§ 193.25 4-amino-6-(1,1-dimethylethyl)-3-methylthio)-1,2,4-triazin-5(4H)-one.

Tolerances are established for combined residues of the herbicide 4-amino-6-(1,1-dimethylethyl)-3-(methylthio)-1,2,4-triazin-5(4*H*)-one and its triazinone metabolites in or on the following processed foods when present therein as a result of application of this herbicide to growing crops:

Food:	Parts per million
Barley, milled fractions (except flour)	3
Potatoes, processed (inc. potato chips)	3
Sugarcane molasses	2
Wheat milled fractions (except flour)	3

PART 561—TOLERANCES FOR PESTICIDES IN ANIMAL FEEDS ADMINISTERED BY THE ENVIRONMENTAL PROTECTION AGENCY

2. Part 561, § 561.41 is amended by revising the table to include the milled fractions of barley (except flour) and wheat (except flour) at 3 ppm as follows:

§ 561.41 4-Amino-6-(1,1-dimethylethyl)-3-(methylthio)-1,2,4-triazin-5(4H)-one.

* * * * *

Feed:	Parts per million
Barley, milled fractions (except flour)	3
Potato waste, processed (dried)	3
Sugarcane bagasse	0.5
Sugarcane molasses	2
Tomato pomace, dried	2
Wheat, milled fractions (except flour)	3

[FR Doc. 79-21308 Filed 7-9-79; 8:45 am]

BILLING CODE 6560-01-M

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Food and Drug Administration

21 CFR Part 522

Implantation or Injectable Dosage Form New Animal Drugs Not Subject To Certification; Oxytocin Injection

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: This document amends the animal drug regulations to reinstate a sponsor which was inadvertently dropped by an earlier document.

EFFECTIVE DATE: July 10, 1979.

FOR FURTHER INFORMATION CONTACT: Robert S. Brigham, Bureau of Veterinary Medicine (HFV-238), Food and Drug Administration, Department of Health, Education, and Welfare, 5600 Fishers Lane, Rockville, MD 20857, 301-443-6243.

SUPPLEMENTARY INFORMATION: A change of sponsor resulted from the consolidation of Myers-Carter Laboratories Div., Chromalloy Pharmaceuticals, Inc., and Glogau and Co., Inc., and the change of corporate name to Carter-Glogau Laboratories Div., Chromalloy Pharmaceuticals, Inc. A document reflecting this change published in the **Federal Register** of May 1, 1975 (40 FR 18993). In that document, Part 522 was amended in § 522.1680(b) (21 CFR 522.1680(b)) by deleting the sponsor 010469 and inserting in its place the sponsor 000381. In a subsequent **Federal Register** publication of July 9, 1975 (40 FR 28791), this change was accidentally reversed to reestablish sponsor 010469. This document reinstates the May 1, 1975 sponsor change from 010469 to 000381.

Therefore, under the Federal Food, Drug, and Cosmetic Act (sec. 512(i), 82 Stat. 347 (21 U.S.C. 360b(i))), and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.1) and redelegated to the Director of the Bureau of Veterinary Medicine (21 CFR 5.83), Part 522 is amended in § 522.1680 *Oxytocin injection* by deleting from paragraph (b) the number "010469" and inserting in numerical sequence the number "000381."

Effective date. This amendment is effective July 10, 1979.

(Sec. 512(i), 82 Stat. 347 (21 U.S.C. 360b(i)))

Dated: June 28, 1979.

Terence Harvey,

Director, Bureau of Veterinary Medicine.

[FR Doc. 79-20961 Filed 7-9-79; 8:45 am]

BILLING CODE 4110-03-M

21 CFR Part 558

New Animal Drugs for use in Animal Feeds; Oleandomycin

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: The animal drug regulations are amended to reflect approval of a supplemental new animal drug application (NADA) filed by Pfizer, Inc., providing labeling revisions for use of an oleandomycin premix used to manufacture complete feeds for chickens, turkeys, and swine.

EFFECTIVE DATE: July 10, 1979.

FOR FURTHER INFORMATION CONTACT: Jack C. Taylor, Bureau of Veterinary Medicine (HFV-136), Food and Drug Administration, Department of Health, Education, and Welfare, 5600 Fishers Lane, Rockville, MD 20857, 301-443-5247.

SUPPLEMENTARY INFORMATION: Pfizer, Inc., 235 East 42nd St., New York, NY 10017, filed a supplemental NADA (35-287) providing labeling revisions for use of a 5-gram-per-pound oleandomycin (as the resin adsorbate) premix used to manufacture complete feeds for broiler chickens, growing turkeys, and growing-finishing swine. The revisions more clearly define the classes of animals for which the drug is intended and eliminate the need for certain limitations on the labeling. Approval of this application, therefore, poses no increased risk from exposure to residues of oleandomycin. Accordingly, under the agency's supplemental policy (see the **Federal Register** of December 23, 1977 (42 FR 64367)) approval of this application did not require a reevaluation of the safety and effectiveness data in the parent application.

Therefore, under the Federal Food, Drug, and Cosmetic Act (sec. 512(i), 82 Stat. 347 (21 U.S.C. 360b(i))) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.1) and redelegated to the Director of the Bureau of Veterinary Medicine (21 CFR 5.83), § 558.435 is amended by revising paragraph (f) to read as follows:

§ 558.435 Oleandomycin.

* * * * *

(f) *Conditions of use.* It is used in animal feed as follows:

(1) *Chickens and turkeys*—(i) *Amount per ton.* Oleandomycin, 1 to 2 grams.

(ii) *Indications for use.* For increased rate of weight gain and improved feed efficiency for broiler chickens and growing turkeys.

