

## §81.10

## 21 CFR Ch. I (4-1-07 Edition)

Sections Affected, which appears in the Finding Aids section of the printed volume and on GPO Access.

### §81.10 Termination of provisional listings of color additives.

(a) *Ext. D&C Yellow Nos. 9 and 10.* These colors cannot be produced with any assurance that they do not contain  $\beta$ -naphthylamine as an impurity. While it has been asserted that the two colors can be produced without the impurity named, no method of analysis has been suggested to establish the fact.  $\beta$ -Naphthylamine is a known carcinogen; therefore, there is no scientific evidence that will support a safe tolerance for these colors in products to be used in contact with the skin. The Commissioner of Food and Drugs, having concluded that such action is necessary to protect the public health, hereby terminated the provisional listing of Ext. D&C Yellow No. 9 and Ext. D&C Yellow No. 10.

(b) [Reserved]

(c) *FD&C Red No. 1.* Results of recent feeding tests of this color additive have demonstrated it to be toxic upon ingestion:

(1) Groups of 50 rats are being fed diets containing FD&C Red No. 1 at levels of 5 percent, 2 percent, 1 percent, 0.5 percent, and 0 percent. At this stage of the tests, which have now been in progress for from 15 months to 18 months, 116 animals from the 250 being fed FD&C Red No. 1 at various levels and 27 of the 100 controls have died. Of these, 11 being fed at the 5 percent level, 16 being fed at the 2 percent level, 11 being fed at the 1 percent level, and 2 being fed at the 0.5 percent level, have shown liver damage. None of the controls that have died have shown liver damage.

(2) Groups of 100 mice are being fed diets containing 2 percent, 1 percent, 0.5 percent, and 0.1 percent FD&C Red No. 1, with 400 mice as controls. All mice on dosage levels of 2 percent and 1 percent died before the seventieth week. Gross liver damage has been observed in all groups fed at the 0.5 percent diet and above.

(3) Groups of 4 dogs are being fed diets containing 2 percent, 1 percent, 0.25 percent, and 0 percent FD&C Red No. 1. Three of the dogs on the 2 percent dosage level died before 32 weeks;

the other is living. Three of the dogs on the 1 percent dosage level died or were sacrificed within 13 months. All deceased or sacrificed dogs have shown liver damage grossly and/or microscopically. Deceased dogs on the 1 percent and 2 percent dosage level showed poor physical condition.

The Commissioner of Food and Drugs having concluded that ingestion of this color additive over a long period of time would be unsafe, and in order to protect the public health, hereby terminates the provisional listing of FD&C Red No. 1 for use in foods, drugs, and cosmetics.

(d) *FD&C Red No. 4.* Feeding tests of this color additive have been conducted with three species:

(1) Rats of the Osborne-Mendel and Sprague-Dawley strains were fed FD&C Red No. 4 for 2 years at levels of 5 percent, 2 percent, 1 percent, and 0.5 percent of the diet. No effect was found.

(2) Mice of the C3Hf and C57BL strains were fed FD&C Red No. 4 for 2 years at levels of 2 percent and 1 percent of the diet. No effect was found.

(3) Dogs were fed FD&C Red No. 4 at levels of 2 percent and 1 percent of the diet. Adverse effects were found at both levels in the urinary bladder and in the adrenals. Three dogs of five fed on the 2-percent level died after 6 months, 9 months, and 5½ years on the test. Two of the dogs on the 2-percent level and all five of the dogs on the 1-percent level survived to the completion of the 7 year study.

The Commissioner of Food and Drugs has concluded that available data do not permit the establishment of a safe level of use of this color additive in food, ingested drugs and ingested cosmetics. In order to protect the public health, the Commissioner hereby terminates the provisional listing of FD&C Red No. 4 for use in food and ingested drugs. The Commissioner has previously terminated the provisional listing of FD&C Red No. 4 for use in ingested cosmetics. FD&C Red No. 4 is listed for use in externally applied drugs and cosmetics by §§74.1304 and 74.2304 of this chapter, respectively. Section 82.304 of this chapter is retained in part 82 of this chapter to permit the use of lakes of FD&C Red No.

4 in externally applied drugs and cosmetics.

(e) *FD&C Violet No. 1*. The Commissioner of Food and Drugs, in order to protect the public health, hereby terminates the provisional listing of FD&C Violet No. 1 for use in foods, drugs, and cosmetics.

(f) *FD&C Red No. 2*. The Commissioner of Food and Drugs, in order to protect the public health, hereby terminates the provisional listing of FD&C Red No. 2 for use in food, drugs, and cosmetics.

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

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

(i) *Ext. D&C Yellow No. 1*. The Commissioner has learned of the contamination of Ext. D&C Yellow No. 1 with 4-aminobiphenyl. The Commissioner concludes that this color cannot be produced with any reasonable assurance that it will not contain 4-aminobiphenyl as an impurity or not yield benzidine from the decomposition

of a subsidiary reaction product that might be present in the color. 4-Aminobiphenyl and benzidine are known carcinogens; therefore, there is no scientific evidence that will support a safe tolerance for these colors in drugs or cosmetics. In addition, insufficient data have been submitted to permit establishment of appropriate specifications for the batch certification of the color. The Commissioner of Food and Drugs, in order to protect the public health, hereby terminates the provisional listing of Ext. D&C Yellow No. 1 for use in externally applied drugs and cosmetics, effective December 13, 1977.

