PART 82—LISTING OF CERTIFIED PROVISIONALLY LISTED COLORS AND SPECIFICATIONS

5. The authority citation for 21 CFR Part 82 continues to read as follows:

Authority: Secs. 701, 706, 52 Stat. 1055–1056 as amended, 74 Stat. 399–407 as amended (21 U.S.C. 371, 376); 21 CFR 5.10.

6. Part 82 is amended by revising § 82.705 to read as follows:

§ 82.705 FD&C Yellow No. 5.

The color additive FD&C Yellow No. 5 shall conform in identify and specifications to the requirements of § 74.2705 (a) and (b) of this chapter.

Dated: August 23, 1985.

Frank E. Young,

Commissioner of Food and Drugs.

[FR Doc. 85–21082 Filed 8–30–85; 8:45 am]

BILLING CODE 4160-01-M

---

21 CFR Part 81

[Docket No. 76N–0366]

Provisional Listing of Certain Color Additives; Postponement of Closing Dates

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is postponing the closing dates for the use of nine provisionally listed color additives, FD&C Red No. 3 and its lakes, FD&C Yellow No. 6, D&C Red No. 8, D&C Red No. 9, D&C Red No. 19, D&C Red No. 33, D&C Red No. 36, D&C Red No. 37, and D&C Orange No. 17. This postponement will permit the uninterrupted use of these color additives while (1) FDA receives and evaluates the report of a scientific review panel on six color additives (FD&C Red No. 3, D&C Red No. 8, D&C Red No. 9, D&C Red No. 19, D&C Red No. 37, D&C Orange No. 17) and then takes final action on those additives; (2) the agency evaluates newly submitted information on the results of the chronic study on one color additive (FD&C Yellow No. 6); and (3) expert scientific review continues with respect to the evidence on two other color additives (D&C Red No. 33 and D&C Red No. 36), proponents of the use of these additives have an opportunity to submit additional evidence on their use, and FDA takes final action on these color additives.

DATES: Effective September 3, 1985, the new closing dates for FD&C Red No. 3 and its lakes will be September 3, 1986; for D&C Red No. 8, D&C Red No. 9, D&C Red No. 19, D&C Red No. 37, D&C Orange No. 17, and FD&C Yellow No. 6 will be June 6, 1986; for D&C Red No. 33 and D&C Red No. 36 will be March 3, 1987.

FOR FURTHER INFORMATION CONTACT: Gerad L. McCowin, Center for Food Safety and Applied Nutrition (HFF–330), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202–472–5676.

SUPPLEMENTARY INFORMATION:

I. Introduction

Under Title II of the Color Additive Amendments of 1960 (the transitional provisions) (Pub. L. 86–618, sec. 203 (21 U.S.C. 376, note)), FDA is authorized to postpone the closing date of the provisional listing of a color additive. The agency's discretion in issuing such postponements is limited in only two respects: "Such postponements must be consistent with the public health, and the Commissioner must judge that the scientific investigations are going forward in good faith and will be completed as soon as reasonably practicable." *McIlwain* v. *Hayes*, 690 F.2d 1041, 1047 (D.C. Cir. 1982).

In the **Federal Register** of June 26, 1985 (50 FR 26377), FDA proposed to postpone the closing date for 9 (FD&C Red No. 3 and its lakes, FD&C Yellow No. 6, D&C Red No. 8, D&C Red No. 9, D&C Red No. 19, D&C Red No. 33, D&C Red No. 36, D&C Red No. 37, and D&C Orange No. 17) of the 11 color additives that remain on the provisional list. (As for the other two additives, FDA is permanently listing one, FD&C Yellow No. 5, elsewhere in this issue of the **Federal Register**, and the closing date for the other, FD&C Blue No. 2, is postponed indefinitely pending the outcome of an administrative hearing on the permanent listing of that additive.) FDA proposed this postponement after a series of short extensions of the provisional listings of these nine additives because it had become clear to the agency that appropriate resolution of the complex issues presented by the uses of these additives would require additional time.

In response to the proposal, FDA received approximately 40 comments from farmers, farm cooperatives, food processors, unions, State legislators, public interest groups, and trade associations. These comments are summarized below.

FDA has carefully considered these comments and has also considered whether, in light of these comments, the extensions that it has proposed are appropriate under the standards set forth in *McIlwain* v. *Hayes*. The conclusions that the agency has reached follow.

II. General Comments

A. Authority To Extend the Provisional List

1. One comment asserted that "25 years after the enactment of the Color Additive amendments," FDA "has no legal authority to use the provisional list to sanction the continued sale of color additives." The comment stated that FDA must either find these color additives to be safe or not permit their use in foods, cosmetics, and drugs. Another comment stated that continued provisional listing "makes a mockery" of permanent listing.

FDA finds no merit in these comments. As noted in the proposal, as scientific sophistication has increased and testing methodology has become more refined, new and increasingly complex issues have been raised concerning the provisionally listed additives.

Less than 3 years ago, in *McIlwain* v. *Hayes, supra*, 690 F.2d at 1047, the Court of Appeals specifically rejected the argument that the passage of time had deprived the agency of its authority to list color additives provisionally. The court noted that the transitional provisions of the Color Additive Amendments set no limit on the number of extensions of the provisional list that the Commissioner may grant and no time limit upon provisional listings. *Id.* at 1046. Consequently, the court found that FDA had authority to extend the provisional list even though 22 years had passed since the passage of the Color Additive Amendments. *Id.* at 1047.

Thus, based on the *McIlwain* decision, FDA can continue to extend the provisional listing of a color additive so long as it finds that continued use of the additive is consistent with the public health, and that the scientific investigations necessary for a decision on the additive, or the analysis of those investigations, are going forward in good faith and will be completed as soon as reasonably practicable. Because the agency has determined that it can make these findings for each of the color additives at issue, FDA has authority to adopt the extensions of the provisional list that it is announcing in this final rule.

