prescribed manner when such use is in accordance with the label and labeling registered pursuant to FIFRA, as amended (86 Stat. 973, 89 Stat. 751, 7 U.S.C. 135 et seq.) and is established as set forth below.

Any person adversely affected by this regulation may, within 30 days after the date of publication in the **Federal Register**, file written objections with the Hearing Clerk (address above). Such objections should be submitted in quintuplicate and specify the provisions of the regulation deemed objectionable and the grounds for the objections. If a hearing is requested, the objections must state the issues for the hearing. A hearing will be granted if the objections are legally sufficient to justify the relief sought.

The Office of Management and Budget (OMB) has exempted this regulation from OMB requirements of Executive Order 12291 pursuant to section 8(b) of that Order.

Pursuant to the requirements of the Regulatory Flexibility Act (Pub. L. 96–354, 94 Stat. 1164 (5 U.S.C. 601–612)), the Administrator has determined that regulations establishing new tolerances or raising tolerance levels or establishing exemptions from tolerance requirements do not have a significant economic impact on a substantial number of small entities. A certification statement to this effect was published in the **Federal Register** of May 4, 1981 (46 FR 24950).

(Sec. 408(c), 72 Stat. 1786 (21 U.S.C. 346(c))

List of Subjects in 21 CFR Parts 193 and 561

Food additives, Feed additives, Pesticides and pests.

Dated: January 5, 1988.

Douglas D. Campt,

Director, Office of Pesticide Programs.

Therefore, Chapter I of Title 21 of the Code of Federal Regulations is amended as follows:

1. Part 193 is amended as follows:

PART 193—[AMENDED]

a. The authority citation for Part 193 continues to read as follows:

Authority: 21 U.S.C. 348.

b. In § 193.98, paragraph (a), which is currently designated "reserved," is added to read as follows:

§ 193.98 Cyano(4-fluoro-3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate).

(a) A tolerance of 2.0 parts per million is established for residues of the insecticide cyano(4-fluoro-3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate) in cottonseed oil resulting from application of the insecticide to cottonseed.

* * * * *

2. Part 561 is amended as follows:

PART 561—[AMENDED]

a. The authority citation for Part 561 continues to read as follows:

Authority: 21 U.S.C. 348.

b. In § 561.96, paragraph (a), which is currently designated "reserved," is added to read as follows:

§ 561.96 Cyano(4-fluoro-3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate).

(a) A tolerance of 2.0 parts per million is established for residues of the insecticide cyano(4-fluoro-3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate) in cottonseed hulls resulting from application of the insecticide to cottonseed.

* * * * *

[FR Doc. 88–1381 Filed 1–22–88; 8:45 am]

BILLING CODE 6560–50–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 312

[Docket No. 82N–0394]

Technical Revision in Requirement for Serial Numbering of Amendments to Investigational New Drug Application

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is adopting revised procedures for numbering amendments to investigational new drug applications (IND's). Previously, IND amendments were required to be numbered serially by scientific discipline. Under the new system, a single, three-digit sequential numbering system will apply to all submissions relating to an IND. This action is intended to assist both IND sponsors and FDA in processing IND amendments.

DATE: Effective January 25, 1988. Comments by March 25, 1988.

ADDRESS: Written comments to the Dockets Management Branch (HFA–305), Food and Drug Administration, Rm. 4–62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Adele S. Seifried, Center for Drug Evaluation and Research (HFN–362), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–295–8046.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of March 19, 1987 (52 FR 8798), FDA adopted new regulations governing the submission and review of investigational new drug applications. The new regulations are called the IND Rewrite. Among other changes, the IND Rewrite adopted new regulations for the format and content of IND amendments. The agency is now revising formatting requirements for IND amendments.

The amendment procedures adopted in the IND Rewrite divided amendments into two classes—protocol amendments and information amendments. Protocol amendments include new protocols, changes in existing protocols, and new investigators added to existing protocols; information amendments cover new information pertinent to each of the scientific disciplines involved in IND review. To assist FDA in processing amendments, the final rule required that both information and protocol amendments prominently identify their contents (e.g., "Information Amendment: Pharmacology-Toxicology," "Protocol Amendment: New Protocol"). In addition, the final regulation required that all amendments be numbered and that all information amendments be serially numbered by discipline (21 CFR 312.31(b)). In numbering amendments, sponsors were expected to adopt separate and unique numbering sequences for chemistry, pharmacology, and clinical information amendments and for protocol amendments. This meant that each IND could have at least four separate sequences of amendment numbers.

