

§ 82.1254 (21 CFR 82.1254) to reference § 74.1254.

Two objections were filed in response to the order. A hearing was not requested. One letter, received from a manufacturer of the color and supported by a second letter from a copetitioner for listing of the color, objected to the limitations placed on the specifications for D&C Orange No. 4. The objections stated that total color should be "not less than 87 percent" instead of "90 percent" and that the sum of volatile matter (at 135° C) and chlorides and sulfates (calculated as sodium salts) should be "not more than 13 percent" instead of "10 percent." The objections further noted that under provisional listing those specifications for D&C Orange No. 4 were 85 percent and 15 percent, respectively. The objections state that the increase in labor and energy required for all batches of D&C Orange No. 4 to meet the specifications of 90 percent for total color and 10 percent for volatile matter and salts would serve only to lower the content of moisture and salt and would lead to increased expenses to producers and consumers.

After evaluating the objections and reviewing the available data, the Commissioner concurs that specifications for the color may be safely revised by the reduction of the specification for total color from 90 percent to 87 percent and an increase of the specifications for volatile matter (water) plus salts (sodium chloride and sodium sulfate) from 10 percent to 13 percent.

Therefore, under the Federal Food, Drug, and Cosmetic Act (sec. 706 (b), (c), and (d), 74 Stat. 399-403 (21 U.S.C. 376 (b), (c), and (d))) and under authority delegated to the Commissioner (21 CFR 5.1), there being no other objections or any request for a hearing in response to the order of September 30, 1977, the amendments to parts 74, 81, and 82 promulgated thereby became effective on November 1, 1977, and part 74 is amended in § 74.1254(b) by revising the listings therein for "sum of volatile matter" and "total color," to read as follows:

§ 74.1254 D&C Orange No. 4.

(b) * * *

Sum of volatile matter (at 135° C) and chlorides and sulfates (calculated as sodium salts), not more than 13 percent.

Total color, not less than 87 percent.

Effective dates: (1) The amendments promulgated by the regulation of September 30, 1977, became effective on

November 1, 1977; (2) the amendment set forth above is effective April 7, 1978.

(Sec. 706 (b), (c), and (d), 74 Stat. 399-403 (21 U.S.C. 376 (b), (c), and (d))).

Dated: March 20, 1978.

WILLIAM F. RANDOLPH,
Acting Associate Commissioner
for Compliance.

[FR Doc. 78-8941 Filed 4-6-78; 8:45 am]

[4110-03]

[Docket No. 76N-0366]

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

Provisionally Listed Color Additives; Postponement of Closing Dates; Restatement of Conditions for Con- tinued Provisional Listing

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: This document amends the color additive regulations by extending the closing dates for four color additives (D. & C. Red No. 6, D. & C. Red No. 7, D. & C. Red No. 30 and caramel) and revising the dates by which certain reports must be submitted to the Food and Drug Administration. This action permits the continued use of these color additives until the new closing dates and amends the color additive regulations by updating the conditions that certain color additives must meet to remain on the provisional list.

EFFECTIVE DATE: April 7, 1978.

FOR FURTHER INFORMATION CONTACT:

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

SUPPLEMENTARY INFORMATION: In the FEDERAL REGISTER of December 13, 1977 (42 FR 62497), the Commissioner of Food and Drugs, on his own initiative, proposed to postpone the closing date for the use of five provisionally listed color additives beyond January 31, 1978. The proposed postponement was conditioned on the completion of appropriate scientific investigations and the submission of data to FDA on a prescribed schedule. The proposal also discussed the extent to which the petitioners have complied with the conditions of provisional list-

ing that are set forth in § 81.27 *Conditions of provisional listing of additives* (21 CFR 81.27), and it proposed to revise certain of these conditions. The conditions in § 81.27 were initially prescribed in regulations published in the FEDERAL REGISTER of February 4, 1977 (42 FR).

In response to the proposal the Commissioner received one comment from the Environmental Defense Fund which contended that the closing date for the provisional listing of lead acetate should not be extended beyond January 31, 1978 because lead acetate is a known carcinogen. An analysis of this comment was subsequently received on January 27, 1978 from Combe, Inc., a manufacturer of lead acetate hair colors. The provisional listing of lead acetate, including a discussion of these comments, was considered in a separate document that was published in the FEDERAL REGISTER of March 3, 1978 (43 FR 8790).