2. A comment from a public interest group asserted that to extend the provisional list again, without proof of the safety of the additives, would put the public at unnecessary risk.

FDA disagrees with this comment. As stated above, to postpone the

provisional listing of a color additive, FDA must find that the postponement is consistent with the public health. *McIlwain* v. *Hayes, supra*, 690 F.2d at 1047. Thus, protection of the public health is one of the agency's specific concerns in deciding whether to extent the provisional list.

The purpose of provisional listing is to allow continued use of a color additive while interested persons gather evidence on the issue of whether use of that additive is safe. Until definitive evidence on that issue is available, the agency can continue to list an additive provisionally so long as the testing that is available on the color additive does not show that it presents a hazard to the public. See FDA's response to petition of Public Citizen Health Research Group for termination of provisional listing for 10 color additives, Docket No. 84P-0429, p. 13 (June 21, 1985). (A copy of this response has been filed with the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fisher Lane, Rockville, MD 20857, in the record of the present proceeding.)

FDA has reviewed all of the evidence available on each of the color additives that are the subject of this rulemaking and has found that none of them presents a hazard requiring an immediate cessation of their use. Therefore, the public is being appropriately protected.

B. De Minimis and the Delaney Clause

3. The statutory provisions governing permanent listing of color additives state that a color additive shall be deemed to be unsafe if it has been shown to cause cancer in appropriate testing (21 U.S.C. 376(b)(5)(B)). In the proposal, however, the agency stated: "If the agency were to treat extremely small carcinogenic risks as being *'de minimis,'* that is, as being of no regulatory significance, it could [permanently] list a carcinogenic color additive if it found that the risk from its use was *de minimis*, and that, in all other respects, there was a reasonable certainty of no harm from the use of the additive" (50 FR 26379). This statement was the subject of much public comment. FDA received five comments that encouraged the agency to apply the *de minimis* concept. These comments all argued that the statutory language, legislative history, and case law support an interpretation of 21 U.S.C. 376(b)(5)(B) that does not require FDA to ban color additives that present a *de minimis* risk of cancer. One comment argued that substances that pose no greater than a one in one million lifetime cancer risk present a *de minimis* risk and are safe. This comment also argued that the agency could permanently list eight of the nine color additives at issue on the ground that the carcinogenic risk they present, if any, is *de minimis*.

On the other hand, one comment argued that the suggestion that a *de minimis* risk assessment might be an appropriate basis on which to permit permanent listing of a color additive is inconsistent with the legislative intent of the Federal Food, Drug, and Cosmetic Act (the act) and its historical interpretation by FDA. That comment argued that under the Delaney Clause, "only risk-free, non-cancer causing color additives can be permitted in the American marketplace." A second comment also urged the agency to reject the *de minimis* concept.

FDA has not made a definitive determination about the application of the Delaney Clause to the color additives at issue here. However, as it has indicated in the proposal and in the agency's response to Public Citizen Health Research Group's petition, the agency believes that the law would support the treatment of certain situations arguably covered by that provision as *de minimis*.

The courts have made it clear that the concept of *"de minimis,"* which is based on the common understanding that the law does not concern itself with trifles, may appropriately be applied to situations like those in question here. As the United States Court of Appeals for the District of Columbia Circuit explained in *Alabama Power Co.* v. *Costle*, 636 F.2d 323, 360-361 (D.C. Cir. 1979): "Unless Congress has been extraordinarily rigid, there is likely a basis for an implication of *de minimis* authority to provide exemption when the burdens of regulation yield a gain of trivial or no value."

The legislative history of the Color Additive Amendments shows that Congress was not being extraordinarily rigid in adopting the Delaney Clause, and that it clearly contemplated that those administering that provision would have discretion to implement it in a reasonable way. Both in the Senate (see 106 Congressional Record 15381 (July 1, 1960)) and in the House (see 106 Congressional Record 14372 (June 25, 1960)), statements were made that the Delaney Clause should be applied in accord with the rule of reason. Moreover, the concept of *de minimis* has been applied by the courts to the regulation of carcinogenic or potentially carcinogenic substances regulated by FDA. See, e.g., *Monsanto* v. *Kennedy*, 613 F.2d 947 (D.C. Cir. 1079). Thus, it is clear that FDA does have the option to use the *de minimis* concept in interpreting the Delaney Clause. (FDA has discussed this issue at greater length in its response to the Public Citizen Health Research Group petition and in two documents (Reply Memorandum in Support of Federal Defendants' Motion to Dismiss and Memorandum in Support of Federal Defendants' Motion for Summary Judgment) that it filed in pending litigation on the provisional list, *Public Citizen* v. *Dept. of Health and Human Services*, Civil Action No. 85-0209 (D.D.C.). FDA incorporates those discussions herein by reference and has included copies of those documents in the record of this proceeding.)

FDA has not made a determination about whether it would be appropriate to invoke the *de minimis* concept with respect to the color additives at issue here because it believes that such a determination must await resolution of the factual circumstances in which the concept may be applied. Such scientific factual resolution is necessary so that the agency can fully judge the significance of applying the *de minimis* concept to the facts before it. Therefore, the agency has not made a determination about what level of risk, if any, is *de minimis*, or, as explained below, whether any of the color additives at issue can be approved on the basis, at least in part, of the *de minimis* concept.

C. Amount of Color Certified

4. One comment argued that in considering the total amount of color additives to which the population is exposed, it is erroneous to add the poundage of lakes and dyes together. The comment asserted that because lakes are made from certified dyes, the amount of dye certified gives the total exposure to color.

The agency's proposal to extend the closing date for provisionally listed color additives did not address the issue of exposure calculations for these color additives. The comment appears to respond to the Commissioner's reply to the petition submitted by the Public Citizen Health Research Group. In its petition, Public Citizen estimated the exposure to provisionally listed color additives used in food and the total exposure to provisionally listed color additives.