Serial numbering was adopted to give the agency a method of assuring that all IND amendments are properly received, identified, and processed. However, both drug firms and the agency have found that serial numbering of amendments by discipline is confusing and difficult to implement, creates unnecessary work, and adds complexity to a system that was intended to be simple. The agency has, therefore, decided to abandon serial numbering by discipline. In its place, FDA is establishing a single, three-digit sequential numbering system.

Under the new numbering system that is being adopted in this final rule, each initial IND will be numbered "000." The

first submission to the established IND (amendment, report, or other correspondence) will be numbered "001." Subsequent submissions will be numbered consecutively in the order in which they are submitted. Numbers will be entered on the IND cover sheet (Form FDA–1571). This new system should significantly improve the agency's ability to track amendments.

Sponsors who are already serially numbering their submissions with a three-digit number may either continue or restart at 001. Prior submissions should not be renumbered. Sponsors who have adopted separate numbering sequences to identify protocol and information amendments should combine future submissions into a single numbering sequence, either by restarting the next new submission at 001 or by continuing in one of the prior numbering sequences.

Although previously only protocol and information amendments were expressly required to be numbered, under the new system all submissions relating to an IND, including reports and correspondence, will be required to be numbered. This action is intended to enhance processing of IND's by improving the identification and tracking of all submissions.

A letter discussing FDA's new policy on numbering of amendments has been sent to all current applicants and holders of new drug applications (NDA's). This technical revision is intended to clarify FDA's policy, and to make all current and future IND sponsors and other interested persons fully aware of the agency's requirements.

Notice and comment is not necessary before issuing this technical revision (see 5 U.S.C. 553(b)(B), 21 CFR 10.40(e)(1)). The requirement for the numbering of all amendments was proposed in the IND Rewrite proposal of June 9, 1983 (48 FR 26720), and adopted in the IND Rewrite final rule (52 FR 8798). This regulation, therefore, does not impose new substantive requirements but merely represents a minor technical revision of the numbering system already in place. The revision is intended to assist both IND sponsors and FDA in processing IND amendments. No purpose would be served by notice and comment or by delaying the effective date. Under FDA's procedural regulations at 21 CFR 10.40(e)(1), the agency has determined for good cause that notice and comment are impracticable, unnecessary, and contrary to the public interest.

This technical revision becomes effective on January 25, 1988, for all new IND submissions.

Environmental Impact

The agency has determined under 21 CFR 25.24(a)(9) that this technical revision 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.

Economic Impact

In accordance with Executive Order 12291 and the Regulatory Flexibility Act (Pub. L. 96–354), the agency has carefully analyzed the economic consequences of this final rule. This final rule is merely a technical revision of an existing rule which will have no economic consequences, and the agency has determined that it is, therefore, not a major rule as defined in Executive Order 12291. Further, the agency certifies that this clarifiction will not have a significant impact on a substantial number of small entities, as defined in the Regulatory Flexibility Act.

Paperwork Reduction Act

The rule relates to sections that contain collection of information requirements already submitted to the Office of Management and Budget (OMB) under section 3507 of the Paperwork Reduction Act of 1980. Sections 312.23, 312.30, and 312.31 have been previously approved under OMB control number 0910–0014.

Interested persons may, on or before March 25, 1988, submit to the Dockets Management Branch (address above), written comments about this clarification. 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. Such comments will be considered in determining whether amendments, modifications, or revisions to the final rule are warranted. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

List of Subjects in 21 CFR Part 312

Drugs, Medical research.

