supplemental structural inspections to detect fatigue cracking, and repair or replacement, if necessary; or the installation of specific modifications on certain Airbus Industrie Model A300 series airplanes. Paragraph (j) of AD 93–01–24 specifies that accomplishment of the requirements of that AD constitutes terminating action for the 14 AD's listed previously. AD 93–01–24 became effective on March 9, 1993, and the actions specified in that AD were required to be accomplished within one year after that date.

Since the actions required by AD 93–01–24 were required to be accomplished by March 9, 1994, and because such accomplishment constitutes terminating action for the requirements of the 14 AD's listed previously, the FAA has determined that it is necessary to rescind those AD's in order to eliminate redundant requirements.

Since this action rescinds requirements that have been rendered moot by subsequent AD action, it has no adverse economic impact and imposes no additional burden on any person. For the same reason, the FAA has determined that there is no particular public interest in this action. Therefore, notice and public procedures hereon are unnecessary and the rescission may be made effective upon publication in the **Federal Register**.

The Rescission

Accordingly, pursuant to the authority delegated to me by the Administrator, the Federal Aviation Administration amends part 39 of the Federal Aviation Regulations (14 CFR part 39) as follows:

## PART 39—AIRWORTHINESS DIRECTIVES

1. The authority citation for part 39 continues to read as follows:

**Authority:** 49 U.S.C. App. 1354(a), 1421 and 1423; 49 U.S.C. 106(g); and 14 CFR 11.89.

**§ 39.13 [Amended]**

2. Section 39.13 is amended by removing Amendments 39–6404, 39–6417, 39–6468, 39–6482, 39–6483, 39–6491, 39–6533, 39–6536, 39–6535, 39–6534, 39–6542, 39–6543, 39–6552, and 39–6576.

94–17–04 **Airbus Industrie:** Amendment 39–8999. Docket No. 94–NM–49–AD. Rescinds the following AD's:

| AD No. | Amendment No. |
|---|---|
| 89–25–07 | 39–6404 |
| 89–26–03 | 39–6417 |
| 90–02–20 | 39–6468 |
| 90–02–21 | 39–6482 |
| 90–03–01 | 39–6483 |
| 90–03–14 | 39–6491 |
| 90–06–01 | 39–6533 |
| 90–06–05 | 39–6536 |
| 90–06–08 | 39–6535 |
| 90–06–11 | 39–6534 |
| 90–06–15 | 39–6542 |
| 90–06–17 | 39–6543 |
| 90–07–03 | 39–6552 |
| 90–08–19 | 39–6576 |

Applicability: All Model A300 series airplanes, certificated in any category.

This rescission is effective August 10, 1994.

Issued in Renton, Washington, on August 4, 1994.

**James V. Devany,**

*Acting Manager, Transport Airplane Directorate, Aircraft Certification Service.*

[FR Doc. 94–19479 Filed 8–9–94; 8:45 am]

BILLING CODE 4910–13–U

## 14 CFR Part 71

**[Airspace Docket No. 93–ANE–77]**

## Establishment of Class E Airspace; Lyndonville, VT

**AGENCY:** Federal Aviation Administration, DOT.

**ACTION:** Final rule.

**SUMMARY:** This action establishes Class E airspace at Lyndonville, VT. This action is a result of a modification of the nondirectional beacon (NDB) standard instrument approach procedure (SIAP) for Runway 2 at the Caledonia County Airport which showed a need for controlled airspace upward from 700 feet above the surface to contain instrument flight rules (IFR) operations at the airport. The intended effect of this action is to provide adequate Class E airspace for IFR operators who will be executing the NDB SIAP at Caledonia County Airport.

**EFFECTIVE DATE:** 0901 UTC, October 13, 1994.

**FOR FURTHER INFORMATION CONTACT:** Charles M. Taylor, Airspace Specialist, System Management Branch, ANE–530, Federal Aviation Administration, 12 New England Executive Park, Burlington, MA 01803–5299; telephone (617) 238–7532; fax (617) 238–7560.

**SUPPLEMENTARY INFORMATION:**

**History**

On March 11, 1994, the FAA published a Notice of Proposed Rulemaking (NPRM) to amend part 71 of the Federal Aviation Regulations (14 CFR Part 71) to establish Class E airspace at Lyndonville, VT (59 FR 11565). The proposal was prompted by a modification of the nondirectional beacon (NDB) standard instrument approach procedure (SIAP) for Runway 2 at the Caledonia Airport which showed a need for controlled airspace upward from 700 feet above the surface to contain instrument flight rules (IFR) operations at the airport. The intended effect of this action is to provide adequate Class E airspace for IFR operators who will be executing the NDB SIAP at Caledonia County Airport. Interested parties were invited to participate in this rulemaking proceeding by submitting written comments on the proposal of the FAA. No comments on the proposal were received.

Class E airspace designations for airspace areas extending upward from 700 feet or more above ground level are published in Paragraph 6005 of the FAA Order 7400.9A dated June 17, 1993, and effective September 16, 1993, which is incorporated by reference in 14 CFR 71.1 (58 FR 36298, July 6, 1993).

The Class E airspace establishment listed in this document will be published in the Order.

**The Rule**

This amendment of part 71 of the Federal Aviation Regulations establishes the Class E Airspace at Claremont, NH. This action is a result of a modification of the nondirectional beacon (NDB) standard instrument approach procedure (SIAP) for Runway 2 at the Caledonia County Airport which showed a need for controlled airspace upward from 700 feet above the surface to contain instrument flight rules (IFR) operations at the airport. The intended effect of this action is to provide adequate Class E airspace for IFR operators who will be executing the NDB SIAP at Caledonia County Airport.

The FAA has determined that this regulation involves only an established body of technical regulations for which frequent and routine amendments are necessary to keep these regulations operationally current. It, therefore—(1) is not a "significant regulatory action" under Executive Order 12866; (2) is not a "significant rule" under DOT Regulatory Policies and Procedures (44 FR 11034, February 26, 1979); and (3) does not warrant preparation of a Regulatory Evaluation as the anticipated economic cost will be so minimal. Since this is a routine matter that will only affect air traffic procedures and air navigation, the FAA certifies that this rule will not have a significant economic impact on a substantial

number of small entities under the criteria of the Regulatory Flexibility Act.

**List of Subjects in 14 CFR Part 71**

Airspace, Incorporation by reference, Navigation (air).

**Adoption of the Amendment**

In consideration of the foregoing, the Federal Aviation Administration amends 14 CFR part 71 as follows:

**PART 71—[AMENDED]**

1. The authority citation for part 71 continues to read as follows:

**Authority:** 49 U.S.C. app. 1348(a), 1354(a), 1510; E.O. 10854, 24 FR 9565, 3 CFR, 1959–1963, Comp., p. 389; 49 U.S.C. 106(g); 14 CFR 11.69.

**§ 71.1 [Amended]**

2. The incorporation by reference in 14 CFR 71.1 of the Federal Aviation Administration Order 7400.9A, Airspace Designations and Reporting Points, dated June 17, 1993, and effective September 16, 1993, is amended as follows:

*Paragraph 6005 Class E airspace areas extending upward from 700 feet or more above the surface of the earth.*

* * * * *

**ANE VT E5 Lyndonville, VT [New]**

Lyndonville, Caledonia County Airport, VT, ME
(Lat. 44°34'09" N, long. 72°01'04" W)
Lyndonville NDB
(Lat. 44°30'15" N, long. 72°01'45" W)

That airspace extending upward from 700 feet above the surface within a 6.3-mile radius of the Caledonia County Airport, and within 2.5 miles on each side of the Lyndonville NDB 188° bearing extending from the 6.3-mile radius to 7 miles south of the Lyndonville NDB.