(2) *Swine*—(i) *Amount per ton.* Oleandomycin, 5 to 11.25 grams.

(ii) *Indications for use.* For increased rate of weight gain and improved feed efficiency in growing-finishing swine.

Effective date. This regulation is effective July 10, 1979.

(Sec. 512(i), 82 Stat. 347 (21 U.S.C. 360b(i)))

Dated: June 29, 1979.

Terence Harvey,

Director, Bureau of Veterinary Medicine.

[FR Doc. 79-20900 Filed 7-9-79; 8:45 am]

BILLING CODE 4110-03-M

21 CFR Part 573

[Docket No. 76F-0280]

Food Additives Permitted in Feed and Drinking Water of Animals; Anhydrous Ammonia

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: This document amends the food additive regulations to provide for the direct mixing of 15 to 30 percent ammonia solutions with corn plant material prior to ensiling, when the food additive is to be used as a source of nonprotein nitrogen for dairy cattle.

Ruminant Nitrogen Products Co. filed a petition for such use.

DATES: Effective July 10, 1979; objections by August 9, 1979.

ADDRESS: Written objections to the Hearing Clerk (HFA–305), Rm. 4–65, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: William D. Price, Bureau of Veterinary Medicine (HFV–123), Food and Drug Administration, Department of Health, Education, and Welfare, 5600 Fishers Lane, Rockville, MD 20857, 301–443–3442.

SUPPLEMENTARY INFORMATION: The Food and Drug Administration (FDA) announced, in a notice published in the **Federal Register** of October 8, 1976 (41 FR 44442), that a petition (MF–3555) had been filed by Ruminant Nitrogen Products Co., 2347 Science Parkway, Okemos, MI 48864, proposing to amend § 121.209 *Anhydrous ammonia* (21 CFR 121.209), recodified § 573.180 *Anhydrous ammonia* (21 CFR 573.180), to provide for the direct mixing of 15 to 30 percent ammonia solutions with freshly chopped corn plant material before ensiling when the food additive is used as a source of nonprotein nitrogen in dairy cattle feed.

The agency, having evaluated data in the petition and other relevant material, concludes that the food additive regulations should be amended as set forth below.

In addition, the current regulation concerning use of anhydrous ammonia is editorially revised.

Therefore, under the Federal Food, Drug, and Cosmetic Act (sec. 409(c)(1), 72 Stat. 1786 (21 U.S.C. 348(c)(1))) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.1), Part 573 is amended by revising § 573.180 to read as follows:

§ 573.180 Anhydrous ammonia.

(a) The food additive anhydrous ammonia is applied directly to corn plant material and thoroughly blended prior to ensiling. It is used or intended for use as a source of nonprotein nitrogen in cattle feed in accordance with paragraphs (a)(1), (2), or (3) as follows:

(1)(i) The food additive anhydrous ammonia is applied as a component of an aqueous premix containing 16 to 17 percent ammonia, with molasses, minerals, and not less than 83 percent crude protein. The premix is a source of nonprotein nitrogen and minerals.

(ii) In addition to the requirements of paragraph (b) of this section, the labeling shall bear an expiration date of not more than 10 weeks after date of manufacture; a statement that additional protein should not be fed to lactating dairy cows producing less than 32 pounds of milk per day nor beef cattle consuming less than 1 percent of body weight daily in shelled corn; and a warning not to use additional trace mineral supplementation with treated silage.

(2)(i) The food additive anhydrous ammonia is applied directly to corn plant material for use in dairy or beef cattle rations.

(ii) The anhydrous ammonia is applied at a rate not to exceed the equivalent of 0.35 percent of the corn plant material.

(iii) It is applied to corn plant material containing 30 to 35 percent dry matter.

(iv) It is applied so that 75 to 85 percent of the additive is liquid at ambient pressure.

(3)(i) The food additive anhydrous ammonia is applied after being diluted to a 15 to 30 percent aqueous ammonia solution (by weight).

(ii) The anhydrous ammonia solution is applied at a rate not to exceed anhydrous ammonia equivalent to 0.3 percent of the corn plant material.

(iii) It is applied to corn plant material containing 28 to 38 percent dry matter.

(iv) The silage treated with aqueous ammonia is to be fed to dairy cattle only.

(b) Its labeling shall bear, in addition to the other requirements of the act, the name of the additive, the concentration of ammonia, the maximum percentage of equivalent crude protein from nonprotein nitrogen, and directions for use consistent with this section.

Any person who will be adversely affected by the foregoing regulation may at any time on or before August 9, 1979 submit to the Hearing Clerk (HFA–305), Food and Drug Administration, Rm. 4–65, 5600 Fishers Lane, Rockville, MD 20857, written objections thereto and may make a written request for a public hearing on the stated objections. Each objection shall be separately numbered and each numbered objection shall specify with particularity the provision of the regulation to which objection is made. 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. Four copies of all documents shall be submitted and shall be identified with the Hearing Clerk docket number found in brackets in the heading of this regulation. Received objections may be seen in the above office between the hours of 9 a.m. and 4 p.m., Monday through Friday.

Effective date. This regulation shall become effective July 10, 1979.

(Sec. 409(c)(1), 72 Stat. 1786 (21 U.S.C. 348(c)(1)))

Dated: June 29, 1979.

William F. Randolph,

Acting Associate Commissioner for Regulatory Affairs.