The petitioners for caramel have recently requested that the proposed deadline of March 31, 1978 for the submission of the full written report on the subchronic study for caramel be extended for a short time because unforeseen problems have delayed its completion. In view of the short amount of time necessary to furnish the final report, the Commissioner concludes that a 30-day extension of the deadline for the final report is reasonable. This short additional extension to April 30, 1978, however, will not effect the "interim" closing date for caramel which is being extended as originally proposed to July 31, 1978.

In the absence of other comments, the Commissioner advises that the dates for submission of data and "interim" closing dates for the three remaining color additives discussed in the December 13, 1977 proposal are being extended as proposed. These three color additives include: D. & C. Red No. 6, D. & C. Red No. 7, and D. & C. Red No. 30. In addition, as proposed, the regulations set forth below add a new paragraph (e) to § 81.27 prescribing additional testing requirements to be met as conditions of the continued provisional listing of F.D. & C. Red No. 3 and D. & C. Red No. 33.

Certain conditions of § 81.27, for continued provisional listing of the color additives, established on February 4, 1977, have been complied with and are now obsolete. Additionally, the provisional listing of certain colors has been terminated since February 4, 1977. The regulation set forth below reflects these actions by deleting § 81.27(a) and reserving it for future use and deleting certain listings for colors from the requirements of paragraphs (b), (c), and (d) of § 81.27.

Therefore, under the transitional provisions of the Color Additive Amendments of 1960 (Title II, Pub. L.

86-316; sec. 203, 74 Stat. 404-407 (21 U.S.C. 376 note)) and under authority delegated to the Commissioner (21 CFR 5.1), § 81.27 is amended by revoking paragraph (a) and reserving it for future use; by revising paragraphs (b), (c), and (d); and by adding new paragraph (e), to read as follows:

§ 81.27 Conditions of provisional listing.

(a) [Reserved]

(b) The closing date for caramel is postponed until July 31, 1978, while a subchronic study is conducted and evaluated, and for lead acetate until December 31, 1978, while a short-term skin penetration study is conducted and evaluated, and subject to compliance with the requirements of this paragraph.

(1) At least one petitioner for caramel shall agree in writing by March 7, 1977 to undertake the subchronic study on the color additive.

(2) A full written report on the subchronic study for caramel shall be submitted by April 30, 1978, and on the short-term skin penetration study for lead acetate by September 30, 1978, to the Division of Food and Color Additives (HFF-334), Food and Drug Administration, 200 C Street SW., Washington, D.C. 20204.

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

(c) The closing date for the following three color additives is postponed until October 31, 1978, while chemistry data and analytical methods to establish specifications for them are developed and evaluated, and subject to compliance with the requirements of this paragraph: D. & C. Red No. 6, D. & C. Red No. 7, and D. & C. Red No. 30.

(1) At least one petitioner for each of the three color additives listed in paragraph (c) of this section shall agree in writing by March 7, 1977 to undertake to develop the necessary chemistry data and analytical methods for the color additives.

(2) The required chemistry data and analytical methods shall be submitted to the Division of Food and Color Additives, Food and Drug Administration, 200 C Street SW., Washington, D.C. 20204, by July 31, 1978.

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

(d) The closing date for the following 25 color additives is postponed until January 31, 1981, while chronic toxicity feeding studies for 24 of the colors and, in the case of caramel, a lifetime mouse skin-painting study, are

conducted and evaluated, and subject to compliance with the requirements of this paragraph: F.D. & C. Yellow No. 5, F.D. & C. Yellow No. 6, D. & C. Yellow No. 10, F.D. & C. Red No. 3, D. & C. Red No. 6, D. & C. Red No. 7, D. & C. Red No. 8, D. & C. Red No. 9, D. & C. Red No. 19, D. & C. Red No. 21, D. & C. Red No. 22, D. & C. Red No. 27, D. & C. Red No. 28, D. & C. Red No. 30, D. & C. Red No. 33, D. & C. Red No. 36, D. & C. Red No. 37, F.D. & C. Green No. 3, D. & C. Green No. 5, D. & C. Green No. 6, F.D. & C. Blue No. 1, F.D. & C. Blue No. 2, D. & C. Orange No. 5, D. & C. Orange No. 17, and caramel.