Therefore, under the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act, 21 CFR Chapter I, Part 312 is amended as follows:

PART 312—INVESTIGATIONAL NEW DRUG APPLICATION

1. The authority citation for 21 CFR Part 312 continues to read as follows:

Authority: Secs. 501, 502, 503, 505, 506, 507, 701, 52 Stat. 1049–1053 as amended, 1055–1056 as amended, 55 Stat. 851, 59 Stat. 463 as amended (21 U.S.C. 351, 352, 353, 355, 356, 357, 371); sec. 351, 58 Stat. 702 as amended (42 U.S.C. 262); 21 CFR 5.10, 5.11.

2. Section 312.23 is amended by adding new paragraph (e) to read as follows:

§ 312.23 IND content and format.

* * * * *

(e) *Numbering of IND submissions.* Each submission relating to an IND is required to be numbered serially using a single, three-digit serial number. The initial IND is required to be numbered 000; each subsequent submission (e.g., amendment, report, or correspondence) is required to be numbered chronologically in sequence.

§ 312.30 [Amended]

3. Section 312.30 is amended in paragraph (d) introductory text by removing the phrase "to be serially numbered,".

§ 312.31 [Amended]

4. Section 312.31 is amended in paragraph (b) introductory text by removing the phrase "to be numbered serially by discipline,".

Dated: December 24, 1987.

John M. Taylor,

Associate Commissioner for Regulatory Affairs.

[FR Doc. 88–1352 Filed 1–22–88; 8:45 am]

BILLING CODE 4160–01–M

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21 CFR Parts 436 and 452

[Docket No. 87N–0154]

Antibiotic Drugs; Erythromycin Estolate Bulk; Thin-Layer Chromatographic, PH, and Identity Testing Methods

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the antibiotic drug regulations by revising the accepted standards for erythromycin estolate bulk to add a thin-layer chromatographic (TLC) test method to identify and limit unesterified erythromycin, and by revising the pH and the identity test methods. These actions are being taken to provide better quality control of this product.

DATES: Effective January 25, 1988; comments, notice of participation, and request for hearing by February 24, 1988; data, information, and analyses to justify a hearing by March 25, 1988.

ADDRESS: Written comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Peter A. Dionne, Center for Drug Evaluation and Research (HFN-815), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-4290.

SUPPLEMENTARY INFORMATION: In the Federal Register of July 6, 1987 (52 FR 25252), FDA proposed to amend the antibiotic drug regulations for erythromycin estolate bulk to: (1) Add a TLC test for free (unesterified) erythromycin content with an upper limit of not more than 3 percent, (2) revise the quantity of sample used in the pH assay procedure from 100 milligrams per milliliter (mg/mL) to 10 mg/mL, and (3) revise the sample preparation method used in the identity test by infrared spectrophotometry from a 1 percent solution of the sample in chloroform to a 1 percent mixture of sample in potassium bromide.

As discussed in the proposal, the TLC test method is intended as a specific test for the detection of an unwanted impurity (unesterified erythromycin) in erythromycin estolate bulk. It has been demonstrated that the proposed test method employs common laboratory equipment and solvents, requires minimal sample preparation, has excellent sensitivity and separation, and can be completed in less than 30 minutes. The agency has determined that the TLC test method provides a fast, sensitive, easily performed inexpensive test that would allow a limit to be set for an unwanted impurity.

The current pH assay procedure for erythromycin estolate bulk uses an aqueous suspension of the sample at a concentration of 100 mg/mL. Because the solubility of erythromycin estolate in water is 0.024 mg/mL, the current sample concentration of 100 mg/mL is excessive for purposes of the test. The agency has determined that a sample concentration of 10 mg/mL would be sufficient for the pH determination of erythromycin estolate bulk.

The current sample preparation method for the identity test by infrared spectrophotometry for erythromycin estolate bulk is a 1 percent solution of the sample in chloroform. It has been determined, however, that erythromycin estolate samples diluted in chloroform show changes in the 1,500 to 2,000 centimeters^{-1} region of the infrared spectrum with time. The agency has determined that a change to a 1 percent mixture of the sample in potassium bromide for the sample preparation method will improve the stability of the erythromycin estolate sample.

Interested persons were given until September 24, 1987, to submit written comments on this proposal and until August 5, 1987, to submit requests for an informal conference. No comments or requests for an informal conference were received in response to the proposal.