In his response to the petition, the Commissioner did not contest the figures cited by Public Citizen, which were apparently based on the agency's certification poundage for these color additives, including lakes. The Commissioner did note that FD&C color additives are used not only in food but

also in drugs and cosmetics, so that certification poundage for an FD&C color additive does not equal the poundage actually used in food. Public Citizen's estimates of exposure to FD&C Red No. 3, FD&C Yellow No. 5, and FD&C Yellow No. 6 were based on the amount of color certified and did not count the poundage from lakes twice.

However, in estimating total exposure to the provisionally listed D&C color additives, Public Citizen did add the total amount of color certified to the amount of lakes used. This was necessary because D&C lakes are not required to be made from certified D&C colors.

Estimating exposure in this way would lead to an overstatement of the total exposure to the straight color additive, unless the substrata of the lakes is subtracted from the total weight. Public Citizen failed to make this subtraction and FDA, as the comment correctly points out, failed to correct Public Citizen's estimate in replying to the petition, because the agency felt that such a correction would not have significantly altered the thrust of Public Citizen's argument.

FDA wishes to assure the public that when it calculates exposure to color additives as part of a safety evaluation, it does so correctly. Although the agency does include the contribution from D&C lakes in its computations, it factors out the substratum weight before arriving at an exposure estimate.

5. The comment also argued that it is misleading to compare, as FDA did in its response to the Public Citizen Health Research Group, the amount of color additives certified in 1974 with the amount certified in 1984. That comparison shows a 42 percent growth. The comment claimed that if the pounds certified each year between 1975 and 1984 were averaged, the result would be 5.3 million pounds per year for that period. According to the comment, that number is exactly the poundage certified in 1975 and approximately the poundage that the comment projected would be certified in 1985. The comment claimed that, thus, there really had not been an increase in the amount of color additives certified each year since 1974.

The agency has reevaluated the certification poundage for FD&C color additives from 1974 to 1985. The figures cited in the comment are correct; however, the figure for 1976 (4.998 million pounds) represents five quarters rather than four because of a change in the fiscal year from July 1 to October 1. The agency agrees that the data do not show an increase of 42 percent in the amount of color additive certified. However, the agency does not agree that there has been no growth in color additive certification in the past 10 years. If one looks at the 5-year averages over this period, the 5-year average increases from 4.929 million pounds (1975–1979, 5¼ years) to 5.340 million pounds (1979–1983). This represents about a 10 to 15 percent increase over that timespan.

II. Color Additives That Are Subject to Review by the Scientific Review Panel

6. In the proposal, FDA stated that treatment-related increases in the incidence of tumors were found in chronic testing for six of the provisionally listed color additives, but that questions had been raised about the significance of these results. The agency stated that it had formed a color additive scientific review panel (the panel) to look into these questions and proposed to extend the provisional listing of these color additives to allow the panel to do its work. The agency received 33 comments about these 6 color additives.

A. D&C Red No. 8, D&C Red No. 9, D&C Red No. 19, D&C Red No. 37, and D&C Orange No. 17

7. A comment from the petitioner for these color additives argued that the data currently before FDA support the permanent listing of these additives. This comment argued that the quantitative risk assessments that have been conducted on the uses of these additives show that none of them poses a significant risk of human cancer, and that therefore they should be permanently listed under a *de minimis* interpretation of the Delaney Clause.

FDA is unable to agree with this comment. As discussed in the proposal, questions have been raised that create doubts about whether a valid risk assessment can be performed on the basis of the chronic testing that has been done on these color additives. See 50 FR 26379. The Commissioner created the panel to address these issues. Because the panel has not completed its work, the questions about the risk assessments that the petitioner submitted remain. Therefore, the agency is unable to act on the permanent listing of these color additives at this time.

8. The comment argued in the alternative that FDA's proposal to extend the provisional list to permit evaluation of the data on these five color additives by the panel represents a rational exercise of the agency's authority under the Color Additive Amendments. The comment asserted that the panel's evaluation will help the agency to resolve the issues on the uses of these color additives. However, the agency also received two comments that argued that because these additives had been shown to be carcinogens, they should be banned.

With respect to the latter comments, as discussed in paragraph 3 in this preamble, FDA believes that an interpretation of the act is possible that does not require the agency to ban color additives that have been shown to cause cancer in animals, if the risk associated with the use of such additives is essentially negligible. Therefore, FDA does not accept these comments.

The Commissioner has reviewed the proposed extension under the standards established in *McIlwain* v. *Hayes, supra*, 690 F.2d at 1047. He has reexamined the evidence on these color additives and has confirmed his conclusion that their continued provisional use for 9 months is consistent with the public health. The Commissioner has also concluded that the review of the scientific evidence on these color additives is going forward in good faith. The panel has prepared a preliminary draft report, and it presented an oral report to the Commissioner in June. The panel has now sent its draft report to 49 scientists around the country for review. The Commissioner expects to receive the final report of the panel this fall.

Once the panel completes its report, the Commissioner will review it and decide how the agency will proceed with regard to these additives. Documents setting forth the agency's conclusions about the safety of these additives (announcing further action, permanent listing, or removal of the additives from the provisional list) will then be prepared for publication in the **Federal Register.** The Commissioner concludes that allowing 9 months for completion of this process is reasonable.

Therefore, the Commissioner finds that an extension of the provisional listing of D&C Red No. 8, D&C Red No. 9, D&C Red No. 19, D&C Red No. 37, and D&C Orange No. 17 until June 6, 1986, fully complies with the standards in *McIlwain* v. *Hayes, supra.*

9. The petitioner for these color additives stated in its comment that it had initiated new testing of D&C Red No. 9, D&C Red No. 19, and D&C Orange No. 17. It stated that these studies include efforts to prepare pure colors for research purposes, to determine oral bioavailability of the pure color and its metabolites, and to compare the short-term toxicity of the purified colors with the toxicities generally shown in the tests of the commercial color additives. The comment stated that these studies provided an additional basis for

extending the provisional listings of these color additives.