(1) At least one petitioner for each of the 25 color additives listed in paragraph (d) of this section shall agree in writing by March 7, 1977 to undertake the required studies on the color additives.

(2) The petitioner undertaking the studies shall submit a protocol for the conduct of the studies to the Division of Food and Color Additives (HFF-334), Food and Drug Administration, 200 C Street SW., Washington, D.C. 20204, for review and acceptance or rejection, by April 5, 1977.

(3) An initial progress report of the studies on the color additives shall be submitted to the Division of Food and Color Additives by December 31, 1977. Further progress reports shall be submitted at 6-month intervals thereafter. A full report of the studies conducted on the color additives shall be submitted to the Division of Food and Color Additives by August 4, 1980.

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

(e) The closing date for the following two color additives is postponed until January 31, 1981, while multigeneration reproduction studies are conducted and evaluated, and subject to compliance with the requirements of this paragraph: F.D. & C. Red No. 3 and D. & C. Red No. 33.

(1) At least one petitioner for each of the two color additives listed in paragraph (e) of this section shall agree in writing by May 8, 1978, to undertake multigeneration reproduction studies on the color additives.

(2) An initial progress report of the studies on the color additives shall be submitted by July 1, 1978 and at 6-month intervals thereafter. A full report of the studies conducted on the color additives shall be submitted to the Division of Food and Color Additives by August 4, 1980.

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

Effective date: April 7, 1978.

(Title II, Pub. L. 86-316; sec. 203, 74 Stat. 404-407 (21 U.S.C. 376 note).)

Dated: March 20, 1978.

WILLIAM F. RANDOLPH,
Acting Associate Commissioner
for Compliance.

[FR Doc. 78-8954 Filed 4-6-78; 8:45 am]

[4110-03]

SUBCHAPTER B—FOOD FOR HUMAN CONSUMPTION

[Docket No. 77N-0131]

BEESWAX

Affirmation of GRAS Status as a Direct Human Food Ingredient

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: This rule affirms that beeswax is generally recognized as safe (GRAS) as a direct human food ingredient. The safety of this ingredient has been evaluated under the comprehensive safety review being conducted by the agency.

EFFECTIVE DATE: May 8, 1978.

ADDRESS: Written objections to the office of the Hearing Clerk (HFC-20), Food and Drug Administration, Room 4-65, 5600 Fishers Lane, Rockville, Md. 20857.

FOR FURTHER INFORMATION CONTACT:

Corbin I. Miles, Bureau of Foods (HFF-335), Food and Drug Administration, Department of Health, Education, and Welfare, 200 C Street SW., Washington, D.C. 20204, 202-472-4750.

SUPPLEMENTARY INFORMATION: In the FEDERAL REGISTER of July 29, 1977 (42 FR 38609), a proposal was published to affirm that beeswax (yellow and white) is generally recognized as safe for use as a direct human food ingredient. The proposal was based on safety information developed by the Select Committee on GRAS substances. The proposal was published in accord with the announced FDA review of the safety of GRAS and prior-sanctioned food ingredients.

In accordance with § 170.35 (21 CFR 170.35), relating to the affirmation of GRAS food ingredients, copies of the Scientific Literature Review on beeswax, data on mutagenic evaluation, and the report of the Select Committee on GRAS substances have been made available for public review in the office of the Hearing Clerk (HFC-20), Food and Drug Administration, Room 4-65, 5600 Fishers Lane, Rockville, Md. 20857. Copies of these documents have

also been made available for public purchase from the National Technical Information Service as announced in the proposal.

In addition to proposing to affirm the GRAS status of beeswax, the Commissioner of Food and Drugs gave public notice that he was unaware of any prior-sanctioned food ingredient use for this ingredient other than for the proposed conditions of use. Persons asserting additional or extended uses, in accordance with approval granted by the U.S. Department of Agriculture or the Food and Drug Administration prior to September 6, 1958, were given notice to submit proof of such a sanction so that the safety of prior-sanctioned uses could be determined at this time. That notice was also an opportunity to have prior-sanctioned uses of beeswax (yellow and white) approved by issuance of an appropriate regulation under Part 181 (21 CFR 181) "Prior-Sanctioned Food Ingredient," provided prior-sanctioned use could be affirmed as safe on the basis of data now available to the Commissioner. Notice was also given that failure to submit proof of an applicable prior sanction in response to the proposal would constitute a waiver of the right to assert sanction at any future time.