[FR Doc. 79–20965 Filed 7–9–79; 8:45 am]

BILLING CODE 4110–03–M

---

21 CFR Parts 601, 610, and 650

[Docket No. 76N–0480]

Skin Test Antigens; Implementation of Efficacy Review

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending certain licensing and standards provisions of the biologics regulations in response to the recommendations of the Panel on Review of Skin Test Antigens. The agency is announcing its adoption of the Panel Report, with modifications of certain portions, based on comments received. The modifications are made for clarity and regulatory accuracy and to reflect any new information that has come to the agency's attention. In addition, the agency is reclassifying Histoplasmin, manufactured by Parke, Davis & Co. and Tuberculin, PPD, Multiple Puncture Device (Heaf), manufactured by Connaught Laboratories Limited from Category IIIA to Category I.

DATES: Effective July 10, 1979, except that recommended labeling changes become effective January 7, 1980.

ADDRESS: Additional background data and information are on public display in the office of the Hearing Clerk (HFA–305), Food and Drug Administration, Rm. 4–65, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Michael L. Hooton, Bureau of Biologics (HFB–620), Food and Drug Administration, Department of Health, Education, and Welfare, 8800 Rockville Pike, Bethesda, MD 20205, 301–443–1306.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of September 30, 1977

(42 FR 52674), FDA published a proposal containing findings of the Panel on Review of Skin Test Antigens. The Panel evaluated the safety and effectiveness of 23 skin test antigen products and recommended that: (a) 5 products be placed in Category I (those biological products determined to be safe, effective, and not misbranded); (b) 2 products be placed in Category II (those biological products determined to be unsafe, ineffective, or misbranded); (c) 6 products be placed in Category IIIA (those biological products for which available data are insufficient to classify their safety and effectiveness but which may remain in the interstate commerce pending completion of testing and conformance with the recommendations of the Panel); and (d) 10 products be placed in Category IIIB (those biological products for which available data are insufficient to classify their safety and effectiveness and which should not continue in interstate commerce).

The Commissioner of Food and Drugs agreed with the Panel's recommendations concerning the classification of these products and accordingly announced the intention to publish a Notice of Opportunity for Hearing to revoke the licenses for those products placed in Categories II and IIIB. At the request of the licensees, the licenses for the 2 products in Category II and 2 of the 10 products in Category IIIB were revoked before publication of the Notice of Opportunity for Hearing. The Notice of Opportunity for Hearing for the remaining 8 Category IIIB products was published in the **Federal Register** of October 28, 1977 (42 FR 56800). Interested persons were advised that they could submit additional data in response to the revocation notices; for products placed in Category IIIA, comments or additional data concerning the classification were also invited. Because manufacturers of those licensed products placed in Category IIIB either did not request a hearing, requested a hearing and submitted additional data that justified reclassification of products without the need for the requested hearing, or requested that the licenses be revoked, FDA published in the **Federal Register** of October 27, 1978 (43 FR 50250), a notice reclassifying certain products into Category IIIA and revoking the remaining product licenses.

In addition, the September 1977 proposal contained the Commissioner's responses to other panel recommendations concerning the testing, content, and labeling of skin test antigens. In view of these recommendations, the Commissioner proposed the following amendments to the biologics regulations:

(1) In § 601.25(h) (21 CFR 601.25(h)), to require that the labeling for Category IIIA skin test antigens contain a prominent boxed statement referencing the Panel's findings of insufficient data on safety and effectiveness, and that written informed consent be obtained from participants in the additional studies performed pursuant to § 601.25(h);

(2) In § 610.13 (21 CFR 610.13), to clarify the regulation by specifying that products need to be free of avoidable extraneous material;

(3) In § 650.13 (21 CFR 650.13), to require chemical characterization of each batch of powdered tuberculin material; and

(4) To redesignate existing § 650.15 as § 650.16 *Equivalent methods* and add new § 650.15 to require potency testing of each batch of tuberculin material in humans.

Interested persons were given until November 29, 1977 to file comments on these proposals with the Hearing Clerk. Eleven letters were received, many of which contained more than one comment. This final rule announces the agency's adoption of the Panel's conclusions and recommendations for classifying skin test antigens, as modified on the basis of comments received and FDA's independent evaluation of the Panel Report. Modifications have been made for clarity and regulatory accuracy, and to reflect any new information that has come to the agency's attention. FDA's agreement with comments suggesting modification of the Panel's findings is reflected in the following summary of the comments and FDA's responses to them.

Panel Report

Basis of Evaluation

1. One comment concerning the Panel's statement on the characteristics of an ideal skin test antigen (42 FR 52675–6) suggested that the skin test material should not cause a local (irritant) reaction, i.e., it should be used at the concentration that produces an antigenic response only.

FDA agrees and interprets the Panel's use of the phrase "immune response" to mean that the skin test antigen should be used at a concentration that induces a specific skin reaction only and not a local irritant reaction.

2. One comment concerning test material (paragraph (2) *Test material*, 42 FR 52675) suggested that diluents should be used as control materials and should be injected separately and simultaneously when the skin test antigen is injected.

The Panel recommended that the solution (diluents) into which the testing material is dissolved must neither sensitize the immune system nor elicit any other form of host reaction, local or systemic. As a requisite for approval of a license application for skin test antigens, a product must be tested in nonsensitive individuals, thereby detecting any reactions that may be attributed to the diluent used. Therefore, it is unnecessary to subject a person to an additional and unwarranted injection of control diluent. Accordingly, FDA rejects the comment.

3. One comment concerning the test method (paragraph (3) *Test method*, 42 FR 52675) stated that it is difficult precisely to inject skin test antigens with resulting clear-cut reproducible reactions in the host as prescribed for an ideal skin test method. The comment suggested that it would be more realistic to provide a range of reaction sizes (in millimeters) for each concentration of antigen.

The Panel noted in its report that the ideal skin test method is a conceptualization that the scientific community should strive to achieve. The agency agrees with the comment that given the current state of the art, it is not possible to require all the characteristics of the ideal skin test method. New and modified methods will be required as they are developed and are proven to be more sensitive and accurate.