* * * * *

Issued in Burlington, Massachusetts, on August 2, 1994.

**Francis J. Johns,**

*Manager, Air Traffic Division, New England Region.*

[FR Doc. 94–19405 Filed 8–9–94; 8:45 am]

BILLING CODE 4910–13–M

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**14 CFR Part 71**

**[Airspace Docket No. 93–ANE–75]**

## Establishment of Class E Airspace; Eastport, ME

**AGENCY:** Federal Aviation Administration, DOT.

**ACTION:** Final rule.

**SUMMARY:** This action establishes Class E airspace at Eastport, ME. This action is a result of a review of standard instrument approach procedures (SIAP's) for Eastport Municipal Airport, which showed a need for controlled airspace upward from 700 feet above the surface to contain instrument flight rules (IFR) operations at the airport. The intended effect of this action is to provide adequate Class E airspace for IFR operators who will be executing the SIAP's.

**EFFECTIVE DATE:** 0901 UTC, October 13, 1994.

**FOR FURTHER INFORMATION CONTACT:** Charles M. Taylor, Airspace Specialist, System Management Branch, ANE–530, Federal Aviation Administration, 12 New England Executive Park, Burlington, MA 01803–5299; telephone (617) 238–7532; fax (617) 238–7560.

**SUPPLEMENTARY INFORMATION:**

**History**

On March 11, 1994, the FAA published a Notice of Proposed Rulemaking (NPRM) to amend part 71 of the Federal Aviation Regulations (14 CFR part 71) to establish Class E airspace at Eastport, ME (59 FR 11563). The proposal was prompted by a review of proposed standard instrument approach procedures (SIAP's) for Eastport Municipal Airport which showed a need for controlled airspace upward from 700 feet above the surface to contain instrument flight rules (IFR) operations at the airport.

Interested parties were invited to participate in this rulemaking proceeding by submitting written comments on the proposal of the FAA. No comments on the proposal were received.

Class E airspace designations for airspace areas extending upward from 700 feet or more above ground level are published in Paragraph 6005 of FAA Order 7400.9A dated June 17, 1993, and effective September 16, 1993, which is incorporated by reference in 14 CFR 71.1 (58 FR 36298, July 6, 1993).

The Class E airspace establishment listed in this document will be published in the Order.

**The Rule**

This amendment of part 71 of the Federal Aviation Regulations establishes the Class E airspace at Eastport, ME. This action is a result of a review of proposed standard instrument approach procedures (SIAP's) for Eastport Municipal Airport, which showed a need for controlled airspace upward from 700 feet above the surface to contain instrument flight rules (IFR) operations at the airport.

The FAA has determined that this regulation only involves an established body of technical regulations for which frequent and routine amendments are necessary to keep these regulations operationally current. It, therefore—(1) Is not a "significant regulatory action" under Executive Order 12866; (2) is not a "significant rule" under DOT Regulatory Policies and Procedures (44 FR 11034, February 26, 1979); and (3) does not warrant preparation of a Regulatory Evaluation as the anticipated economic cost will be so minimal. Since this is a routine matter that will only affect air traffic procedures and air navigation, the FAA certifies that this rule will not have a significant economic impact on a substantial number of small entities under the criteria of the Regulatory Flexibility Act.

**List of Subjects in 14 CFR Part 71**

Airspace, Incorporation by reference, Navigation (air).

**Adoption of the Amendment**

In consideration of the foregoing, the Federal Aviation Administration amends 14 CFR part 71 as follows:

**PART 71—[AMENDED]**

1. The authority citation for part 71 continues to read as follows:

**Authority:** 49 U.S.C. app. 1348(a), 1354(a), 1510; E.O. 10854, 24 FR 9565, 3 CFR, 1959–1963, Comp., p. 389; 49 U.S.C. 106(g); 14 CFR 11.69.

**§ 71.1 [Amended]**

2. The incorporation by reference in 14 CFR 71.1 of the Federal Aviation Administration Order 7400.9A, Airspace Designations and Reporting Points, dated June 17, 1993, and effective September 16, 1993, is amended as follows:

*Paragraph 6005 Class E airspace areas extending upward from 700 feet or more above the surface.*

* * * * *

**ANE ME E5 Eastport, ME [New]**

Eastport Municipal Airport, ME
(Lat. 45°54'35" N, long. 67°00'44" W)

That airspace extending upward from 700 feet above the surface within a 7.4-mile radius of the Eastport Municipal Airport, excluding that airspace outside of the United States.

* * * * *

Issued in Burlington, Massachusetts, on August 2, 1994.

**Francis J. Johns,**

*Manager, Air Traffic Division, New England Region.*

[FR Doc. 94–19404 Filed 8–9–94; 8:45 am]

BILLING CODE 4910–13–M

14 CFR Part 71

[Airspace Docket No. 93-ANE-76]

## Establishment of Class E Airspace; Claremont, NH

AGENCY: Federal Aviation Administration, DOT.

ACTION: Final rule.

SUMMARY: This action establishes Class E airspace at Claremont, NH. This action is a result of a review of a nondirectional beacon (NDB) standard instrument approach procedure (SIAP) for Claremont Airport, which showed a need for controlled airspace upward from 700 feet above the surface to contain instrument flight rules (IFR) operations executing that NDB SIAP at the airport. The intended effect of this action is to provide adequate Class E airspace for IFR operators who will be executing the NDB SIAP at Claremont, NH.

EFFECTIVE DATE: 0901 UTC, October 13, 1994.

FOR FURTHER INFORMATION CONTACT: Charles M. Taylor, Airspace Specialist, System Management Branch, ANE-530, Federal Aviation Administration, 12 New England Executive Park, Burlington, MA 01803-5299; telephone (617) 238-7532; fax (617) 238-7560.

SUPPLEMENTARY INFORMATION:

### History

On March 11, 1994, the FAA published a Notice of Proposed Rulemaking (NPRM) to amend part 71 of the Federal Aviation Regulations (14 CFR part 71) to establish Class E airspace at Claremont, NH (59 FR 11564). The proposal was prompted by a review of a proposed nondirectional beacon (NDB) standard instrument approach procedure (SIAP) for Claremont Airport, which showed a need for controlled airspace upward from 700 feet above the surface to contain instrument flight rules (IFR) operations executing that NDB SIAP at the airport. The intended effect of this action is to provide adequate Class E airspace for IFR operators who will be executing the proposed NDB SIAP at Claremont, NH.

Interested parties were invited to participate in this rulemaking proceeding by submitting written comments on the proposal of the FAA. No comments on the proposal were received.

Class E airspace designations for airspace areas extending upward from 700 feet or more above ground level are published in Paragraph 6005 of FAA Order 7400.9A dated June 17, 1993, and effective September 16, 1993, which is incorporated by reference in 14 CFR 71.1 (58 FR 36298, July 6, 1993).

The Class E airspace establishment listed in this document will be published in the Order.

