents used to prepare this substratum. If such comments are received and the information provided is satisfactory, the agency will list barium sulfate prepared in situ as a substratum in lakes for use in drugs and cosmetics.

The agency is also proposing to substitute the name ''barium sulfate'' for ''blanc fixe.'' CTFA's comment on the 1979 NOI suggested this change in terminology. The agency notes that, in the past, the name ''blanc fixe'' was typically used to identify the substratum composed of barium sulfate in requests for certification of lakes. However, more recently, the name typically used for this substratum in requests for certification is ''barium sulfate.'' Therefore, the agency agrees with CTFA's comment and is proposing to substitute the name ''barium sulfate'' for the name ''blanc fixe.''

d. *Gloss white.* Section 82.3(i) defines gloss white as ''a suspension in water of co-precipitated aluminum hydroxide and barium sulfate''. As discussed above, the agency is proposing to permit both alumina and barium sulfate as substrata in lakes for drug or cosmetic use.

Therefore, the agency is proposing not to list gloss white as a substratum in lakes for drug and cosmetic use, because the proposed regulations provide for combinations of substrata.

e. *Kaolin (clay).* In the 1979 NOI, the agency stated that the term ''clay'' does not adequately identify the chemical structure of this material. The NOI requested comments identifying the material and suggesting specifications to ensure its safe use as a substratum in lakes. CTFA's comment, submitted in response to the 1979 NOI, identified kaolin as the substratum material used in lakes.

The USP (23d ed., 1995) defines kaolin as ''a native hydrated aluminum silicate, powdered and freed from gritty particles by elutriation,'' and provides specifications. The agency has affirmed clay (kaolin) as GRAS in § 186.1256 as an indirect food ingredient. Section 186.1256 identifies clay (kaolin) as hydrated aluminum silicate ($Al_2O_3.2SiO_2.nH_2O$) and provides a CAS Registry number of 1332–58–7.

The agency has reviewed data relating to the safety of ingested and dermal uses of kaolin and bentonite (a related

mineral containing magnesium aluminum silicate). These data included data developed for the GRAS review of these compounds and data in a color additive master file, which included dermal toxicity data. The agency also considered a 90-day feeding study on magnesium aluminum silicate.

Based on its review, the agency finds that kaolin is inert when applied externally and is not absorbed by the gastrointestinal tract. A search of the scientific literature revealed no reports of adverse effects resulting from topical use of kaolin. Therefore, the agency tentatively concludes that kaolin that meets USP specifications is safe for use as a substratum in lakes for drug and cosmetic use (Ref. 13).

f. *Titanium dioxide.* The color additive regulation for titanium dioxide (§ 73.575) identifies titanium dioxide as ''synthetically prepared TiO_2'' and provides specifications. Titanium dioxide is listed as a color additive exempt from certification for use in food (§ 73.575), in drugs generally (§ 73.1575), in cosmetics generally (§ 73.2575), and in certain medical devices (§ 73.3126). The USP (23d ed., 1995) recognizes titanium dioxide, defines it as ''TiO_2 79.88; Titanium oxide (TiO_2); Titanium oxide (TiO_2) [13463–67–7],'' and provides specifications.

The agency has evaluated the available data relating to the safety of ingested and dermal uses of titanium dioxide, including data supporting its use as a color additive, and more recent genetic and chronic toxicity studies in rats and mice. Based on these data, the agency tentatively concludes that titanium dioxide that meets the requirements of § 73.575 (a)(1) and (b) is safe for use as a substratum in lakes for drug and cosmetic use (Ref. 13).

g. *Zinc oxide.* The color additive regulation for zinc oxide (§ 73.1991) identifies zinc oxide as ''a white or yellow-white amorphous powder manufactured by the French process (described as the indirect process whereby zinc metal isolated from the zinc-containing ore is vaporized and then oxidized).'' Section 73.1991(b) provides specifications for zinc oxide. The USP (23d ed., 1995) recognizes zinc oxide, defines it as ''ZnO 81.39; Zinc oxide; Zinc Oxide [1314–13–2],'' and provides specifications.

Zinc oxide is listed as a color additive exempt from certification for use in externally applied drugs (§ 73.1991) and in cosmetics generally (§ 73.2991). Zinc oxide is also GRAS for use as a dietary supplement (§ 182.5991) and as a nutrient (§ 182.8991).

The agency has evaluated data relating to the safety of ingested and dermal uses of zinc oxide, including a safety review of zinc compounds as food ingredients by the Select Committee on GRAS Substances of the Federation of American Societies for Experimental Biology and the data supporting the safety of zinc oxide as a color additive. Based on these data, the agency tentatively concludes that zinc oxide that meets the requirements of § 73.1991 (a)(1) and (b) is safe for use as a substratum in lakes for drug and cosmetic use (Ref. 13).

h. *Talc.* The color additive regulation for talc (§ 73.1550) identifies talc as ''a finely powdered, native, hydrous magnesium silicate sometimes containing a small proportion of aluminum silicate'' and provides specifications. Talc is a color additive exempt from certification for use in coloring drugs generally (§ 73.1550) and is GRAS for certain indirect food uses (§§ 182.70 and 182.90). The USP (23d ed., 1995) defines talc as ''a native, hydrous magnesium silicate, sometimes containing a small proportion of aluminum silicate,'' and provides specifications.

The agency has evaluated the available data relating to the safety of ingested and dermal uses of talc, including a safety review of silicates (including talc) as food ingredients by the Select Committee on GRAS Substances of the Federation of American Societies for Experimental Biology and the data supporting the safety of talc as a color additive. Based on these data, the agency tentatively concludes that talc that meets the requirements of § 73.1550 (a)(1) and (b) is safe for use as a substratum in lakes for drug and cosmetic use (Ref. 13).

i. *Aluminum benzoate.* During the preparation of a lake with aluminum benzoate as a substratum, aluminum benzoate is produced in situ using benzoic acid and the aluminum cation. The Merck Index (11th ed., 1989) identifies aluminum benzoate as $C_{21}H_{15}AlO_6$ or $Al(C_6H_5COO)_3$ with a molecular weight of 390.30. The USP (23d ed., 1995) recognizes aluminum chloride, aluminum sulfate, and benzoic acid (the components used to prepare aluminum benzoate). The USP (23d ed., 1995) defines benzoic acid as ''$C_7H_6O_2$ 122.12; Benzoic acid; Benzoic acid [65–85–0]'' and provides specifications. The U.S.P. (23d ed., 1995) defines aluminum chloride as ''$AlCl_3$ $6H_2O$; Aluminum chloride, hexahydrate; Aluminum chloride hexahydrate [7784–13–6]; Anhydrous 133.34 [7446–70–0]'' and provides specifications. The USP (23d ed., 1995) defines aluminum sulfate as ''$Al_2(SO_4)_3$ xH_2O (anhydrous) 342.16; Sulfuric acid, aluminum salt (3:2), hydrate; Aluminum sulfate (2:3) hydrate [17927–65–0]; Anhydrous 342.16 [10043–01- 3]'' and provides specifications.

The agency has affirmed benzoic acid (§ 184.1021) and sodium benzoate (§ 184.1733) as GRAS for use in food as flavoring agents and adjuvants and as antimicrobial agents. In addition, the standard of identity for margarine (21 CFR 166.110) permits the use of the sodium, potassium, and calcium salts of benzoic acid as preservatives. The agency has also reviewed safety data on the ingested and dermal uses of benzoic acid and benzoates, including a safety review of benzoic acid and benzoates as food ingredients by the Select Committee on GRAS Substances of the Federation of American Societies for Experimental Biology and information identified in a search of the scientific literature published from 1981 to 1987 on benzoic acid and benzoates. The agency's review found no reports of adverse toxicological effects of ingested or topically administered benzoic acid.

The agency's evaluation of the safety of aluminum salts, including aluminum chloride and aluminum sulfate, is discussed in section IV.A.2. of this document under the safety of alumina as a substratum in lakes for food use.

Based on these data, the agency tentatively concludes that aluminum benzoate prepared from benzoic acid and aluminum chloride or aluminum sulfate that meet the USP specifications for these compounds is safe for use as a substratum in lakes for drug and cosmetic use (Ref. 13).

j. *Calcium carbonate.* The color additive regulation for calcium carbonate (§ 73.1070) identifies calcium carbonate as ''a fine, white, synthetically prepared powder consisting essentially of precipitated calcium carbonate ($CaCO_3$).'' Calcium carbonate is listed as a color additive exempt from certification for use in drugs generally (§ 73.1070). Calcium carbonate has also been affirmed as GRAS for general food use (§ 184.1191) and is GRAS for dietary supplement use (§ 182.5191).

The agency has evaluated the available data relating to the safety of ingested and dermal uses of calcium salts, including calcium carbonate. These data, including a safety review of calcium salts as food ingredients by the Select Committee on GRAS Substances of the Federation of American Societies for Experimental Biology and data supporting the safety of calcium carbonate as a color additive, establish that calcium is ubiquitous in nature and

that its salts are commonly found in food. Based on its review, the agency tentatively concludes that calcium carbonate that meets the requirements of § 73.1070 (a)(1) and (b) is safe for use as a substratum in lakes for drug and cosmetic use (Ref. 13).

k. *Rosin.* ''Rosin'' is a generic term encompassing a variety of substances that may vary considerably in their composition. For example, the Merck Index (11th ed., 1989) defines rosin as ''Residue left after distilling off the volatile oil from the oleoresin obtained from'' various species of *Pinus.* Gum rosin is obtained from the oleoresin of living pine trees and wood rosin is extracted from the wood of the stumps of pine trees. Another type of rosin is tall oil rosin, a by-product of the wood pulp industry. The CRC Handbook of Chemical Synonyms and Trade Names (8th ed., 1978) also lists rosin under its synonym 'colophony' and defines it as ''The residue which remains after the volatile oils have been removed by the distillation of crude turpentine.'' The CRC Handbook lists several varieties of rosins obtained from different species of pine.

Rosin is approved as a food additive for use as a natural flavoring substance for alcoholic beverages (§ 172.510). Various rosins and rosin derivatives are approved for other food additive uses: In coatings of fresh citrus fruits (§ 172.210) and as plasticizing materials or softeners in chewing gum base (§ 172.615). Rosin and rosin derivatives are approved as diluents in color additive mixtures for use in inks for marking food supplements in tablet form, gum, confectionery, fruit, and vegetables (§ 73.1(b)) and, by reference, in inks for branding pharmaceutical forms (§ 73.1001(a)(2)). Numerous rosins and rosin derivatives are approved as indirect food additives (substances that are not added to food directly but that may become part of food through migration from materials in contact with the food) (§ 178.3870).

The agency has evaluated the available data relating to the safety of rosin and related compounds, including data supporting the food additive and color additive diluent uses of rosin and rosin derivatives, and data obtained by the agency from searches of the scientific literature in 1988 and 1994 for information concerning rosin. The agency's literature searches did not find any reports of adverse toxicological effects from ingested rosin. However, many publications reported cases of allergic contact dermatitis and occupational asthma resulting from exposure to certain rosin materials (Ref. 13).

In the 1979 NOI, the agency requested information on the chemical composition of rosin and suggestions for specifications to ensure its safe use in lakes for drug and cosmetic use. CTFA's comment on the 1979 NOI provided general information on rosin, but did not identify the specific types of rosin that are used as substrata in lakes. However, the monograph for rosin in the CTFA International Cosmetic Ingredient Dictionary, 5th ed., 1993 defines rosin as ''the residue left after distilling off the volatile oil from the oleoresin obtained from *Pinus palustris* and other species of *Pinaceae* (Ref. 29). Because this definition clearly identifies gum rosin, and not wood rosin or tall oil rosin, the agency tentatively concludes that the rosin used in cosmetic products is gum rosin.

Based on its review of available data (Refs. 29 and 30), the agency has tentatively identified the rosin used as a substratum in lakes for drug and cosmetic use as gum rosin, and is proposing to define and set specifications for rosin based on this tentative conclusion. It is unclear, however, whether all lake manufacturers who use rosin as a substratum are using gum rosin. Therefore, any manufacturer who uses rosin other than gum rosin that meets the requirements in the proposed regulation as a substratum in lakes for drug or cosmetic use should submit information about the identity and specifications of such rosin as a comment on this proposal. The comment should include the manufacturer's product specifications and any analytical data that establish the identity and purity of the rosin. The agency will consider modifying the identity and specifications for rosin if it receives information to substantiate the safe use of rosin other than gum rosin.

In response to the concerns raised by the agency about the topical safety of rosin lakes, the CTFA submitted reports of numerous human sensitization and photosensitization studies on cosmetic products colored with rosinated lakes of D&C Red No. 6, D&C Red No. 7, and D&C Red No. 34. The studies involved a total of 2,381 subjects for sensitization and 312 subjects for photosensitization; products tested included lipsticks, lip liner, blush, rouge, and nail polish. No skin sensitization/photoallergic reactions were reported in any of the test subjects. The agency tentatively concludes that these studies show that there is little risk of developing a skin sensitization reaction from skin contact with various cosmetic products that contain rosinated color additive lakes at levels found in such products, and, therefore, that use of rosin as a substratum in color additive lakes for external drug and cosmetic use is safe (Ref. 14).

3. Precipitants

a. *Aluminum (Al^{+3}), barium (Ba^{+2}), and calcium (Ca^{+2}) cations.* The safety of salts of the cations aluminum, barium, and calcium is discussed in the safety evaluations of alumina (sections IV.A.2. and V.A.2.b. of this document), barium sulfate (blanc fixe) (section V.A.2.c. of this document), and calcium carbonate (section V.A.2.j. of this document). Based on those evaluations, the agency tentatively concludes that these cations are safe as components of precipitants used in the preparation of lakes for drug and cosmetic use (Ref. 13). However, as stated in the discussion of the safety of barium sulfate as a substratum (section V.A.2.c.), the agency is proposing to retain the current specification for soluble barium (0.05 percent) in lakes for drug or cosmetic use.

b. *Zirconium cation (Zr^{+4}).* Zirconium is a rare earth metal that closely resembles aluminum in pharmacological and chemical properties. The agency has evaluated data relating to the safety of ingested and dermal uses of zirconium salts. These data, including a review of published literature on the toxicity, physiological effects, and medicinal uses of zirconium and its salts, revealed nothing to indicate any likelihood of harm from topical administration or ingestion of low levels of zirconium salts (Ref. 13). Therefore, the agency tentatively concludes that zirconium is safe as a component of precipitants used in lakes for drug and cosmetic use.

c. *Sodium (Na^+) and potassium (K^+) cations.* The salts of the sodium and potassium cations, sodium chloride and potassium chloride, are ubiquitous in nature. Sodium chloride (table salt) is GRAS (§ 182.1(a)) and potassium chloride has been affirmed as GRAS for food use (§ 184.1622). Most of the permanently listed water-soluble straight colors subject to certification, including all the straight colors used as components of lakes under § 82.51, are sodium salts. By virtue of their GRAS status, sodium chloride and potassium chloride are permitted under § 73.1(a)(1) for use as diluents in color additive mixtures for coloring food, and under § 73.1001(a)(1) and (b) are also permitted for use as diluents in color additive mixtures for coloring ingested drugs and externally applied drugs. Therefore, the agency tentatively concludes that these salts are safe for

use as components of precipitants in lakes for drug or cosmetic use.

d. *Strontium cation (Sr^{+2}).* Strontium is an alkaline earth element and is a metabolic analog of calcium. The agency has evaluated published data on the safety of strontium cation. Because strontium can substitute for calcium, it can influence certain physiological parameters; however, the concentrations required to adversely affect these parameters are significantly higher than the levels encountered when strontium is used as a precipitant in a lake. Based on its review of the published data, the agency tentatively concludes that the use of strontium cation is safe as a component of precipitants used in lakes for drug and cosmetic use (Ref. 13).

e. *Accompanying anions.* In section IV.A.3.c. of this document, the agency considered the safety of soluble chlorides and sulfates as components of precipitants in lakes for food use. As discussed more fully in that section, chloride and sulfate anions are found in many GRAS ingredients. In the safety reviews conducted as part of the GRAS rulemakings for these ingredients, the agency found that ingestion of chlorides and sulfates (in the presence of the accompanying cation) was safe at levels that vastly exceed the possible level of exposure to these anions as components of lakes. Therefore, the agency tentatively concludes that the presence of these anions in lakes prepared for food use is safe (Ref. 13). Furthermore, by virtue of their GRAS status, the salts of chloride and sulfate are permitted under § 73.1(a)(1) for use as diluents in color additive mixtures for coloring food, and under § 73.1001 (a)(1) and (b) are also permitted for use as diluents in color additive mixtures for coloring ingested drugs and externally applied drugs. Therefore, the agency tentatively concludes that these anions are safe for use as components of precipitants in lakes for drug or cosmetic use.

f. *Tentative conclusions.* The agency tentatively concludes that the water-soluble chloride and sulfate salts of aluminum, barium, calcium, zirconium, sodium, potassium, and strontium are safe for use as components of precipitants in the preparation of lakes for drug or cosmetic use. The agency notes that, although these substances are discussed as distinct chemical compounds, the proposal would permit their use in other forms to prepare lakes, provided that no substance or ion that is not provided for in the regulation is introduced. For example, the proposal would allow the use of a precipitant formed in situ from the combination of a listed cation (as the hydroxide) and either hydrochloric or sulfuric acid.

4. Diluents in Color Additive Mixtures Containing Lakes

The agency is not proposing any limitations on the diluents permitted in color additive mixtures for cosmetic use that are made with lakes. The part 74 listings for the straight colors that are components of lakes for cosmetic use do not limit the use of diluents in mixtures for coloring cosmetics. Moreover, no regulation in part 73 specifies safe diluents for cosmetic use. However, the agency notes that cosmetic products containing color additive mixtures are subject to the adulteration provisions of section 601 of the act.

B. Specifications for Lakes for Use in Drugs and Cosmetics

1. Intermediates and Other Impurities Derived from Straight Colors

The provisional listing regulations for lakes for drug or cosmetic use (§§ 82.1051 and 82.2051) contain specifications for ether extracts (not more than 0.5 percent) and intermediates (not more than 0.2 percent) in such lakes. The agency established these specifications to limit the levels of intermediates and other impurities in lakes prepared from uncertified batches of straight colors. However, as discussed in section IV.A.1.b. of this document, proven methodology to analyze all lakes for intermediates and other impurities is not available. Therefore, the agency is proposing to require the use of certified batches of straight colors to ensure safe levels of intermediates and other impurities in lakes. In light of this proposed requirement, the agency tentatively concludes that specifications for ether extracts, intermediates, and subsidiary colors in lakes for drug or cosmetic use are unnecessary to ensure the safety of such lakes.

2. Precipitants

Because lakes are washed when prepared in accordance with CGMP, the agency anticipates that only low levels of water-soluble contaminants from these precipitants will remain in the finished lake. Furthermore, the proposed specifications for the lake would limit the levels of contaminants of toxicological concern (primarily heavy metals) permitted in the end product. However, the agency tentatively concluded in its discussion of barium sulfate as a substratum (section V.A.2.c. of this document) and barium as a precipitant (section V.A.3.a. of this document) that a specification to limit soluble barium in lakes for drug or cosmetic use should be retained to provide an extra margin of safety. Based on these considerations, the agency tentatively concludes that specifications for residues from precipitants used in lakes for drug or cosmetic use, except for soluble barium, are unnecessary.

3. Heavy Metals

As discussed in section IV.B.2. of this document, the manufacturing processes for lakes involve reagents that are sources of potential contamination by metals. Currently, lakes are subject to the following general specifications in § 82.5 for provisionally listed colors for drug or cosmetic use: 20 ppm lead, 2 ppm arsenic, 0.003 percent total heavy metals (except for lead and arsenic), and, for those colors that contain a barium salt, a limit of 0.05 percent on soluble barium. As discussed in section IV.B.2. of this document, FDA is proposing limits for lead, arsenic, and mercury in lakes for food use. The agency tentatively concludes that specifications to limit the levels of lead, arsenic, mercury, and soluble barium are also necessary to ensure safe use of lakes in drugs and cosmetics. The agency is unaware of any other heavy metals that have a significant level of toxicity and that would be expected to occur in lakes. Therefore, the agency tentatively concludes that a general heavy metal specification is unnecessary to ensure the safety of lakes for drug or cosmetic use.