No reports of a prior-sanctioned use for beeswax were submitted in response to the proposal. Therefore, in accordance with that proposal, any right to assert a prior sanction for use of beeswax under conditions different from those set forth in this regulation has been waived.

No comments were received in response to the Commissioner's proposal and supporting data and information on beeswax (yellow and white). The Commissioner therefore concludes that no change in the proposal to affirm the GRAS status of beeswax (yellow and white) is warranted. Accordingly, it is being promulgated without change.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 201(s), 409, 701(a), 52 Stat. 1055, 72 Stat. 1784-1788 as amended (21 U.S.C. 321(s), 348, 371(a))) and under authority delegated to the Commissioner (21 CFR 5.1), Chapter I of Title 21 of the Code of Federal Regulations is amended as follows:

PART 172—FOOD ADDITIVES PERMITTED FOR DIRECT ADDITION TO FOOD FOR HUMAN CONSUMPTION

§ 172.510 [Amended]

1. In Part 172, § 172.510 *Natural flavoring substances and natural substances used in conjunction with flavors*, by deleting the entry for "Beeswax, white (Cire d'abeille)" from the list of substances in paragraph (b).

PART 182—SUBSTANCES GENERALLY RECOGNIZED AS SAFE

§§ 182.1973, 182.1975 [Deleted]

2. In Part 182, by deleting § 182.1973 *Beeswax* and § 182.1975 *Bleached beeswax*.

PART 184—DIRECT FOOD SUBSTANCES AFFIRMED AS GENERALLY RECOGNIZED AS SAFE

3. In Part 184, by adding new § 184.1973 to read as follows:

§ 184.1973 Beeswax (yellow and white).

(a) Beeswax (CAS Registry No. MX 8012-89-3 and MX 8006-40-4) is a secretory product of honey bees used as a structural material in honeycombs. Beeswax is prepared from honeycombs after removal of the honey by draining or centrifuging. The combs are melted in hot water or steam or with solar heat, and strained. The wax is refined by melting in hot water to which sulfuric acid or alkali may be added to extract impurities. The resulting wax is referred to as yellow beeswax. White beeswax is produced by bleaching the constituent pigments of yellow beeswax with peroxides, or preferably it is bleached by sun light.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 2d Ed. 1972.¹

(c) The ingredient is used as a flavoring agent and adjuvant as defined in § 170.3(o)(12) of this chapter, as a lubricant as defined in § 170.3(o)(18) of this chapter, and as a surface-finishing agent as defined in § 170.3(o)(30) of this chapter.

(d) The ingredient is used in food, in accordance with § 184.1(b)(1) of this chapter, at levels not to exceed good manufacturing practice. Current good manufacturing practice results in a maximum level, as served, of: 0.065 percent for chewing gum as defined in § 170.3(n)(6) of this chapter; 0.005 percent for confections and frostings as defined in § 170.3(n)(9) of this chapter; 0.04 percent for hard candy as defined in § 170.3(n)(25) of this chapter; 0.1 percent for soft candy as defined in § 170.3(n)(38) of this chapter; and 0.002 percent or less for all other food categories.

Effective date. This regulation is effective May 8, 1978.

(Secs. 201(s), 409, 701(a), 52 Stat. 1055, 72 Stat. 1784-1788 as amended (21 U.S.C. 321(s), 348, 371(a)).)

¹Copies may be obtained from: National Academy of Sciences, 2101 Constitution Avenue NW., Washington, D.C. 20037.

Dated: March 20, 1978.

WILLIAM F. RANDOLPH,
*Acting Associate Commissioner
for Compliance.*

NOTE.—Incorporation by reference approved by the Director of the Office of the Federal Register on July 10, 1973 and is on file in the Federal Register's library.

[FR Doc. 78-8951 Filed 4-6-78; 8:45 am]

[1505-01]

[Docket No. 76N-0460]

PART 173—SECONDARY DIRECT FOOD ADDITIVES IN FOOD FOR HUMAN CONSUMPTION

Subpart D—Specific Usage Additives

Correction

In FR Doc. 78-6039 appearing at page 11301 in the FEDERAL REGISTER issue of Friday, March 17, 1978, please make the following corrections:

At page 11302, in the third column under paragraph 6., in the third line of the second paragraph "oxzone" should be changed to "ozone";

At page 11305, in the 31st line of the third column, the word "degrated" should be changed to "degraded";

At page 11315, in the 11th line of the third column, the word "ustin" should be changed to "using"; and

At page 11317, in § 173.345(c)(1)(i), "chloropentafluoroethane" should appear as "chloropentafluoroethane".