Histoplasmin by Parke, Davis & Co.

4. The Panel recommended in its report that Histoplasmin manufactured by Parke, Davis and Company be placed in Category IIIA because the available data were insufficient to satisfy its safety and effectiveness. Since publication of the Panel's report, the firm has submitted data with an amended license application demonstrating safety and effectiveness of its product. FDA has reviewed the data and found them adequate to approve the license amendment and reclassify the product to Category I. Accordingly, Histoplasmin manufactured by Parke, Davis and Company is reclassified from Category IIIA to Category I.

Mumps Skin Test Antigen

5. One comment requested that Mumps Skin Test Antigen manufactured by Eli Lilly & Co. be placed in Category IIIA rather than IIIB for its use in assessing immunocompetence.

FDA advises that Mumps Skin Test Antigen manufactured by Eli Lilly & Co. was assigned to Category IIIB by the Panel for its licensed and labeled use for identifying immunity to mumps virus infection. However, the Panel noted the widespread use and apparent value of the product for the purpose of ascertaining immunocompetence and recommended that additional data be submitted to demonstrate the product's safety and effectiveness for this use. Eli Lilly & Co. has submitted data in support of using the product for testing immunocompetence. As stated in the October 1978 notice, the Commissioner decided to hold in abeyance a ruling on Eli Lilly & Co.'s request for a hearing, pending receipt from the firm and evaluation by FDA of an appropriate license amendment and a commitment to undertake additional studies as required by § 601.25(h)(1) (21 CFR 601.25(h)(1)). The amendment has been submitted and Mumps Skin Test Antigen has been placed into Category IIIA for further evaluation of its use for immunocompetence testing. Therefore, no hearing will be necessary.

Tuberculin, Old, General Statement; Characteristics of Effectiveness

6. One comment concerning the measurement in the test method for Tuberculin, Old suggested that a statement be added to distinguish the type of reaction produced by Tuberculin Mono-Vacc and other multiple puncture devices.

Although the comment does not require a change in the regulation, the agency agrees that it would be appropriate to distinguish the type of reaction described in the comment. Thus, the Panel Report is adopted with a modification in paragraph (ii)(2) *Measurement* (42 FR 52700) to delete the last sentence and add a new sentence as follows:

The close spacing of the Mono-Vacc points usually produces a single area of induration while the more distant spacing of other multiple puncture devices may produce multiple areas of induration which may coalesce to form a circular reaction.

Tuberculin, Old (Tine Test) by Lederle; Characteristics of Effectiveness

7. The agency advises that in the **Federal Register** of July 29, 1977 (42 FR 38567), FDA amended § 650.14 (21 CFR 650.14) to change the assay requirements for multiple puncture devices from ±50 percent of the tuberculin units claimed by the manufacturer in its license application to ±20 percent of the tuberculin units.

The Panel Report to the agency did not reflect the amendment to § 650.14 published in the **Federal Register** of July 29, 1977. Therefore, to reflect the correct assay requirement accurately, the Panel Report is adopted with a modification in paragraph (i)(3) *Standardization* in the discussion concerning test material for Tuberculin, Old (Tine Test) by Lederle, (42 FR 52702), to revise the phrase "the average potency for each Tine Test unit must be equivalent to $\frac{1}{2700}$ to $\frac{1}{1350}$ of the undiluted U.S. Standard Old Tuberculin (an allowable variation of 33 percent)" to read "the average potency of each Tine Test unit must be equivalent to $\frac{1}{1666}$ to $\frac{1}{2500}$ of the undiluted U.S. Standard Old Tuberculin (an allowable variation of 20 percent)."

8. One comment concerning certain Panel recommendations on Lederle's Tuberculin, Old (Tine Test), (paragraph 4). *Recommendations* (b), 42 FR 52703) stated that use of individuals with bacteriologically confirmed tuberculosis in in vivo testing with tuberculin may create a legal dilemma for manufacturers because tuberculin testing of infective persons may reactivate quiescent or healed-over lesions. No data accompanied the comment.

The agency is not aware of any information to support the suggestion that tuberculin testing of infected persons may reactivate quiescent foci. Skin testing of individuals, both infected and noninfected, has been carried out for many years in millions of persons and when the correct doses are properly administered, adverse reactions to tuberculin are limited only to those who are very sensitive. These reactions are localized and usually self limited. Accordingly, the comment is rejected.

Tuberculin, Old by Institut Merieux; Characteristics of Effectiveness

9. One comment on test material standardization for Institut Merieux's Tuberculin, Old recommended that, to ensure reproducibility, the degree of reactivity should be tested with material derived from 20 randomly selected Mono-Vacc test devices as required for the Lederle Laboratories Division product (characteristics of effectiveness, (i)(3) *Standardization*) at 42 FR 52702.

Although the comment does not require a change in the regulation, the agency agrees that it would be appropriate to clarify the procedure for standardization of Institut Merieux's Tuberculin, Old test material. Thus, the Panel Report is adopted with a modification in characteristics of effectiveness, (i)(3) *Standardization*, (42 FR 52708) to revise the first paragraph to read as follows:

The standardization of each lot is accomplished by injecting 0.5, 1, 2, and 4 TU of the U.S. Standard tuberculin (Bureau of Biologics) intracutaneously by the Mantoux method into hypersensitive guinea pigs and comparing the degree of reactivity to four comparative levels of activity of the test lot with material derived from 20 randomly selected Mono-Vacc test devices.