The agency is proposing to maintain the specifications of not more than 20 ppm lead and 0.05 percent soluble barium for lakes for drug or cosmetic use and to raise the arsenic specification from not more than 2 ppm to not more than 3 ppm. The agency is also proposing to include a mercury specification of not more than 1 ppm. The proposed levels for arsenic and mercury are the levels that the agency tentatively concludes are necessary to ensure the safety of color additives used in drugs and cosmetics, based on safety evaluations in rulemakings for the permanent listing of numerous straight colors.

4. Soluble Chlorides and Sulfates

Current §§ 82.1051 and 82.2051 contain a specification that limits the content of the soluble chloride and sulfate anions in lakes for drug and cosmetic use. As noted in section IV.B.3. of this document, most of the water-soluble chloride and sulfate anions are washed out during preparation of the lake under CGMP conditions. In its safety review, the agency found that these anions are safe in foods, drugs, and cosmetics at levels considerably greater than those found in lakes (Ref. 13). Therefore, the agency

tentatively concludes that a specification to limit the levels of soluble chlorides and sulfates is unnecessary to ensure the safety of lakes prepared in conformity with CGMP for drug or cosmetic use.

5. Other Residues

The 1979 NOI requested information on certain other chemicals occasionally used in the laking process, such as citrate, acetate, and surfactants. CTFA's comment did not provide a list of such substances, but stated that the substances used were GRAS. A comment from a color manufacturer identified specific substances that the company uses in the manufacture of lakes and characterized them as food additives or GRAS substances. The company stated that the surfactants were used at very low concentrations and that the nature of the use prevented any significant amount from being present in the final lake.

The agency recognizes that it is impracticable to set specifications for every chemical used in the manufacture of a color additive. The agency generally sets specifications to limit the substances that are normally expected to be present in the final additive, especially those substances that could present a safety hazard at foreseeable levels of exposure. The agency agrees with the comment that the surfactants and other chemicals mentioned are used at low concentrations. The agency further agrees that, because of the washing of lakes during manufacture, these chemicals are unlikely to be present at significant levels in a lake that has been prepared under conditions of CGMP and that is otherwise in compliance with applicable regulations. Therefore, the agency is not proposing specifications for residues of these substances in lakes for drug and cosmetic use.

6. Other Impurities and Contaminants

The agency has tentatively concluded above that specifications to limit the levels of total heavy metals (except lead, arsenic, mercury, and soluble barium), soluble chlorides and sulfates, and residues of other chemicals are unnecessary to ensure the safety of lakes for drug and cosmetic use, as long as a general provision is included in the specifications for lakes to ensure that they are prepared in conformity with CGMP. Therefore, the agency is proposing to continue the requirement in existing § 82.5 that lakes be free from all impurities other than those named in the specifications, to the extent that such impurities can be avoided by CGMP.

C. Certification Requirement

As discussed in section IV.C. of this document, the agency has evaluated the necessity for the certification of lakes and has tentatively concluded that certification is necessary to protect the public health. The simplified procedure the agency is proposing for certification of lakes is described in section VI.B. of this document.

D. Provisions of Proposed Regulations

1. Proposed Section 74.1050 Lakes for Use in Drugs

The agency is proposing a new § 74.1050 to list lakes permanently for use in drugs as color additives subject to certification. Paragraphs (a)(1), (a)(2), and (a)(3) would designate the components permitted for use in preparing lakes for coloring drugs. These paragraphs would permit the use of one or more certified batches of one or more of the color additives FD&C Blue No. 1, FD&C Blue No. 2, FD&C Green No. 3, FD&C Yellow No. 5, FD&C Yellow No. 6, FD&C Red No. 4, FD&C Red No. 40, D&C Blue No. 4, D&C Orange No. 4, D&C Orange No. 5, D&C Orange No. 10, D&C Red No. 6, D&C Red No. 7, D&C Red No. 21, D&C Red No. 22, D&C Red No. 27, D&C Red No. 28, D&C Red No. 31, D&C Red No. 33, D&C Red No. 34, and D&C Yellow No. 10 (see Table 1); one or more of the substrata alumina, aluminum benzoate, barium sulfate, calcium carbonate, kaolin, rosin, talc, titanium dioxide, and zinc oxide; and one or more precipitants that form the cation aluminum (Al^{+3}), barium (Ba^{+2}), calcium (Ca^{+2}), potassium (K^{+}), sodium (Na^{+}), strontium (Sr^{+2}), or zirconium (Zr^{+4}), and the anion chloride (Cl^{-}) or sulfate (So^{4-2}). Paragraph (a)(3) would require that the substrata (except alumina), or for aluminum benzoate, the components of the substrata, conform to the identity and purity requirements of the applicable color additive regulation or, if no such regulation exists, to the requirements of the USP 23d ed. (1995). The paragraph would require that alumina conform to the requirements of § 74.50(a)(3).

Proposed § 74.1050(a)(4) would limit the diluents used in color additive mixtures containing lakes to those diluents that are suitable and that are listed in § 73.1001 as diluents for drug use. This requirement is consistent with the existing requirements for mixtures of color additives for drug use and will ensure that color additive mixtures containing lakes are safe for drug use. As discussed in section III.C.2.b. of this document, the agency is proposing to amend § 73.1001 to permit additional diluents in color additive mixtures for drug use.

Proposed § 74.1050(b) would prescribe the following specifications for lakes for drug use: lead (not more than 20 ppm); arsenic (not more than 3 ppm); mercury (not more than 1 ppm); soluble barium (not more than 0.05 percent). It would also state that such lakes shall be free from impurities other than those named in the specifications, to the extent that such impurities may be avoided by CGMP.

Proposed § 74.1050(c)(1) would restrict the use of a lake to uses common to all of the straight colors in the lake. For example, use of a lake of the straight colors FD&C Red No. 4 and FD&C Blue No. 1 would be limited to externally applied drugs and cosmetics because of the limitations on the use of FD&C Red No. 4. Proposed § 74.1050(c)(2) would also specify that where regulations for the straight color impose quantitative limitations for the use of such straight color in drug products, the amount of such straight color in a lake shall be considered as a part of the total amount of such straight color permitted in a drug product.

Proposed § 74.1050(d) would identify each lake made as prescribed in § 74.1050(a) as a listed color and would prescribe the formation of its name from the names of the straight colors present in the lake (in descending order of predominance), followed by the names of the cations of the precipitants, and followed by the words ''Lake on _____ and _____'' (inserting the listed names of the substrata in descending order of predominance). For example, the name of a lake prepared by the extension of FD&C Yellow No. 5, FD&C Yellow No. 6 and D&C Orange No. 5 on alumina using aluminum chloride as the precipitant would be ''FD&C Yellow No. 5, FD&C Yellow No. 6 and D&C Orange No. 5 Aluminum Lake on Alumina''. The anion component of the precipitant would not be included in the name of the lake because this anion is removed during processing and is not a component of the finished lake.

Proposed § 74.1050(e)(1) would require that the label of the lake and of any mixtures prepared from it for coloring purposes conform to the requirements of § 70.25 of this chapter. Proposed § 74.1050(e)(2) would require that drug products that contain a lake of FD&C Yellow No. 5 comply with the label declaration requirements of § 74.1705(c)(2) and (c)(3). Proposed § 74.1050(e)(3) would require that drug products that contain a lake of FD&C Yellow No. 6 comply with the label declaration requirements of proposed § 74.1706(c)(2). These proposed labeling

provisions are discussed more fully in sections VI.C.2. and VI.C.3. of this document.

Proposed § 74.1050(f) would require that all batches of lakes be certified in accordance with proposed regulations in part 80.

2. Proposed § 74.2050 Lakes for Use in Cosmetics

The agency is proposing new § 74.2050 to list lakes permanently for use in cosmetics as color additives subject to certification. Proposed paragraph (a) would identify the components permitted for use in preparing lakes for coloring cosmetics by incorporating the identity provisions proposed in § 74.1050(a)(1), (a)(2), and (a)(3) for lakes for use in drugs, except that FD&C Blue No. 2 would not be permitted as a straight-color component in lakes for cosmetic use. Proposed § 74.2050(a) also would incorporate the specifications in proposed § 74.1050(b).

Proposed § 74.2050(b) would prescribe the same uses and restrictions for lakes for cosmetic use as proposed for lakes for drug use in § 74.1050(c).

Proposed § 74.2050(c) would identify each lake made as prescribed in § 74.2050(a) as a listed color and would prescribe the formation of its name in the same manner as proposed in § 74.1050(d).

Proposed § 74.2050(d)(1) would require that the label of the lake and of any mixtures prepared from it for coloring purposes conform to the requirements of § 70.25. Proposed § 74.2050(d)(2) would require the ingredient labeling of lakes in cosmetic products to comply with proposed § 701.3(c)(1)(i). These proposed labeling provisions are discussed more fully in sections VI.C.2. and VI.C.3. of this document.

Proposed § 74.2050(e) would require that all batches of lakes be certified in accordance with proposed regulations in part 80.

VI. Other Proposed Actions

A. Removal of Provisional Listings

1. Removal of 21 CFR Part 81

The agency is proposing to remove Part 81 *General Specifications and General Restrictions for Provisional Color Additives for Use in Foods, Drugs, and Cosmetics.* This part was originally issued in 1960 (25 FR 9759, October 12, 1960) to provide for the listing of commercially established color additives permitted for provisional use under the transitional provisions of the 1960 amendments, and to establish conditions for the continued provisional listing of these color additives pending completion of studies required to establish their safety for permanent listing.

Currently, only lakes are listed in § 81.1 *Provisional lists of color additives.* The final rule based on this proposal will remove these entries. When the final rule becomes effective, the section will no longer be necessary. The remaining three sections, § 81.10 *Termination of provisional listings of color additives;* § 81.30 *Cancellation of certificates;* and § 81.32 *Limitations of certificates,* concern past agency actions on provisionally listed color additives and are purely of historical interest, as the color additives referred to in these sections are no longer permitted for use in FDA-regulated products. In addition, after FDA completes action on this proposal and the final rule terminating all provisional color additive listings becomes effective, no further additions to part 81 will be possible. Therefore, the agency is proposing to remove the entire part.

2. Removal of 21 CFR Part 82

The agency is proposing to remove Part 82—*Listing of Certified Provisionally Listed Colors and Specifications.* The purpose of this part was to prescribe the identity, specifications, and uses of provisionally listed color additives. Currently, the regulations in this part apply only to lakes. When the final rule resulting from this proposal becomes effective, all remaining provisional listings in part 82 will terminate. Therefore, the agency is proposing to remove the entire part.

B. Certification Procedure for Lakes

1. Overview

The current requirements and procedures for batch certification of lakes are described in part 80. Under the provisions of § 80.21, a firm that has prepared or repacked a batch of lake submits a request for certification of the batch to FDA. The request provides the name, batch number, and batch weight of the lake or repack; information on storage pending certification; and the uses for which certification is requested. For a newly manufactured batch of lake, the request also provides the name, quantity, and (where applicable) the lot number of the straight color used, the identity of the precipitant used, the identity and quantity of the substratum used, and the identity (name and address) of the manufacturer of the lake. For a repack of a certified batch of lake, the request provides the original lot number, certified color content, and name and address of the source from which the repacker obtained the lake. (See section III.A.7. of this document for the proposed definition of ''repack.'') The request must be accompanied by the required certification fee, which varies according to the type of request and weight of the batch (§ 80.10), and a representative sample from the batch accompanied by any label or labeling intended for use with the batch (§ 80.22).

The agency evaluates the request and analyzes the sample to ensure that they meet the requirements of part 82, including identity, specifications, and uses of the lake. After evaluation of the information in the request and laboratory analysis of the sample, the agency determines whether the request meets the requirements for certification. For those requests that meet these requirements, the agency issues the requester a certificate (§ 80.31). The certificate states the name of the requester, the name of the color additive, the FDA certification lot number, the uses and restrictions that apply to the color additive, and the results of the agency's analyses of the batch. Upon receipt of the certificate, the requester then labels the batch with the certification lot number, the percent total color, uses and restrictions, and other labeling as required in § 70.25. The requester is also required to maintain the batch, both before and after certification, under conditions that ensure that the composition of the batch does not change and that the sample submitted to FDA for certification remains representative of the batch until the batch has been packaged and labeled as required by §§ 70.20 and 70.25 (§§ 80.37 and 80.38). The person to whom the certificate is issued is required to keep complete records showing the disposal of all color additive from the batch covered by the certificate until at least 2 years after disposal of the batch (§ 80.39).

The requirement for certification of lakes and repacks ensures that the agency can identify each firm that manufactures or repacks a lake. Under its inspectional authority, the agency can then inspect these establishments and determine compliance with labeling and storage requirements and verify the disposal of the batch. The regulations enable the agency to ensure the continued safety of lakes and other color additives after certification by establishing conditions (§ 80.32) under which a certificate will expire and the batch will be deemed to be uncertified. In addition, the agency can refuse certification service (§ 80.34) to firms that submit requests for certification but fail to comply with requirements designed to ensure the safety of certified

color additives, including recordkeeping and allowing inspection of the firm's color additive inventory and records.

This batch certification procedure provides the agency with an integrated system for ensuring the safety of lakes for use in foods, drugs, and cosmetics. For each batch of lake certified, the agency maintains, as records, the original request for certification and a copy of the certificate for the batch, which includes the results of agency analysis of the representative sample. The agency's analysis of the representative sample includes tests for total color, heavy metals, and impurities derived from the straight color used to prepare the lake.

As discussed in section IV.C. of this document, the agency has tentatively concluded that many requirements of the current batch certification system are necessary to ensure that lakes are safe for use in foods, drugs, and cosmetics, and thus to protect the public health. However, the agency also tentatively concludes that FDA analysis of a representative sample of the batch is not necessary in light of the other requirements for lakes being proposed. Therefore, the agency is proposing to establish a simplified procedure in § 80.31(b) for certification of batches of lakes and lake repacks. The agency notes that both new batches of lakes and repacks of previously certified batches of lakes would be subject to the new procedure. In subsequent discussion of the proposed certification requirements for lakes, the agency will address requirements for lakes generically and will distinguish between new batches and repacks only when it is necessary to identify specific requirements relating to only one type of batch. In the remainder of this document, the term ''batch of lake'' should be understood to encompass both new batches and repacks.

Under the proposed procedure, certification of a batch of lake would rely on the certificates for the batches of straight colors that are used in the lake, either directly to prepare the lake or indirectly as components of a certified batch of lake that is blended into the new batch. The certification of the batch would also rely on representations by the manufacturer or repacker that the batch complies with the requirements of parts 74 and 80.

The proposed procedure would require that a batch of lake meet the requirements of the proposed listing regulation for the lake in part 74, that the manufacturer of the lake be the same firm that was issued the certificates for all batches of straight color in the batch of lake, and that the firm complete the requirements of proposed § 80.33 for notifying the agency of the firm's claim to certification for the batch. The proposed procedure would also require that the firm submitting the notice maintain records of the composition and disposal of the batch, including the certificates for the straight colors used to make the batch. Repackers would be required to retain proof that the original batch of lake was certified, in lieu of the certificates for the batches of straight color used to prepare the lake. The manufacturer or repacker would also be required to retain a representative sample of the batch.

This proposed procedure would provide for routine agency review of only the information necessary to ensure the use of certified batches of straight color and to verify that the straight color in the lake did not degrade significantly during the laking process. Under this proposed procedure, the agency would not routinely monitor compliance with the remaining requirements for the preparation and repacking of lakes under the regulations in part 74. However, as noted above, the certification of a batch of lake would be based both on the agency's review of the critical factors in lake manufacturing and repacking and on the manufacturer's and repacker's representations of compliance with the remaining requirements. The agency would be able to verify these representations by inspecting the manufacturer's or repacker's records, and violations of the requirements for certification would be addressed under proposed §§ 80.32 and 80.34.

Under the proposed procedure, a manufacturer or repacker of a batch of lake would submit to FDA a notice claiming certification for the batch and providing the information and fee specified in proposed §§ 80.10(c) and 80.33. The notice would provide the same information about the batch that is currently provided in a request for certification under § 80.21(j), or generated by the agency as part of its evaluation of the certification request. However, the person submitting the notice would not be required to submit a representative sample of the batch for analysis by the agency. The agency would review the notice and, if the information in the notice was complete and appeared to comply with the requirements of parts 74 and 80, would issue an acceptance of the notice. Upon FDA's issuance of its acceptance of the notice, the batch covered by the notice would be a certified batch.

As noted above, the proposed certification procedure for batches of lakes and certified lake repacks would not require submission of a representative sample for agency analysis. Instead, the proposed new procedure would require that the manufacturer or repacker of the batch provide certain analyses and maintain certain records for agency inspection. Under the proposed procedure, the agency also would not issue a certificate for the batch. As noted above, the proposed certification procedure would rely on the certificates issued by the agency for the straight-color components of batches of lake and the representations of the manufacturer or repacker about the composition of the batch. Under this proposed procedure, certification of a batch of lake would be complete upon the agency's acceptance of the firm's notice claiming certification. This notice would provide information that would allow the agency to identify the certificates for the straight colors on which the certification of the lake relies and to ensure that the batch otherwise complies with the requirements of parts 74 and 80.

The agency is proposing to continue the application of the current storage and labeling requirements for batches pending certification and after certification (§§ 80.37 and 80.38) to batches of lakes certified under the proposed new procedure.

Amended § 80.39 would continue the application of the current recordkeeping requirements for certified color additives to lakes, including repacks, and would add recordkeeping requirements for lakes only to support the information and affirmations contained in the firm's notice to FDA.

Amended § 80.32 would provide for conditions under which the certification of a batch of lake would expire, and would add a provision to allow a certified color additive, including a lake, to be used in a batch of lake without losing its certification.

Amended § 80.34 would continue the agency's authority to refuse certification service to manufacturers and repackers of lakes who falsify records, obtain certification by fraud, or otherwise abuse the certification system.

The proposed certification procedure would provide a simplified system for assuring the safety of a certified batch of lake. For the reasons discussed in section VI.B.2.b. of this document, preparation of a lake would be limited to the firm issued the certificates for the straight colors used in the batch of lake. For each certified batch of lake, the agency would retain the original notice claiming certification for the batch and a copy of its response to the notice. The notice for each new certified batch of lake would contain the lot numbers for

the batches of straight colors used to prepare the batch of lake. This information would allow the agency to ensure that the batch of lake meets the requirements in part 74. The proposed requirement for submission of a premarket notice claiming certification would ensure that the agency could identify every firm that prepares or repacks certified batches of lakes. Under its inspectional authority, the agency could then inspect these establishments and their records to ensure compliance with the composition requirements of part 74 and the certification requirements of part 80, including the recordkeeping requirements of amended § 80.39. As part of a typical inspection, the agency might look at the facility, verify the records of the disposal of the batch, and check compliance with storage and labeling requirements.

The current batch certification procedure for lakes does not provide for certification of mixtures containing lakes. Color additive mixtures containing lakes are exempted from certification under § 80.35(b), subject to the conditions in that regulation. The agency is proposing to retain this exemption.

2. Certification Requirements

a. *Current provisions for batch certification.* The current requirements for batch certification of color additives in § 80.31 include references to parts 81 and 82. As discussed in section VI.A. of this document, the agency is proposing to delete parts 81 and 82 in this rulemaking. Therefore, the agency is proposing to amend § 80.31 to delete all references to parts 81 and 82.

Currently, § 80.31(a)(2) requires that a certified color additive conform to specifications and other conditions in parts 81 and 82. The section does not make any reference to specifications and other conditions in part 74, however. Because it appears that this omission was an oversight, the agency is proposing to amend § 80.31(a)(2) to add a reference to part 74. This action will clarify that permanently listed straight colors are subject, as a condition of certification, to the specifications and other conditions in part 74 of this chapter.