[4110-03]

SUBCHAPTER D—DRUGS FOR HUMAN USE

[Docket No. 77N-00601]

PART 361—PRESCRIPTION DRUGS FOR HUMAN USE GENERALLY RECOGNIZED AS SAFE AND EFFECTIVE AND NOT MISBRANDED: DRUGS USED IN RESEARCH

Radioactive Drugs for Certain Research Uses; Amended Reporting Requirements

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: This amendment revises the reporting requirements for research studies in which radioactive drugs are used. It deletes the requirement for detailed measurements and calculations for each subject in the study; instead, it permits submission of data on a representative subject. The effect will be to decrease the burden in reporting required of the

Radioactive Drug Research Committee, but still provide the agency with data to evaluate the risk attributable to radioactive drugs.

EFFECTIVE DATE: May 8, 1978.

FOR FURTHER INFORMATION CONTACT:

Robert D. Bradley, Bureau of Drugs (HFD-30), Food and Drug Administration, Department of Health, Education, and Welfare, 5600 Fishers Lane, Rockville, Md. 20857, 301-443-5220.

SUPPLEMENTARY INFORMATION: In the FEDERAL REGISTER of May 6, 1977 (42 FR 23161), the Commissioner of Food and Drugs proposed revising § 361.1(c)(3) (21 CFR 361.1(c)(3)) to lessen the reporting workload of Radioactive Drug Research Committees (RDRC), while still providing FDA with sufficient information to evaluate the total risk that radioactive drugs pose to the public health. This document implements the proposed rule without change.

Twelve comments responded to the proposal. They came from professionals associated with colleges, universities, and medical centers; from a city health department; and from a pharmaceutical association. The substantive comments and the Commissioner's response to each follow:

1. Most comments supported the proposal. Several suggested that the regulations be further amended to simplify the RDRC's task, but were not specific about how to do it. Two comments said that FDA receives no useful information from data on radiation doses absorbed by the eye lens and that this requirement should be revoked.

The Commissioner advises that FDA is constantly seeking, and soliciting comment on, ways to simplify reporting requirements. All justifiable requests to accomplish this will be considered. Regarding the comments on absorbed doses to the lens of the eye, however, the Commissioner is concerned about the risk to the public health from such doses and believes that useful information is obtained from these data. He therefore rejects the recommendation to revoke requirements for data on radiation doses absorbed by the eye lens.

2. One comment said there should be a threshold for total radiation doses, and the regulations should require data submission only when the threshold is exceeded—for example, when the dose exceeds 75 percent of the maximum allowable dose per year.

The Commissioner advises that § 361.1(b)(3) (21 CFR 361.1(b)(3)) requires that the amount of radioactive material administered to a subject be the smallest radiation dose with which it is practical to perform the study without jeopardizing the benefits to be

obtained from the study. If the RDRC were to report only doses above a certain threshold level, FDA would not be able to judge how effectively the RDRC is enforcing compliance with this requirement. The Commissioner therefore rejects the comment.

3. One comment said the proposed regulation appears impossible to comply with because subjects would be relied on to provide information that they may not have record of, such as the name of a radioactive drug, the dates of administration, and the drug's activity.

The Commissioner disagrees. Section 361.1(d)(5) requires the investigator to select appropriate subjects for the study; and § 361.1(b)(3)(i) sets the limit on radiation dose from a single study or cumulatively from a number of studies. The Commissioner realizes that the physician accepts much of the medical history information from the subject. Physicians must rely on their own expertise to determine the suitability of the subject and if follow-up is needed to establish the amount of radiation absorbed from previous studies.

4. One comment said that reporting estimates of the dose from any associated X-ray procedure for each subject is a new requirement.

The Commissioner disagrees. He advises that this amendment is for clarification of requirements that are already in effect. In paragraph 28 of the preamble to the final regulation establishing part 361 (see the FEDERAL REGISTER of July 25, 1975 (40 FR 31303)), the Commissioner stated specifically that the dose limitations under § 361.1(b)(3) include "any doses from X-ray procedures which are considered an integral part of the research study, i.e., would not have occurred but for the study." To further clarify this, the Commissioner has modified the first paragraph of § 361.1(c)(3)(6) to clearly state that required X-ray dose estimates are those associated with the study.