### The Rule

This amendment of part 71 of the Federal Aviation Regulations establishes the Class E airspace at Claremont, NH. This action is a result of a review of a proposed nondirectional beacon (NDB) standard instrument approach procedure (SIAP) for Claremont Airport which showed a need for controlled airspace upward from 700 feet above the surface to contain instrument flight rules (IFR) operations executing that NDB SIAP at the airport. The intended effect of this action is to provide adequate Class E airspace for IFR operators who will be executing the proposed NDB SIAP at Claremont, NH.

The FAA has determined that this regulation involves only an established body of technical regulations for which frequent and routine amendments are necessary to keep these regulations operationally current. It, therefore—(1) is not a "significant regulatory action" under Executive Order 12866; (2) is not a "significant rule" under DOT Regulatory Policies and Procedures (44 FR 11034, February 26, 1979); and (3) does not warrant preparation of a Regulatory Evaluation as the anticipated economic cost will be so minimal. Since this is a routine matter that will only affect air traffic procedures and air navigation, the FAA certifies that this rule will not have a significant economic impact on a substantial number of small entities under the criteria of the Regulatory Flexibility Act.

### List of Subjects in 14 CFR Part 71

Airspace, Incorporation by reference, Navigation (air).

### Adoption of the Amendment

In consideration of the foregoing, the Federal Aviation Administration amends 14 CFR part 71 as follows:

## PART 71—[AMENDED]

1. The authority citation for part 71 continues to read as follows:

Authority: 49 U.S.C. app. 1348(a), 1354(a), 1510; E.O. 10854, 24 FR 9565, 3 CFR, 1959–1963, Comp., p. 389; 49 U.S.C. 106(g); 14 CFR 11.69.

§ 71.1 [Amended]

2. The incorporation by reference in 14 CFR 71.1 of the Federal Aviation Administration Order 7400.9A, Airspace Designations and Reporting Points, dated June 17, 1993, and effective September 16, 1993, is amended as follows:

*Paragraph 6005 Class E airspace areas extending upward from 700 feet or more above the surface.*

* * * * *

ANE NH E5 Claremont, NH [New]

Claremont NDB

(Lat. 43°22'10" N, long. 72°22'16" W)

That airspace extending upward from 700 feet above the surface within a 5.5-mile radius of the Claremont NDB; excluding that airspace within the Springfield, VT and Lebanon, NH class E5 areas.

* * * * *

Issued in Burlington, Massachusetts, on August 2, 1994.

**Francis J. Johns,**

*Manager, Air Traffic Division, New England Region.*

[FR Doc. 94-19403 Filed 8-9-94; 8:45 am]

BILLING CODE 4910-13-M

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

21 CFR Part 74

[Docket No. 92C-0294]

## Listing of Color Additives Subject to Certification; D&C Green No. 5

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the color additive regulations to provide for the safe use of D&C Green No. 5 for coloring drugs and cosmetics intended for use in the area of the eye. This action is in response to a petition filed by the Cosmetic, Toiletry, and Fragrance Association (CTFA).

DATES: Effective September 12, 1994, except as to any provisions that may be stayed by the filing of proper objections: written objections and requests for a hearing by September 9, 1994.

ADDRESSES: Submit written objections to the Dockets Management Branch (HFA-305), Food and Drug Administration, rm. 1-23, 12420 Parklawn Dr., Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Robert L. Martin, Center for Food Safety and Applied Nutrition (HFS-217), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202-254-9519.

SUPPLEMENTARY INFORMATION:

### I. Introduction

In a notice published in the **Federal Register** of August 11, 1992 (57 FR

35833), FDA announced that a color additive petition (CAP 6C0204) had been filed by CTFA, 1101 17th St. NW., suite 300, Washington, DC 20036. The petition proposed that the color additive regulations for D&C Green No. 5 be amended to provide for the safe use of D&C Green No. 5 for coloring drugs and cosmetics intended for use in the area of the eye. The petition was filed under section 706 (currently section 721) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 376) (currently 21 U.S.C. 379e).

## II. Regulatory History

The regulatory history of D&C Green No. 5 is summarized in a final rule that was published in the **Federal Register** of June 4, 1982 (47 FR 24278). In that final rule, FDA permanently listed D&C Green No. 5 for use in drugs and cosmetics excluding use in the area of the eye. These actions were taken in response to a color additive petition (CAP 8C0084).

## III. Definitions

Section 70.3(s) (21 CFR 70.3(s)) defines the term "area of the eye" as "the area enclosed within the circumference of the supra-orbital ridge and the infra-orbital ridge, including the eyebrow, the skin below the eyebrow, the eyelids and the eyelashes, and conjunctival sac of the eye, the eyeball, and the soft areolar tissue that lies within the perimeter of the infra-orbital ridge." 21 CFR 70.5(a) states that "No listing or certification of a color additive shall be considered to authorize the use of any such color additive in any article intended for use in the area of the eye unless such listing or certification of such color additive specifically provides for such use." The petitioner has requested that the uses for D&C Green No. 5 be expanded to include drug and cosmetic uses in the area of the eye.

## IV. The Color Additive

D&C Green No. 5 is principally the disodium salt of 2,2'-[(9,10-dihydro-9,10-dioxo-1,4-anthracenediyl)diimino]bis-[5-methylbenzenesulfonic acid] (CAS Reg. No. 4403–90–1). The manufacture of D&C Green No. 5 is accomplished by the sulfonation of D&C Green No. 6 with fuming sulfuric acid. Because D&C Green No. 6 is the starting material in this manufacturing process, the possibility exists that the chemicals used in the synthesis of D&C Green No. 6 may be present in minor amounts in D&C Green No. 5. D&C Green No. 6 is formed by chemically reacting one molecule of quinizarin with two molecules of *p*-toluidine. The significance of these components is that Weisburger et al. have demonstrated that *p*-toluidine is a carcinogen in mice (Ref. 1). Residual amounts of reactants, such as *p*-toluidine and related manufacturing aids, are commonly found among the constituents of many color additives. The presence of such constituents, however, is not unique to color additives. Numerous contaminants are unavoidably present in all chemical products, even in highly purified reagent grade chemicals.

Although D&C Green No. 5 has itself not been shown to cause cancer, it does contain minor amounts of a carcinogenic impurity, *p*-toluidine. The carcinogenicity of *p*-toluidine was discussed in the final rule, published in the of **Federal Register** June 4, 1982 (47 FR 24278), permanently listing D&C Green No. 5 for use in drugs and cosmetics, excluding use in the area of the eye.

## V. Determination of Safety

Under section 721(b)(4) of the act (21 U.S.C. 379e(b)(4)), the so-called "general safety clause" for color additives, a color additive cannot be listed for a particular use unless a fair evaluation of the data available to FDA establishes that the color additive is safe for that use. FDA's color additive regulations (§ 70.3(i)) define safe as "convincing evidence that establishes with a reasonable certainty that no harm will result from the intended use of the color additive."

The anticancer or Delaney clause of the Color Additive Amendments (section 721(b)(5)(B) of the act) provides that a noningested color additive shall be deemed unsafe and shall not be listed if, after tests that are appropriate for evaluating the safety of the additive for such use, it is found to induce cancer in man or animal. Importantly, however, the Delaney clause applies to the additive itself and not to constituents of the additive. That is, where an additive itself has not been shown to cause cancer, but contains a carcinogenic impurity, the additive is properly evaluated under the general safety clause using risk assessment procedures to determine whether there is a reasonable certainty that no harm will result from the proposed use of the additive (*Scott* v. *FDA*, 728 F.2d 322 (6th Cir. 1984)).