Tuberculin, PPD, Multiple Puncture Device (Aplitest) by Parke-Davis

10. One comment concerning the Panel's quality control recommendations for Parke-Davis' Tuberculin, PPD, Multiple Puncture Device (Aplitest) (paragraph 4. *Recommendations* (a), 42 FR 52715) suggested that the required quality control test is unnecessary because, except for human error, the mechanical dipping process will always coat tines.

FDA believes that the required testing is necessary to compensate for human error and to ensure that all tines are dipped satisfactorily, thus preventing the marketing of inadequately coated tines that would result in false negative reactions. Accordingly, the comment is rejected.

Tuberculin, PPD (Mantoux) by Connaught

11. One comment concerning Connaught's Tuberculin, PPD (Mantoux) suggested that the title should include the trade name, "Tubersol®," after the word "Mantoux."

The agency advises that the trade name "Tubersol®" for Connaught's Tuberculin, PPD (Mantoux) was inadvertently omitted from the September 30, 1977 proposal. Wherever the name "Tuberculin, PPD (Mantoux)" by Connaught appears in the proposal, it should be considered to include the trade name "Tubersol®." For consistency, the agency also advises that the name of the Parke, Davis & Co. Tuberculin, PPD product should read "Tuberculin, PPD (Mantoux) Aplisol®" wherever it appears.

12. Connaught Laboratories Limited commented that certain portions of the Panel Report under the heading "Characteristics of Effectiveness" should be clarified to reflect accurately the characteristics of Tuberculin, PPD (Mantoux) Tubersol®. Although the comment does not require a change in the regulation, the agency agrees that it would be appropriate to clarify the Panel Report. Therefore, the Panel

Report is adopted with the following modifications:

(a) Paragraph (i)(1) *Chemical composition* (42 FR 52716) is modified by revising the last sentence to read as follows:

The Kjeldahl nitrogen content is used in the preparation of a 1 mg/ml stock solution from the Master Batch PPD–CT68. One mg PPD–CT68 has been found by the Kjeldahl method to correspond to 0.91 plus or minus 0.02 mg of proteins.

(b) In (i)(3) *Standardization* (42 FR 52716), the last paragraph is modified to read as follows:

Bioequivalency of PPD–CT68 to PPD–S was determinded in man, and the 5 TU bioequivalent PPD–CT68 preparation is confirmed on the basis of the guinea pig potency test. The 1 TU and 250 TU strengths are made by appropriate dilutions of the stock material in reference to the 5 TU dose. They are therefore calculated potencies and not directly bioequivalent to a standard, although each strength is standardized in guinea pigs against PPD–S and the Connaught Laboratories Limited house standard Tuberculin, PPD. This would seem to be an acceptable compomise, however, since most of the clinical data on which interpretation of reaction sizes are based have been collected only with the 5 TU dose. One TU and 250 TU PPD are used only in special instances and interpretations of reactions with these doses are limited.

(c) The typographical error in paragraph (i)(4) *Stability* (42 FR 52716) is corrected by revising the phrase "50 PPm" to read "50 ppm."

(d) In 4. *Recommendations*, the first sentence of paragraph (b) (42 FR 52717) is modified to read as follows:

The labeling should indicate that storage in secondary containers (such as a syringe) is not recommended because of possible contamination of the product during transfer from container to container.

Tuberculin, PPD, Multiple Puncture Device (Heaf) by Connaught

13. Connaught Laboratories Limited also commented that certain portions of the Panel Report under discussion of "Tuberculin, PPD, Multiple Puncture Device (Heaf)" should be clarified to describe this product accurately. Although the comment does not require a change in the regulation, the agency agrees that it would be appropriate to clarify the Panel Report. Thus, the Panel Report is adopted with the following modifications:

(a) The typographical error "250 TP" in paragraph 3. (a) *Effectiveness* (42 FR 52717), in the next to the last sentence is corrected to read "250 TU."

(b) The third sentence of paragraph 3. (a)(i)(3) *Standardization* (42 FR 52717) is modified to read as follows:

The reaction sites are randomized and the reactions are read blindly.

(c) Paragraph 3. (a)(i)(1)(7) *Diluent* (42 FR 52717) is modified to read as follows:

The material itself is prepared in a solution which contains sodium phosphate, sodium chloride, 50 percent w/v glycerol, and 0.5 percent w/v phenol, and is not known to be sensitizing. No further diluent is used.

14. Connaught Laboratories Limited also requested reclassification of its Tuberculin, PPD, Multiple Puncture Device (Heaf) from Category IIIA to Category I and submitted data from clinical studies performed on 50 individuals with bacteriologically confirmed tuberculosis.

FDA finds that the data submitted adequately support reclassification of the Tuberculin, PPD, Multiple Puncture Device from Category IIIA to Category I. Accordingly, the product is reclassified to Category I.

Proposed Amendments to the Regulations

15. One comment concerning proposed § 601.25(h)(4) objected to the requirement that labeling and promotional material for products requiring additional studies contain a box statement concerning the effectiveness of the product because the statement will result in a marked reduction in the use of the product by the medical community.

FDA does not agree. Section 601.25(h)(4), requiring the boxed labeling referred to in the comment, was codified in the final rule concerning Bacterial Vaccines and Bacterial Antigens with "No U.S. Standards of Potency," which was published in the **Federal Register** of January 5, 1979 (44 FR 1544). The response to comment 8 of that final rule (see 44 FR 1547) sets forth the reasons for the adoption of the boxed labeling, which references the need for further data to establish effectiveness of Category IIIA products fully.