5. One comment said that § 361.1(c)(3) should be amended to require that the investigator immediately notify FDA, through the RDRC, of any untoward effect.

The Commissioner advises that § 361.1(d)(8) requires immediate reporting of all adverse reactions associated with the use of a radioactive drug. Such an amendment to the annual report provisions in § 361.1(c)(3) is therefore unnecessary.

6. One comment recommended that the reporting requirements be amended to include a requirement to report any abnormal pathology for a subject, and to identify normal pathology in terms of standard reference work. The comment said the pathology requirement would be important in assessing risks and would not be an additional

burden because abnormal pathologies would already be included in medical records. The only additional reporting when normal subjects were used would be a one-time designation of the standard for normal organ mass.

Although the pathology of a particular subject is an important consideration, the Commissioner does not believe that its inclusion as a requirement is necessary. Potential subjects for the research covered by part 361 are, for the most part, healthy volunteers for whom a standard for normal organ mass would apply. It would be the responsibility of the investigator to assure that a subject is a suitable candidate for a study and that meaningful data can be obtained from that subject.

7. One comment requested clarification of who is responsible for monitoring the dose commitment and asked if the burden is being transferred from the RDRC to FDA.

The Commissioner advises that the RDRC continues to be responsible for determining that the dose commitment is within the limits described in § 361.1(b)(1), and FDA continues to review the activities of the RDRC, as described in § 361.1(c)(5). Only the reporting requirements in § 361.1(c)(3) are being changed.

8. One comment said the regulation would limit to a maximum of 5 rems per year, studies that use X-rays only.

The Commissioner advises that § 361.1 applies to research studies involving radioactive drugs. It does not apply to research studies that involve the use of X-rays only and does not impose limits on such use. Because the safety of a given study depends on the total radiation dose, the limits in § 361.1(b)(3) include the dose from X-ray exposure that occurs as an integral part of the study. Section 361.1(c)(3) requires the reporting of the dose contribution from X-ray procedures so that the subject's total exposure to radiation can be determined.

9. One comment asked for clarification of the requirement in item 6(c), that for each subject who has participated in other radioactive drug research studies involving X-ray procedures, the report include an estimate of the subject's absorbed radiation doses. The comment asked if the Commissioner intended to require reporting skin exposure, absorbed dose to specific organs, or both.

The Commissioner advises that for such a subject, the report should include the doses to the whole body and to each organ specified in § 361.1(b)(3)(i), i.e., active blood-forming organs, lens of the eye, gonads, and other organs. The requirement does not include skin exposure as one of the "other organs."

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 505,

701(a), 52 Stat. 1052-1053 as amended, 1055 (21 U.S.C. 355, 371(a)) and under authority delegated to the Commissioner (21 CFR 5.1), part 361 is amended in § 361.1(c)(3) by revising item 6 in the "Report on Research Use of Radioactive Drugs" therein, to read as follows:

§ 361.1 Radioactive drugs for certain research uses.

(c) * * *

(3) * * *

REPORT ON RESEARCH USE OF RADIOACTIVE DRUG

6. Radiation absorbed dose. Provide the maximum dose commitment to the whole body and each organ specified in 21 CFR 361.1(b)(3)(i) that was received by a representative subject and the calculations or references that were used to estimate these maximum dose commitments. The report shall include the dose contribution of both the administered radionuclide(s) and any X-ray procedures associated with the study. If the study elicits data on the uptake or excretion of the radioactive drug pertinent to the estimation of dose commitment, report the mean value and range of values. For each subject provide:

- Age, sex, and approximate weight.
- Total activity of each radionuclide administered for each radioactive drug used in the study. Report each X-ray procedure used in conjunction with the study.
- If the subject has participated in other radioactive drug research studies, report the name of the radioactive drug used in these other studies, the date of administration, and the total activity of each radionuclide administered. If any X-ray procedures were used, identify the X-ray procedure(s) and include an estimate of the absorbed radiation doses.

Effective date: May 8, 1978.

(Secs. 505, 701(a), 52 Stat. 1052-1053 as amended, 1055 (21 U.S.C. 355, 371(a)).)