## VI. Safety of the Petitioned Use of the Additive

FDA estimates from the data submitted and other relevant information that the exposure to D&C Green No. 5 from its use in drugs and cosmetics intended for use in the area of the eye, is 0.56 milligrams per person per day (mg/p/d), based upon a maximum frequency of application and maximum quantity applied.

FDA does not ordinarily consider chronic toxicological testing to be necessary to determine the safety of an additive whose use will result in such low exposure levels (Ref. 2), and the agency has not required such testing here. Although the agency does not normally require such testing, chronic studies supporting current listings for the use of D&C Green No. 5 are available in the agency's files, and FDA's safety evaluation for the proposed use of the color additive in drugs and cosmetics intended for use in the area of the eye included a consideration of these studies. Two-year carcinogenicity studies of D&C Green No. 5 showed no indication of carcinogenicity.

FDA has evaluated the safety of this additive under the general safety clause, considering all available data. The agency has used risk assessment procedures to estimate the upper-bound limit of risk presented by *p*-toluidine, the carcinogenic chemical that may be present as an impurity in the additive. The risk evaluation of this chemical has two aspects: (1) Assessment of the exposure to the impurity from the proposed use of the additive, and (2) extrapolation of the risk observed in the animal bioassays to the conditions of probable exposure to humans.

FDA estimates that the maximum total lifetime exposure to *p*-toluidine that will result from the use of D&C Green No. 5 in drugs and cosmetics intended for use in the area of the eye that complies with the applicable specifications is 8.4 nanograms (ng)/p/d. This exposure estimate was based on the use of this color additive in eyebrow pencil, eyeliner, eye shadow, eye lotion, eye makeup remover, mascara, eye cream, eye shadow base, and eye stick.

The agency used data reported by the National Cancer Institute which demonstrated that *p*-toluidine was carcinogenic for male and female Charles River CD–1 (HaM/ICR derived) mice, causing an increased incidence of hepatomas (liver tumors) (Ref. 1) to estimate the upper-bound limit of lifetime human risk from exposure to this chemical stemming from the proposed use of D&C Green No. 5 as a color additive in drugs and cosmetics intended for use in the area of the eye (Ref. 3).

Based on a potential exposure of 8.4 ng/p/d, FDA estimates that the upper-bound limits of individual lifetime risk from the potential exposure to *p*-toluidine from the proposed use of D&C Green No. 5 as a color additive in eye

area drugs and cosmetics is $2 \times 10^{-9}$ or 2 in 1 billion (Ref. 4). Moreover, FDA points out that in an earlier determination of the risk from exposure to *p*-toluidine from all other uses of D&C Green No. 5, the agency calculated the upper-bound limits of individual lifetime risk to be in the 1 in 30 million to 1 in 300 million range (47 FR 24278). Thus, the use of D&C Green No. 5 in eye area drugs and cosmetics does not increase this risk in any way. The agency also points out that because of the numerous conservative assumptions used in calculating the exposure estimate, actual lifetime-averaged individual exposure to *p*-toluidine is expected to be substantially less than the worst-case exposure. Therefore, the actual upper-bound limits of risk would be less than that cited above. Thus, the agency concludes that there is a reasonable certainty of no harm from exposure to *p*-toluidine that might result from the proposed use of D&C Green No. 5 for coloring drugs and cosmetics intended for use in the area of the eye.

In its evaluation of the safety of the proposed use of the subject additive, FDA has also considered other safety data submitted previously to support current listings for the use of D&C Green No. 5. These toxicity studies of D&C Green No. 5, involving dogs, rats, and mice, included acute oral toxicity studies, subchronic studies, and chronic toxicity studies in which animals were exposed to the color additive through diet and skin applications, and reproductive toxicity studies. These studies did not produce any evidence that D&C Green No. 5 would be unsafe for the petitioned uses.

In addition, FDA evaluated the ocular toxicity studies that the petitioner provided to support the proposed use of D&C Green No. 5 in drugs and cosmetics intended for use in the area of the eye. Almost all of the animals were free of signs of ocular irritation. The effects noted in most animals that exhibited irritation were slight conjunctival redness or discharge. These irritations were seen sporadically in both control and test animals. Based on its review of these studies, FDA finds that there were no significant adverse clinical findings in the ocular irritation studies.

## VII. Conclusions

### *A. Safety*

Based upon the available toxicity data and other relevant considerations discussed above, FDA concludes that there is a reasonable certainty that no harm will result from the use of D&C Green No. 5 as a color additive in drugs and cosmetics intended for use in the area of the eye. The agency also concludes on the basis of available data that the color additive will perform its intended technical effect and thus is suitable for the petitioned uses. The agency, therefore, is amending §§ 74.1205(c)(2) and 74.2205(b) of the color additive regulations to provide for the use of D&C Green No. 5 in drugs and cosmetics intended for use in the area of the eye.

### *B. Specifications*

D&C Green No. 5 is currently produced as a certifiable color additive for use in drugs and cosmetics excluding use in the area of the eye in amounts consistent with current good manufacturing practices in accordance with 21 CFR part 80. Based upon the low level of exposure to *p*-toluidine that results under the current specifications for D&C Green No. 5 in §§ 74.1205 and 74.2205 (21 CFR 74.1205 and 74.2205), the agency concludes that the specifications listed in § 74.1205 are adequate to ensure the safe use of this color additive and to control the amount of *p*-toluidine that may exist as an impurity in the color additive when used in drugs and cosmetics intended for use in the area of the eye.

## VIII. Inspection of Documents

In accordance with § 71.15 (21 CFR 71.15), the petition and the documents that FDA considered and relied upon in reaching its decision to approve the petition are available for inspection at the Center for Food Safety and Applied Nutrition (address above) by appointment with the information contact person listed above. As provided in § 71.15, the agency will delete from the documents any materials that are not available for public disclosure before making the documents available for inspection.

## IX. Environmental Impact

The agency has carefully considered the potential environmental effects of this action. FDA has concluded that the action will not have a significant impact on the human environment, and that an environmental impact statement is not required. The agency's finding of no significant impact and the evidence supporting that finding, contained in an environmental assessment, may be seen in the Dockets Management Branch (address above) between 9 a.m. and 4 p.m., Monday through Friday.

## X. Objections

Any person who will be adversely affected by this regulation may at any time on or before September 9, 1994, file with the Dockets Management Branch (address above) written objections thereto. Each objection shall be separately numbered, and each numbered objection shall specify with particularity the provisions of the regulation to which objection is made and the grounds for the objection. Each numbered objection on which a hearing is requested shall specifically so state. Failure to request a hearing for any particular objection shall constitute a waiver of the right to a hearing on that objection. Each numbered objection for which a hearing is requested shall include a detailed description and analysis of the specific factual information intended to be presented in support of the objection in the event that a hearing is held. Failure to include such a description and analysis for any particular objection shall constitute a waiver of the right to a hearing on the objection. Three copies of all documents shall be submitted and shall be identified with the docket number found in brackets in the heading of this document. Any objections received in response to the regulation may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday. FDA will publish notice of the objections that the agency has received or lack thereof in the **Federal Register.**

## XI. References

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

1. Weisburger, E. K. et al., "Testing of Twenty-one Environmental Aromatic Amines or Derivatives for Long-Term Toxicity or Carcinogenicity," *Journal of Environmental Pathology and Toxicology*, 2:325–356, 1978.