Section 601.25(h)(5), requiring written informed consent from participants in the requisite additional studies on Category IIIA products, was also codified in the January 5, 1979 final rule concerning Bacterial Vaccines and Bacterial Antigens with "No U.S. Standards of Potency." No comments were received on the proposal to require informed consent for studies on skin test antigens. The agency has now concluded that § 601.25 should be amended as proposed for skin test antigens (1) in paragraph (h)(4) to preclude misleading labeling, which results in misbranding of the products, by requiring disclosure in the boxed labeling that the data in support of the products' safety and effectiveness are currently insufficient, and (2) in paragraph (h)(5) to give participants in the additional studies an explanation of the product and purpose of the study, and provide them a clear opportunity to refuse to participate in the study. Accordingly, the comment is rejected and § 601.25(h) (4) and (5) is amended by requiring skin test antigens to meet the labeling provisions set forth in each paragraph.

16. One comment concerning §§ 650.13 and 650.15 recommended use of the term "master lot" rather than "batch" in the regulations.

FDA believes that the term "batch" is more appropriate. "Master lot" may be confused with the term "lot," which is used in the biologics field to identify final production material. In addition, use of the term "batch" for tuberculin products is consistent with its use for other drug products (see § 210.3(b)(2) (21 CFR 210.3(b)(2)). Each batch of tuberculin material is intended to last for a number of years and is chemically characterized and tested for potency in humans. Tuberculin production lots are final material manufactured from a batch of material. Accordingly, the comment is rejected and the term "batch" is retained in §§ 650.13(c) and 650.15 (a) and (b).

17. Four comments on the Panel's recommendations for tuberculin products and proposed § 650.15(a) expressed concern over the requirement that multiple puncture devices for screening purposes be sufficiently sensitive to elicit reactions in 100 percent of at least 50 persons who are known to have had bacteriologically confirmed tuberculosis. The comments suggested that a margin be permitted for human error and that there is no practical difference in the effectiveness of tuberculin materials that elicit positive reactions in 95 percent of persons tested.

FDA acknowledges, and experience has demonstrated, that certain false positive and false negative reactions are associated with all tuberculin tests. Consequently, the 100 percent reactivity requirement may result in rejection of a satisfactory batch of tuberculin material. Accordingly, the comment is accepted and § 650.15(a) is amended to require that the sensitivity of each batch of tuberculin material be demonstrated to

be sufficient to elicit positive reactions at a 95 percent rate.

18. One comment concerning proposed § 650.15(a) requested a definition of what constitutes a positive skin test reaction for multiple puncture devices. Another comment recommended that a positive test for certain multiple puncture devices be defined as an induration of 2 millimeters (mm) or more at one or more of the puncture sites and a positive Mantoux test be defined as an induration of 5 mm or more.

FDA agrees that the reaction sizes recommended in the comment will ensure that the batch being tested is at least as sensitive as the standard and will define the testing requirements for batches of both liquid tuberculins and tuberculins dried on tines in § 650.15(a). Accordingly, the comment is accepted and § 650.15(a) is amended to require minimum reaction sizes of 2 mm or more at one or more of the puncture sites or at a coalescence of more than one site for all multiple puncture devices and 5 mm or more for the Mantoux test.

19. One comment concerning proposed § 650.15(a) recommended that the proposed standards include defined retest provisions, as has been permitted under § 650.14 concerning animal potency testing.

FDA advises that § 650.15(a) permits additional data to be accumulated to obtain the 95 percent reactivity rate in bacteriologically confirmed tuberculosis subjects by testing additional individuals who react to the 5 TU dose in the Mantoux test. To clarify the retest provisions concerning animal potency tests, the agency is amending § 650.14 by revising the title of the section and by adding the phrase "using results from all valid tests performed" to the last sentence in paragraph (b).

20. One comment on proposed § 650.15(a) questioned the availability of PPD–S for use in characterizing master lots of tuberculin.

FDA advises that the Bureau of Biologics will supply adequate amounts of PPD–S reference material to all manufacturers for use in characterizing tuberculin products.

21. One comment on proposed § 650.15(b) suggested that the requirement for potency testing in the population subgroups specified under paragraph (b)(2) may not be achievable because of the problem of finding such individuals in certain locations in the United States.

FDA believes that manufacturers will be able to locate the population subgroups specified under § 650.15(b). Moreover, the testing is required only for a batch. A batch may be manufactured from large volumes of pooled material and should last for a number of years. Accordingly, the burden imposed by the testing requirement will not be frequent or continuous. For these reasons, the comment is rejected.

22. One comment suggested that proposed § 650.15(b) be modified to require that the effectiveness of each batch of tuberculin material for use by the Mantoux method include a determination of the bioequivalent dose by comparing the product with a standard using dose response curves for two population subgroups known or presumed to be infected with *Mycobacterium tuberculosis* and a third population subgroup composed of persons presumed to be infected with other mycobacteria. The comment suggested that the bioequivalent dose then be verified by comparing the distribution of reaction sizes of the product and standard separately for each of those three population subgroups and a fourth subgroup composed of persons presumed to be without mycobacterial infection.

FDA believes that the use of four separate population subgroups for testing each batch of tuberculin is not warranted. Tuberculin products are primarily intended to diagnose people infected with *Mycobacterium tuberculosis*, and it is necessary only that the selective dose be bioequivalent to the 5 TU of the standard as determined by the dose response assays identified in § 650.15(b). Accordingly, the comment is rejected.

23. One comment on proposed § 650.15 suggested that persons performing the tests will anticipate that their subjects should be positive. Because of this bias, borderline negative reactions for both tests may be read as positive. The comment also suggested that bias would not necessarily be predictive for both the testing material and the control in the same subject because the two tests may be read by different persons and because bias may play a part in one test and not in the other.