Currently, § 80.31(b) specifies the conditions under which the agency shall refuse to certify a batch and the procedures for contesting such refusal. The agency is proposing to modify this paragraph to cover the proposed changes in the procedure for certification of lakes. The agency is also proposing to redesignate this paragraph as paragraph (c) to allow the addition of the proposed new procedure in new paragraph (b).

b. *Proposed certification provisions for lakes.* The agency is proposing to add new § 80.31(b) to specify the conditions under which a batch of lake or certified lake repack is a certified batch. Proposed § 80.31(b) would require that a certified batch of lake or certified lake repack meet the specifications and any other conditions set forth in part 74 of this chapter. The agency tentatively concludes that this is an essential condition for certification because proposed §§ 74.50, 74.1050, and 74.2050 specify the conditions under which lakes are safe for use in foods, drugs, and cosmetics.

Proposed § 80.31(b) would also require, as a condition of certification for a batch of lake, that the firm preparing the batch be the same firm that was issued the certificate for each batch of straight color used in the lake. The agency tentatively concludes that this provision is a necessary condition for certification because, under the proposed procedure, certification of a batch of lake relies on the certificates issued for the batches of straight colors that were used to prepare the lake.

Under the proposed procedure, the agency would not issue a separate certificate for the batch of lake. Instead, the certificates for the straight colors in the lake would remain in effect provided that the lake was prepared in accordance with the regulations in part 74, including the requirement of preparation under conditions of CGMP such that the straight color does not significantly degrade. The agency recognizes that during the preparation of a lake, some change in the composition of the straight color inevitably occurs because the color goes from a water-soluble form in the straight color to a water-insoluble form in the lake. However, it is the responsibility of the manufacturer of the lake to prevent avoidable changes in the composition of the straight color so that the certificates for all straight colors used in the lake remain valid. The agency tentatively concludes that the responsibility for assuring the validity of the certificates of the straight colors in a lake should be retained by the firm issued the certificates.

The agency notes that a repacker of a certified lake would not be the same firm that was issued the certificates for the straight-color components of the lake. However, the handling of a lake during repacking is significantly less than during the preparation of the lake because no reprocessing occurs and no chemical reaction takes place; thus, the potential for change in composition is much less. Furthermore, a repack is derived from a single batch of lake, and the agency would keep on file all notices claiming certification for a batch of lake under § 80.31(b) and all agency acceptances of such notices. Therefore, the agency would have the necessary information on the certification of the original batch of lake to compare to the information submitted in a notice claiming certification for a repack of the batch.

Proposed § 80.31(b) would require that a firm that prepares or repacks a batch of lake comply with the notification requirements of § 80.33 as a condition of certification. Proposed § 80.33 would require that the firm submit and obtain FDA acceptance of a notice claiming certification of the batch. The proposed notice would provide FDA with the same information, except for the representative sample of the batch, that is currently provided by the request for certification of a batch of lake or generated by the agency when it analyzes the sample and evaluates the request for certification.

Proposed § 80.31(b) would also require that a firm that prepares or repacks a batch of lake comply with the recordkeeping requirements of § 80.39 as a condition of certification. Currently, § 80.39 requires that the person issued a certificate for a batch of color additive maintain records showing the disposal of all the color additive from the batch covered by the certificate. This section also specifies the types of records required to be kept and the required length of time for keeping the records, as well as requiring that such records be made available to agency representatives. This section further provides the agency access to check the correctness of the records. The agency is proposing to maintain the current recordkeeping requirements for lakes. The agency is also proposing to amend § 80.39 to require additional records that would apply to lakes only. These additional records would allow the agency to verify the information provided in the notice claiming certification. The proposed new recordkeeping requirements are essential to the success of the simplified certification procedure for lakes, as they would provide the means for the agency to verify that a batch of lake has been prepared, repacked, and maintained in compliance with safety requirements, and to trace any batches that are found to have problems.

The agency would review the notice claiming certification and, if the batch of lake covered by the notice appeared to comply with these requirements and the notice appeared to contain no

untrue statement of a material fact, would issue an acceptance of the notice. Upon issuance of the acceptance, the batch covered by the notice, subject to the terms, conditions and restrictions prescribed in part 74, would be a certified batch.

3. Notification Requirements

a. *General requirements.* An essential component of the agency's proposed certification procedure for lakes is the proposed requirement that a firm claiming certification for a batch of lake comply with the notification requirements in § 80.33. The proposed notice would be the primary vehicle for providing the agency with the information needed to verify that the batch is safe for use in foods, drugs, and cosmetics.

Proposed § 80.33 (a), (b), (c), and (d) would require that a notice claiming certification for a batch of lake be addressed to the Commissioner of Food and Drugs, be prepared in the format specified in § 80.33(i), be submitted in duplicate, and be signed by a responsible officer of the company (or, for a foreign manufacturer or repacker, by a responsible officer of the firm and by an agent of the firm who resides in the United States). Except for the format of the notice, these requirements are identical to the requirements for a request for certification of a batch of lake or repack under § 80.21.

Proposed § 80.33(e) would require that a notice claiming certification for a batch of lake show the name and address of the firm submitting the notice. This information is needed to issue a response to the notice and also to identify the location of the batch and the records supporting the notice.

Like existing § 80.21(f), proposed § 80.33(f) would require that the notice be accompanied by the fee prescribed in § 80.10 unless the firm has advanced a deposit to be used for prepayment of such fees. Currently, the fee for certification of lakes and lake repacks is based on the poundage of the color additive, with a minimum fee of $192.00 for a batch of lake and $30.00 for a repack. Under proposed § 80.10(c), the fee for a notice claiming certification for a batch of lake or lake repack would be $30.00 regardless of the size of the batch. This proposed fee is based on the agency's estimate that reviewing and responding to a notice claiming certification would require approximately 1 hour. The agency estimates that average total personnel costs for these activities would be approximately $25.00 per notice with an additional $5.00 per notice for recordkeeping and other overhead costs. The agency is proposing a flat fee rather than a fee based on the poundage of lake certified because the manufacturer of a lake has already paid a fee based on poundage for the certification of the straight colors used in the lake. The agency estimates that the resources required for the administrative handling, review, and response to a notice claiming certification for a new batch of lake or a lake repack would be essentially the same. Therefore, the agency is proposing the same fee for both types of notices.

Proposed § 80.33(g) would require that a copy of the label or labeling intended to be used with the batch accompany the notice. This proposed requirement is comparable to the current requirement (§ 80.22(c)(5)) that the sample submitted with the request for certification be accompanied by a copy of the label or labeling intended to be used with the batch. The agency notes, however, that under proposed § 80.33, no sample would be submitted with the notice.

Proposed § 80.33(h) would state that the name of the lake is derived as prescribed in part 74. This proposed provision is comparable to § 80.21(h), which cross-references the regulations that prescribe the naming of straight colors, mixtures, and repacks.

Under proposed § 80.33(j), the agency would respond to the notice claiming certification for a batch of lake within 5 working days of receipt. The agency's response would either accept or reject the notice, as discussed in section VI.B.3.d. of this document.

b. *Requirements for new batches of lakes.* Proposed § 80.33(i)(1) would prescribe the format and content of a notice claiming certification for a newly prepared batch of lake. The notice would be required to contain the name of the lake, as prescribed in §§ 74.50, 74.1050, or 74.2050; the batch number (manufacturer's number); the weight of the batch; conditions of storage pending certification; and proposed uses. This information is comparable to that currently required for an application for certification of a lake under § 80.21(j)(2).

Proposed § 80.33(i)(1) would also require that the notice state the total color content of the batch and the color content (as a percent of the batch) for each straight-color component of the lake. The total color content of a lake is essential to the identity of the lake, and necessary for the user of a lake to determine product formulation requirements and to ensure compliance with any quantitative limitations on the use of the straight-color component of a lake. Currently, in its routine certification analysis of the representative sample, the agency determines the total color content of a lake. This information is an essential part of the basis for the certificate issued by the agency. Under the proposed simplified certification procedure for lakes, the agency would not analyze a sample of the batch and determine the total color content. Rather, the manufacturer would provide this information in the notice, based on its analysis of the lake. These analyses would be part of the records that the manufacturer would be required to maintain for the batch of lake.

Proposed § 80.33(i)(1) would also require the notice to contain the following information for the components of the lake: the name, quantity used, and certification lot number of each batch of straight color used in the preparation of the lake; the name and quantity used of each precipitant or substratum ingredient in the lake, including the source of the chloride or sulfate anion; and, for each certified batch of lake blended into the batch, the name, quantity used, and certification lot number or FDA acceptance number (the number assigned to FDA's acceptance of the notice claiming certification). This information is comparable to that currently required for an application for certification of a lake under § 80.21(j)(2). Although § 80.21(j)(2) does not currently require information on certified batches of lakes that are blended into a new batch of lake, such information is important for describing the composition of a batch of lake and reflects a practice that is common in the industry. Such information is routinely included in current requests for certification of lakes under § 80.21.

In evaluating requests it has received for certification of batches of lakes, the agency has noted that, although the regulations for lakes in part 82 specify precipitants and substrata as distinct functional entities, the functions of ingredients that are added to the lake preparation for these purposes may overlap. Also, in some instances, acid is added to make a component water-soluble so that it can function as a precipitant in the laking process. Under proposed § 80.33(i)(1), the required information on ingredients of the lake in the notice claiming certification would encompass all ingredients that are either identified in §§ 74.50(a), 74.1050(a), or 74.2050(a) as components of lakes, or are added to form these components of lakes in situ. This information, together with the name of the lake, would provide the agency with the necessary information on the components of the lake and the ingredients used to form

these components in the preparation of the lake.

Proposed § 80.33(i)(1) would also require statements affirming that the batch meets the requirements of 21 CFR parts 74 and 80; that the records required by § 80.39, including a representative sample of the batch, are available for inspection by FDA; and that the firm submitting the notice is the manufacturer of the batch. These proposed affirmations are necessary to ensure that the batch of lake meets all the requirements of proposed § 80.31(b) and, therefore, that the batch is safe for use in foods, drugs, or cosmetics.

As discussed in section VI.B.1. of this document, the agency is proposing to provide for the certification of batches of lakes based on its review of the critical factors in lake manufacture and on the manufacturer's representations that the remaining requirements have been met. Under this proposed procedure, the agency would not routinely verify compliance with every requirement for the preparation and repacking of lakes in part 74; therefore, affirmations of compliance with these requirements from the manufacturer of each batch are necessary as a condition of certification.

c. *Requirements for repacks of certified lakes.* Proposed § 80.33(i)(2) would prescribe the format and content of a notice claiming certification for a repack of a previously certified batch of lake. The notice would be required to contain the name of the lake, as prescribed in proposed §§ 74.50, 74.1050, or 74.2050, and the following information for the original certified batch of lake that was repacked: FDA acceptance number for the manufacturer's notice claiming certification (or the certification lot number, if the batch was certified under the old procedure); total color content of the batch; color content for each straight color in the batch; and the manufacturer's name and place of business. Proposed § 80.33(i)(2) would also require the following information about the repacked batch of lake: The batch number, weight of batch, total color content, and the color content of each straight color in the batch, as well as conditions of storage pending certification and proposed uses. This information is comparable to that currently required for an application for certification of a repack under § 80.21(j)(3).

Proposed § 80.33(i)(2) would also require statements affirming that the batch meets the requirements of 21 CFR parts 74 and 80; that the records required by § 80.39, including a representative sample of the batch, are available for inspection by FDA; and that the firm submitting the notice is the repacker of the batch.

d. *Agency action on the notice.* Under proposed § 80.33(j), the agency would furnish a response to each notifier within 5 working days of receipt of the notice. The agency would review the notice and, if the information in the notice was complete and appeared to comply with the requirements of parts 74 and 80, would issue an acceptance of the notice. Upon issuance of the acceptance, the batch would be a certified batch. To facilitate identification of the batch, the acceptance document would be assigned a number.

If the information in the notice claiming certification was incomplete or did not appear to comply with the requirements of parts 74 and 80, the agency would issue a rejection of the notice. Proposed § 80.33(j)(2) would state that a batch of lake covered by a rejected notice has not complied with the requirements of § 80.31(b) and is not a certified batch. The proposed procedure would not provide for interim responses by the agency or for amendment of a notice by the submitter. The agency recognizes that a rejection of a notice may result from an oversight on the part of the submitter, such as the inadvertent omission of required information. If the deficiency in the notice was such that it could be corrected, the firm could submit a new notice that contained all the required information or otherwise corrected the deficiency. However, the resubmission would be considered a new notice. In addition, under proposed § 80.31(c), the notifier would also have the option to request a hearing on the rejection.

4. Recordkeeping Requirements

The current recordkeeping requirements for certified color additives are found in § 80.39 *Records of distribution.* This section requires that the person to whom a certificate is issued keep complete records showing the disposal of all the color additive from the batch covered by such certificate. The section also specifies the length of time the records must be kept (2 years after disposal of the batch) and permits FDA access to the facility to check the accuracy of these records. It also specifies that these records must be kept separately from all other records. The agency is proposing to maintain these recordkeeping requirements for certified batches of lakes by modifying the language of § 80.39 to conform to the proposed changes in the certification procedure for lakes.

The agency is also proposing to require in § 80.39(b) that a firm submitting a notice claiming certification for a batch of lake keep additional records that confirm the information submitted in the notice. Under proposed § 80.39(b)(1), a manufacturer or repacker of a batch of lake certified under § 80.31(b) would be required to retain records of all documents that the firm relied upon to establish the certified status of the batch of lake. For the manufacturer of a lake, such documents would include copies of the notice submitted to FDA claiming certification for the batch of lake, the FDA acceptance of the notice, the certificate for each batch of straight color used to prepare the batch of lake, the FDA acceptance (or, for batches certified before the effective date of this final rule, the certificate) for each batch of lake used as an ingredient in the batch of lake, and the manufacturer's specifications for the substrata used to prepare the batch of lake. For the repacker of a lake, such documents would include copies of the notice submitted to FDA claiming certification for the batch of lake, and the FDA acceptance of the notice.

These records would also include complete reports of any chemical analyses performed on the batch or its components, including records of analyses that show the total color content of the batch as a percentage and, if the batch contains more than one straight color, the color content of each straight-color component of the batch of lake. As noted above in section VI.B.3.b. of this document, an accurate statement of total color content is essential for identification and proper use of a lake. Complete records of the analyses would include a method description in sufficient detail to allow the analysis to be repeated, the experimental data, the final results and a clear description or calculations that show how the final results were obtained from the experimental data. The agency tentatively concludes that complete records of the analyses for total color in a batch of lake are necessary to allow the agency to verify the accuracy of the identity of the lake.

For new batches of lakes, proposed § 80.39 would require that, for each batch of lake that contains a barium salt, as permitted under §§ 74.1050 and 74.2050, the manufacturer maintain complete records of the analyses that show that the batch of lake conforms to the specification for soluble barium. Barium is a heavy metal whose safety in lakes is based on its insolubility (see section V.A.2.c. of this document). In lakes containing barium salts, soluble

barium is either deliberately introduced as a precipitant, or could form under the conditions of laking. Therefore, the agency tentatively concludes that analysis of the batch for soluble barium is necessary to ensure the safety of lakes that contain barium salts.

For new batches of lakes, the agency is proposing that the records for the batch would also include the manufacturer's specifications for substratum and precipitant ingredients used in the lake, as well as a copy of the certificate for each batch of straight color used to prepare the lake and a copy of the acceptance of the notice claiming certification (or the certificate, during the transition between the old and new procedures) for each batch of lake that was used as an ingredient in the lake. These additional records would allow the agency to verify the information and the affirmations about the identity and composition of the lake in the notice claiming certification.

Under proposed § 80.39(b)(2), the manufacturer or repacker of a batch of lake certified under proposed § 80.31(b) would be required to retain an 8-ounce sample of the batch. The requirements for taking, storing, and labeling this sample are provided in proposed § 80.22(b). The requirements are similar to those in existing § 80.22 for samples to accompany a request for certification. However, proposed § 80.22(b) also specifies when the sample is to be taken; storage conditions for the sample; and additional labeling to show the total color, the date the sample was taken, and (following FDA acceptance of the notice claiming certification) the FDA acceptance number.

The agency is proposing that the timeframes and conditions for agency access to these additional records, including the sample of the batch retained by the firm, be the same as currently specified in § 80.39 for records of distribution for certified color additives.

5. Treatment of Batches of Lakes Pending Certification and After Certification

Current § 80.37 *Treatment of batch pending certification* and § 80.38 *Treatment of batch after certification* contain requirements to ensure that the composition of a batch of color additive subject to certification does not change from the composition of the representative sample of the batch that was submitted to the agency and that formed the basis for the agency's issuance of the certificate for the batch; that the batch remains under control of the person requesting certification until it has been certified; and that the batch is clearly identified as the batch for which certification was requested or obtained. The proposed revision of these sections would maintain these requirements or comparable requirements for batches of lakes to be certified under § 80.31(b).

a. *Treatment of batches of lakes pending certification.* Section 80.37 specifies the storage and labeling requirements for a batch of color additive pending certification. The requirements of this section are triggered by the act of taking a representative sample from the batch of color additive for submission to FDA with the request for certification, and they continue until the requested certificate has been issued. The agency is proposing to amend § 80.37 to continue the requirements and conditions of this section for lakes subject to certification under proposed § 80.31(b). Specifically, the agency is proposing to amend the description of the sample in § 80.37 to include a sample taken and held as a record by the manufacturer or repacker of a batch of lake certifiable under proposed § 80.31(b). The agency is also proposing to amend § 80.37(b) to specify that the batch must be held under the control of the person requesting or claiming certification until certified. Finally, the agency is proposing to amend § 80.37(c) to specify that the batch must be marked in a manner such that there can be no question that the batch may not be used until the issuance of the certificate for the batch or, for lakes, the issuance of FDA's acceptance of the required notice claiming certification.

b. *Treatment of batches after certification.* Section 80.38 specifies the storage, labeling and use requirements, and limitations that apply to a batch of color additive after certification. The agency is proposing to amend § 80.38 to continue the requirements and conditions of this section for lakes under the proposed certification procedures in § 80.31(b). Specifically, the agency is proposing to amend § 80.38 to divide it into two subsections: (a) Labeling and (b) Storage. The agency is also proposing to establish two subparagraphs under § 80.38(a) to describe the labeling requirements for batches of color additives certified under § 80.31(a) and § 80.31(b), respectively. In both cases, the trigger for labeling would be notification from FDA that the batch is a certified batch. However, a batch certified under proposed § 80.31(b) would be identified by labeling it with the FDA acceptance number, rather than with the certified lot number. The agency is also proposing to amend § 80.38(b) to clarify that the person responsible for the storage and use of the batch after certification is the person requesting or claiming certification.

6. Color Additive Mixtures

Current § 80.35 refers to ''straight colors'' in describing the ingredients in color additive mixtures to be certified (§ 80.35(a)) and in color additive mixtures exempt from certification (§ 80.35(b)). Currently, the term ''straight color'' is defined to include lakes. As noted in section III.A.1. of this document, the agency is proposing to amend the definition of ''straight color'' to exclude lakes and to define a new term ''listed color'' that would include both straight colors and lakes. Therefore, the agency is proposing a conforming amendment to substitute the term ''listed color'' or ''listed colors'' for the term ''straight color'' or ''straight colors'' in § 80.35.

7. Enforcement Provisions

a. *Limitations of certification.* Current § 80.32 specifies conditions under which the certificate for a batch of color additive expires. The agency is proposing to adapt the provisions of § 80.32 to the proposed new procedure for certification of lakes.

As explained in section VI.B.1. of this document, under the proposed new certification procedure for lakes, the agency would not issue a certificate for a batch of lake. Instead, the certification of a batch of lake would rely on the certification of the straight colors used in the batch of lake, on the affirmations in the notice claiming certification, and on agency acceptance of the notice. The certification of a repacked batch of lake would rely on the certification of the original batch of lake rather than directly on the certification of the straightcolor components of the lake. The agency is proposing to amend § 80.32 to clarify that the certification of a batch of lake is inextricably linked to the certificates for the straight colors used to prepare the lake. As proposed, the expiration of the certificate for a batch of straight color would result in the expiration of the agency's acceptance of all notices claiming certification of batches of lakes made from that batch of straight color, including any repacks of such batches.

The agency is proposing to change the title of § 80.32 from ''Limitations of Certificates'' to ''Limitations of Certification'' to expand the application of § 80.32 to the proposed certification procedure for lakes, which would not result in the issuance of a certificate by the agency.