2. Kokoski, C. J., "Regulatory Food Additive Toxicology," in "Chemical Safety Regulation and Compliance," edited by F. Homburger and J. K. Marquis, S. Karger, NY, pp. 24–33, 1985.

3. Memorandum of Conference of the Cancer Assessment Committee, "Para-Toluidine," February 24, 1981.

4. Report of the Quantitative Risk Assessment Committee, "Estimation of the Upper-Bound Lifetime Risk from Para-Toluidine in D&C Green No. 5 for Uses Requested in CAP 6C0204, Cosmetic, Toiletry, and Fragrance Association," September 28, 1993.

## List of Subjects in 21 CFR Part 74

Color additives, Cosmetics, Drugs.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 74 is amended as follows:

## PART 74—LISTING OF COLOR ADDITIVES SUBJECT TO CERTIFICATION

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

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

2. Section 74.1205 is amended by revising paragraph (c)(2) to read as follows:

**§ 74.1205 D&C Green No. 5.**

* * * * *

(c) * * *

(2) D&C Green No. 5 may be safely used for coloring drugs generally, including drugs intended for use in the area of the eye, in amounts consistent with current good manufacturing practice.

* * * * *

3. Section 74.2205 is amended by revising paragraph (b) to read as follows:

**§ 74.2205 D&C Green No. 5.**

* * * * *

(b) *Uses and restrictions.* D&C Green No. 5 may be safely used for coloring cosmetics generally, including cosmetics intended for use in the area of the eye, in amounts consistent with current good manufacturing practice.

* * * * *

Dated: August 4, 1994.

**Michael R. Taylor,**

*Deputy Commissioner for Policy.*

[FR Doc. 94–19483 Filed 8–9–94; 8:45 am]

BILLING CODE 4160–01–F

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## 21 CFR Parts 430, 436, and 455

**[Docket No. 94N–0184]**

## Antibiotics Drugs; Rifabutin and Rifabutin Capsules

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Final rule.

**SUMMARY:** The Food and Drug Administration (FDA) is amending the antibiotic drug regulations to include accepted standards for a new antibiotic drug, rifabutin, and the use of the antibiotic drug in a dosage form, rifabutin capsules. The manufacturer has supplied sufficient data and information to establish its safety and efficacy.

**DATES:** Effective September 9, 1994; written comments, notice of participation, and requests for a hearing by September 9, 1994; data, information, and analyses to justify a hearing by October 11, 1994.

**ADDRESSES:** Submit written comments to the Dockets Management Branch (HFA–305), Food and Drug Administration, rm. 1–23, 12420 Parklawn Dr., Rockville, MD 20857.

**FOR FURTHER INFORMATION CONTACT:** James Timper, Center for Drug Evaluation and Research (HFD–520), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–443–6714.

**SUPPLEMENTARY INFORMATION:** FDA has 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 a request for approval of (1) a new antibiotic drug, rifabutin, and (2) its use in a dosage form, rifabutin capsules. The agency has concluded that the data supplied by the manufacturer concerning these antibiotic drugs are adequate to establish their safety and efficacy when used as directed in the labeling and that the regulations should be amended in 21 CFR parts 430, 436, and 455 to include accepted standards for these products.

### Environmental Impact

The agency has determined under 21 CFR 25.24(c)(6) 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.

### Submitting Comments and Filing Objections

This final rule announces standards that FDA has accepted in a request for approval of an antibiotic drug. Because this final rule is not controversial and because when effective it provides notice of accepted standards, FDA finds that notice and comment procedure is unnecessary and not in the public interest. This final rule, therefore, is effective September 9, 1994. However, interested persons may, on or before September 9, 1994, submit written comments to the Dockets Management Branch (address above). Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Any person who will be adversely affected by this final rule may file objections to it and request a hearing. Reasonable grounds for the hearing must be shown. Any person who decides to seek a hearing must file (1) on or before September 9, 1994, a written notice of participation and request for a hearing, and (2) on or before October 11, 1994, the data, information, and analyses on which the person relies to justify a hearing, as specified in 21 CFR 314.300. A request for a hearing may not rest upon mere allegations or denials, but must set forth specific facts showing that there is a genuine and substantial issue of fact that requires a hearing. If it conclusively appears from the face of the data, information, and factual analyses in the request for a hearing that no genuine and substantial issue of fact precludes the action taken by this order, or if a request for a hearing is not made in the required format or with the required analyses, the Commissioner of Food and Drugs will enter summary judgment against the person(s) who request(s) the hearing, making findings and conclusions and denying a hearing. All submissions must be filed in three copies, identified with the docket number appearing in the heading of this document and filed with the Dockets Management Branch.

The procedures and requirements governing this order, a notice of participation and request for a hearing, a submission of data, information, and analyses to justify a hearing, other comments, and grant or denial of a hearing are contained in 21 CFR 314.300.

All submissions under this order, except for data and information prohibited from public disclosure under 21 U.S.C. 331(j) or 18 U.S.C. 1905, may be seen in the Dockets Management Branch (address above) between 9 a.m. and 4 p.m., Monday through Friday.

### List of Subjects

*21 CFR Part 430*

Administrative practice and procedure, Antibiotics.

*21 CFR Parts 436 and 455*

Antibiotics.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR parts 430, 436, and 455 are amended as follows:

## PART 430—ANTIBIOTIC DRUGS; GENERAL

1. The authority citation for 21 CFR part 430 continues to read as follows:

**Authority:** Secs. 201, 501, 502, 503, 505, 507, 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 351, 352, 353, 355, 357, 371); secs. 215, 301, 351 of the Public Health Service Act (42 U.S.C. 216, 241, 262).

2. Section 430.4 is amended by adding new paragraph (a)(69) to read as follows:

**§ 430.4 Definitions of antibiotic substances.**

(a) * * *

(69) *Rifabutin.* Rifabutin is an antibiotic substance having the chemical structure described by the following name: (9*S*,12*E*,14*S*,15*R*,16*S*,17*R*,18*R*,19*R*, 20*S*,21*S*,22*E*, 24*Z*)-6,16, 18,20-tetrahydroxy-1′-isobutyl-14-methoxy-7,9,15,17,19,21,25-heptamethylspiro[9,4-(epoxypentadeca[1,11,13]trienimino)-2*H*-furo[2′,3′:7,8]naphth[1,2-d]imidazole-2,4′-piperidine]-5,10,26-(3*H*,9*H*)-trione-16-acetate.

* * * * *

3. Section 430.5 is amended by adding new paragraphs (a)(104) and (b)(106) to read as follows:

**§ 430.5 Definitions of master and working standards.**

(a) * * *

(104) *Rifabutin.* The term "rifabutin master standard" means a specific lot of rifabutin that is designated by the Commissioner as the standard of comparison in determining the potency of the rifabutin working standard.

(b) * * *

(106) *Rifabutin.* The term "rifabutin working standard" means a specific lot of a homogeneous preparation of rifabutin.

4. Section 430.6 is amended by adding new paragraph (b)(106) to read as follows:

**§ 430.6 Definitions of the terms "unit" and "microgram" as applied to antibiotic substances.**

* * * * *

(b) * * *

(106) *Rifabutin.* The term "microgram" applied to rifabutin means the rifabutin (potency) contained in 1.022 micrograms of the rifabutin master standard.