Economic Impact

The agency has considered the economic impact of this final rule and has determined that it does not require a regulatory flexibility analysis, as defined in the Regulatory Flexibility Act (Pub. L. 96-354). Specifically, the final rule imposes an insubstantial amendment to existing requirements and refines existing technical provisions without imposing more stringent requirements. Accordingly, the agency certifies that this rulemaking will not have a significant economic impact on a substantial number of small entities.

Submitting Comments and Filing Objections

Any person who will be adversely affected by this regulation 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 February 24, 1988, a written notice of participation and request for hearing, and (2) on or before March 25, 1988, 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 hearing that no genuine and substantial issue of fact precludes the action taken by this order, or if a request for 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 order and filed with the Dockets Management Branch (address above).

The procedures and requirements governing this order, a notice of appearance and request for 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 436

Antibiotics.

21 CFR Part 452

Antibiotics.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under the authority delegated to the Commissioner of Food and Drugs, Parts 436 and 452 are amended as follows:

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

1. The authority citation for 21 CFR Part 436 continues to read as follows:

Authority: Sec. 507, 59 Stat. 463 as amended (21 U.S.C. 357); 21 CFR 5.10.

2. Section 436.362 is added to read as follows:

§ 436.362 Thin-layer chromatographic test for free erythromycin content in erythromycin estolate bulk.

(a) *Equipment*—(1) *Chromatography tank.* A rectangular tank approximately 23 centimeters long, 23 centimeters high, and 9 centimeters wide, equipped with a glass solvent trough in the bottom and a tight-fitting cover for the top.

(2) *Plates.* Use a 20- by 20-centimeter precoated silica gel 60 F-254 thin-layer chromatography plate. Before using, place the plate in an unlined developing chamber containing approximately 100 milliliters of anhydrous methanol and allow the solvent front to travel to the top of the plate, marking the direction of travel. Remove the plate and allow to drip dry. Store in a dry place.

(b) *Reagents*—(1) *Developing solvent.* Mix 15 milliliters of chloroform and 85 milliliters of anhydrous methanol. Use fresh developing solvent for each test.

(2) *Spray solution.* Dissolve 150 milligrams of xanthydrol in a mixture of 7.5 milliliters of glacial acetic acid and 92.5 milliliters of 37 percent hydrochloric acid.

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

Note.—It is advisable to prepare the sample and standard solutions immediately before spotting to minimize the possibility of degradation in solution.)

(2) *Standard solution.* Prepare a solution of erythromycin base reference standard in anhydrous methanol to contain 1 milligram per milliliter. Weigh 99.5, 99.0, and 97.0 milligrams of erythromycin estolate (propionyl erythromycin lauryl sulfate) reference standard and transfer to separate 10-milliliter volumetric flasks. To these flasks add 0.5, 1.0, and 3.0 milliliters, respectively, of the 1-milligram-per-milliliter solution of erythromycin base reference standard and dilute to volume with anhydrous methanol. These solutions contain, respectively, 0.5 percent, 1.0 percent, and 3.0 percent erythromycin base in erythromycin estolate. Prepare a solution of erythromycin estolate reference standard in anhydrous methanol to contain 10 milligrams per milliliter. Prepare a solution of erythromycin base reference standard in anhydrous methanol to contain 0.1 milligram per milliliter.

(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 plate, apply 1.0 microliter of each of the following solutions:

(1) 10-milligrams-per-milliliter solution of erythromycin estolate reference standard, equivalent to 10 micrograms of erythromycin estolate;

(2) 0.5 percent base-in-estolate solution, equivalent to 0.05 microgram of base and 9.95 micrograms of estolate;

(3) 1.0 percent base-in-estolate solution, equivalent to 0.10 microgram of base and 9.90 micrograms of estolate;

(4) 3.0 percent base-in-estolate solution, equivalent to 0.30 microgram of base and 9.70 micrograms of estolate;

(5) 0.1-milligram-per-milliliter solution of erythromycin base reference standard, equivalent to 0.1 microgram of erythromycin base; and

(6) Sample solution, equivalent to 10 micrograms of erythromycin estolate. Allow the spots to dry. Place the plate directly in the chromatograph tank. Cover and seal the tank. Allow the solvent front to travel a distance of 7 centimeters (about 27 minutes). Remove the plate from the tank, and allow it to air dry under a hood. With the plate still under the hood, spray uniformly with the spray solution. Heat the sprayed plate in an oven at 100 °C for 5 minutes. (CAUTION: Avoid exposure to the acid fumes while removing the plate from the oven.)