Current § 80.32(a) provides that a certificate that is obtained through fraud or misrepresentation of a material fact shall not be effective, and that any color additive from the batch covered by the fraudulently obtained certificate shall be considered to be from an uncertified batch. Proposed § 80.32(a) would continue the applicability of this provision to batches of lakes certified under the proposed new procedure by replacing the term ''certificate'' with the phrase ''certificate or acceptance of a notice claiming certification''. Proposed § 80.32(a) would also clarify that any lake prepared with the color additive covered by the fraudulently obtained certificate or acceptance would lose its certification.

Current § 80.32(b) provides that if, between the time a representative sample is taken from a batch of color additive and the time a certificate for the batch is received by the person to whom it is issued, the color additive becomes changed in composition, the certificate shall not be effective, and the changed color additive shall be considered to be from an uncertified batch. Proposed § 80.32(b) would continue the applicability of this provision to batches of lakes certified under the proposed new procedure by amending the description of the sample to include a sample retained by a firm claiming certification for a batch of lake and by replacing the word ''a certificate'' by ''a certificate or an acceptance of a notice claiming certification.'' The agency is also proposing to amend § 80.32(b) to state that if a certificate or acceptance of a notice claiming certification for a batch of color additive ceases to be effective, then any batch of lake prepared with such color additive is also an uncertified batch.

Current § 80.32(c) provides that if, at any time after a certificate is received by the person to whom it is issued, any color additive from the batch covered by the certificate becomes changed in composition, the certificate expires. Proposed § 80.32(c) would continue the applicability of this provision to batches of lakes certified under the proposed new procedure by replacing the term ''a certificate'' with the phrase ''a certificate or an acceptance of a notice claiming certification.'' The agency is also proposing to amend the second sentence in § 80.32(c) to indicate clearly that the expiration of a certificate or an acceptance of a notice claiming certification of a batch of color additive would cause any lake prepared with such color additive to be an uncertified batch.

To allow certain specified uses of the color additive, current § 80.32(c) provides three exceptions to the expiration of the certificate when a change in composition occurs. A change in composition does not cause the certificate to expire if the change in composition resulted solely from use of the color additive: (1) For coloring a food, drug, or cosmetic; (2) for the purpose of certifying a batch of a mixture in which the color additive was used as an ingredient; or (3) for use in preparing a batch of a mixture for which exemption from certification has been authorized. Proposed § 80.32(c) would add another exception to provide that a change in composition would not cause the certification of a color additive to expire if the change in composition resulted solely from use of the color additive as a component or ingredient in a batch of lake for which certification was claimed under § 80.31(b) of this chapter. This provision would allow the use of certified batches of straight color to prepare a lake, or the use of a portion of a certified batch of lake as an ingredient in another certified batch of lake.

As amended, § 80.32(c) would permit any changes in the straight-color components of a lake that would normally occur during lake manufacture under conditions consistent with CGMP. For example, if the straight color was a sodium salt (e.g. D&C Yellow No. 10), and the lake was prepared with aluminum cation, this provision would allow for the change in the cation associated with the straight color from sodium to aluminum. However, this provision could not be used to justify a claim for certification of a batch of lake containing a straight color that had degraded during preparation of the lake. Such a batch of lake would not meet the requirement in part 74 that lakes be free from impurities other than those named in the specifications, to the extent that such impurities may be avoided by CGMP. Therefore, the batch would not comply with the conditions of § 80.31(b) and could not be a certified batch.

Current § 80.32(d) provides that a certificate expires if the package in which the color additive was closed for shipment or delivery is opened. Current § 80.32(d)(1) through (d)(5) specify five exceptions to the expiration of the certificate. These exceptions allow a package of certified color additive to be opened and the color additive used (1) in coloring a food, drug, or cosmetic (subject to certain restrictions); (2) for the purpose of certifying a batch made by repacking the color additive; (3) for the purpose of certifying a batch of a mixture in which the color additive is used as an ingredient; (4) for the purpose of preparing a batch of a mixture for which exemption from certification has been authorized; and (5) when the package is reopened solely for repackaging by the person to whom the certificate was issued. Proposed § 80.32(d) would continue the applicability of these provisions to certified batches of lakes or certified repacks of such batches by replacing the term ''a certificate'' by the phrase ''a certificate or an acceptance of a notice claiming certification.''

Current §§ 80.32(e), (f), and (g) describe additional conditions under which a certificate ceases to be effective with respect to a package of color additive and under which the color additive is therefore considered to be from an uncertified batch. Proposed § 80.32(e), (f), and (g) would continue the applicability of these provisions to batches of lakes certified under the proposed new procedure by replacing the term ''a certificate'' by the phrase ''a certificate or an acceptance of a notice claiming certification.''

Current § 80.32(h) describes the consequences of revocation or amendment of the listing or specifications for a color additive. Section 80.32(h) states that on the date specified in the order effecting the revocation or amendment, all certificates for existing batches and portions of batches of the color additive issued under the revoked or amended regulations cease to be effective, and any such lots of the color additive are regarded as uncertified after the date specified unless a new certificate can be and is obtained in conformity with the new regulation. Proposed § 80.32(h) would continue the applicability of this provision to batches of lakes certified under the proposed new procedure by replacing the term ''a certificate'' by the phrase ''a certificate or an acceptance of a notice claiming certification.'' Proposed § 80.32(h) would also provide that any batch of lake prepared from a batch or portion of a batch of color additive that was certified under the revoked or amended regulations is also regarded as uncertified unless a new certificate is obtained.

b. *Authority to refuse certification.* Certification requirements are enforced through the provisions of § 80.34 *Authority to refuse certification service.* This section currently provides four conditions for refusing certification service to a firm requesting certification. Paragraph 80.34(a)(1) authorizes the agency to deny certification service to a firm that has ''obtained or attempted to obtain a certificate through fraud or misrepresentation of a material fact.''

The remaining three paragraphs (§ 80.34(a)(2), (a)(3), and (a)(4)) authorize the agency to deny certification service to a firm that violates the recordkeeping requirements of § 80.39 by falsifying the required records; failing to keep the records or to make them available to the agency; or by refusing to permit duly authorized FDA employees full access to inspect the manufacturing facilities, processes and formulae involved in the manufacture of color additives and of intermediates from which such color additives are derived. Proposed § 80.34 would continue the application of these provisions to firms certifying batches of lakes under the proposed new procedure by amending § 80.34 to replace the phrase ''a certificate'' with the phrase ''a certificate or acceptance of a notice claiming certification.'' Proposed § 80.34(a)(4) would also authorize FDA to examine processes and formulae for substrata, as substances from which color additives are derived.

C. Amendments to Other Regulations

1. Listings in Part 74

a. *Listings for FD&C Red No. 40 lakes.* Except for FD&C Red No. 40, all the straight colors used in lakes were provisionally listed in 1960. FD&C Red No. 40 was never provisionally listed and, when FD&C Red No. 40 was listed (permanently) in 1971 (food and drugs: 36 FR 23552, December 10, 1971) and 1975 (cosmetics: 39 FR 28278, August 6, 1974, and 39 FR 44198, December 23, 1974), the lakes of FD&C Red No. 40 were included, for convenience, in §§ 74.340, 74.1340, and 74.2340. These permanent listings for FD&C Red No. 40 lakes cross-reference the specifications and labeling requirements in the provisional listings for lakes. For consistency, the agency is proposing to move the current listings of lakes of FD&C Red No. 40 in §§ 74.340, 74.1340, and 74.2340 to §§ 74.50, 74.1050, and 74.2050, respectively, to conform the permanent listing of the lakes of FD&C Red No. 40 to the permanent listings for other lakes.

b. *Reference to lakes in listings for straight colors.* The proposed permanent listings for lakes (§§ 74.50, 74.1050, and 74.2050) would specify the straight colors that are permitted as components of a lake. The agency tentatively concludes that the regulations for the straight colors should specify that lakes made with the straight color must conform to the requirements for lakes (§§ 74.50, 75.1050, or 74.2050, as appropriate). Therefore, the agency is proposing to amend the listings in part 74, subpart A, for the straight colors used to prepare lakes for food use to specify that ''lakes made with (name of straight color) shall conform to the requirements of § 74.50''; to amend the listings in part 74, subpart B, for the straight colors used to prepare lakes for drug use to specify that ''lakes made with (name of straight color) shall conform to the requirements of § 74.1050''; and to amend the listings in part 74, subpart C, for the straight colors used to prepare lakes for cosmetic use to specify that ''lakes made with (name of straight color) shall conform to the requirements of § 74.2050.''

c. *Listings for eye-area use of lakes.* In 1994, the agency permanently listed the aluminum lakes on alumina of the straight colors FD&C Blue No. 1 and FD&C Red No. 40 (February 16, 1994, 59 FR 7635) and FD&C Yellow No. 5 (November 29, 1994, 59 FR 60893), for use in drugs and cosmetics intended for use in the area of the eye. Because § 81.1 specifically precludes use of provisionally listed lakes in eye-area products, these lakes were included in the permanent listings of the straight color. The agency tentatively concludes that it is appropriate to include the eye-area uses of lakes with the other permanently listed uses of lakes and is therefore proposing to move these eye-area uses from the permanent listings for the straight colors to §§ 74.1050 and 74.2050.

2. Color Additive Labeling

Currently, provisionally listed lakes are subject to the general labeling requirements for color additives in § 70.25. FDA is proposing to continue the applicability of these requirements to permanently listed lakes by including a provision in proposed §§ 74.50, 74.1050, and 74.2050 to prescribe that the label of a lake conform to the requirements of § 70.25.

To reflect the proposed deletion of the provisional listings for color additives, the agency is also proposing to amend § 70.25(a) by removing the reference to part 81. As a result of the proposed change in the definition of ''straight color'' and the proposed new definition of ''listed color,'' the agency is proposing to maintain the general labeling requirements for color additives by amending § 70.25(a)(1) and (a)(3) to replace the term ''straight color'' with the term ''listed color.'' As amended, § 70.25(a)(1) would require the label of a package of lake to include the name of the lake, as prescribed in part 74 (§§ 74.50, 74.1050, or 74.2050).

As a result of the proposed new certification procedure for batches of lakes, the agency is also proposing to amend § 70.25(a)(3), which requires that the label of certified colors that are subject to a tolerance (quantitative limitation on use) bear directions to prevent products to which the color may be added from exceeding the tolerance. As amended, § 70.25(a)(3) would provide that, where regulations impose a tolerance for a general or specific use of a straight color, the amount of a straight color present in a lake would be included in the total amount of the straight color.

In addition, the agency is proposing to amend § 70.25(d) *Special labeling for color additives not exempt from certification* to establish separate labeling requirements for color additives subject to the certification procedures of § 80.31(a) and lakes subject to the certification procedures of § 80.31(b). Proposed § 70.25(d)(1) would apply to color additives subject to certification under § 80.31(a) and would incorporate the provisions of current § 70.25(d). Proposed § 70.25(d)(2) would prescribe special labeling requirements for lakes subject to certification procedures under § 80.31(b). The proposed paragraph would require that the labeling for such lakes include the total color content of the lake, the amount of color contributed by each straight-color component of the lake, and FDA's acceptance number for the notice claiming certification of the batch. The information on the total color content and content of each straight color in the lake would enable the user of the lake to comply with any quantitative limitations on the use of the straight-color component of a lake. This information would also assist the user in the formulation of products using the lake. The inclusion of the FDA acceptance number for the notice claiming certification for the batch would facilitate agency verification of the records and other information for the batch.

3. Product Labeling

a. *Food ingredient labeling.* i. *Statutory authority.* Currently, lakes are provisionally listed colors subject to certification. Therefore, under section 403(i) of the act (21 U.S.C. 343), as amended by the Nutrition Labeling and Education Act of 1990 (Pub. L. 101–535) (the NLEA), lakes must be listed as ingredients on the label of food products that contain them. Before the NLEA was enacted, the act provided that color additives added to food need not be declared individually by their common or usual names but could be designated by the collective term ''colorings.'' In 1990, the NLEA amended section 403(i) of the act to exempt from label

declaration only colors not required to be certified. To implement amended section 403(i), the agency revised its labeling regulations in § 101.22 by adding new paragraph (k), which became effective on May 8, 1993. Under § 101.22(k)(1), the lake of a color additive subject to certification must be individually identified on the food label. Because all lakes for food use are made from straight colors subject to certification and are themselves certified color additives, the presence of a lake in a food product must always be individually identified on the label of the product under § 101.22(k)(1). The agency is now proposing to list lakes permanently as color additives subject to certification. Therefore, in accordance with section 403(i) of the act (21 U.S.C. 343(i)), the agency is proposing to retain the requirement that lakes be declared on the food label under their individual names rather than as ''colorings.''

Section 721(b)(3) of the act (21 U.S.C. 379e(b)(3)) provides that regulations for the listing of a color additive ''shall, to the extent deemed necessary * * * to assure the safety of the use or uses for which a particular color additive is listed, prescribe the conditions under which such additive may be safely employed for such use or uses (including, but not limited to * * * directions or other labeling or packaging requirements for such additive).'' The straight colors FD&C Yellow No. 5 and FD&C Yellow No. 6 have been reported to cause hypersensitivity in some individuals. Declaration of the lakes of FD&C Yellow No. 5 and FD&C Yellow No. 6 on the label of foods that contain them will provide the means for consumers who are sensitive to these color additives to identify the foods that contain them and thereby avoid suffering a reaction. Therefore, the agency tentatively concludes that such a label declaration requirement is necessary.

Label declaration of the straight color FD&C Yellow No. 5 is required under § 74.705 for all foods that contain this color additive, including butter, cheese, and ice cream (foods exempted under section 403(k) of the act (21 U.S.C. 343(k)) from the requirement to declare the presence of certified color additives). In the Federal Register of July 21, 1995 (60 FR 37611), the agency published a proposal to require declaration of FD&C Yellow No. 6 on the labels of butter, cheese, and ice cream (hereinafter referred to as the July 1995 proposal). Declaration of FD&C Yellow No. 6 in other foods is already required under § 101.22(k)(1). The agency notes that both its original proposal to require the labeling of FD&C Yellow No. 5 in foods and ingested drugs (42 FR 6835, February 4, 1977) and the pending proposal to require the labeling of FD&C Yellow No. 6 in butter, cheese, and ice cream refer to the need for label declaration of the presence of the color additive in food for humans—whether added as a straight color, a mixture, or a lake—to enable persons intolerant to the color additive to minimize exposure to it. Therefore, the agency tentatively concludes that the lakes of FD&C Yellow No. 5 and FD&C Yellow No. 6 should be subject to the same label declaration requirements for foods as the straight colors. Accordingly, this proposal modifies the July 1995 proposal to include lakes.

Proposed § 74.50(e)(2) would require that the label of food products for human use that contain a lake declare the presence of the lake in accordance with § 101.22(k) of this chapter. Proposed § 74.50(e)(3) would require that the labels of butter, cheese, and ice cream that contain a lake of FD&C Yellow No. 5 or FD&C Yellow No. 6 declare such lake in the list of ingredients.

ii. *Format.* Currently, § 101.22(k)(1) provides for the declaration of certified color additives, including lakes, in the ingredient listing on the food label and cites part 74 or 82 as the source of the name of such color additive. In this rulemaking, the agency is proposing to list lakes permanently in part 74 and to remove parts 81 and 82. Therefore, the agency is proposing to remove the reference to part 82 as a source of the name for a certified color additive for declaration on the food label.

Section 101.22(k)(1) states that it is not necessary to include the ''FD&C'' prefix or the term ''No.'' in the declaration of a color additive on the food label, but that the term ''Lake'' must be included in the declaration of a lake. However, the example given in § 101.22(k)(1) (''Blue 1 Lake'') to illustrate the declaration of a lake does not include the identity of the precipitant cation, although the precipitant cation is part of the listed name of the lake under current § 82.51. In addition, in this rulemaking, the agency is proposing in § 74.50 to include the substratum as well as the precipitant cation in the listed name of a lake.

The agency tentatively concludes that the current abbreviated nomenclature (e.g., Blue 1 Lake) for food ingredient labeling is still appropriate and that the inclusion of the identity of the precipitant cation and substratum in the name of the lake on the food label is unnecessary and may be confusing to consumers. Inclusion of these components of lakes as part of the name of the lake in the ingredient list would greatly lengthen the name of the lake on the food label without providing any additional information about the color additive, since the agency is proposing to permit only the aluminum cation and the substratum alumina in lakes for food use.

As discussed in section IV.A.1.d. of this document, the agency is also proposing in new § 74.50 to allow the use of more than one straight color in a lake. Accordingly, the agency is proposing to amend § 101.22(k)(1) to require that all straight colors used to prepare a lake be included in the name of the lake. Amended § 101.22(k)(1) would also specify that it is not necessary to include the name of the precipitant cation or the substratum in the name of a lake when listing it as an ingredient in a food product. Thus, a lake would be identified on a food label by a name consisting of the names of the straight colors (in descending order of predominance) present in the lake (without the ''FD&C'' designation or the term ''No.'') followed by the word ''Lake.'' For example, a lake that contains 10 percent FD&C Yellow No. 5, 5 percent FD&C Blue No. 1, the aluminum cation, and alumina substratum would be declared on the food label as ''Yellow 5 and Blue 1 Lake.''

b. *Cosmetic ingredient labeling.* Currently, § 701.3 requires that the label of each package of a cosmetic bear a declaration of the name of each ingredient in descending order of predominance. Section 701.3(c) also designates, in order of priority, the sources from which the names of cosmetic ingredients are to be derived for the purpose of declaration of ingredients. Under § 701.3(c)(1), if FDA has established a name for the ingredient in § 701.30, that name is used. However, § 701.3(c)(1) does not cite the color additive regulations as the preferred source for names of color additives. The agency is proposing to correct this oversight by amending § 701.3(c) to include the color additive listings in parts 73 and 74 as the preferred source of names for the declaration of ingredients on the cosmetic label.

Currently, under § 701.3(c)(2) (21 CFR 701.3(c)(2)), a lake is declared on the cosmetic label by the name under which it is listed in the CTFA Cosmetic Ingredient Dictionary, 2d ed. (1977). This name is the same as the listed name of the color additive, which, under §§ 82.51, 82.1051, and 82.2051, is formed from the name of the straight color, the name of the precipitant

cation, and the word ''lake.'' As discussed in previous sections of this document, the agency is proposing in § 74.2050(c) to change the listed name of a lake to include the name of the substrata used in the lake, and is also proposing to allow the use of more than one straight color to make a lake. The agency recognizes that these proposed changes would result in a long listed name for a lake. As with food labels, the agency is concerned that the additional information that such a name on a cosmetic label would provide to consumers would be overshadowed by consumer confusion about the identity and composition of the color additive.

Unlike lakes added to food (which, under the proposed regulation, would be permitted to contain only one cation precipitant (aluminum) and one substratum (alumina)), however, lakes added to cosmetics would continue to contain a range of possible cation precipitants and substrata. The straight color and the substrata are the principal components of the lake by weight, making up over 95 percent of the total weight of the lake. Currently, the name of a lake provides only the identity of the straight color and the precipitant. The complete name of a lake would provide additional information to consumers about the substrata present in lakes. On the other hand, the space available for ingredient declaration on a cosmetic label is limited, and under the proposed new nomenclature that would be required by § 74.2050, the name of a lake would occupy a significantly greater amount of space than currently. Furthermore, the amount of space on the label that would be allocated to declaring the presence of a lake would give undue prominence to the lake as an ingredient and overshadow the other ingredients of the cosmetic product, although lakes are not necessarily more important to the consumer.

Therefore, the agency tentatively concludes that the abbreviated nomenclature permitted for declaring lakes as ingredients on the food label under § 101.22(k) should be permitted for cosmetic labels as well. The agency believes that the abbreviated name would provide consumers with more understandable information about the identity of the color additive because it would clearly identify the ingredient as a color additive and highlight the color component of the lake, which is its primary characterizing feature from the consumer's point of view. The agency tentatively finds that adopting uniform nomenclature for color additives, including lakes, on food and cosmetic ingredient labels would assist consumers in identifying these ingredients as color additives. Therefore, the agency tentatively concludes that the extension of abbreviated nomenclature for ingredient labeling of lakes to cosmetics as well as foods will provide maximum benefit to consumers.