## PART 436—TESTS AND METHODS OF ASSAY OF ANTIBIOTIC AND ANTIBIOTIC-CONTAINING DRUGS

5. The authority citation for 21 CFR part 436 continues to read as follows:

**Authority:** Sec. 507 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 357).

6. Section 436.215 is amended by alphabetically adding a new entry to the table in paragraph (b) and by adding new paragraph (c)(18) to read as follows:

**§ 436.215 Dissolution test.**

* * * * *

(b) * * *

| Dosage form | Dissolution medium | Rotation rate[1] | Sampling time(s) | Apparatus |
|---|---|---|---|---|
| * * | * * | * | * | * |
| Rifabutin capsules | 900 mL 0.01*N* hydrochloric acid | 100 | 45 min | 1 |
| * * | * * | * | * | * |

[1]Rotation rate of basket or paddle stirring element (revolutions per minute).

(c) * * *

(18) *Rifabutin*—(i) *Preparation of the working standard solution.* Accurately weigh approximately 45 milligrams of the rifabutin working standard into a suitable-sized volumetric flask. Dissolve and dilute to volume with 0.01*N* hydrochloric acid (prepared by diluting 5.0 milliliters of hydrochloric acid (37 percent) to 6 liters with distilled water) to obtain a concentration of approximately 13 micrograms rifabutin activity per milliliter.

(ii) *Preparation of sample solutions.* Forty-five minutes after the beginning of the rotation, withdraw a 10-milliliter aliquot from the vessel. Dilute a 2-milliliter portion of the sample to 25 milliliters with 0.01*N* hydrochloric acid.

(iii) *Procedure.* Using a suitable spectrophotometer and 0.01*N* hydrochloric acid as the blank, determine the absorbance of each standard and sample solution at the absorbance maximum at approximately 280 nanometers. Determine the exact position of the absorbance maximum for the particular instrument used.

(iv) *Calculations.* Determine the total amount of rifabutin dissolved as follows:

$$T = \frac{A_U \times c \times d \times 900}{A_S \times 1{,}000}$$

where:

$T$ = Total milligrams of rifabutin activity dissolved;

$A_U$ = Absorbance of sample;

$A_S$ = Absorbance of the standard;

$c$ = Rifabutin activity of the working standard solution in micrograms per milliliter; and

$d$ = Dilution factor of the sample filtrate.

* * * * *

7. New §§ 436.369 and 436.370 are added to subpart F to read as follows:

**§ 436.369 Thin layer chromatography test for free *N*-isobutylpiperidone content in rifabutin.**

(a) *Equipment*—(1) *Chromatography tank.* A rectangular tank, approximately 23 X 23 X 9 centimeters, with a glass solvent trough on the bottom and a tight-fitting cover.

(2) *Iodine vapor chamber.* A rectangular tank, approximately 23 X 23 X 9 centimeters, with a suitable cover, containing iodine crystals.

(3) *Plates.* Use 20 X 20 centimeter thin layer chromatography plates coated with silica gel 60F 254 or equivalent to a thickness of 250 microns.

(b) *Reagents*—(1) *Developing solvent.* Mix petroleum ether (b.p. 60 to 80 °C) and acetone in volumetric proportions of 100:30, respectively.

(2) *Spray solution.* Prepare a 1 percent solution of soluble starch in water (containing 0.01 percent mercuric iodide).

(c) *Preparation of spotting solutions*—(1) *Sample solution.* Prepare a solution of the rifabutin sample in 1:1 chloroform/methanol to contain 10 milligrams per milliliter.

(2) *Standard solution.* Prepare a solution of *N*-isobutylpiperidone standard in 1:1 chloroform/methanol to contain 1 milligram per milliliter. Transfer aliquots of 0.5, 1.0, 2.0, 5.0, and 10.0 milliliters into separate 100-milliliter volumetric flasks and dilute to volume with 1:1 chloroform/methanol. These solutions contain, respectively, the equivalent of 0.05, 0.1, 0.2, 0.5, and 1.0 percent of *N*-isobutylpiperidone.

(d) *Procedure.* Pour 100 milliliters of developing solvent into the glass trough on the bottom of the unlined chromatography tank. Cover and seal

the tank. Allow it to equilibrate while the plate is being prepared. Prepare a plate as follows: on a line 2.0 centimeters from the base of the thin layer chromatography plate, and at intervals of 2.0 centimeters, apply 10 microliters of each of the standard solutions and the sample solution prepared as directed above. After the spots are thoroughly dry, place the plate into the trough in the bottom of the tank. Cover and tightly seal the tank, allow the solvent front to travel about 15 centimeters from the starting line and then remove the plate from the tank. Air dry the plate. Warm the iodine vapor chamber to vaporize the iodine crystals and place the dry plate in the iodine vapor chamber until the spots are visible (usually about 5 minutes). Remove the plate from the iodine vapor chamber and spray with 1 percent starch solution.

(e) *Evaluation.* Measure the distance the solvent front traveled from the starting line and the distance the spots are from the starting line. Calculate the $R_f$ value by dividing the latter by the former. *N*-isobutylpiperidone has an $R_f$ value of about 0.3. Rifabutin has an $R_f$ value of about 0.1. Compare the size and intensity of any *N*-isobutylpiperidone spots in the sample lane with the *N*-isobutylpiperidone spots in the standard lanes, and report the percentage of *N*-isobutylpiperidone in the sample.

**§ 436.370 Spectrophotometric identity test for rifabutin capsules.**

(a) *Equipment.* A suitable spectrophotometer capable of recording the ultraviolet spectrum in the 200 to 400 nanometer range, using suitable quartz cells of 1 centimeter pathlength.

(b) *Preparation of working standard and sample solution*—(1) *Working standard solution.* Suspend approximately 200 milligrams of rifabutin working standard in 20 milliliters of methanol and sonicate for approximately 5 minutes. Filter the resulting solution through a suitable 0.5 micrometer filter. Transfer a 2-milliliter aliquot of the filtered solution to a 100-milliliter volumetric flask and fill to volume with methanol. Further dilute with methanol to obtain a solution containing 20 micrograms of rifabutin activity per milliliter.

(2) *Sample solution.* Empty and combine the contents of five capsules. Suspend a quantity of the capsule contents equivalent to 200 milligrams of rifabutin in 20 milliliters of methanol. Sonicate for about 5 minutes and then filter through an appropriate 0.5 micrometer filter. Transfer a 2-milliliter aliquot to a 100-milliliter volumetric flask and dilute to volume with methanol. Further dilute with methanol to obtain a solution containing 20 micrograms of rifabutin activity per milliliter (estimated).

(c) *Procedure.* Using a suitable spectrophotometer equipped with 1.0 centimeter cells and methanol as the blank, determine the absorbance spectra of the working standard and sample solutions over the ultraviolet range of 250 to 300 nanometers.

(d) *Evaluation.* Compare the spectrum of the sample to that of the working standard. The identity of the rifabutin capsules is confirmed by quantitative comparison of the two spectra with an absorbance maximum being observed at about 275 nanometers.