The agency is aware that the petitioner has asserted that it has initiated new studies on D&C Red No. 9, D&C Red No. 19, and D&C Orange No. 17. The details of the protocols and the rationale for these studies have not been submitted to the agency. Consequently, the agency is not aware of how these studies could contribute to an appropriate resolution of the issues raised with respect to these color additives. Therefore, on the basis of available information, the agency is unable to agree with the comment's assertion that the initiation of these studies provides an additional basis for extending the provisional listing of these color additives.

B. FD&C Red No. 3

10. Comments from three trade associations asserted that the evidence before the agency on FD&C Red No. 3 establishes the safety of the use of this color additive. These comments reviewed the results of recently conducted studies that were designed to explore whether the tumors observed in the chronic study of this color additive were the result of hormonal stimulation rather than of the direct action of FD&C Red No. 3. Among these studies were two short-term studies in rats, and in vitro study, pharmacokinetic studies, and a study of the effects of FD&C Red No. 3 on humans.

The comments asserted that these studies suggest that the tumors observed in the chronic rat study resulted from a hormonal mechanism that was indirectly mediated by FD&C Red No. 3; that there is a threshold for this effect; that the compound is not mutagenic and does not accumulate in the thyroid; and that when consumed by humans, nearly all of the administered compound is excreted in the feces. The comments asserted that the data demonstrate that FD&C Red No. 3 is safe, and that its provisionally listed uses should be permanently listed.

FDA is unable to agree with these comments. The agency's initial review of the information from these studies indicated that they do not provide a sufficient basis upon which to draw a definite conclusion on whether FD&C Red No. 3 is a secondary carcinogen. This initial review raised questions about whether the submission actually supported the sponsor's hypothesis that there was a hormonal mechanism of tumor induction. The agency has not been able to complete its evaluation of these studies because much of the raw data from them was not submitted to FDA until July 25, 1985. Moreover, on July 25, 1985, the sponsor also submitted two additional studies that address the issue of a possible secondary mechanism. The agency has not yet completed its evaluation of these new studies. Thus, at least at the present time, FDA is unable to find that the evidence before the agency on FD&C Red No. 3 establishes the safety of the use of this color additive.

11. One trade association commented that even if FDA concludes that FD&C Red No. 3 does not act by a secondary mechanism, FDA can permanently list this color additive for cosmetic uses based on the quantitative risk assessment that this trade association performed and the application of the *de minimis* concept to the results.

FDA disagrees. The risk assessment that this trade association has submitted is subject to many of the questions that have been raised about the risk assessments on the five color additives discussed above. See response to Public Citizen Health Research Group petition, p. 20. Because of these questions, the Commissioner referred the risk assessment on FD&C Red No. 3 to the panel for review. Thus, the Commissioner concludes that it would be inappropriate for the agency to take any action on the basis of the risk assessment at this time. Moreover, as discussed in paragraph 3 of this preamble, FDA has not made a definitive determination about the appropriateness or applicability of the *de minimis* concept.

12. This trade association also argued in its comment that FDA should permanently list the cosmetic uses of FD&C Red No. 3 without regard to the secondary mechanism issue because any risk from the cosmetic uses of this additive would be *de minimis* against the background of its permanently listed food uses. The comment argued that such action would be consistent with FDA's lead acetate decision (45 FR 72122; October 30, 1980).

FDA does not agree that the lead acetate decision is directly applicable in all respects to the immediate case at this time. In the lead acetate decision, FDA pointed out that its conclusion was "based upon the unusual combination of scientific facts peculiar to lead acetate in hair dyes" (45 FR 72115). Among the unique factors in the lead acetate case were that lead is ubiquitous in the environment, and that humans normally have lead in their blood (45 FR 72113). FDA determined that the amount of human lead absorption from the use of lead acetate in hair dyes would have no discernible effect on the level of lead in human blood (45 FR 72114). The agency is not able to make these findings for FD&C Red No. 3.

13. The three trade associations, in the alternative, all supported FDA's proposal to extend the provisional listing of FD&C Red No. 3, so that the panel could consider the evidence on the mechanism of action of this additive. There were 28 other comments that also supported this proposed action. Two comments opposed this proposal, stating that FD&C Red No. 3 has been shown to be a carcinogen.

FDA rejects the latter two comments for the same reasons that, in paragraph 8 of this preamble, it rejected the arguments that it terminate the provisional listing of the five other color additives. Moreover, questions about the mechanism of action of RD&C Red No. 3 remain to be resolved.

The Commissioner has reviewed the proposed extension under the *McIlwain* standards. He has concluded that a 1-year extension of the provisional list will ensure that the review of the data on FD&C Red No. 3 is completed as quickly as reasonably practicable. Such an extension will allow time for the agency to complete its review of the data and of the new studies that were recently submitted. It will also allow the panel to review the results of the scientific investigations of this color additive and to report to the agency on its findings. The Commissioner considers review by the panel to be necessary before he can decide whether the petitioners have demonstrated that this additive works by a secondary mechanism; whether they have shown that there is a safe level of use for this additive (and, if so, what that level is); and whether, if they have not done so, new studies of FD&C Red No. 3 are necessary. The 1-year extension will allow the agency time to review the panel report and the other evidence on this color additive and to take appropriate action.

In addition, the Commissioner has reviewed the evidence on this color additive and confirmed his conclusion that continued use of FD&C Red No. 3 for its provisionally listed uses for 1 year is consistent with the public health. Therefore, FDA is adopting a final rule extending the provisional listing of this additive until September 3, 1986.