For consistency, the agency also tentatively concludes that this abbreviated nomenclature for cosmetic ingredient labeling should apply to all certified color additives, not just to lakes. Currently, straight colors are declared on the cosmetic label by the listed name of the straight color (e.g., FD&C Blue No. 2). However, as discussed above, under § 101.22(k) the agency permits the use of abbreviated names for identifying straight colors in the ingredient statement on the food label. The agency tentatively concludes that the abbreviated name now being used on the food label (the listed name without the prefix ''FD&C'' or ''D&C,'' and without the term ''No.'') would meet the purpose of ingredient declaration on the cosmetic label to prevent consumer deception and to facilitate value comparisons (38 FR 28912, October 17, 1973).

However, for cosmetics, the prefix ''Ext.'' would still be required as part of the abbreviated name to uniquely identify different color additives. For example, D&C Yellow No. 7 (21 CFR 74.1707 and 74.2707) and Ext. D&C Yellow No. 7 (21 CFR 74.1707a and 74.2707a) are different chemical compounds, although they are both listed as color additives for use in externally applied drug and cosmetic products. Under the proposed abbreviated nomenclature, Ext. D&C Yellow No. 7 would be declared as Ext. Yellow 7, whereas D&C Yellow No. 7 would be declared as Yellow 7.

Adopting this abbreviated nomenclature for ingredient declaration of certified colors on cosmetic labels would eliminate the current inconsistency between the nomenclature used to identify certified colors on food labels and the nomenclature used on cosmetic labels, as well as any resulting consumer confusion. Therefore, the agency is further proposing to adopt as an option, for the purpose of declaring certified colors as ingredients on the labels of cosmetics, the same abbreviated nomenclature currently permitted under § 101.22(k) for declaring certified colors on the food label, except that the ''Ext.'' prefix must be included where applicable. For example, the color additive D&C Red No. 28 could be declared on the cosmetic label as ''Red 28,'' and a lake containing 10 percent FD&C Yellow No. 5, 5 percent D&C Red No. 28, the precipitant cations aluminum and calcium, and 50 percent barium sulfate and 35 percent rosin, could be declared on the cosmetic label as ''Yellow 5 and Red 28 Lake.'' The requirement that the prefix ''Ext.'' be included on cosmetic labels would not create an inconsistency with the nomenclature for food labels because, by definition, ''Ext.'' color additives are for external use and cannot be used in foods.

To accomplish the changes discussed above, the agency is proposing to amend § 701.3(c) by establishing new paragraphs (c)(1)(i) and (c)(1)(ii). Proposed paragraph (c)(1)(ii) would incorporate the existing citation to § 701.30 as a source of names. Proposed paragraph § 701.30(c)(1)(i) would identify the color additive regulations in parts 73 and 74 as the preferred source of names for color additives. This proposed paragraph would further state that for color additives listed in part 74 it is not necessary to include the prefix ''FD&C'' or ''D&C'' or the term ''No.'' in the ingredient declaration, but that the prefix ''Ext.'' shall be included in the declaration. For lakes, it would also not be necessary to include the identity of precipitant cations or substrata, but the term ''Lake'' would have to be included in the name.

c. *Labeling of drug products.* Under §§ 201.20 (a) and (b) (21 CFR 201.20 (a) and (b)) and § 74.1705(c), certain over-the-counter and prescription drug products intended for human use must declare the presence of FD&C Yellow No. 5 as a color additive. The regulations specify that the labeling for these drug products shall bear a statement such as ''Contains FD&C Yellow No. 5 (tartrazine) as a color additive'' or ''Contains color additives including FD&C Yellow No. 5 (tartrazine),'' and prescribe a more detailed warning that must be included in the ''Precautions'' section of the labeling.

Under the July 1995 proposal, the labels of certain over-the-counter and prescription drug products would be required to declare the presence of FD&C Yellow No. 6 as a color additive. The agency had previously published a final rule adopting the same requirement for such drug products (51 FR 41765, November 19, 1986), but subsequently, in compliance with a stipulation for the dismissal of a lawsuit challenging the 1986 final rule, the agency published a notice in the Federal Register of December 6, 1988 (53 FR 49138), announcing that the requirement would not be enforced pending a reproposal of the action.

The provisional listings of the lakes of FD&C Yellow No. 5 (§ 82.705) and FD&C Yellow No. 6 (§ 82.706) do not contain any reference to the declaration of these lakes in drug products. However, FDA's proposal to require the labeling of FD&C Yellow No. 5 in foods and ingested drugs (42 FR 6835, February 4, 1977) explicitly states that ''a label declaration of the presence of FD&C Yellow No. 5 in food for humans, whether added as the straight color, a mixture, or a lake, would enable persons intolerant to FD&C Yellow No. 5 to minimize exposure to the color.'' The July 1995 proposal contains almost identical language in the foods section of the proposal (60 FR 37611 at 37613 to 37614). Although these proposals were silent as to whether the labeling requirement would encompass all forms (straight color, mixture, or lake) of the color additive when added to drugs, the safety issue necessitating such labeling in drugs is the same as for foods. Therefore, the agency tentatively concludes that the presence of FD&C Yellow No. 5 should be declared as prescribed by § 74.1705 (c)(2) and (c)(3) and by § 201.20 (a) and (b) when a lake of FD&C Yellow No. 5 is used in these products, and that the presence of FD&C Yellow No. 6 should be declared as prescribed by proposed §§ 74.1706(c)(2) and 201.20(c) when a lake of FD&C Yellow No. 6 is used. Accordingly, this proposal modifies the July 1995 proposal to include lakes of FD&C Yellow No. 5 and FD&C Yellow No. 6. The agency notes that the declaration of FD&C Yellow No. 5 and FD&C Yellow No. 6 in these drug products is intended as a warning statement about the presence of these color additives, not as an ingredient declaration.

To minimize confusion, the agency is proposing that the declaration for the presence of a lake of FD&C Yellow No. 5 in drug products should be the same as that required for the straight color in §§ 74.1705(c) and 201.20. Therefore, the agency is proposing to require in § 74.1050(e)(2) that drugs that contain a lake of FD&C Yellow No. 5 be labeled in accordance with § 74.1705 (c)(2) and (c)(3). Similarly, the agency is proposing to require in § 74.1050(e)(3) that drugs that contain a lake of FD&C Yellow No. 6 be labeled in accordance with proposed § 74.1706(c)(2). The agency is also proposing to amend § 201.20 to state that a drug product that contains a lake of FD&C Yellow No. 5 or a lake of FD&C Yellow No. 6 is subject to the same labeling requirements as a drug product that contains the straight color. Finally, the agency is proposing to amend § 74.1705 (c)(2) and (c)(3) to clarify that drugs made with a lake of FD&C Yellow No. 5 are subject to the same label declaration requirements as drugs made with the straight color, and to modify proposed § 74.1706(c)(2) to clarify that drugs made with a lake of FD&C Yellow No. 6 are subject to the same label declaration requirements as drugs made with the straight color.

Under the current regulations, certain drug products that are also cosmetics, such as antibacterial mouthwashes and fluoride toothpastes, need not comply with the label declaration requirements for FD&C Yellow No. 5 in §§ 74.1705(c) and 201.20, provided that they comply with the ingredient labeling provisions for cosmetics in § 701.3. The pending July 1995 proposal for declaration of FD&C Yellow No. 6 in ingested drugs contains the same proviso. The agency is proposing to allow the labeling of such drug/cosmetic products that contain lakes of FD&C Yellow No. 5 or FD&C Yellow No. 6 to use the abbreviated nomenclature for ingredient declaration of lakes in proposed § 701.3(c)(1), which is discussed in section VI.C.3.b. of this document.

4. Other Amendments

As a result of the proposed change in the definition of ''straight color'' and the proposed new definition of ''listed color,'' the agency is also proposing to amend §§ 70.20, 73.1, and 73.1001 to replace the term ''straight color'' with the term ''listed color.''

As a result of the deletion of the provisional listings (parts 81 and 82), the agency is also proposing to amend § 178.3297(d) by removing the references to parts 81 and 82.

VII. Summary of Information Requested

To protect the confidentiality of the requested identity and process information, interested parties may submit such information, as well as reference samples of rosin products, directly to the Office of Cosmetics and Colors (address above).

A. In Situ Manufacturing Processes

As discussed in section V.A.2. of this document, the agency is aware that some substrata, including aluminum benzoate, alumina, barium sulfate (blanc fixe), and gloss white, may be currently prepared in situ during the manufacture of lakes. The agency is proposing conditions for the in situ preparation of alumina and aluminum benzoate as substrata and is requesting, as comments on this proposal, information on appropriate methods of preparation and ingredient specifications for barium sulfate produced in situ. If such comments are received, the agency will consider modifying the proposal to permit the in situ preparation of barium sulfate as a substratum.

B. Identity and Specifications for Rosin

As discussed in section V.A.2.k. of this document, the agency is requesting, as comments on this proposal, information (e.g., a manufacturer's product specification sheet or analytical data sheet) about identity and specifications for any type of rosin that does not meet the identity and specifications proposed in this document, but that is currently used as the substratum ''rosin'' under §§ 82.1051 or 82.2051. The agency is also requesting a 5-pound reference sample of each type of rosin identified in a comment. Comments should identify the specific type(s) of rosins used by the lake manufacturer and describe any treatment of the rosin prior to incorporation in a lake. Furthermore, the agency requests data concerning the dermal safety of any rosin intended for use as a diluent in color additives for externally applied drug use.

If the agency receives satisfactory information for additional types of rosin, the agency will expand the definition of rosin in its final action on this rulemaking to provide for the use of the additional products as substrata in lakes for drug or cosmetic use. In addition, to alleviate the concerns raised by literature reports of allergic reactions and dermal irritation caused by some forms of free rosin, the agency is requesting information on the safety of rosin as a diluent in color additive mixtures used in externally applied drugs. If the requested data are received and they demonstrate that rosin used as a diluent in externally applied drugs is safe, the agency will consider listing rosin for such use in the final rule.

C. Anions in Precipitants

As discussed above, the agency is proposing to allow only the anions chloride (Cl^{-1}) and sulfate (SO_4^{-2}) for use as components of precipitants. However, because the provisional listing regulations did not specify the anions that could be used in lakes, the agency is requesting comments on the use of other anions in the preparation of lakes for food, drug, or cosmetic use. This information should include data to document the current use of such anions in preparing lakes and to demonstrate their safety for such use. If the agency receives information to confirm the current safe use of anions other than chloride and sulfate in lakes, the agency will consider listing these anions in the final rule.

VIII. Effective Date

Section 701(e) of the act (21 U.S.C. 371(e)) allows 30 days for the filing of objections to a final rule listing a color additive and states that such a final rule may not become effective until the period for filing objections is over. Thus, the earliest possible effective date for a final rule listing a color additive is 31 days after publication. FDA typically sets a longer effective date for changes in labeling requirements.

In accordance with section 701(e) of the act, the agency is proposing that the final rule resulting from this proposal become effective 31 days following its publication, except for the proposed provisions of §§ 201.20, 74.1050(e), 74.1705(c), and 74.1706(c)(2) concerning declaration of lakes of FD&C Yellow No. 5 and FD&C Yellow No. 6 on the labels of certain drug products, and the proposed provisions of §§ 74.50(e)(3) and 74.706(d)(2) concerning declaration of lakes of FD&C Yellow No. 6 on the labels of butter, cheese, and ice cream. FDA is proposing that these provisions, which are part of the rulemaking initiated by the July 1995 proposal (as modified by this proposal), become effective when the final rule resulting from that proposal takes effect.

Although this proposal contains changes in the ingredient labeling provisions applicable to cosmetics, the proposed abbreviated nomenclature for declaration of lakes as ingredients in these products is optional, and manufacturers may continue to use the old labeling nomenclature if they wish. Therefore, FDA tentatively concludes that the amendments to the labeling regulations for lakes in cosmetics do not necessitate a delay in the effective date of the final rule.

IX. Inspection of Documents

The documents that FDA considered and relied upon in developing this proposal are available for inspection at the Center for Food Safety and Applied Nutrition by appointment with the information contact person (address above). As provided in § 71.15 (21 CFR 71.15), the agency will delete from the documents any materials that are not available for public disclosure before making the documents available for inspection.

X. Environmental Impact

The agency has determined under 21 CFR 25.24(b)(3) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

XI. Paperwork Reduction Act

This proposed rule contains collections of information that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (Pub. L. 104–13). Therefore, in accordance with 44 U.S.C. 3506(c)(2)(B) and 5 CFR part 1320, FDA is providing below the title, description, and respondent descriptions for the collections of information contained in this proposal along with an estimate of the resulting annual collection of information burden. Included in the estimate is the time needed to review instructions, to gather the required information, and to disclose the information.

FDA invites comments on the following:

(1) Whether the proposed collection of information is necessary for the proper performance of the functions of the agency, including whether the information will have practical utility;

(2) The accuracy of the agency's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used;

(3) Ways to enhance the quality, utility, and clarity of the information to be collected; and

(4) Ways to minimize the burden of the collection of information on those who are to respond, including through the use of automated collection techniques, where appropriate, or other forms of information technology.

Title: Certification and Labeling Requirements for Color Additive Lakes.

Description: Section 721(c) of the act requires the certification of color additives where a certification requirement is necessary in the interest of the public health. Currently, lakes are subject to certification under §§ 80.21 and 80.31 and recordkeeping as required in § 80.39. The proposed rule would establish a new simplified procedure for certification of batches of lakes. Under § 80.33 of the proposed rule, the manufacturer or repacker of a lake would submit a notice claiming certification, in lieu of a request for certification. The notice would contain information about the ingredients and chemical composition of the batch. The manufacturer or repacker would be required to keep records, including a sample taken from the batch, to document the information in the notice. After certification, the manufacturer or repacker would be required to keep records of the disposition of the batch. The proposal would also require that these records be made available to FDA upon request. Because most of the records that would be required by the proposed rule are already kept in the usual course of business, the agency believes that the proposed provisions will add only a minor additional record retention burden for firms subject to the proposed provisions.

Section 721(b)(3) of the act provides that a color additive regulation shall prescribe the conditions under which the additive may be safely employed for use in foods, drugs, or cosmetics, including any labeling or packaging requirements necessary to ensure the safety of the additive. The presence of FD&C Yellow No. 5 or FD&C Yellow No. 6 in food has been reported to cause allergic-type reactions. To ensure that consumers who are sensitive to these color additives will be able to identify and avoid them, the agency is proposing to require in § 74.50(e)(3) that lakes of FD&C Yellow No. 5 and FD&C Yellow No. 6 that are used as ingredients in butter, cheese, and ice cream be declared on the labels of these foods. (Declaration of these lakes in all foods is already required both by statute and regulation.) However, because the agency is unaware of any current use of lakes of FD&C Yellow No. 5 or FD&C Yellow No. 6 in butter, cheese, or ice cream, the agency tentatively concludes that no burden would result from this proposed change.

Proposed § 701.3(c)(1)(i) changes the reference for the names under which color additives, including lakes, are declared on the cosmetic label, and provides for the optional use of abbreviated nomenclature for the declaration of color additives as ingredients on the cosmetic label. Proposed § 701.3(c)(1)(i) would also allow continued use of the current nomenclature, however. The agency does not anticipate that cosmetic manufacturers will change their labels immediately to take advantage of the abbreviated nomenclature; rather, the agency expects that manufacturers will start using the abbreviated nomenclature when they institute a label change for some other reason. Therefore, the agency tentatively concludes that proposed § 701.3(c)(1)(i) would introduce no startup costs or other burden.

To avoid double-counting, certain labeling provisions in this proposal have not been included in the burden estimate because they merely cross-reference labeling requirements contained in other regulations. Accordingly, proposed §§ 74.50(e)(1) and (e)(2), 74.1050(e), and 74.2050(d) do

not appear in the burden estimate table. Provisions that merely continue existing labeling requirements, such as proposed § 101.22(k)(1), also have not been included in the burden estimate for this proposal.

Other proposed labeling changes do not constitute collections of information because they provide for disclosure of information supplied by FDA. Proposed §§ 201.20, 74.1705(c)(2) and (c)(3), and 74.1706(c)(2) would require disclosure of the presence of FD&C Yellow No. 5 and FD&C Yellow No. 6 on the labels and in the labeling of certain drug products. The proposed regulations specify the wording of the required disclosures. Also, proposed § 70.25(d)(2) would require disclosure, on the package label of the lake, of the number assigned by FDA to its acceptance of the notice claiming certification for the batch of lake. These labeling requirements provide for ''public disclosure of information originally supplied by the Federal government to the recipient for the purpose of disclosure to the public'' and are, therefore, exempt from OMB review under 5 CFR 1320.3(c)(2). Finally, some proposed requirements have been excluded from the burden estimate because the agency tentatively concludes that the resources necessary to comply with these requirements would be expended by businesses in the normal course of their activities and that the reporting, recordkeeping, or disclosure activities required by the proposed regulation are, thus, usual and customary (5 CFR 1320.3(b)(2)). For example, the information on percent total color and percent color from each straight color used in a batch of lake that must appear on the package label of the lake under proposed § 70.25(d)(2)(i) and (ii) is needed by the purchaser of the lake to properly formulate the purchaser's food, drug, or cosmetic product. Therefore, as a matter of business necessity, a manufacturer or repacker would obtain and disclose this information to clients, regardless of FDA requirements.

Description of Respondents: Businesses, including small businesses.

ESTIMATED ANNUAL REPORTING BURDEN

CFR Section	Number of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours	Total Operating and Maintenance Costs
21 CFR 74.50(e)(3)	0	0	0	0	0	0
21 CFR 80.33	20	80	1,600	0.25	400	$48,000
21 CFR 701.3(c)(1)(i)	0	0	0	0	0	0
Totals	.....	.....	.....	.....	400	48,000

ESTIMATED ANNUAL RECORDKEEPING BURDEN

CFR Section	Number of Recordkeepers	Annual Frequency of Recordkeeping	Total Annual Records	Hours per Recordkeeper	Total Hours
21 CFR 80.22	20	1	20	2.65	53
21 CFR 80.39	20	1	20	37.35	747
Totals	.....	.....	.....	40	800

The agency expects that the number of respondents and the annual burden hours will not change significantly over succeeding years because it believes that the use of lakes in foods, drugs, and cosmetics will remain constant. There are no anticipated capital or startup costs associated with the proposed information collection requirements.

The agency has submitted copies of the proposed rule to OMB for review of the portions of the proposal that are within the ambit of the Paperwork Reduction Act of 1995. Interested persons are requested to send comments regarding information collection by April 3, 1996, but not later than May 3, 1996, to the Office of Information and Regulatory Affairs, OMB, New Executive Office Building, rm. 10235, Washington, DC 20503, ATTN: Desk Officer for FDA.

XII. Comments

As noted in section XI. of this document, interested parties may, on or before May 3, 1996, submit to the Office of Information and Regulatory Affairs, OMB (address above) written comments regarding the collections of information contained in this proposal. For other issues in the proposed rule, interested persons may, on or before June 3, 1996, submit to the Dockets Management Branch (address above) written comments regarding this proposal. Four copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number of the rulemaking or rulemakings to which the comment is relevant. Comments on modifications to the July 1995 proposal regarding label declaration of FD&C Yellow No. 6 should be identified with both docket numbers found in brackets in the heading of this document; comments on other aspects of this proposal should be identified with docket number 79N–0043 only. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

In addition, interested persons may, on or before June 3, 1996, submit to the Office of Cosmetics and Colors (address above) written comments containing process information relating to the identity and current use of substrata (including rosin) in lakes, and samples of such substrata. Written comments regarding the use of anions other than chloride and sulfate in precipitants may also be submitted to this address. Two copies of each comment and one 5-pound sample are to be submitted, and each submission is to be identified with the docket number (79N–0043) found in

brackets in the heading of this document.

XIII. References

The following references have been placed on display in the Dockets Management Branch (address above) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Kubo, Y., T. Iijima, ''Dye Elution from Aluminum Lake Synthetic Food Colors (VI) Brilliant Blue FCF Lakes,'' *Shikisai*, 60(1): 2–13, 1987.

2. Kubo, Y., M. Shirai, T. Iijima, ''Dye Elution from Aluminum Lake Synthetic Food Colors (VII) Lakes Produced by One-Step Method,'' *Shikisai*, 60(2):83–93, 1987.