## PART 455—CERTAIN OTHER ANTIBIOTIC DRUGS

8. The authority citation for 21 CFR part 455 continues to read as follows:

**Authority:** Sec. 507 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 357).

9. New § 455.88 is added to subpart A to read as follows:

**§ 455.88 Rifabutin.**

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Rifabutin is an amorphous red-violet powder. It is (9*S*,12*E*,14*S*,15*R*,16*S*,17*R*,18*R*,19*R*,20*S*,21*S*, (9*S*,12*E*,14*S*,15*R*,16*S*,17*R*,18*R*,19*R*,20*S*,21*S*)-6,16,18,20-tetrahydroxy-1′-isobutyl-14-methoxy-7,9,15,17,19,21,25-heptamethylspiro[9,4-(epoxypentadeca[1,11,13]trienimino)-2*H*-furo[2′,3′:7,8]naphth[1,2-d]imidazole-2,4′-piperidine]-5,10,26-(3*H*,9*H*)-trione-16-acetate. It is very slightly soluble in water, sparingly soluble in ethanol, and soluble in chloroform and methanol. It is so purified and dried that:

(i) Its potency is not less than 950 micrograms and not more than 1,020 micrograms of rifabutin activity per milligram on an anhydrous basis.

(ii) Its content for the four major related substances detected by high-performance liquid chromatography (HPLC) is not more than 1.0 percent each. All other unknown related substances are not more than 0.5 percent. The total of all related substances is not more than 3.0 percent.

(iii) Its moisture content is not more than 2.5 percent.

(iv) Its *N*-isobutylpiperidone content is not more than 0.5 percent.

(v) It gives a positive identity test.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for rifabutin potency, related substances, moisture, *N*-isobutylpiperidone, and identity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research: 10 packages each containing approximately 300 milligrams.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.216 of this chapter, using ambient temperature, an ultraviolet detection system operating at a wavelength of 254 ± 1 nanometers, an 11 centimeters X 4.7 millimeters (i.d.) column packed with microparticulate (5 to 7 micrometers in diameter) packing material such as octylsilane chemically bonded to porous silica (U.S. Pharmacopeia designation L7), a flow rate of about 1.0 milliliter per minute, and a manual or automatic injector capable of injecting 10 microliters. The retention time for rifabutin is between 9 and 11 minutes. Reagents; working standard, sample, and resolution solutions; system suitability requirements; and calculations are as follows:

(i) *Reagents*—(A) *Hydrochloric acid, 2N.* Dilute 85 milliliters of hydrochloric acid (37 percent) with distilled water to 500 milliliters.

(B) *Potassium dihydrogen phosphate, 0.1M.* Prepare a solution containing 15.4 grams of potassium dihydrogen phosphate monohydrate (potassium phosphate monobasic) per liter of distilled water.

(C) *Sodium hydroxide, 2N.* Dissolve 8 grams of sodium hydroxide pellets in 100 milliliters of distilled water.

(D) *Mobile phase.* Acetonitrile:phosphate buffer, pH 6.5, 50:50. Mix equal quantities of acetonitrile and 0.1*M* potassium dihydrogen phosphate and adjust to an apparent pH of 6.5 ± 0.1 by dropwise addition of 2*N* sodium hydroxide. Filter through a suitable filter capable of removing particulate matter 0.5 micron in diameter and degas it just prior to its introduction into the chromatograph. Slight adjustments of the mobile phase components ratio may be made in order to meet the system suitability requirements described in the system suitability tests in paragraph (b)(1)(iii) of this section.

(ii) *Preparation of working standard, sample, and resolution test solution*—(A) *Working standard solution.* Accurately weigh approximately 25 milligrams of the rifabutin working reference standard into a 50-milliliter volumetric flask. Add 5 milliliters of acetonitrile. Dissolve and dilute to volume with mobile phase and mix to

obtain a solution having a known concentration of about 0.5 milligram of rifabutin per milliliter.

(B) *Sample solution.* Accurately weigh approximately 25 milligrams of sample into a 50-milliliter volumetric flask. Add 5 milliliters of acetonitrile. Dissolve and dilute to volume with mobile phase and mix to obtain a solution containing 0.5 milligram of rifabutin per milliliter (estimated).

(C) *Resolution test solution.* Dissolve approximately 10 milligrams of rifabutin in 2 milliliters of methanol and add 1 milliliter of 2*N* sodium hydroxide. Allow to stand for 3 to 4 minutes and then add 1 milliliter of 2*N* hydrochloric acid. Mix and dilute to 50 milliliters with mobile phase. Store aliquots of this solution in the frozen state for future use.

(iii) *System suitability requirements.* Using the apparatus and conditions described in this section, test the chromatographic system by injecting the resolution test solution. The chromatogram shows one major degradation peak and two minor degradation peaks eluting at relative retention times (RRT) of 0.5–0.6, 0.65–0.75, and 0.8–0.9, respectively, followed by the rifabutin peak.

(A) *Asymmetry factor.* The asymmetry factor ($A_S$) is satisfactory if it is not less than 1.0 and not more than 4.0 for the rifabutin peak.

(B) *Efficiency of the column.* The absolute efficiency ($h_r$) is satisfactory if it is not more than 11 for the rifabutin peak, equivalent to 2,000 theoretical plates for a 11-centimeter column of 5-micrometer particles.

(C) *Resolution factor.* The resolution factor ($R$) between the peak for rifabutin and its closest eluting degradation product (generated in situ as described in paragraph (b)(1)(iii) of this section and eluting at RRT of 0.8–0.9) is satisfactory if it is not less than 1.3.

(D) *Coefficient of variation (relative standard deviation).* The coefficient of variation ($S_R$ in percent of 5 replicate injections of the rifabutin working standard solution) is satisfactory if it is not more than 2.0 percent. If the system suitability parameters have been met, then proceed as described in § 436.216(b) of this chapter.

(iv) *Calculations.* Calculate the micrograms of rifabutin per milligram of sample on an anhydrous basis as follows:

$$\text{Micrograms of rifabutin per milligram} = \frac{A_U \times P_S \times 100}{A_S \times C_U \times (100 - m)}$$

where:

$A_U$ = Area of the rifabutin peak in the chromatogram of the sample (at a retention time equal to that observed for the standard);

$A_S$ = Area of the rifabutin peak in the chromatogram of the rifabutin working standard;

$P_S$ = Rifabutin activity in the rifabutin working standard solution in micrograms per milliliter;

$C_U$ = Milligrams of sample per milliliter of sample solution; and

$m$ = Percent moisture content of the sample.

(2) *Related substances.* Proceed as directed in paragraph (b)(1) of this section for potency using the sample prepared as described in paragraph (b)(1)(ii)(B) of this section and calculating the amounts of related substances as follows.

(i) *Calculations.* Calculate the percentage of related substances as follows:

$$\text{Percent individual HPLC-related substance} = \frac{A_i \times 100}{A_t}$$

$$\text{Percent total HPLC-related substances} = \frac{A \times 100}{A_t}$$

where:

$A_i$ = Area of the individual related substance peak;

$A$ = The sum of areas of all peaks minus the area due to the rifabutin peak and solvent front peak; and

$A_t$ = The sum of areas of all peaks in the chromatogram excluding the solvent peak.

(ii) [Reserved]

(3) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(4) *N-Isobutylpiperidone.* Proceed as directed in § 436.369 of this chapter.

(5) *Identity.* (i) Proceed as directed in § 436.211 of this chapter, using the sample preparation method described in paragraph (b)(1) of that section using a 1 to 2 percent mixture in potassium bromide.

(ii) The identity of rifabutin is confirmed by the qualitative comparison of the HPLC of the sample to the rifabutin working standard as directed in paragraph (b)(1) of this section.