14. Two trade associations commented that until FDA heard from the panel, it would be premature to evaluate whether further chronic testing of FD&C Red No. 3 is necessary to establish a secondary mechanism. Both comments urged that if the agency should come to believe that such testing is necessary, it should propose that

testing in a separate rulemaking. One trade association stated that if the agency should conclude than an additional study on FD&C Red No. 3 is necessary, the association will seriously consider sponsoring study.

FDA agrees that it would be premature to require a new chronic study on FD&C Red No. 3. The agency advises, however, that if, after hearing from the panel and completing its own review, it appears that such a study is necessary, it will move as quickly as possible to propose to require such a study, even if there is a significant amount of time left before the September 3, 1986, closing date.

IV. The Color Additive About Which Additional Information Is Being Developed—FD&C Yellow No. 6

15. In the proposal, FDA explained that it had not completed its review of the scientific investigations on FD&C Yellow No. 6. The agency reported that rare tumors had been found in the kidneys of female rats fed the color additive in a chronic study, but that agency scientists have doubts as to whether this effect was actually caused by the color additive. The agency stated that to clarify this issue, it had asked the petitioner to prepare and submit additional kidney slides. It proposed to extend the provisional listing of FD&C Yellow No. 6 for 9 months to give itself an opportunity to review and to evaluate these slides and the other data on this additive. The agency stated that it also needed time to evaluate the carcinogenic impurities that may be present in this color additive (50 FR 26380).

FDA received six comments on its proposed action.

16. One comment asserted that FD&C Yellow No. 6 has been shown to be an animal carcinogen.

FDA does not agree with this comment. Although there was a suggestion of a dose-related increase of relatively rare tumors in the kidneys of Charles River CD rats tested with this additive, the agency has not yet confirmed that these tumors are compound-related. The agency has completed an initial review of the additional kidney slides that it received at the time the proposal was published and has found a higher incidence of proliferative-type lesions in the kidneys of the treated than in the control rats. However, because an unexpectedly high incidence of proliferative lesions was found in the controls on reexamination, the agency believes that there is reason to question the significance of this observation. Therefore, the agency finds that additional review of the evidence on this color additive is necessary before a decision on its safety can appropriately be made.

17. This comment also asserted that FD&C Yellow No. 6 is an allergen.

The agency has investigated the two studies cited by the comment and has concluded that these studies do not provide a basis for finding that FD&C Yellow No. 6 is an allergen. The studies included a very limited number of subjects, and these subjects had complicating medical conditions. The agency is, however, attempting to locate any additional scientific articles relating to the allergenicity of FD&C Yellow No. 6 to determine whether the available data support a finding that FD&C Yellow No. 6 is an allergen.

FDA's review of the possible allergenicity of FD&C Yellow No. 6 is separate from its review of the petition for permanent listing of this color additive. If the agency determines that sufficient data exist to demonstrate the allergenicity of FD&C Yellow No. 6 for a portion of the population, other options may be considered. For example, the agency could propose labeling requirements for this color additive similar to those for FD&C Yellow No. 5. Such labeling requirements could apply to the use of the color additive regardless of whether it is provisionally or permanently listed.

18. FDA received four comments that supported the proposed extension of the provisional listing of this color additive and two that opposed it.

The Commissioner has reviewed the proposed extension under the *McIlwain* standards. FDA received the new kidney slides from the petitioner in June, and agency scientists are already well into their review. After all necessary reviews are complete, the agency will make decisions about the significance of their findings. In addition, the agency will make decisions about the carcinogenic impurities found in this additive. The latter decisions will be made more difficult by the fact that FD&C Yellow No. 6 shares some impurities with FD&C Yellow No. 5. When FDA has decided whether the use of this color additive is safe, it will prepare a **Federal Register** document announcing its decision.

Based on these facts, the Commissioner believes that FDA's review of the scientific investigations on FD&C Yellow No. 6 is going forward in good faith, and that a 9-month extension of the provisional listing of this additive will ensure that that review is completed as soon as reasonably practicable. In addition, based on his review of the evidence presently before FDA on FD&C Yellow No. 6, the Commissioner has confirmed his conclusion that continued provisional use of this color additive for 9 months, under its current conditions of use, is consistent with the public health. Therefore, FDA is extending the closing date for FD&C Yellow No. 6 until June 3, 1986.

V. Color Additives for Which FDA Proposed Further Study

19. In the proposal, FDA reported that the chronic testing of D&C Red No. 33 and D&C Red No. 36 did not reveal a carcinogenic effect in the animals in which they were tested, but that for both color additives there were a few uncommon tumors and numerous lesions of the spleen that are rare but not neoplastic. The agency stated that these proliferative effects indicated that there was a similarity between these color additives and certain other compounds, such as D&C Red No. 9 (which is presently before the panel), which have indicated carcinogenic effects. The agency also reported that a panel of experts from the National Toxicology Program (NTP) had examined the data on D&C Red No. 33 in conjunction with the data on D&C Red No. 9 and agreed with agency scientists that there is a clear relationship between the two color additives that provides a basis for concern about the possible carcinogenicity of D&C Red No. 33 (50 FR 26381). FDA received several comments that addressed the NTP review.

20. In the proposal, FDA stated that the NTP panel suggested that there might be some short-term testing that could be done to resolve the question of the possible carcinogenicity of D&C Red No. 33, but that it was not clear to FDA whether the NTP panel had any type of short-term testing specifically in mind. The agency stated that it had contacted NTP to resolve this question (50 FR 26381). FDA received one comment that asked that FDA announce NTP's response as quickly as possible.

In July, the agency was advised by a representative of NTP that the NTP panel had not recommended that further research on D&C Red No. 33 include short-term studies (Memorandum dated July 16, 1985, to Director, NTP, from Assistant to the Director, "Comments on NTP Peer Review Panel Evaluation of the Carcinogenicity Data on D and C Red No. 33"). Therefore, FDA concludes that its statement in the proposal was in error, and that there was no recommendation by NTP of short-term studies.