3. Kubo, Y., H. Kawaguchi, ''Dye Elution from Aluminum Lake Synthetic Food Colors (V) Indigo Carmine Lakes,'' *Shikisai*, 59(11):663–669, 1986.

4. U.S. Patent 2,418,416 to Locke, R. C., Salem, NJ assignor to E.I. du Pont de Nemours and Co., Wilmington, DE, ''Manufacture of Azo Lakes,'' April 1, 1947.

5. U.S. Patent 2,478,768 to Locke, R. C., Salem, NJ assignor to E.I. du Pont de Nemours and Co., Wilmington, DE, ''Manufacture of Azo Lakes,'' August 9, 1949.

6. Clark, G. R., ''Report on Pure Dye, Impurities, and Substrata in Pigments,'' *Journal of the Association of Official Agricultural Chemists*, 28(4):938–941, 1942.

7. Clark, G. R., ''Report on Lakes and Pigments,'' *Journal of the Association of Official Agricultural Chemists*, 24(4):904–906, 1941.

8. Holtzman, H., ''The Hydrous Oxides of Aluminum and Color Lake Formation,'' agency internal progress report, 1942.

9. Zuckerman, S., ''Color in Cosmetics: *Cosmetics, Science and Technology*,'' edited by E. Sagarin, Interscience Publishers, New York, NY, pp. 539–572, 1974.

10. United States Department of Agriculture, Food Inspection Decision 76, July 13, 1907.

11. United States Department of Agriculture, ''Certification of Coal-Tar Colors Begun by Food and Drug Administration,'' information for the press, May 11, 1939.

12. Faulkner, E. B., ''Coping with International Color Regulations,'' *Cosmetics & Toiletries*, 107:45–49, 1992.

13. Memorandum dated June 27, 1988, from the Additives Evaluation Branch, FDA, to the Division of Food and Color Additives, FDA.

14. Memoranda dated July 13, 1994, and August 22, 1994, from Research Chemist, Office of Cosmetics and Colors, FDA (HFS-128), to Aydin Örstan, FDA (HFS–217).

15. Memorandum dated December 3, 1986, from the Division of Food and Color Additives, FDA, to the Division of Colors and Cosmetics, FDA.

16. *Color Index*, 3d ed., vol. 4, Society of Dyers and Colourists, Bradford, Yorkshire, England, pp. 4003, 4009–4011, 4013, 4379, 4417, 4435, 4593–4594, 1971.

17. Marmion, D. M., *Handbook of U.S. Colorants for Foods, Drugs, and Cosmetics*, 2d ed., John Wiley and Sons, New York, NY, pp. 48, 64–89, 1984.

18. Food and Drug Administration, ''Report on the Certification of Color Additives, Foreign and Domestic Manufacturers, fiscal year 1995.''

19. Color Additive Master File No. 9, entry nos. 550, 550A, and 550-addendum 1, dated September 3, 1986, October 8, 1986, and June 3, 1987.

20. Memoranda from the Division of Colors and Cosmetics, FDA, to the Division of Food and Color Additives, FDA, dated October 2, 1986, November 21, 1986, and October 7, 1987.

21. Food and Drug Administration, Office of Cosmetics and Colors, ''Intermediates and Subsidiary Colors in FD&C Blue No. 2 Straight Color and Lake,'' September 14, 1995.

22. Lykens, D. N., ''Thermal Stability of FD&C Lake Pigments,'' *Plastics Compounding*, pp. 35 to 40, November/December, 1986.

23. Memorandum from the Food and Color Additives Review Section, FDA, to the Direct Additives Branch, FDA, dated March 19, 1991.

24. Memorandum from the Additives Evaluation Branch, FDA, to the Direct Additives Branch, FDA, dated April 17, 1991.

25. Committee on GRAS List Survey—Phase III, ''The 1977 Survey of Industry on the Use of Food Additives,'' vol. 1, National Academy of Sciences, Washington, DC, pp. 1175 to 1192, 1979.

26. King, J., ''Method for Determination of Color Stability in Laking; The Results of Experiments with the Method of Establishing the Stability of Color in Laking for FD&C Red No. 4 and D&C Orange No. 4,'' January 28, 1980.

27. Food and Drug Administration, ''Report of FY–95 Certification Results for Batches of D&C Lakes of D&C Orange No. 5, D&C Red Nos. 21, 22, 27 and 28,'' December 1, 1995.

28. Food and Drug Administration, ''Report of FY–95 Certification Results for Batches of D&C Yellow No. 10 Lakes Prepared from Certified Batches of Straight Color,'' December 1, 1995.

29. The Cosmetic, Toiletry, and Fragrance Association, edited by Wenninger, J. A., and G. N. McEwen, ''International Cosmetic Ingredient Dictionary, 5th ed.,'', vol. 1, Washington, DC, p. 640, 1993.

30. Hercules, Product Data Sheet no. 7248, for Dresinate Dry Powder Soaps.

List of Subjects

21 CFR Part 70

Color additives, Cosmetics, Drugs, Labeling, Packaging and containers.

21 CFR Part 73

Color additives, Cosmetics, Drugs, Medical devices.

21 CFR Part 74

Color additives, Cosmetics, Drugs, Incorporation by reference.

21 CFR Part 80

Color additives, Cosmetics, Drugs, Reporting and recordkeeping requirements.

21 CFR Part 81

Color additives, Cosmetics, Drugs.

21 CFR Part 82

Color additives, Cosmetics, Drugs.

21 CFR Part 101

Food Labeling, Nutrition, Reporting and recordkeeping requirements.

21 CFR Part 178

Food additives, Food packaging.

21 CFR Part 201

Drugs, Labeling, Reporting and recordkeeping requirements.

21 CFR Part 701

Cosmetics, Labeling, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act, the transitional provisions of the Color Additive Amendments of 1960, and under authority delegated to the Commissioner of Food and Drugs and redelegated to the Associate Commissioner for Regulatory Affairs, it is proposed that 21 CFR parts 70, 73, 74, 80, 81, 82, 101, 178, 201 and 701 be amended as follows:

PART 70—COLOR ADDITIVES

1. The authority citation for 21 CFR part 70 continues to read as follows:

Authority: Secs. 201, 401, 402, 403, 409, 501, 512, 601, 701, 721 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 341, 342, 343, 348, 351, 360b, 361, 371, 379e).

2. Section 70.3 is amended by revising paragraphs (j), (k), (l), and (n), and by adding new paragraphs (w) and (x) to read as follows:

§ 70.3 Definitions.

* * * * *

(j) The term *straight color* means a color additive listed in parts 73 or 74 of this chapter, but does not include color additive mixtures or lakes.

(k) The term *mixture* means a color additive made by mixing two or more listed colors, or one or more listed colors and one or more diluents, without an accompanying chemical reaction.

(l) The term *lake* means a color additive made by extending one or more straight colors on one or more substrata by adsorption, coprecipitation, or chemical combination, but does not include mixtures.

* * * * *

(n) The term *substratum* means the substance on which the straight color in a lake is extended.

* * * * *

(w) The term *listed color* means a color additive listed in parts 73 or 74 of this chapter and includes lakes.

(x) The term *repack* means all or a portion of a batch of certified color additive that has been sealed in accordance with § 70.20 and labeled in accordance with § 70.25, but has been reopened solely for repackaging without further processing, or relabeled for shipment or delivery, by a person other than the person to whom the certificate or acceptance of a notice claiming certification was issued.

3. Section 70.20 is amended by revising the section heading and first sentence to read as follows:

§ 70.20 Packaging requirements for listed colors and mixtures (other than hair dyes).

Listed colors and mixtures shall be packaged in containers which prevent changes in composition. * * *

* * * * *

4. Section 70.25 is amended in paragraph (a), introductory text, by removing from the first sentence ''80, and 81'' and adding in its place ''and 80''; in paragraph (a)(1) by removing the words ''straight color'' and adding in their place the words ''listed color''; in paragraph (a)(3) by removing the words ''straight color'' and adding in their place the words ''listed color'' the two times they appear and by adding a new sentence at the end of the paragraph; and by revising paragraph (d) to read as follows:

§ 70.25 Labeling requirements for color additives (other than hair dyes).

(a) * * *

(3) * * * The amount of such straight color in a lake shall be considered part of the total amount of such straight color.

* * * * *

(d) *Special labeling for color additives not exempt from certification.* (1) Color additives subject to the certification procedures of § 80.31(a) of this chapter shall in addition include in the labeling the lot number assigned by the Color Certification Branch, Center for Food Safety and Applied Nutrition (CFSAN), Food and Drug Administration, except that in the case of any mixture for household use which contains not more than 15 percent of pure color and which is in packages containing not more than 3 ounces there appears on the label, a code number which the manufacturer has identified with the lot number by giving to the Food and Drug Administration written notice that such code number will be used in lieu of the lot number.

(2) Lakes subject to the certification procedures of § 80.31(b) of this chapter shall in addition include in the labeling:

(i) The total color content of the lake;

(ii) The amount of color contributed by each straight-color component of the lake; and

(iii) The FDA acceptance number assigned to the firm's notice claiming certification for the batch.

PART 73—LISTING OF COLOR ADDITIVES EXEMPT FROM CERTIFICATION

5. The authority citation for 21 CFR part 73 continues to read as follows:

Authority: Secs. 201, 401, 402, 403, 409, 501, 502, 505, 601, 602, 701, 721 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 341, 342, 343, 348, 351, 352, 355, 361, 362, 371, 379e).

§ 73.1 [Amended]

6. Section 73.1 *Diluents in color additive mixtures for food use exempt from certification* is amended in the introductory text by removing the words ''straight color'' and adding in their place the words ''listed color''.

7. Section 73.1001 is amended in the first sentence of the introductory text by removing the words ''straight color'' and adding in their place the words ''listed color'', and in the table in paragraph (a)(1) by alphabetically adding four new entries to read as follows:

§ 73.1001 Diluents in color additive mixtures for drug use exempt from certification.

* * * * *

(a) * * *

(1) * * *

Substances	Definitions and specifications	Restrictions
* *	* * * * * *	*
Aluminum benzoate	As set forth in § 74.1050(a)(3)(ii) of this chapter	
Barium sulfate	As set forth in § 74.1050(a)(3)(iii) of this chapter	
* *	* * * * * *	*
Kaolin	As set forth in § 74.1050(a)(3)(v) of this chapter	
* *	* * * * * *	*
Rosin	As set forth in § 74.1050(a)(3)(vi) of this chapter	For use only in ingested drugs.
* *	* * * * * *	*

* * * * *

PART 74—LISTING OF COLOR ADDITIVES SUBJECT TO CERTIFICATION

8. The authority citation for 21 CFR part 74 continues to read as follows:

Authority: Secs. 201, 401, 402, 403, 409, 501, 502, 505, 601, 602, 701, 721 of the Federal Food, Drug, and Cosmetic Act.

(21 U.S.C. 321, 341, 342, 343, 348, 351, 352, 355, 361, 362, 371, 379e)

9. Section 74.50 is added to subpart A to read as follows:

§ 74.50 Lakes for use in foods.

(a) *Identity.* (1) Lakes listed in this section are color additives made by extending one or more certified batches of one or more straight colors listed in paragraph (a)(2) of this section on a substratum of alumina that conforms to the requirements of paragraph (a)(3) of this section using one or more precipitants that form aluminum (Al^{+3}) cation and chloride (Cl^{-1}) or sulfate (SO_4^{-2}) anion.

(2) Lakes listed in this section may contain one or more of the following straight colors:

(i) FD&C Blue No. 1;

(ii) FD&C Blue No. 2;

(iii) FD&C Green No. 3;

(iv) FD&C Red No. 40;

(v) FD&C Yellow No. 5; and

(vi) FD&C Yellow No. 6.

(3) Lakes listed in this section shall contain the substratum alumina, which may either conform to the requirements for alumina under § 73.1010(a)(1) and (b) of this chapter, or may be a suspension in water of precipitated aluminum hydroxide that is formed from aluminum sulfate that meets the requirements of the Food Chemicals

Codex, 2d. ed., 1972, pp. 39–40, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51, and sodium carbonate or sodium hydroxide that meets the specifications of the Food Chemicals Codex, 3d. ed., 1981, p. 280 (sodium carbonate) or p. 287 (sodium hydroxide), which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies of this publication are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or may be examined at the Center for Food Safety and Applied Nutrition's Library, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(4) Color additive mixtures for food use (including dietary supplements) made with lakes listed in this section may contain only those diluents that are suitable and that are listed in part 73 of this chapter as safe for use in color additive mixtures for coloring foods. Such mixtures shall be used in accordance with paragraph (c) of this section.

(b) *Specifications.* Lakes listed in this section shall conform to the following specifications and shall be free from impurities other than those named, to the extent that such other impurities may be avoided by current good manufacturing practice:

(1) Lead (as Pb), not more than 10 parts per million;

(2) Arsenic (as As), not more than 3 parts per million; and

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

(c) *Uses and restrictions.* Lakes listed in this section may be safely used for coloring foods generally (including dietary supplements) in amounts consistent with current good manufacturing practice, except that:

(1) They may not be used to color foods for which standards of identity have been promulgated under section 401 of the act unless added color is authorized by such standards; and

(2) Any restriction on the use of a straight color shall also apply to the use of a lake of such straight color. If a lake is prepared using a single straight color, the lake may be used in the same manner as permitted for the straight color. If a lake is prepared using more than one straight color, its use shall be restricted to those uses common to all of the component straight colors.

(d) *Identification.* Each lake made as prescribed in paragraph (a) of this section shall be considered to be a listed color and to be listed therein under the name that is formed as follows:

(1) The listed names of the straight colors present in the lake (in descending order of predominance);

(2) The name of the cation precipitant ''Aluminum,'' followed by the words ''Lake on Alumina.'' (For example, the name of a lake prepared by the extension of FD&C Yellow No. 5 and FD&C Blue No. 1 on alumina using aluminum chloride as a precipitant is ''FD&C Yellow No. 5 and FD&C Blue No. 1 Aluminum Lake on Alumina.'')

(e) *Labeling.* (1) The label of each lake listed in this section and any mixtures prepared from them that are intended solely or in part for coloring purposes shall conform to the requirements of § 70.25 of this chapter.

(2) Foods for human use that contain lakes listed in this section shall declare the presence of such lakes in accordance with § 101.22(k)(1) of this chapter.

(3) Butter, cheese, and cream that contain a lake of FD&C Yellow No. 5 or FD&C Yellow No. 6 shall be labeled in accordance with § 101.22(k)(1) of this chapter.

(f) *Certification.* All batches of lakes listed in this section shall be certified in accordance with regulations in part 80 of this chapter.

10. Section 74.101 is amended by adding new paragraph (a)(3) to read as follows:

§ 74.101 FD&C Blue No. 1.

(a) * * *

(3) Lakes made with FD&C Blue No. 1 shall conform to the requirements of § 74.50.

* * * * *

11. Section 74.102 is amended by adding new paragraph (a)(3) to read as follows:

§ 74.102 FD&C Blue No. 2.

(a) * * *

(3) Lakes made with FD&C Blue No. 2 shall conform to the requirements of § 74.50.

* * * * *

12. Section 74.203 is amended by adding new paragraph (a)(3) to read as follows:

§ 74.203 FD&C Green No. 3.

(a) * * *

(3) Lakes made with FD&C Green No. 3 shall conform to the requirements of § 74.50.

* * * * *

13. Section 74.340 is amended by revising paragraph (a)(3); in paragraph (d) by removing the words ''lakes or''; and in paragraph (e) by removing the words ''and lakes thereof'', to read as follows:

§ 74.340 FD&C Red No. 40.

(a) * * *

(3) Lakes made with FD&C Red No. 40 shall conform to the requirements of § 74.50.

* * * * *

14. Section 74.705 is amended by revising paragraph (a)(3) to read as follows:

§ 74.705 FD&C Yellow No. 5.

(a) * * *

(3) Lakes made with FD&C Yellow No. 5 shall conform to the requirements of § 74.50.

* * * * *

15. Section 74.706 is amended by adding new paragraph (a)(3) to read as follows:

§ 74.706 FD&C Yellow No. 6.

(a) * * *

(3) Lakes made with FD&C Yellow No. 6 shall conform to the requirements of § 74.50.

* * * * *

16. Section 74.1050 is added to subpart B to read as follows:

§ 74.1050 Lakes for use in drugs.

(a) *Identity.* (1) Lakes listed in this section are color additives made by extending one or more certified batches of one or more straight colors specified in paragraph (a)(2) of this section on one or more substrata specified in paragraph (a)(3) of this section, using one or more precipitants that form aluminum (Al^{+3}), barium (Ba^{+2}), calcium (Ca^{+2}), potassium (K^{+1}), sodium (Na^{+1}), strontium (Sr^{+2}), or zirconium (Zr^{+4}) cation, and chloride (Cl^{-1}) or sulfate (SO_4^{-2}) anion.

(2) Lakes listed in this section may contain one or more of the following straight colors:

(i) FD&C Blue No. 1;
(ii) FD&C Blue No. 2;
(iii) FD&C Green No. 3;
(iv) FD&C Yellow No. 5;
(v) FD&C Yellow No. 6;
(vi) FD&C Red No. 4;
(vii) FD&C Red No. 40;
(viii) D&C Blue No. 4;
(ix) D&C Orange No. 4;
(x) D&C Orange No. 5;
(xi) D&C Orange No. 10;
(xii) D&C Red No. 6;
(xiii) D&C Red No. 7;
(xiv) D&C Red No. 21;
(xv) D&C Red No. 22;
(xvi) D&C Red No. 27;
(xvii) D&C Red No. 28;
(xviii) D&C Red No. 31;
(xix) D&C Red No. 33;
(xx) D&C Red No. 34; and
(xxi) D&C Yellow No. 10.

(3) Lakes listed in this section may contain one or more of the following substrata:

(i) Alumina that conforms to the requirements of § 74.50(a)(3) of this chapter; and

(ii) Aluminum benzoate that is prepared from aluminum chloride or aluminum sulfate that conforms to the requirements of the United States Pharmacopeia, 23d ed. (1995), p. 64 (aluminum chloride) or p. 68 (aluminum sulfate), which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51, and benzoic acid that conforms to the requirements of the United States Pharmacopeia, 23d ed. (1995), pp. 176 and 177, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the United States Pharmacopoeial Convention, Inc., 12601 Twinbrook Pkwy., Rockville, MD 20852, or may be examined at the Center for Food Safety and Applied Nutrition's Library, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(iii) Barium sulfate that conforms to the requirements of the United States Pharmacopeia, 23d ed. (1995), pp. 165 and 166, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. The availability of this incorporation by reference is given in paragraph (a)(3)(ii) of this section.

(iv) Calcium carbonate that conforms to the requirements of § 73.1070(a)(1) and (b) of this chapter.

(v) Kaolin that conforms to the requirements of the United States Pharmacopeia, 23d ed. (1995), p. 863, which are incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. The availability of this incorporation by reference is given in paragraph (a)(3)(ii) of this section.

(vi) Rosin, which is the pale, cream-colored sodium soap of the residue left after distilling off the volatile oil from the oleoresin obtained from *Pinus palustris* and other species of *Pinus*, and which conforms to the following specifications:

(A) Solids, not less than 95 percent;

(B) Acid number, not greater than 7.5; and

(C) Free alkali, not greater than 2.5 percent.

(vii) Talc that conforms to the requirements of § 73.1550(a)(1) and (b) of this chapter.

(viii) Titanium dioxide that conforms to the requirements of § 73.575 (a)(1) and (b) of this chapter.

(ix) Zinc oxide that conforms to the requirements of § 73.1991(a)(1) and (b) of this chapter.

(4) Color additive mixtures for drug use made with lakes listed in this section may contain only those diluents that are suitable and that are listed in part 73 of this chapter as safe for use in color additive mixtures for coloring drugs. Such mixtures shall be used in accordance with paragraph (c) of this section.

(b) *Specifications.* Lakes listed in this section shall conform to the following specifications and shall be free from impurities other than those named, to the extent that such other impurities may be avoided by current good manufacturing practice:

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

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

(3) Mercury (as Hg), not more than 1 part per million; and

(4) For a lake that contains a barium salt, soluble barium (in dilute HCl) as $BaCl_2$, not more than 0.05 percent.