(j) *Graphite*. Data have been developed that show the contamination of graphite with polynuclear aromatic hydrocarbons (PNA's). There is no reasonable assurance this color can be produced so that it will not contain PNA's as an impurity. The presence of certain PNA's in graphite would indicate that PNA's known to be carcinogenic to animals and humans may also be present. Therefore, there is no scientific evidence that will support a safe tolerance for this color in drugs or cosmetics. The Commissioner of Food and Drugs, in order to protect the public health, hereby terminates the provisional listing of graphite for use in externally applied cosmetics, effective November 29, 1977.

(k) *Ext. D&C Green No. 1*. The Commissioner concludes that there are inadequate analytical methods to permit certification of the color additive Ext. D&C Green No. 1. In addition, the Commissioner has found that there was a failure to comply with the conditions attached to the postponement of the closing date in accordance with section 203(a)(2) of the transitional provisions of the Color Additive Amendments of 1960. The Commissioner of Food and Drugs hereby terminates the provisional listing of Ext. D&C Green No. 1 for use in externally applied drugs and cosmetics, effective November 29, 1977.

(l) [Reserved]

(m) *D&C Orange Nos. 10 and 11*. In the absence of a petition to list D&C Orange No. 10 and D&C Orange No. 11 for use in ingested drugs and cosmetics, there no longer exists a basis for provisional listing for such uses. Therefore, FDA is terminating the provisional

## §81.30

## 21 CFR Ch. I (4-1-07 Edition)

listing of D&C Orange No. 10 and D&C Orange No. 11 for use in ingested drugs and cosmetics, effective April 28, 1981.

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

(o) *D&C Green No. 6*. In the absence of a petition to list D&C Green No. 6 for use in ingested drugs and cosmetics, there no longer exists a basis for provisional listing for such uses. Accordingly, the Commissioner of Food and Drugs hereby terminates the provisional listing of D&C Green No. 6 for use in ingested drugs and cosmetics, effective March 27, 1981.

(p) [Reserved]

(q)(1) *D&C Red No. 19 and D&C Red No. 37*. Having concluded that, when ingested, D&C Red No. 19 causes cancer in rats and mice, the agency hereby terminates the provisional listings of D&C Red No. 19 and chemically related D&C Red No. 37 for use in ingested drugs and ingested cosmetics, effective February 4, 1983.

(2) *D&C Red No. 37*. In the absence of a petition to list D&C Red No. 37 for external uses, there no longer exists a basis for provisional listing for such uses. Accordingly, the Commissioner of Food and Drugs hereby terminates the provisional listings of D&C Red No. 37 for use in externally applied drugs and cosmetics, effective June 6, 1986.

(r) [Reserved]

(s) *D&C Orange No. 17*. Having concluded that, when ingested, D&C Orange No. 17 causes cancer in rats and mice, the agency has terminated the provisional listing of D&C Orange No. 17 for use in ingested drugs and ingested cosmetics, effective March 31, 1983.

(t) *D&C Red No. 8 and D&C Red No. 9*. In the absence of a petition to list D&C Red No. 8 and D&C Red No. 9 for mouthwash, dentifrices, and ingested drugs, except ingested drug lip products, there no longer exists a basis for provisional listing for such uses. Accordingly, the Commissioner of Food and Drugs hereby terminates the provisional listings of D&C Red No. 8 and

D&C Red No. 9 for use in mouthwash, dentifrices, and ingested drugs, except ingested drug lip products, effective January 6, 1987.

(u) *FD&C Red No. 3*. Having concluded that FD&C Red No. 3 causes cancer in rats, the agency hereby terminates the provisional listing of FD&C Red No. 3 for use in cosmetics and externally applied drugs and the provisional listing of the lakes of FD&C Red No. 3 for use in food, drug, and cosmetic products, effective January 29, 1990.

[42 FR 15665, Mar. 22, 1977]

EDITORIAL NOTE: For FEDERAL REGISTER citations affecting §81.10, see the List of CFR Sections Affected, which appears in the Finding Aids section of the printed volume and on GPO Access.

### §81.30 Cancellation of certificates.

(a) Certificates issued heretofore for colors being removed from the provisional list (§81.10(a)) are cancelled and of no effect after December 1, 1960, and use of such color additives in drugs or cosmetics after that date will result in adulteration.

(b)(1) Certificates issued heretofore for the color additive designated FD&C Red No. 1 are cancelled as of the date of the publication of this Order, and use of this color additive in the manufacture of foods, drugs, or cosmetics after that date will result in adulteration.

(2) The Commissioner finds that no action needs to be taken to remove foods, drugs, and cosmetics containing this color additive from the market on the basis of the scientific evidence before him, taking into account that the additive is not an acute toxic substance and that it is only used in small amounts in foods, drugs, and cosmetics.

(c) Certificates issued for FD&C Red No. 4 and all mixtures containing this color additive are cancelled and have no effect after September 23, 1976 insofar as food, ingested drugs, and ingested cosmetics are concerned, and use of this color additive in the manufacture of food, ingested drugs, and ingested cosmetics after this date will result in adulteration. The certificates shall continue in effect for the use of FD&C Red No. 4 in externally applied