21. One comment from a trade association asserted that the NTP panel

had concluded that D&C Red No. 33 was not a carcinogen.

This comment does not accurately characterize the NTP's conclusions. The NTP panel's report concludes that while the quantitative evidence was insufficient to demonstrate a carcinogenic response to treatment, the qualitative observations revealed a treatment-related toxic effect on the spleen that was similar to the toxic effects produced by known splenic carcinogens among the other aromatic azo compounds. The NTP panel stated that further research is needed to develop an understanding of the mechanism of the toxic action of this family of compounds in the spleen of rats.

22. Two comments stated that the NTP panel found that the maximum tolerated dose had been exceeded in the rat bioassay of D&C Red No. 33.

FDA has reviewed the transcript of the NTP panel's deliberations. The agency believes that the sense of the NTP panel's discussion is that while the high dose in the rat study may have exceeded the maximum tolerated dose, the study nonetheless provided meaningful results.

23. FDA received two comments that argued that the currently available data on D&C Red No. 33 and D&C Red No. 36 are adequate to justify their permanent listing. One comment argued that because the chronic testing of both additives did not reveal a carcinogenic effect, FDA approval of these additives is appropriate.

FDA disagrees with these comments. The Color Additive Amendments require that the petitioner demonstrate the safety of a color additive to justify its permanent listing. Because the evidence as currently interpreted on these color additives provides a basis for concern about possible carcinogenicity that has not been adequately resolved, FDA finds that permanent listing of D&C Red No. 33 and D&C Red No. 36 is not appropriate at this time.

24. Two comments argued that even if there is a need for additional studies of D&C Red No. 33 and D&C Red No. 36, a new bioassay is not necessary. One comment said that because the concern about these color additives is their splenic toxicity in male Sprague-Dawley rats, there is no reason to conduct a full lifetime study, with attendant evaluation of all tissues and organs. Both comments asserted that the NTP panel rejected the need for new chronic studies of these additives in a different strain of rat.

The summary minutes (p. 4) of the NTP meeting show that the panel did not reject the need for another cancer study. The NTP panel felt that such a study would be useful, but that its focus should be on the mechanism of splenic effects. The NTP panel recommended that further research be done to gain a better understanding of "the mechanisms of toxic action." The NTP panel pointed out that a neoplastic response is one phase of a toxic response. An investigation of the toxic response in this situation would mean an investigation of the neoplastic response and therefore would be likely to require a long-term study, although not necessarily of the conventional bioassay type.

25. The comments suggested alternatives to chronic testing. One comment suggested calculating a risk assessment based on the comparative toxicity of D&C Red No. 9, D&C Red No. 33, and D&C Red No. 36 in Sprague-Dawley rats. This trade association also stated that it had begun to explore the possibility of conducting studies designed to elucidate the mechanism of splenic tumor development associated with monoazo compounds such as D&C Red No. 33 and D&C Red No. 36. These comments also suggested that to permit further consideration of the scientific evaluations and studies that are necessary on D&C Red No. 33 and D&C Red No. 36, FDA should extend the provisional listing of these color additives for 1 year, until September 3, 1986. FDA also received two comments that urged the agency to take these additives off the provisional list. One of these comments said the petitioner would have an opportunity to submit data even if the color additives were no longer provisionally listed.

FDA has carefully considered these comments. The agency believes that a risk assessment based on the comparative toxicity of D&C Red No. 9, D&C Red No. 33, and D&C Red No. 36 may be possible. If the splenic toxicity associated with the use of these additives is produced by their principal color components, it should be possible to predict, within reasonable limits, the potency of these color additives. Insight into the relative potency of these additives would enable the agency to make a determination about the safety of D&C Red No. 33 and D&C Red No. 36 without new long-term studies on these additives. Because the Color Additive Amendments enjoin the Commissioner to reach a decision on the provisional list as soon as reasonably practicable, he has decided to pursue the approach suggested by the comment rather than require new long-term studies. Therefore, this final rule extends the provisional listing of D&C Red No. 33 and D&C Red No. 36 for 18 months, until March 3, 1987, rather than the 5 years that the agency proposed (50 FR 26382) or the 1 year that the comments requested.

FDA is unable to proceed immediately to conduct a comparative risk assessment because questions have been raised about whether a relative potency determination can be made. If the splenic toxicity of these additives or the observed carcinogenicity of D&C Red No. 9 were likely to be caused by an impurity in any of these additives, available evidence may not be adequate to determine whether that impurity is a common ingredient. Consequently, a determination of relative potency would not be possible.

The agency believes that resolution of the questions about the feasibility of determining relative potency is likely to derive from two sources. First, the panel is currently reviewing the toxicity of D&C Red No. 9. Consequently, its report should provide important insights. In addition, after the agency has received the panel's report on D&C Red No. 9, the Commissioner will arrange for expert review that will address specifically whether a determination of the relative potency of D&C Red No. 9, D&C Red No. 33, and D&C Red No. 36 is possible.

The Commissioner invites interested parties to submit skin penetration studies and any other information relevant to the issue of relative risk as quickly as possible. The Commissioner is committed to meeting the March 3, 1987, closing date for these color additives.

The Commissioner has considered whether this extension meets the standards set forth in *McIlwain* v. *Hayes*, 690 F.2d at 1047, and concludes that it does. To complete its evaluation of the studies on D&C Red No. 33 and D&C Red No. 36 and reach a decision on these additives, the agency must hear from the panel on D&C Red No. 9, receive the results of the expert review, consider these reports and all other available data, and prepare an appropriate **Federal Register** document. Consequently, the Commissioner believes that 18 months is as soon as a decision on D&C Red No. 33 and D&C Red No. 36 can practicably be made. The Commissioner also finds that continuing to permit the provisionally listed uses of D&C Red No. 33 and D&C Red No. 36 for 18 months is consistent with the public health.