(c) *Uses and restrictions.* Lakes listed in this section may be safely used for coloring drugs generally in amounts consistent with current good manufacturing practice, except that:

(1) Any restriction on the use of a straight color shall also apply to the use of a lake of such straight color. If a lake is prepared using a single straight color, the lake may be used in the same manner as permitted for the straight color. If a lake is prepared using more than one straight color, its use shall be restricted to those uses common to all of the component straight colors. (For example, a lake produced using two straight colors, one listed for use in coloring drugs generally and one listed for use in coloring externally applied drugs only, may be used only for coloring externally applied drugs.)

(2) Where regulations impose quantitative limitations for a general or specific use of a straight color, the amount of such straight color in a lake shall be considered part of the total amount of such straight color in a drug product.

(3) The aluminum lakes on alumina of FD&C Blue No. 1, FD&C Red No. 40, and FD&C Yellow No. 5, prepared in accordance with the requirements of § 74.50, may be safely used for coloring drugs intended for use in the area of the eye, in amounts consistent with current good manufacturing practice. Use of these lakes in the area of the eye is subject to the limitations in § 70.5 (b) and (c) of this chapter and does not include use in articles intended for use in injections or as a surgical suture in the area of the eye.

(d) *Identification.* Each lake made as prescribed in paragraph (a) of this section shall be considered to be a listed color and to be listed therein under the name that is formed as follows:

(1) The listed names of the straight colors present in the lake (in descending order of predominance);

(2) The names of the cations of the precipitants, followed by the words ''Lake on _____'';

(3) The names of the substrata (in descending order of predominance). (For example: The name of a lake prepared by the extension of FD&C Red No. 40 and D&C Orange No. 5 on alumina and titanium dioxide using aluminum chloride and calcium chloride as precipitants is ''FD&C Red No. 40 and D&C Orange No. 5 Aluminum/Calcium Lake on Alumina and Titanium Dioxide.'')

(e) *Labeling.* (1) The label of each lake listed in this section and any mixtures prepared from them that are intended solely or in part for coloring purposes shall conform to the requirements of § 70.25 of this chapter.

(2) Drugs that contain a lake of FD&C Yellow No. 5 shall be labeled in accordance with § 74.1705 (c)(2) and (c)(3).

(3) Drugs that contain a lake of FD&C Yellow No. 6 shall be labeled in accordance with § 74.1706(c)(2).

(f) *Certification.* All batches of lakes listed in this section shall be certified in accordance with regulations in part 80 of this chapter.

17. Section 74.1101 is amended by adding a new paragraph (a)(4), by removing paragraphs (b)(2) and (c)(2) and redesignating paragraph (b)(1) and (c)(1) as paragraphs (b) and (c), respectively, to read as follows:

§ 74.1101 FD&C Blue No. 1.

(a) * * *

(4) Lakes made with FD&C Blue No. 1 shall conform to the requirements of § 74.1050.

* * * * *

18. Section 74.1102 is amended by adding new paragraph (a)(3) to read as follows:

§ 74.1102 FD&C Blue No. 2.

(a) * * *

(3) Lakes made with FD&C Blue No. 2 shall conform to the requirements of § 74.1050.

* * * * *

19. Section 74.1104 is amended by adding new paragraph (a)(3) to read as follows:

§ 74.1104 FD&C Blue No. 4.

(a) * * *

(3) Lakes made with FD&C Blue No. 4 shall conform to the requirements of § 74.1050.

* * * * *

20. Section 74.1203 is amended by adding a new paragraph (a)(3) to read as follows:

§ 74.1203 FD&C Green No. 3.

(a) * * *

(3) Lakes made with FD&C Green No. 3 shall conform to the requirements of § 74.1050.

* * * * *

21. Section 74.1254 is amended by adding new paragraph (a)(3) to read as follows:

§ 74.1254 D&C Orange No. 4.

(a) * * *

(3) Lakes made with D&C Orange No. 4 shall conform to the requirements of § 74.1050.

* * * * *

22. Section 74.1255 is amended by adding new paragraph (a)(3) to read as follows:

§ 74.1255 D&C Orange No. 5.

(a) * * *

(3) Lakes made with D&C Orange No. 5 shall conform to the requirements of § 74.1050.

* * * * *

23. Section 74.1260 is amended by adding new paragraph (a)(3) to read as follows:

§ 74.1260 D&C Orange No. 10.

(a) * * *

(3) Lakes made with D&C Orange No. 10 shall conform to the requirements of § 74.1050.

* * * * *

24. Section 74.1304 is amended by adding new paragraph (a)(3) to read as follows:

§ 74.1304 FD&C Red No. 4.

(a) * * *

(3) Lakes made with FD&C Red No. 4 shall conform to the requirements of § 74.1050.

* * * * *

25. Section 74.1306 is amended by adding new paragraph (a)(3) to read as follows:

§ 74.1306 D&C Red No. 6.

(a) * * *

(3) Lakes made with D&C Red No. 6 shall conform to the requirements of § 74.1050.

* * * * *

26. Section 74.1307 is amended by adding new paragraph (a)(3) to read as follows:

§ 74.1307 D&C Red No. 7.

(a) * * *

(3) Lakes made with D&C Red No. 7 shall conform to the requirements of § 74.1050.

* * * * *

27. Section 74.1321 is amended by adding new paragraph (a)(3) to read as follows:

§ 74.1321 D&C Red No. 21.

(a) * * *

(3) Lakes made with D&C Red No. 21 shall conform to the requirements of § 74.1050.

* * * * *

28. Section 74.1322 is amended by adding new paragraph (a)(3) to read as follows:

§ 74.1322 D&C Red No. 22.

(a) * * *

(3) Lakes made with D&C Red No. 22 shall conform to the requirements of § 74.1050.

* * * * *

29. Section 74.1327 is amended by adding new paragraph (a)(3) to read as follows:

§ 74.1327 D&C Red No. 27.

(a) * * *

(3) Lakes made with D&C Red No. 27 shall conform to the requirements of § 74.1050.

* * * * *

30. Section 74.1328 is amended by adding new paragraph (a)(3) to read as follows:

§ 74.1328 D&C Red No. 28.

(a) * * *

(3) Lakes made with D&C Red No. 28 shall conform to the requirements of § 74.1050.

* * * * *

31. Section 74.1331 is amended by adding new paragraph (a)(3) to read as follows:

§ 74.1331 D&C Red No. 31.

(a) * * *

(3) Lakes made with D&C Red No. 31 shall conform to the requirements of § 74.1050.

* * * * *

32. Section 74.1333 is amended by adding new paragraph (a)(3) to read as follows:

§ 74.1333 D&C Red No. 33.

(a) * * *

(3) Lakes made with D&C Red No. 33 shall conform to the requirements of § 74.1050.

* * * * *

33. Section 74.1334 is amended by adding new paragraph (a)(3) to read as follows:

§ 74.1334 D&C Red No. 34.

(a) * * *

(3) Lakes made with D&C Red No. 34 shall conform to the requirements of § 74.1050.

* * * * *

34. Section 74.1340 is amended by revising paragraph (a)(3); by removing paragraph (b)(2); by redesignating paragraph (b)(1) as paragraph (b); by amending newly redesignated paragraph (b) by removing the phrase ''and FD&C Red No. 40 Aluminum Lake''; by amending paragraph (c) by removing the phrase ''lakes or''; and by amending paragraph (d) by removing the phrase ''and lakes thereof'' to read as follows:

§ 74.1340 FD&C Red No. 40.

(a) * * *

(3) Lakes made with FD&C Red No. 40 shall conform to the requirements of § 74.1050.

* * * * *

35. Section 74.1705 is amended by revising paragraph (a)(2); by removing paragraph (b)(2); by redesignating paragraph (b)(1) as paragraph (b); and by removing in the first sentence of paragraph (c)(2) and paragraph (c)(3), the phrase ''containing FD&C Yellow No. 5'' and adding in its place the phrase ''containing FD&C Yellow No. 5 or a lake of FD&C Yellow No. 5''.

§ 74.1705 FD&C Yellow No. 5.

(a) * * *

(2) Lakes made with FD&C Yellow No. 5 shall conform to the requirements of § 74.1050.

* * * * *

36–37. Section 74.1706 is amended by adding new paragraphs (a)(3) and (c)(2) to read as follows:

§ 74.1706 FD&C Yellow No. 6.

(a) * * *

(3) Lakes made with FD&C Yellow No. 6 shall conform to the requirements of § 74.1050.

* * * * *

(c) * * *

(2) The label of over-the-counter and prescription drug products intended for human use and administered orally, nasally, rectally, or vaginally containing FD&C Yellow No. 6, or a lake of FD&C Yellow No. 6, shall specifically declare the presence of FD&C Yellow No. 6 by listing the color additive using the name FD&C Yellow No. 6. The labels of certain drug products subject to this labeling requirement that are also cosmetics, such as antibacterial mouthwashes and fluoride toothpastes, need not comply with this requirement provided they comply with the requirements of § 701.3 of this chapter.

38. Section 74.1710 is amended by adding new paragraph (a)(3) to read as follows:

§ 74.1710 D&C Yellow No. 10.

(a) * * *

(3) Lakes made with D&C Yellow No. 10 shall conform to the requirements of § 74.1050.

* * * * *

39. Section 74.2050 is added to subpart C to read as follows:

§ 74.2050 Lakes for use in cosmetics.

(a) *Identity and specifications.* Lakes listed in this section shall conform in identity and specifications to the requirements of § 74.1050(a)(1), (a)(2), (a)(3), and (b), except that the straight color FD&C Blue No. 2 shall not be a component of such lakes.

(b) *Uses and restrictions.* Lakes listed in this section may be safely used for coloring cosmetics generally in amounts consistent with current good manufacturing practice, except that:

(1) Any restriction on the use of a straight color shall also apply to the use of a lake of such straight color. If a lake is prepared using a single straight color, the lake may be used in the same manner as permitted for the straight color. If a lake is prepared using more than one straight color, its use shall be restricted to those uses common to all of the component straight colors. (For example, a lake produced using two straight colors, one listed for use in coloring cosmetics generally and one listed for use in coloring externally applied cosmetics only, may be used only for coloring externally applied cosmetics.)

(2) Where regulations impose quantitative limitations for a general or specific use of a straight color, the amount of such straight color in a lake shall be considered a part of the total amount of such straight color in a cosmetic product.

(3) The aluminum lakes on alumina of FD&C Blue No. 1, FD&C Red No. 40, and FD&C Yellow No. 5, prepared in accordance with the requirements of § 74.50, may be safely used for coloring cosmetics intended for use in the area of the eye, in amounts consistent with current good manufacturing practice. Use of these lakes in the area of the eye is subject to the limitations in § 70.5(b) and (c) of this chapter, and does not include use in articles intended for use in injections or as a surgical suture in the area of the eye.

(c) *Identification.* Each lake made as prescribed in paragraph (a) of this section shall be considered to be a listed color and to be listed therein under the name that is formed as prescribed in § 74.1050(d).

(d) *Labeling.* (1) The label of each lake listed in this section and any mixtures prepared from that are intended solely or in part for coloring purposes shall conform to the requirements of § 70.25 of this chapter.

(2) Cosmetics that contain lakes listed in this section shall declare the presence of such lakes in accordance with § 701.3(c)(1)(i) of this chapter.

(e) *Certification.* All batches of lakes listed in this section shall be certified in accordance with regulations in part 80 of this chapter.

40. Section 74.2101 is amended by removing paragraphs (b)(2) and (c)(2); by redesignating paragraphs (a), (b)(1), and (c)(1) as paragraphs (a)(1), (b), and (c), respectively; and by adding new paragraph (a)(2) to read as follows:

§ 74.2101 FD&C Blue No. 1.

(a) * * *

(2) Lakes made with FD&C Blue No. 1 shall conform to the requirements of § 74.2050.

* * * * *

41. Section 74.2104 is amended by redesignating paragraph (a) as paragraph (a)(1) and by adding new paragraph (a)(2) to read as follows:

§ 74.2104 D&C Blue No. 4.

(a) * * *

(2) Lakes made with D&C Blue No. 4 shall conform to the requirements of § 74.2050.

* * * * *

42. Section 74.2203 is amended by redesignating paragraph (a) as paragraph (a)(1) and by adding new paragraph (a)(2) to read as follows:

§ 74.2203 FD&C Green No. 3.

(a) * * *

(2) Lakes made with FD&C Green No. 3 shall conform to the requirements of § 74.2050.

* * * * *

43. Section 74.2254 is amended by redesignating paragraph (a) as paragraph (a)(1) and by adding new paragraph (a)(2) to read as follows:

§ 74.2254 D&C Orange No. 4.

(a) * * *

(2) Lakes made with D&C Orange No. 4 shall conform to the requirements of § 74.2050.

* * * * *

44. Section 74.2255 is amended by redesignating paragraph (a) as paragraph (a)(1) and by adding new paragraph (a)(2) to read as follows:

§ 74.2255 D&C Orange No. 5.

(a) * * *

(2) Lakes made with D&C Orange No. 5 shall conform to the requirements of § 74.2050.

* * * * *

45. Section 74.2260 is amended by redesignating paragraph (a) as paragraph (a)(1) and adding new paragraph (a)(2) to read as follows:

§ 74.2260 D&C Orange No. 10.

(a) * * *

(2) Lakes made with D&C Orange No. 10 shall conform to the requirements of § 74.2050.

* * * * *

46. Section 74.2304 is amended by redesignating paragraph (a) as paragraph (a)(1) and by adding new paragraph (a)(2) to read as follows:

§ 74.2304 FD&C Red No. 4.

(a) * * *

(2) Lakes made with FD&C Red No. 4 shall conform to the requirements of § 74.2050.

* * * * *

47. Section 74.2306 is amended by redesignating paragraph (a) as paragraph (a)(1) and by adding new paragraph (a)(2) to read as follows:

§ 74.2306 D&C Red No. 6.

(a) * * *

(2) Lakes made with D&C Red No. 6 shall conform to the requirements of § 74.2050.

* * * * *

48. Section 74.2307 is amended by redesignating paragraph (a) as paragraph (a)(1) and by adding new paragraph (a)(2) to read as follows:

§ 74.2307 D&C Red No. 7.

(a) * * *

(2) Lakes made with D&C Red No. 7 shall conform to the requirements of § 74.2050.

* * * * *

49. Section 74.2321 is amended by redesignating paragraph (a) as paragraph (a)(1) and by adding new paragraph (a)(2) to read as follows:

§ 74.2321 D&C Red No. 21.

(a) * * *

(2) Lakes made with D&C Red No. 21 shall conform to the requirements of § 74.2050.

* * * * *

50. Section 74.2322 is amended by redesignating paragraph (a) as paragraph (a)(1) and by adding new paragraph (a)(2) to read as follows:

§ 74.2322 D&C Red No. 22.

(a) * * *

(2) Lakes made with D&C Red No. 22 shall conform to the requirements of § 74.2050.

* * * * *

51. Section 74.2327 is amended by redesignating paragraph (a) as paragraph (a)(1) and by adding new paragraph (a)(2) to read as follows:

§ 74.2327 D&C Red No. 27.

(a) * * *

(2) Lakes made with D&C Red No. 27 shall conform to the requirements of § 74.2050.

* * * * *

52. Section 74.2328 is amended by redesignating paragraph (a) as paragraph (a)(1) and by adding new paragraph (a)(2) to read as follows:

§ 74.2328 D&C Red No. 28.

(a) * * *

(2) Lakes made with D&C Red No. 28 shall conform to the requirements of § 74.2050.

* * * * *

53. Section 74.2331 is amended by redesignating paragraph (a) as paragraph (a)(1) and by adding new paragraph (a)(2) to read as follows:

§ 74.2331 D&C Red No. 31.

(a) * * *

(2) Lakes made with D&C Red No. 31 shall conform to the requirements of § 74.2050.

* * * * *

54. Section 74.2333 is amended by redesignating paragraph (a) as paragraph (a)(1) and by adding new paragraph (a)(2) to read as follows:

§ 74.2333 D&C Red No. 33.

(a) * * *

(2) Lakes made with D&C Red No. 33 shall conform to the requirements of § 74.2050.

* * * * *

55. Section 74.2334 is amended by redesignating paragraph (a) as paragraph (a)(1) and by adding new paragraph (a)(2) to read as follows:

§ 74.2334 D&C Red No. 34.

(a) * * *

(2) Lakes made with D&C Red No. 34 shall conform to the requirements of § 74.2050.

* * * * *

56. Section 74.2340 is amended by revising paragraph (a)(2); by removing in the introductory text of paragraph (b) the phrase ''except that only FD&C Red No. 40 and FD&C Red No. 40 Aluminum Lake may be safely used in coloring'' and adding in its place the word ''including'', in paragaph (b)(2) by removing the words ''additives'' and ''their'' and adding in their place the words ''additive'' and ''its'', respectively, to read as follows:

§ 74.2340 FD&C Red No. 40.

(a) * * *

(2) Lakes made with FD&C Red No. 40 shall conform to the requirements of § 74.2050.

* * * * *

57. Section 74.2705 is amended by redesignating paragraph (a) as paragraph (a)(1) and by adding new paragraph (a)(2), by removing paragraph (b)(2) and (c)(2) and redesignating paragraphs (b)(1) and (c)(1) as paragraphs (b) and (c), respectively, to read as follows:

§ 74.2705 FD&C Yellow No. 5.

(a) * * *

(2) Lakes made with FD&C Yellow No. 5 shall conform to the requirements of § 74.2050.

* * * * *

58–59. Section 74.2706 is amended by redesignating paragraph (a) as paragraph(a)(1) and by adding new paragraph (a)(2) to read as follows:

§ 74.2706 FD&C Yellow No. 6.

(a) * * *

(2) Lakes made with FD&C Yellow No. 6 shall conform to the requirements of § 74.2050.

* * * * *

60. Section 74.2710 is amended by redesignating paragraph (a) as paragraph(a)(1) and by adding a new paragraph (a)(2) to read as follows:

§ 74.2710 D&C Yellow No. 10.

(a) * * *

(2) Lakes made with D&C Yellow No. 10 shall conform to the requirements of § 74.2050.

* * * * *

PART 80—COLOR ADDITIVE CERTIFICATION

61. The authority citation for 21 CFR Part 80 continues to read as follows:

Authority: Secs. 701, 721 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 371, 379e).

62. Section 80.10 is amended in paragraph (a) by revising the paragraph heading and by removing the phrase ''and (j)(2)''; in paragraph (b), introductory text, by revising the paragraph heading and by removing ''§ 80.21(j)(3) and (j)(4)'' and adding in its place ''§ 80.21(j)(2) and (j)(3)''; by redesignating paragraphs (c), (d), (e), and (f) as paragraphs (d), (e), (f), and (g), respectively, by amending newly redesignated paragraph (d) by removing the phrase ''(a) and (b)'' and adding in its place the phrase ''(a), (b), and (c)'', and by adding new paragraph (c) to read as follows:

§ 80.10 Fees for certification services.

(a) *Fees for straight colors.* * * *

* * * * *

(b) *Fees for repacks of certified straight colors and color additive mixtures.* * * *

* * * * *

(c) *Fees for lakes and repacks of certified lakes.* The fee for the services provided under the regulations in this part in the case of each notice claiming certification submitted in accordance with § 80.33 shall be $30.00.

* * * * *

63. Section 80.21 is amended in paragraph (g)(1) by removing the phrase ''and lakes''; by amending paragraph (g)(2) by adding the words ''of straight colors'' at the end of the sentence; by revising paragraph (h)(1); by removing paragraph (h)(2) and redesignating paragraphs (h)(3) and (h)(4) as paragraphs (h)(2) and (h)(3), respectively; by revising newly redesignated paragraph (h)(3); by amending paragraph (j), introductory text, by removing the words ''a lake,'' and by removing the phrase ''previously certified color additive'' and adding in its place the phrase ''previously certified straight color''; by removing paragraph (j)(2) and redesignating paragraphs (j)(3) and (j)(4) as paragraphs (j)(2) and (j)(3), respectively; and by revising the paragraph heading of newly designated paragraph (j)(2) to read as follows:

§ 80.21 Request for certification.