Dated: March 22, 1978.

WILLIAM F. RANDOLPH,
Acting Associate Commissioner
for Compliance.

[FR Doc. 78-8950 Filed 4-6-78; 8:45 am]

[4110-03]

[Docket No. 78N-0035]

PART 442—CEPHA ANTIBIOTIC DRUGS

Sterile Cephradine

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: This document amends the antibiotic drug regulations to provide for the certification of sterile

cephradine for intravenous use. Under section 507 of the Federal Food, Drug, and Cosmetic Act, the manufacturer has supplied sufficient data and information to establish the safety and efficacy of sterile cephradine.

EFFECTIVE DATE: April 7, 1978.

FOR FURTHER INFORMATION CONTACT:

Joan Eckert, Bureau of Drugs (HFD-140), Food and Drug Administration, Department of Health, Education, and Welfare, 5600 Fishers Lane, Rockville, Md. 20857, 301-443-4290.

SUPPLEMENTARY INFORMATION: The Commissioner of Food and Drugs, having evaluated data submitted in accordance with regulations promulgated under section 507 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 357), as amended, with respect to providing for the certification of sterile cephradine for intravenous use, concludes that the data supplied by the manufacturer concerning this antibiotic drug product are adequate to establish its safety and efficacy when used as directed in the labeling and that the regulations should be amended in part 442 (21 CFR part 442) to provide for its certification.

Therefore, under the Federal Food, Drug, and Cosmetic Act (sec. 507, 59 Stat. 463, as amended (21 U.S.C. 357)) and under authority delegated to the Commissioner (21 CFR 5.1), part 442 is amended as follows:

- In § 442.40a, paragraphs (a)(1)(i), (3)(ii), and (b)(1) are revised to read as follows:

§ 442.40a Sterile cephradine.

(a) * * *

(1) * * *

(i) Its potency is not less than 900 and not more than 1,050 micrograms of cephradine per milligram on the anhydrous basis. If it is packaged for dispensing, its cephradine content is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of cephradine that it is represented to contain.

(3) * * *

(ii) Samples required:

(a) If the batch is packaged for repackaging or for manufacturing use:

(1) For all tests except sterility: 10 packages, each containing approximately 500 milligrams.

(2) For sterility testing: 1 package containing approximately 6 grams of a composite sample.

(b) If the batch is packaged for dispensing:

(1) For all tests except sterility: A minimum of 10 immediate containers.

(2) For sterility testing: 20 immediate containers, collected at regular in-

tervals throughout each filling operation.

(b) * * *

(1) *Potency.* Use any of the following methods; however, the results obtained from the microbiological agar diffusion assay shall be conclusive.

(i) *Microbiological agar diffusion assay.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample in sufficient 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to give a stock solution containing 1.0 milligram of cephradine per milliliter (estimated); also, if it is packaged for dispensing, reconstitute the sample as directed in the labeling, except use distilled water in lieu of reconstituting fluid. Then using a suitable hypodermic needle and syringe, remove an accurately measured representative portion from each container. Dilute with solution 1 to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with solution 1 to the reference concentration of 10 micrograms of cephradine per milliliter (estimated).

(ii) *Hydroxylamine colorimetric assay.* Proceed as directed in § 442.40(b)(1)(ii). If packaged for dispensing, reconstitute the sample as directed in the labeling using distilled water instead of the reconstituting fluid. Further dilute an aliquot of this solution with distilled water to 1 milligram of cephradine per milliliter (estimated).

(iii) *Liquid chromatographic assay.* Proceed as directed in § 442.40(b)(1)(iii). If packaged for dispensing, reconstitute the sample as directed in the labeling, using distilled water instead of the reconstituting fluid. Further dilute an aliquot of this solution with distilled water to 1 milligram of cephradine per milliliter (estimated).

2. Section 442.240 is redesignated as § 442.240a and new §§ 442.240 and 442.240b are added to read as follows:

§ 442.240 Cephradine injectable dosage forms.

§ 442.240a Cephradine for injection.

§ 442.240b Sterile cephradine.

The requirements for certification and the tests and methods of assay for sterile cephradine packaged for dispensing are described in § 442.40a.

Since the conditions prerequisite to providing for certification of this drug have been complied with and as the matter is noncontroversial, the Commissioner finds for good cause that prior notice, public procedure, and delay in effective date are unneces-