The Commissioner advises that if at any time before March 3, 1987, he concludes that a risk assessment based on the comparative toxicity of D&C Red No. 9, D&C Red No. 33, and D&C Red No. 36 is not possible, he will notify the

public of that fact and announce what action he will take with regard to these color additives.

VI. Environmental and Economic Impact

The agency has determined under 21 CFR 25.24(a)(8) (April 26, 1985; 50 FR 16636) 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.

FDA has determined that extending the provisional listing of these color additives requires no change in the current industry practice concerning the manufacture or use of these ingredients. Therefore, FDA certifies, in accordance with section 605(b) of the Regulatory Flexibility Act, that no significant economic impact on a substantial number of small entities will derive from this action. Further, the economic effects of this final rule have been analyzed and it has been determined that it is not a major rule as defined by Executive Order 12291.

List of Subjects in 21 CFR Part 81

Color additives, Color additives provisional list, Cosmetics, Drugs.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, Part 81 is amended as follows:

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

1. The authority citation for 21 CFR Part 81 continues to read as follows:

Authority: Secs. 701, 706, 52 Stat. 1055–1056 as amended, 74 Stat. 399–407 as amended (21 U.S.C. 371, 376); Title II, Pub. L. 86–618; sec. 203, 74 Stat. 404–407 (21 U.S.C. 376, note); 21 CFR 5.10.

§ 81.1 [Amended]

2. In § 81.1 *Provisional lists of color additives* in paragraph (a) by revising the closing date for "FD&C Yellow No. 6" to read "June 6, 1986" and by revising the closing date for "FD&C Red No. 3" to read "September 3, 1986" and in paragraph (b) by revising the closing dates for "D&C Orange No. 17," "D&C Red No. 8," "D&C Red No. 9," "D&C Red No. 19," and "D&C Red No. 37" to read "June 6, 1986" and by revising the closing dates for "D&C Red No. 33" and "D&C Red No. 36" to read "March 3, 1987."

3. In § 81.27 by removing paragraph (e) and by revising the introductory text of paragraph (d), to read as follows:

§ 81.27 Conditions of provisional listing.

* * * * *

(d) The closing dates and dates for final reports for the following 10 color additives are postponed in accordance with the following list while chronic toxicity feeding studies are conducted and evaluated and subject to compliance with the requirements of this paragraph:

	Final report due	Closing date
D&C Orange No. 17		June 6, 1986.
D&C Red No. 3		Sept 3, 1986.
D&C Red No. 8		June 6, 1986.
D&C Red No. 9		Do.
D&C Red No. 19		Do.
D&C Red No. 33		Mar. 3, 1987.
D&C Red No. 36		Do.
D&C Red No. 37		June 6, 1986.
FD&C Yellow No. 6		Do.
FD&C Blue No. 2		Date of final decision on permanent listing.

* * * * *

Dated: August 23, 1985.

Frank E. Young,

Commissioner of Food and Drugs.

[FR Doc. 85-21081 Filed 8-30-85; 8:45 am]

BILLING CODE 4160-01-M

---

21 CFR Part 81

[Docket No. 76N-0366]

Provisional Listing of FD&C Yellow No. 5 and Its Lakes; Postponement of Closing Date

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is postponing the closing date for the provisional listing of FD&C Yellow No. 5 for use in coloring cosmetics generally and externally applied drugs and of its lakes for use in coloring food and ingested drugs. The new closing date will be November 5, 1985. This brief postponement will provide time for the receipt and evaluation of any objections submitted in response to the final rule, published elsewhere in this issue of the **Federal Register**, approving the petition for the listing of FD&C Yellow No. 5 in cosmetics generally and in externally applied drugs and also continuing the provisional listing of its lakes.

DATES: Effective September 3, 1985, the new closing date for FD&C Yellow No. 5 and its lakes will be November 5, 1985.

FOR FURTHER INFORMATION CONTACT: George H. Pauli, Center for Food Safety and Applied Nutrition (HFF-330), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202-472-5740.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of June 3, 1985 (50 FR 23294), FDA established the current closing date of September 3, 1985, for the provisional listing of FD&C Yellow No. 5 and of its lakes. The agency extended the closing date until September 3, 1985, to permit consideration of the scientific and policy aspects of the data concerning the safety of its provisionally listed uses. The agency had previously extended the closing date for FD&C Yellow No. 5 and its lakes on several occasions. For a full procedural history of the provisional listing of this color additive, see 48 FR 45760.

After reviewing and evaluating the data, the agency has concluded that FD&C Yellow No. 5 is safe for use in coloring cosmetics and externally applied drugs. Therefore, elsewhere in this issue of the **Federal Register**, FDA is publishing a final rule that lists FD&C Yellow No. 5 for these uses. That rule also continues the provisional listing of the lakes of this additive. FDA is also publishing elsewhere in this issue of the **Federal Register** a proposed rule that would establish a new identity and a uniform set of specifications for all uses of FD&C Yellow No. 5 because the final rule that FDA is publishing establishes a new identity and new specifications for this color additive in 21 CFR 74.2705.

This brief postponement will provide sufficient time for receipt and evaluation of objections submitted in response to the final rule that lists FD&C Yellow No. 5 for use in coloring cosmetics and externally applied drugs.

Because of the shortness of time until the September 3, 1985, closing date, FDA concludes that notice and public procedure on these amendments are impracticable, and that good cause exists for issuing the postponement as a final rule. This final rule will permit the uninterrupted use of FD&C Yellow No. 5 and its lakes until November 5, 1985. Therefore, in accordance with 5 U.S.C. 553(d) (1) and (3), this regulation is being issued as a final rule and is being made effective on September 3, 1985.