FDA agrees that bias may enter into the evaluation of the test results. To preclude such bias, the agency is amending § 650.15 by adding a new paragraph (c) requiring that all trials be performed in randomized double-blind fashion whenever possible and all reactions in each test subject be read by more than one competent and responsible individual.

24. One comment on proposed § 650.15 suggested that the Bureau of Biologics conduct and monitor the human testing that is required of manufacturers in the proposed regulations. The comment provided no reason for the suggestion.

The agency advises that it is the manufacturer's responsibility to conduct testing to develop data supporting the safety, effectiveness, and quality of a drug product. FDA will review the resulting data to determine whether the product is satisfactory for release. Accordingly, the comment is rejected.

Having considered the comments and other relevant information, FDA concludes that the proposal, with changes, is adopted as set forth below.

(a) *Category I. Biological products determined to be safe and effective and not misbranded and which should continue in interstate commerce.* Histoplasmin, Parke, Davis & Co., License No. 1; Tuberculin, Old (Multiple Puncture Device), Lederle Laboratories Division, American Cyanamid Co., License No. 17; Tuberculin, Old (Multiple Puncture Device), Institut Merieux, License No. 384; Tuberculin, PPD (Mantoux) Tubersol®, Connaught Laboratories Limited, License No. 73; Tuberculin, PPD (Mantoux) Aplisol®, Parke, Davis & Co., License No. 1; Tuberculin, PPD, Multiple Puncture Device, (Aplitest) Parke, Davis & Co., License No. 1; and Tuberculin, PPD, Multiple Puncture Device (Heaf), Connaught Laboratories Limited, License No. 73. Licenses remain in effect for these products pending conformance with the Panel's recommendations. Labeling changes recommended by the Panel and now adopted by FDA become effective January 7, 1979.

(b) *Category II. Biological products determined to be unsafe or ineffective or to be misbranded and which should not continue in interstate commerce.* At the request of the manufacturer, Category II product licenses were revoked before publication of the Panel Report, as announced in the **Federal Register** proposal on September 30, 1977 (42 FR 52721).

(c) *Category IIIA. Biological products for which available data are insufficient to classify their safety and effectiveness but which may remain in interstate commerce.* Coccidioidin, Cutter Laboratories, Inc., License No. 8; Coccidioidin, Iatric Corporation, License No. 416; Histoplasmin, Bureau of Laboratories, Michigan Department of Public Health, License No. 99; Diphtheria Toxin for Schick Test, Massachusetts Public Health Biologic Laboratories, License No. 64; and Mumps Skin Test Antigen, Eli Lilly & Co., License No. 56. Licenses remain in

effect for these Category IIIA products pending conformance with the Panel's recommendations and completion of testing in accordance with § 601.25(h) (21 CFR 601.25(h)).

For products now herein classified in Category IIIA for which license revocations have not been issued at the request of the licensee, manufacturers shall submit, on or before August 9, 1979, a written statement of the studies that the licensee proposes to undertake to resolve the questions raised about the products. If no such commitment is made or adequate or appropriate studies are not undertaken, the Commissioner shall institute proceedings to revoke the license (21 CFR 601.25(h)(1)). Licenses for Category IIIA products will remain in effect pending the conduct of studies as recommended by the Panel and adopted by the Commissioner.

Labeling changes recommended by the Panel and now adopted by FDA become effective January 7, 1979.

(d) *Category IIIB. Biological products for which available data are insufficient to classify their safety and effectiveness and which should not continue in interstate commerce.* Product licenses for Category IIIB products were revoked or the products were reclassified to Category IIIA as announced in the **Federal Register** notice of revocations and reclassifications on October 27, 1978 (43 FR 50250).

A summary of the category changes that have been made from those originally recommended by the Panel is as follows:

(1) Data submitted by Eli Lilly & Co. have been found adequate to reclassify its Mumps Skin Test Antigen from Category IIIB to Category IIIA;

(2) Data submitted by Connaught Laboratories Limited have been found adequate to reclassify its Tuberculin, PPD Multiple Puncture Device (Heaf) from Category IIIA to Category I; and

(3) Data submitted by Parke, Davis & Co. with an amended license application for a dye-free, stable product have been found adequate to approve the license amendment and to reclassify the firm's Histoplasmin from Category IIIA to Category I.

In addition, FDA had reclassified Diphtheria Toxin for Schick Test and Schick Test Control, manufactured by Texas Department of Health Resources, from Category IIIB to Category IIIA. However, the establishment and product licenses of this manufacturer were later revoked at the manufacturer's request.

Additional background data and information on which the agency relies in promulgating these regulations are on public display in the office of the Hearing Clerk (HFA-305), Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20857.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 201, 502, 505, 701, 52 Stat. 1040-1042 as amended, 1050-1053 as amended, 1055-1056 as amended (21 U.S.C. 321, 352, 355, 371)), the Public Health Service Act (sec. 351, 58 Stat. 702 as amended (42 U.S.C. 262)), and the Administrative Procedure Act (secs. 4, 10, 60 Stat. 238 and 243 as amended (5 U.S.C. 553, 702, 703, 704)), and under authority delegated to the Commissioner (21 CFR 5.1), Parts 601, 610, and 650 are amended as follows:

PART 601—LICENSING

1. Part 601 is amended in § 601.25 by revising the opening text of paragraph (h)(4) and paragraph (h)(5) to read as follows:

§ 601.25 Review procedures to determine that licensed biological products are safe, effective, and not misbranded under prescribed, recommended, or suggested conditions of use.