10. New § 455.188 is added to subpart B to read as follows:

**§ 455.188 Rifabutin capsules.**

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Rifabutin capsules are gelatin capsules containing rifabutin with a suitable and harmless filler and with or without binders, lubricants, and stabilizers. Each capsule contains rifabutin equivalent to 150 milligrams of rifabutin. Its rifabutin content is satisfactory if it is not less than 90 percent and not more than 110 percent of the number of milligrams of rifabutin that it is represented to contain. Its content of the four major related substances detected by high-performance liquid chromatography (HPLC) is not more than 1.0 percent each. All other unknown related substances are not more than 0.5 percent. The total of all related substances is not more than 4.5 percent. It passes the dissolution test if the quantity (Q) dissolved is 75 percent at 45 minutes. It passes the identity test. The rifabutin used conforms to the standards prescribed by § 455.88(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(A) The rifabutin used in making the batch for potency, related substances, moisture, *N*-isobutylpiperidone, and identity.

(B) The batch for content, related substances, dissolution, and identity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:

(A) The rifabutin used in making the batch: 10 packages, each containing approximately 300 milligrams.

(B) The batch: A minimum of 30 capsules.

(b) *Tests and methods of assay*—(1) *Rifabutin content.* Proceed as directed in § 455.88(b)(1), preparing the sample solution and calculating the rifabutin content as follows:

(i) *Preparation of sample solution.* Empty 20 capsules, collecting the contents quantitatively. Weigh the powder and determine the average capsule fill weight. Mix the powder and accurately weigh a portion containing the equivalent of about 25 milligrams of rifabutin into a 50-milliliter volumetric flask. Add 5 milliliters of acetonitrile. Dilute to volume with mobile phase and mix to yield a solution containing 0.5 milligram of rifabutin per milliliter (estimated). Filter through a suitable filter capable of removing particulate matter 0.5 micron in diameter prior to injection into the chromatographic system.

(ii) *Calculations.* Calculate the rifabutin content as follows:

$$\text{Milligrams of rifabutin per capsule} = \frac{A_U \times C_S \times P_S \times W_a}{A_S \times C_U \times 1{,}000}$$

where:
$A_U$ = Area of the rifabutin peak in the chromatogram of the sample (at a retention time equal to that observed for the standard);
$A_S$ = Area of the rifabutin peak in the chromatogram of the rifabutin working standard;
$C_S$ = Milligrams of rifabutin working standard per milliliter of standard solution;
$C_U$ = Milligrams of sample per milliliter of sample solution;
$P_S$ = Rifabutin activity in the rifabutin working standard solution in micrograms per milliliter; and
$W_a$ = Average capsule fill weight in milligrams.

(2) *Related substances.* Proceed as directed in paragraph (b)(1) of this section for rifabutin content using the sample prepared as described in paragraph (b)(1)(i) of this section and calculating the amounts of related substances as follows.

(i) *Calculations.* Calculate the percentage of related substances as follows:

$$\text{Percent individual HPLC-related substance} = \frac{A_i \times 100}{A_t}$$

$$\text{Percent total HPLC-related substances} = \frac{A \times 100}{A_t}$$

where:
$A_i$ = Area of the individual related substance peak;
$A$ = The sum of areas of all peaks minus the area due to the rifabutin peak and solvent front peak; and
$A_t$ = The sum of areas of all peaks in the chromatogram excluding the solvent peak.

(ii) [Reserved]

(3) *Dissolution test.* Proceed as directed in § 436.215 of this chapter. The quantity (Q) (the amount of rifabutin activity dissolved) is 75 percent within 45 minutes.

(4) *Identity.* (i) The retention time of the rifabutin response in the HPLC procedure described in paragraph (b)(1) of this section as applied to the sample solution compares qualitatively to that of the rifabutin reference standard.

(ii) The identity of rifabutin capsules is also confirmed by the spectrophotometric identity test described in § 436.370 of this chapter.

Dated: August 1, 1994.

**Stephanie R. Gray,**

*Acting Director, Office of Compliance, Center for Drug Evaluation and Research.*

[FR Doc. 94–19484 Filed 8–9–94; 8:45 am]

BILLING CODE 4160–01–F

## DEPARTMENT OF DEFENSE

### Office of the Secretary

### 32 CFR Part 77

[DoD Instruction 1332.37]

RIN 0790–AF70

## Program to Encourage Public and Community Service Employment

**AGENCY:** Department of Defense (DOD).

**ACTION:** Final rule.

**SUMMARY:** The Department of Defense (DoD) is adopting as a final rule, without change, the provisions of a proposed rule establishing guidelines for the registration of public and community service organizations and a listing of separating DoD personnel and their spouses to be maintained by the Department of Defense. The purpose of the public and community service organizational registry is to provide an avenue for public and community service organizations to recruit highly skilled and experienced separating DoD personnel and their spouses. The final rule encourages continuing public and community service for separating Military Service members, as well as to implement the temporary early retirement authority as established in the National Defense Authorization Act for Fiscal Year 1993 (hereinafter, "the Act"). This registry will be maintained indefinitely to encourage separating Service members to enter into public and community service job vacancies, such as in education, conservation, environmental protection, law enforcement, and public health care after separation from active duty. This action provides the necessary guidelines to determine how separating Military Service members, DoD civilian personnel leaving the Government, and their spouses register for public and community service employment, which organizations qualify for registration, and procedures qualifying organizations must take to be placed on the registry.

**EFFECTIVE DATE:** This rule is effective June 29, 1994.

**FOR FURTHER INFORMATION CONTACT:** Lt. Col. David F. Witkowski, (703) 695–1636.

**SUPPLEMENTARY INFORMATION:** This final rule is being issued after publication of a proposed rule on April 4, 1994 (59 FR 15673) in 32 CFR Part 77. There were no public comments to the proposed rule.

This rule is established in order to describe the organizational responsibilities within DoD for the program to encourage public and community service employment and to state the general policy of DoD with respect to this program. It has been certified that this rule would not be a significant rule. The rule would:

(a) Not have an annual effect on the economy of $100 million or more or adversely affect in a material way the economy, a section of the economy, productivity, competition, jobs, the environment, public health or safety, or State, local, or tribal governments or communities;

(b) Not create a serious inconsistency or otherwise interfere with an action taken or planned by another agency;

(c) Not materially alter the budgetary impact of entitlements, grants, user fees, or loan programs or the rights and obligations of recipients thereof; or,

(d) Not raise novel legal or policy issues arising out of legal mandates, the President's priorities, or the principles set forth in Executive Order 12866.

(e) Not become subject to the Regulatory Flexibility Act (5 U.S.C. 601) because it is not likely to have a significant economic impact on a substantial number of small entities. The primary effect on grantees administering the proposed rule will be a reduction in administrative costs and other burdens resulting from the simplification and clarification of certain policies and the elimination of policy differences among the federal agencies promulgating this final rule.

(f) Impose a reporting requirement under the Paperwork Reduction Act of 1980 (44 U.S.C. 3501–3250). The Office of Management and Budget approved the reporting requirement and assigned control number 0704–0324.

**List of Subjects in 32 CFR Part 77**

Employment, Military personnel, civilian personnel.

Accordingly, Title 32, Chapter I, Subchapter C, is amended to add Part 77 to read as follows:

## PART 77—PROGRAM TO ENCOURAGE PUBLIC AND COMMUNITY SERVICE

Sec.
77.1 Purpose.
77.2 Applicability and scope.
77.3 Definitions.
77.4 Policy.
77.5 Responsibilities.
77.6 Procedures.

**Appendix A to Part 77—DD Form 2580, Operation Transition Department of Defense Outplacement and Referral System/Public and Community Service Individual Application**