(e) *Evaluation.* Erythromycin base and erythromycin estolate appear as reddish-violet spots on the sprayed and heated plate. Better visualization of the erythromycin base spots may be gained by viewing the plate under long-wavelength (366 nanometers) ultraviolet light, erythromycin base appearing as dark spots on a yellow-green fluorescent background. Erythromycin base has an R_f value of about 0.3. Erythromycin estolate has an R_f value of about 0.7. Compare the size and intensity of any erythromycin base spots in the sample lane with the erythromycin base spots in the erythromycin base reference standard lane and in the 0.5 percent, 1.0 percent, and 3.0 percent base-in-estolate lanes, and report the percentage of erythromycin base (free erythromycin) in the sample. For a more accurate determination of free erythromycin content, it may be necessary to repeat the test using a different set of standards.

PART 452—MACROLIDE ANTIBIOTIC DRUGS

3. The authority citation for 21 CFR Part 452 continues to read as follows:

Authority: Sec. 507, 59 Stat. 463, as amended (21 U.S.C. 357); 21 CFR 5.10.

4. In § 452.15, paragraph (a)(1)(ii) is added, (a)(3)(i) is revised, (b)(2) is added, and (b)(4) and (6) are revised to read as follows:

§ 452.15 Erythromycin estolate.

(a) * * *

(1) * * *

(ii) Its free erythromycin content is not more than 3.0 percent.

* * * * *

(3) * * *

(i) Results of tests and assays on the batch for potency, free erythromycin content, moisture, pH, crystallinity, and identity.

* * * * *

(b) * * *

(2) *Free erythromycin content.* Proceed as directed in § 436.362 of this chapter.

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(4) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous suspension containing 10 milligrams per milliliter.

* * * * *

(6) *Identity test.* Proceed as directed in § 436.211 of this chapter, preparing the sample as described in paragraph (b)(1) of that section.

Dated: January 12, 1988.

Daniel L. Michels,

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

[FR Doc. 88-1354 Filed 1-22-88; 8:45 am]

BILLING CODE 4160-01-M

DEPARTMENT OF TRANSPORTATION

Federal Highway Administration

23 CFR Part 635

Physical Construction Authorization

AGENCY: Federal Highway Administration (FHWA), DOT.

ACTION: Final rule.

SUMMARY: The Federal Highway Administration (FHWA) is amending its regulation regarding the erection of certain signs on Federal-aid construction projects to implement Section 154 of the Surface Transportation and Uniform Relocation Assistance Act (STURAA) of 1987. Section 154 mandates that those States that currently have a practice of erecting signs identifying funding sources on construction projects without Federal-aid highway assistance shall be required to erect signs displaying sources and amounts of funds on all Federal-aid highway projects. The current regulations provide for the erection of only those signs that conform to the standards developed by the Secretary of Transportation. The FHWA must determine that the States' plans, specifications, and estimates meet these conditions before authorization to advance a Federal-aid project to the physical construction stage. This amendment will allow erection of funding source signs that do not presently conform to standards developed by the Secretary. Furthermore, this amendment requires that provisions be included in the plans, specifications, and estimates, where applicable, that require erection of funding source signs, during the life of the construction project, prior to authorization for physical construction.

EFFECTIVE DATE: January 25, 1988.

FOR FURTHER INFORMATION CONTACT: Mr. William A. Weseman, Chief, Construction and Maintenance Division, (202) 366-0392 or Mr. Michael J. Laska, Office of Chief Counsel, (202) 366-1383, Federal Highway Administration, 400 Seventh Street SW., Washington, DC 20590. Office hours are from 7:45 a.m. to 4:15 p.m., ET, Monday through Friday.

SUPPLEMENTARY INFORMATION: Section 154 of the STURAA of 1987 (Pub. L.