List of Subjects in 21 CFR Part 81

Color additives, Color additives provisional list, Cosmetics, Drugs.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under the transitional provisions of the Color Additive Amendments of 1960 and under authority delegated to the

Commissioner of Food and Drugs, Part 81 is amended as follows:

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

1. The authority citation for 21 CFR Part 81 is revised to read as follows:

Authority: Secs. 701, 706, 52 Stat. 1055–1056 as amended, 74 Stat. 399–407 (21 U.S.C. 371, 376); Title II, Pub. L. 86–618; sec. 203, 74 Stat. 404–407 (21 U.S.C. 376, note); 21 CFR 5.10.

§ 81.1 [Amended]

2. In § 81.1 *Provisional lists of color additives*, by revising the closing date for "FD&C Yellow No. 5" in paragraph (a) to read "November 5, 1985."

§ 81.27 [Amended]

3. In § 81.27 *Conditions of provisional listing*, by revising the closing date for "FD&C Yellow No. 5" in paragraph (d) to read "November 5, 1985."

Dated: August 23, 1985.

Frank E. Young,

Commissioner of Food and Drugs.

[FR Doc. 85–21083 Filed 8–30–85; 8:45 am]

BILLING CODE 4160–01–M

DEPARTMENT OF DEFENSE

Office of the Secretary

32 CFR Part 155

[DoD Directive 5220.6]

Defense Industrial Personnel Security Clearance Review Program

AGENCY: Office of Secretary of Defense, DoD.

ACTION: Final rule.

SUMMARY: This part is revised and reissued to (1) reflect organizational changes in the Department, (2) simplify the language contained in the existing rule, (3) incorporate the Equal Access to Justice (5 U.S.C. 504), standard in the section pertaining to reimbursement for lost earnings, and (4) establish the Adjudication Policy for security clearance determinations under this rule.

EFFECTIVE DATE: This rule was approved and signed by the Deputy Secretary of Defense, August 12, 1985, and is effective as of that date.

FOR FURTHER INFORMATION CONTACT: Mr. James P. Brown, Director, Directorate for Industrial Security Clearance Review, 4019 Wilson Blvd., Suite 101, Arlington, VA 22203, telephone (202) 696–4598.

SUPPLEMENTARY INFORMATION: The Office of the Secretary of Defense published the last edition of this directive in FR Doc. 76–13745 appearing in the **Federal Register** on May 12, 1976 (41 FR 19303). It is now revised and incorporates the changes described in the **SUMMARY** above. While publication of this notice of revision is not required under the Administrative Procedures Act, 5 U.S.C. 553(a), notice is provided voluntarily by the Department of Defense.

1. This rule does not impose a burden under the Paperwork Reduction Act of 1980, 44 U.S.C. 3501 *et seq.*

2. This rule is not subject to the Regulatory Flexibility Act, 5 U.S.C. 601 *et seq.*

3. Although exempt under section 1.(a)(2) of E.O. 12291, the Department of Defense does not consider this rule to be a major rule under section 1.(b), E.O. 12291.

List of Subjects in 32 CFR Part 155

Administrative practice and procedure, Business and industry, Classified information, Security clearance.

Accordingly, 32 CFR is amended by revising Part 155, reading as follows:

PART 155—DEFENSE INDUSTRIAL PERSONNEL SECURITY CLEARANCE REVIEW PROGRAM

Sec.

Authority: 5 U.S.C. 504, E.O. 10865, 3 CFR, 1959–1963 COMP., p. 398.

§ 155.1 Purpose.

This part has been revised to update policy, the criteria, and procedures of the Defense Industrial Personnel Security Clearance Review Program under E.O. 10865.

§ 155.2 Applicability and scope.

This part:

(a) Applies to the Office of the Secretary of Defense, the Military Departments, Organization of the Joint Chiefs of Staff, and the Defense Agencies (hereafter referred to collectively as "DoD Components").

(b) By mutual agreement also extends to other Federal agencies that include:

(1) Department of Agriculture.
(2) Department of Commerce.
(3) Department of Interior.
(4) Department of Justice.
(5) Department of Labor.
(6) Department of State.
(7) Department of Transportation.
(8) Department of Treasury.
(9) Environmental Protection Agency.
(10) Federal Emergency Management Agency.
(11) Federal Reserve System.
(12) General Accounting Office.
(13) General Services Administration.
(14) National Aeronautics and Space Administration.
(15) National Science Foundation.
(16) Small Business Administration.
(17) United States Arms Control and Disarmament Agency.
(18) United States Information Agency.

(c) Applies to cases in which the Defense Industrial Security Clearance Office (DISCO) cannot affirmatively determine that it is clearly consistent with the national interest to grant or continue a security clearance for access to classified information by persons employed by U.S. industry, or to U.S. citizens who are direct-hire employees or selectees for positions with NATO and who require Certificates of Security Clearance in connection with direct employment by agencies of NATO, or to Red Cross or United Service Organizations (USO) employees nominated for assignment with the Military Services overseas. These cases must be referred to the Directorate for Industrial Security Clearance Review (DISCR) for action under this Directive.

(d) Does not apply to cases in which a security clearance is withdrawn for administrative reasons with no finding of prejudice to a later determination as to whether the grant or continuance of applicant's security clearance would be clearly consistent with the national interest, or to cases in which an interim security clearance is withdrawn during an investigation.

(e) Provides a program which may be extended to other cases at the direction of the Deputy Under Secretary of Defense for Policy, or designee.

§ 155.3 Definitions.

Addiction. Psychological or physical dependency to the point of compulsive use.

Appeal Board. A panel designated by the General Counsel, DoD, or designee to make final determinations in cases which are appealed.

Applicant. A person in industry who requires a security clearance for access to classified information and any U.S. citizen who is a direct-hire employee or selectee for a position with NATO and who requires NATO Certificates of Security Clearance, security assurances