* * * * *

(h) * * *

(1) The name of a straight color shall be the name of the color additive as listed in part 74 of this chapter.

* * * * *

(3) The name of a repack shall be the name described in paragraph (h)(1) or (h)(2) of this section, whichever is applicable.

* * * * *

(j) * * *

(2) *Request for certification of a repack of a batch of certified straight color.* * * *

* * * * *

64. Section 80.22 is revised to read as follows:

§ 80.22 Samples to accompany requests for certification or to be held as records.

(a) *Straight colors and their mixtures and repacks.* A sample of a batch of color additive which is to accompany a request for certification shall:

(1) Be taken only after such batch has been so thoroughly mixed as to be of uniform composition throughout;

(2) Be held under the control of the person requesting certification until certified; and

(3) Be labeled to show:

(i) The name of the color additive;

(ii) The manufacturer's batch number;

(iii) The quantity of such batch;

(iv) The name and post office address of the person requesting certification of such batch; and

(v) Be accompanied by any label or labeling intended to be used.

(b) *Lakes and their repacks.* A sample of a batch of lake that is to be held by a firm claiming certification for the batch shall:

(1) Be taken prior to submission of the notice claiming certification;

(2) Be taken only after such batch has been so thoroughly mixed as to be of uniform composition throughout;

(3) Be sealed and stored in such a manner as to prevent change in composition;

(4) Be held by the firm claiming certification for the batch, as required by § 80.39(b)(3); and

(5) Be labeled to show:

(i) The name of the lake;

(ii) The percent total color for the batch and, if the batch contains more than one straight color, the percent color in the batch for each straight color;

(iii) The firm's batch number and the date the sample was taken;

(iv) The quantity of the batch;

(v) The name and place of business of the firm claiming certification for the batch;

(vi) A copy of any label or labeling intended to be used with the batch; and

(vii) After receipt of an acceptance of the notice claiming certification for the batch, FDA's acceptance number.

65. Section 80.31 is amended in paragraph (a) by adding a new heading; by removing in paragraph (a)(2) in the phrase ''parts 81 and 82'' and adding in its place ''part 74'', by removing in paragraph (a)(3) the phrase ''81, and 82'', by revising paragraph (b), and by adding new paragraph (c) to read as follows:

§ 80.31 Certification.

(a) *Straight colors and their mixtures and repacks.* * * *

* * * * *

(b) *Lakes and their repacks.* If the Commissioner determines, after such investigations as the Commissioner considers to be necessary, that:

(1) A notice submitted in accordance with § 80.33 appears to contain no untrue statement of a material fact;

(2) Such lake conforms to the specifications and any other conditions set forth therefor in part 74 of this chapter;

(3) The manufacturer of the lake is the firm that was issued the certificate for each batch of straight color used in the lake;

(4) The manufacturer or repacker of the batch has complied with the notification requirements in § 80.33 and the recordkeeping requirements in § 80.39; and

(5) The batch covered by such notice otherwise appears to comply with the regulations in this chapter, the Commissioner shall issue to the firm that submitted the notice, an acceptance showing the acceptance number assigned to such notice. Upon issuance of such an acceptance, the batch covered by the notice, subject to the terms, conditions and restrictions prescribed by part 74 of this chapter, is a certified batch.

(c) If the Commissioner determines, after such investigation as the Commissioner considers to be necessary, that a request submitted in accordance with § 80.21, or the batch of color additive covered by such request, does not comply with the requirements prescribed by paragraph (a) of this section for the issuance of a certificate, or that a notice submitted in accordance with § 80.33, or the batch of lake covered by such notice, does not comply with the requirements prescribed by paragraph (b) of this section for the issuance of an acceptance of the notice, the Commissioner shall refuse to certify such batch and shall give notice thereof to the person who submitted such request, or such notice, stating the Commissioner's reasons for refusal. Any person who contests such refusal shall have an opportunity for a regulatory hearing before the Food and Drug Administration pursuant to part 16 of this chapter.

66. Section 80.32 is amended by revising the section heading and paragraphs (a), (b), (c), and the introductory text of paragraph (d); in paragraphs (e), (f), introductory text, and (g) by adding the words ''or an acceptance of a notice claiming certification'' after the words ''A certificate''; and in paragraph (h) by revising the first sentence to read as follows:

§ 80.32 Limitations of certification.

(a) If a certificate or an acceptance of a notice claiming certification is obtained through fraud or misrepresentation of a material fact, such certificate or acceptance shall not be effective, and a color additive from the batch on which such certificate or acceptance was issued, or from any batch of lake prepared with such color additive, shall be considered to be from a batch that has not been certified in accordance with the regulations in this part. Whenever the Commissioner learns that any certificate or acceptance of a notice claiming certification has been obtained through fraud or material misrepresentation, the Commissioner shall notify the holder of the certificate or acceptance that it is of no effect.

(b) If, between the time a sample of color additive accompanying a request for certification or retained by a firm that has submitted a notice claiming certification is taken from a batch of color additive and the time a certificate or an acceptance of the notice claiming certification for such batch is received by the person to whom such certificate or acceptance is issued, any such color additive becomes changed in composition, such certificate or such acceptance shall not be effective with respect to such changed color additive, and such changed color additive, and any lake prepared with such color additive, shall be considered to be from a batch that has not been certified in accordance with the regulations in this part.

(c) If, at any time after a certificate or an acceptance of a notice claiming certification is received by the person to whom it is issued, any color additive from the batch covered by such certificate or acceptance becomes changed in composition, such certificate or acceptance shall expire with respect to such changed color additive. After such expiration, such color additive and any lake prepared with such color additive shall be considered to be from a batch that has not been certified in accordance with this part; except that such color additive or lake shall not be so considered when used for coloring a food, drug, or cosmetic, or for the purpose of certifying a batch of a mixture in which such color additive was used as an ingredient, or for use in preparing a batch of a mixture for which exemption from certification has been authorized, or for use in preparing a batch of lake for which certification is claimed under § 80.31(b), if such change resulted solely from such use.

(d) A certificate or an acceptance of a notice claiming certification shall expire with respect to any color additive covered thereby if the package in which such color additive was closed for shipment or delivery is opened. After such expiration such color additive shall be considered to be from a batch that has not been certified, except that such color additive shall not be so considered when the package is opened;

* * * * *

(h) When the listing or the specifications for a color additive are revoked or amended, the final order effecting the revocation or amendment may specify, in addition to its own effective date, a date on which all previous certificates or acceptances of

notices claiming certification for existing batches and portions of batches of such a color additive issued under the revoked or amended regulations shall cease to be effective; and any such lots or batches of the color additive, and any batches of lake prepared from such lots or batches, shall be regarded as uncertified after the date specified unless a new certificate or, for a lake, a new acceptance of a notice claiming certification, can be and is obtained in conformance with the new regulations.

* * *

67. New § 80.33 is added to subpart B to read as follows:

§ 80.33 Notice claiming certification for a batch of lake.

A notice claiming certification for a batch of lake or lake repack shall:

(a) Be addressed to the Commissioner of Food and Drugs;

(b) Be prepared in the manner set forth in paragraph (i) of this section;

(c) Be submitted in duplicate;

(d) Be signed by a responsible officer of the firm submitting the notice. In the case of a foreign company, the notice must be signed by a responsible officer of such firm, and by an agent of the firm who resides in the United States;

(e) Show the name and place of business (street address, city, State, and zip code) of the firm submitting the notice;

(f) Be accompanied by the fee prescribed in § 80.10 unless the firm has established an advanced deposit to be used for prepayment of such fees. In no case shall the Commissioner consider a notice claiming certification for a batch of lake or lake repack if the fee accompanying such notice is less than that required by § 80.10 or if such fee exceeds the amount held in the advance deposit account of the firm submitting such notice; and

(g) Be accompanied by any label or labeling intended to be used with the batch.

(h) The name of a lake shall be the name derived in the manner described in part 74 of this chapter.

(i) The form for submission of the notice shall be one of the following, depending on whether the color additive is a new batch of lake or a repack of a previously certified batch of lake:

(1) *Notice claiming certification for a new batch of lake.*

Date _____

Division of Programs and Enforcement Policy (HFS–105), Center for Food Safety and Applied Nutrition, Food and Drug Administration, 200 C St. SW., Washington, DC 20204.

In accordance with the regulations promulgated under the Federal Food, Drug, and Cosmetic Act, we hereby give notice that we claim certification for a batch of lake.

Name of lake _____

Batch number _____

Batch weighs _____ pounds (or kilograms)

Total color _____ percent of batch

For each straight color used:

Color content _____ percent of batch.

How stored pending certification _____

_____

_____

(State conditions of storage, with kind and size of containers, location, etc.)

For use in _____

_____

_____

(State proposed uses)

Ingredients of batch

Name of each straight color used _____

_____

For each straight color used:

Certified Lot number _____

Quantity used _____ pounds (or kilograms)

For each precipitant or substratum ingredient used:

Name of ingredient used _____

Quantity used _____ pounds (or kilograms)

If any previously certified batches of lake have been used, provide the following information for each such batch.

Name of lake _____

FDA acceptance number (or certified lot number) _____

Quantity used _____ pounds (or kilograms), Required fee, § 30.00 (drawn to the order of Food and Drug Administration.)

This batch of lake was manufactured by the undersigned firm and meets the requirements of 21 CFR parts 74 and 80. The records required by 21 CFR 80.39, including a representative sample of the batch, are available for FDA inspection at the undersigned firm.

(Signed) _____

By _____

(Title)

(2) *Notice claiming certification for a repack of a batch of certified lake.*

Date _____

Division of Programs and Enforcement Policy (HFS–105), Center for Food Safety and Applied Nutrition, Food and Drug Administration, 200 C St. SW., Washington, DC 20204.

In accordance with the regulations promulgated under the Federal Food, Drug, and Cosmetic Act, we hereby give notice that we claim certification for a batch of lake repack.

Name of lake _____

Original batch:

FDA acceptance number (or certified lot number) _____

Total color _____ percent of batch

For each straight color used:

Color content _____ percent of batch.

This lake obtained from (provide name and place of business of manufacturer of the lake)

Batch number _____

Batch weighs _____ pounds (or kilograms)

Repacked batch:

Total color _____ percent of batch

For each straight color used:

Color content _____ percent of batch.

How stored pending certification _____

_____

_____

(State conditions of storage, with kind and size of containers, location, etc.)

Certified for use in _____

_____

_____

_____

(State proposed uses)

Required fee, $30.00 (drawn to the order of Food and Drug Administration).

This batch of lake was repacked by the undersigned firm and meets the requirements of 21 CFR parts 74 and 80. The records required by 21 CFR 80.39, including a representative sample of the batch, are available for FDA inspection at the undersigned firm.

(Signed) _____

By _____

(j) The Food and Drug Administration will furnish a response to each notifier within 5 working days of receipt of the notice. The response will either:

(1) Accept the notice claiming certification; or

(2) Reject the notice claiming certification, in which case the batch of lake covered by the notice has not complied with the requirements of § 80.31(b) of this chapter and is not a certified batch.

§ 80.34 [Amended]

68. Section 80.34 *Authority to refuse certification service* is amended in paragraph (a)(1) by removing the phrase ''a certificate'' and adding in its place the phrase ''a certificate or an acceptance of a notice claiming certification''; and in paragraph (a)(4) by removing the phrase ''color additives and intermediates'' and adding in its place ''color additives, intermediates and substrata''.

§ 80.35 [Amended]

69. Section 80.35 *Color additive mixtures; certification and exemption from certification* is amended in paragraphs (a) and (b) by removing the words ''straight colors'' and adding in their place the words ''listed colors''; and in paragraph (b) by removing the words ''straight color'' and adding in their place the words ''listed color'' the three times they appear.

70. Section 80.37 is revised to read as follows:

§ 80.37 Treatment of batch pending certification.

Immediately after the sample is taken that (for a batch of color additive subject to certification under § 80.31(a)) is to accompany a request for certification of the batch or (for a batch of lake subject to certification under § 80.31(b)) is to be

retained by the firm preparing or repacking the batch, the batch shall be:

(a) Stored in containers of such kind as to prevent change in composition.

(b) Held under the control of the person requesting or claiming certification until certified.

(c) Marked, by labeling or otherwise, in a manner such that there can be no question as to the identity of the batch and no question that it is not to be used until the requested certificate or acceptance of the notice claiming certification has been issued.

71. Section 80.38 is revised to read as follows:

§ 80.38 Treatment of batch after certification.

(a) *Labeling.* (1) Immediately upon notification that a batch of color additive has been certified under § 80.31(a), the person requesting certification thereof shall identify such batch, by labeling, with the certified lot number.

(2) Immediately upon notification that the notice submitted in accordance with § 80.33 has been accepted, the firm claiming certification for the batch shall identify such batch, by labeling, with the FDA acceptance number.

(b) *Storage.* The person requesting or claiming certification shall maintain storage in such manner as to prevent change in composition until such batch has been packaged and labeled as required by §§ 70.20 and 70.25 of this chapter, except that the person requesting or claiming certification may use such color additive for the purpose of coloring a food, drug, or cosmetic.

72. Section 80.39 is revised to read as follows:

§ 80.39 Records.

(a) *Records of distribution.* (1) The person to whom a certificate is issued or the firm to which FDA issues an acceptance of a notice claiming certification shall keep complete records showing the disposal of all the color additive from the batch covered by such certificate or such acceptance. These records shall show:

(i) Each quantity used by such person or firm from such batch and the date and kind of such use.

(ii) The date and quantity of each shipment or delivery from such batch, and the name and post office address of the person to whom such shipment or delivery was made.

(2) Upon the request of any officer or employee of the Food and Drug Administration or of any other officer or employee acting on behalf of the Secretary of Health and Human Services, such person or such firm, at all reasonable hours until at least 2 years after disposal of all such color additive, shall make the records required by paragraph (a)(1) of this section available to any such officer or employee, and shall accord to such officer or employee full opportunity to make inventory of stocks of such color additive on hand and otherwise to check the correctness of such records.

(b) *Certification records for lakes.* (1) The manufacturer or repacker of a lake certified under § 80.31(b) shall keep complete records showing that the batch of lake covered by the notice claiming certificaion is in compliance with parts 74 and 80 of this chapter.

(i) For both manufacturers and repackers, these records shall include:

(A) A copy of the notice claiming certification for the batch;

(B) A copy of FDA's acceptance of the notice; and

(C) Complete reports of all chemical analyses performed on the batch. Such analyses shall include, for each batch, analyses that establish the percent total color for the batch and, if the batch contains more than one straight color, the percent color for each straight color in the batch.

(ii) For manufacturers only, the records shall also include:

(A) A copy of the certificate for each batch of straight color used to prepare the batch of lake;

(B) For each certified batch of lake that was used as an ingredient, a copy of FDA's acceptance of the notice claiming certification for the batch, or if certified before (date of publication of the final rule), a copy of the certificate for the batch;

(C) Manufacturer specifications for substratum and precipitant ingredients used in the preparation of the batch; and

(D) For each batch that contains a barium salt as provided in §§ 74.1050 and 74.2050 of this chapter, analyses that show that the batch meets the specification for soluble barium in § 74.1050(b) of this chapter.

(2) A firm claiming certification for a batch of lake under § 80.31(b) shall retain an 8-ounce sample of the batch as required by § 80.22(b); however, such sample need not be submitted to FDA.

(3) Upon the request of any officer or employee of the Food and Drug Administration or of any other officer or employee acting on behalf of the Secretary of Health and Human Services, such firm, at all reasonable hours until at least 2 years after disposal of all such color additive, shall make the records and the sample required by paragraphs (b)(1) through (b)(3) of this section available to any such officer or employee, and shall accord to such officer or employee full opportunity to make inventory of stocks of such color additive on hand and otherwise to check the correctness of such records.

(c) The records required to be kept by paragraphs (a) and (b) of this section shall be kept separately from all other records.

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

73. The authority citation for 21 CFR part 81 continues to read as follows:

Authority: Secs. 701, 721 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 371, 379e).

PART 81—[REMOVED]

74. Part 81 is removed.

PART 82—LISTING OF CERTIFIED PROVISIONALLY LISTED COLORS AND SPECIFICATIONS

75. The authority citation for 21 CFR part 82 continues to read as follows:

Authority: Secs. 701, 721 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 371, 376, 379e).

PART 82—[REMOVED]

76. Part 82 is removed.

PART 101—FOOD LABELING

77. The authority citation for 21 CFR part 101 continues to read as follows:

Authority: Secs. 4, 5, 6 of the Fair Packaging and Labeling Act (15 U.S.C. 1453, 1454, 1455); secs. 201, 301, 402, 403, 409, 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 331, 342, 343, 348, 371).

78. Section 101.22 is amended in paragraph (k)(1) by revising the first sentence and by removing the phrase ''or part 82'' in the second sentence to read as follows:

§ 101.22 Foods; labeling of spices, flavorings, colorings and chemical preservatives.

* * * * *

(k) * * *

(1) A color additive, including a lake, subject to certification under section 721(c) of the act shall be declared by the name of the color additive listed in the applicable regulation in part 74 of this chapter, except that it is not necessary to include the ''FD&C'' prefix or the term ''No.'' in the declaration, and for lakes it is also not necessary to identify the aluminum cation or alumina substratum, but the term ''Lake'' shall be

included in the declaration (e.g., Blue 1 Lake). * * *

* * * * *

PART 178—INDIRECT FOOD ADDITIVES; ADJUVANTS, PRODUCTION AIDS, AND SANITIZERS

79. The authority citation for 21 CFR part 178 continues to read as follows:

Authority: Secs. 201, 402, 409, 721 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 342, 348, 379e).

§ 178.3297 [Amended]

80. Section 178.3297 *Colorants for polymers* is amended in paragraph (d) by removing the phrase ‘‘, 81, and 82’’.

PART 201—LABELING

81. The authority citation for 21 CFR part 201 continues to read as follows:

Authority: 201, 301, 501, 502, 503, 505, 506, 507, 508, 510 512, 530–542, 701, 704, 721 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 331, 351, 352, 353, 355, 356, 357, 358, 360, 360b, 360gg-360ss, 371, 374, 379e); secs 215, 301, 351, 361 of the Public Health Service Act (42 U.S.C. 216, 241, 262, 264).

§ 201.20 [Amended]

82. Section 201.20 *Declaration of presence of FD&C Yellow No. 5 and/or FD&C Yellow No. 6 in certain drugs for human use* is amended in paragraph (a) by adding the words ‘‘or a lake of FD&C Yellow No. 5’’ before the words ‘‘as a color additive using the names’’, in paragraph (b) by adding the words ‘‘or a lake of FD&C Yellow No. 5’’ before the words ‘‘that are administered’’, and in paragraph (c) by adding the words ‘‘or a lake of FD&C Yellow No. 6’’ before the words ‘‘shall specifically’’.

PART 701—COSMETIC LABELING

83. The authority citation for 21 CFR part 701 continues to read as follows:

Authority: Secs. 201, 502, 601, 602, 603, 701, 704 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 352, 361, 362, 363, 371, 374); secs. 5, 6 of the Fair Packaging and Labeling Act (15 U.S.C. 1454, 1455).

84. Section 701.3 is amended by redesignating paragraph (c)(1) as paragraph (c)(1)(ii) and by adding new paragraph (c)(1)(i) to read as follows:

§ 701.3 Designation of ingredients.

* * * * *

(c) * * *

(1)(i) For color additives, the name of the color additive listed in the applicable regulation in part 73 or 74 of this chapter, except that it is not necessary to include the ‘‘FD&C’’ or ‘‘D&C’’ prefix or the term ‘‘No.’’ in the declaration, but the prefix ‘‘Ext.’’ shall be included in the declaration. (For example, Ext. D&C Yellow No. 7 may be declared as Ext. Yellow 7.) For lakes, it is also not necessary to identify the cation precipitants or the substrata, but the term ‘‘Lake’’ shall be included in the declaration. (For example, the name of a lake prepared by the extension of FD&C Red No. 40 and D&C Yellow No. 10 on alumina and titanium dioxide using aluminum chloride and calcium chloride precipitants is ‘‘Red 40 and Yellow 10 Lake.’’).

* * * * *

Dated: February 16, 1996.

William B. Schultz,

Deputy Commissioner for Policy.

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