* * * * *

(h) * * *

(4) Labeling and promotional material for Bacterial Vaccines and Bacterial Antigens with "No U.S. Standards of Potency" and Skin Test Antigens requiring additional studies shall bear a box statement in the following format: * * *

(5) A written informed consent shall be obtained from participants in the requisite additional studies for Bacterial Vaccines and Bacterial Antigens with "No U.S. Standards of Potency" and Skin Test Antigens, explaining the nature of the product and the investigation. The explanation shall consist of such disclosure and be made so that intelligent and informed consent be given and that a clear opportunity to refuse is presented.

* * * * *

PART 610—GENERAL BIOLOGICAL PRODUCTS STANDARDS

2. Part 610 is amended by revising the introductory paragraph of § 610.13 to read as follows:

§ 610.13 Purity.

Products shall be free of extraneous material except that which is unavoidable in the manufacturing process described in the approved license. In addition, products shall be tested as provided in paragraphs (a) and (b) of this section.

* * * * *

PART 650—ADDITIONAL STANDARDS FOR DIAGNOSTIC SUBSTANCES FOR DERMAL TESTS

3. Part 650 is amended:

a. In § 650.13 by adding new paragraph (c) to read as follows:

§ 650.13 Production.

* * * * *

(c) *Chemical characterization.* Each batch of powdered tuberculin material shall be chemically characterized, including protein, carbohydrate, lipid, and nucleic acid content to assess consistency of production.

b. In § 650.14, by revising the section heading and revising the last sentence of paragraph (b) to read as follows:

§ 650.14 Potency testing in animals.

* * * * *

(b) *Test procedure.* * * * The number of U.S. units in the lot under test shall be estimated from its relationship to the reactivity of the appropriate standard preparation using results from all valid tests performed.

* * * * *

§ 650.15 [Redesignated as § 650.16]

c. By redesignating existing § 650.15 *Equivalent methods* as § 650.16 *Equivalent methods.*

d. By adding new § 650.15 to read as follows:

§ 650.15 Potency testing in humans.

(a) The sensitivity of each batch of tuberculin material for use on multiple puncture devices for screening purposes shall be demonstrated to be sufficient to elicit an induration of 2 millimeters or more at one or more of the puncture sites or at a coalescence of more than one site in at least 95 percent of at least 50 persons who are known to have had bacteriologically confirmed tuberculosis and who are tuberculin positive as demonstrated by a simultaneous Mantoux test that elicits an induration of 5 millimeters or more when tested with 5 TU of Tuberculin, Purified Portein Derivative.

(b) The product effectiveness of each batch of tuberculin material for use by the Mantoux method shall include comparison of the product with the standard by means of (1) dose response curves, and (2) distribution of reaction sizes in persons presumed to be uninfected with *Mycobacterium tuberculosis* or other mycobacteria, in persons known to be infected with *Mycobacterium tuberculosis*, and in persons presumed to be infected with other mycobacteria.

(c) All trials in paragraphs (a) and (b) of this section shall be performed in a

randomized double-blind fashion whenever possible and all reactions in each test subject shall be read by more than one competent and responsible individual.

Effective date. This regulation is effective July 10, 1979, except that recommended labeling changes shall become effective January 7, 1979.

(Secs. 201, 502, 505, 701, 52 Stat. 1040–1042 as amended, 1050–1053 as amended, 1055–1056 as amended (21 U.S.C. 321, 352, 355, 371); sec. 351, 58 Stat. 702 as amended (42 U.S.C. 262); secs. 4, 10, 60 Stat. 238 and 243 as amended (5 U.S.C. 553, 702, 703, 704).)

Dated: June 26, 1979.

Sherwin Gardner,

Acting Commissioner of Food and Drugs.

[FR Doc. 79-21201 Filed 7-9-79; 8:45 am]

BILLING CODE 4110-03-M

FEDERAL EMERGENCY MANAGEMENT AGENCY

44 CFR Part 64

[Docket No. FEMA 5634]

List of Communities With Special Hazard Areas Under the National Flood Insurance Program

AGENCY: Office of Federal Insurance and Hazard Mitigation, Federal Emergency Management Agency.

ACTION: Final rule.

SUMMARY: This rule identifies communities with areas of special flood, mudslide, or erosion hazards as authorized by the National Flood Insurance Program. The identification of such areas is to provide guidance to communities on the reduction of property losses by the adoption of appropriate flood plain management or other measures to minimize damage. It will enable communities to guide future construction, where practicable, away from locations which are threatened by flood or other hazards.

EFFECTIVE DATES: The date listed in the eighth column of the table or 30 days after the date of this **Federal Register** publication (August 9, 1979), whichever is later.

FOR FURTHER INFORMATION CONTACT: Mr. Richard Krimm, National Flood Insurance Program (202) 755–5581 or Toll Free Line 800–424–8872, Room 5270, 451 Seventh Street, SW., Washington, DC 20410.

SUPPLEMENTARY INFORMATION: The Flood Disaster Protection Act of 1973 (Pub. L. 93–234) requires the purchase of flood insurance on and after March 2, 1974, as a condition of receiving any form of Federal or federally related financial assistance for acquisition or construction purposes in an identified flood plain area having special flood hazards that is located within any community participating in the National Flood Insurance Program.

One year after the identification of the community as flood prone, the requirement applies to all identified special flood hazard areas within the United States, so that, after that date, no such financial assistance can legally be provided for acquisition and construction in these areas unless the community has entered the program. The prohibition, however, does not apply to loans by federally regulated, insured, supervised, or approved lending institutions (1) to finance the acquisition of a residential dwelling occupied as a residence prior to March 1, 1976, or one year following identification of the area within which such dwelling is located as an area containing special flood hazards, whichever is later, or made to extend, renew, or increase the financing or refinancing in connection with such a dwelling, (2) to finance the acquisition of a building or structure completed and occupied by a small business concern, as defined by the Director, prior to January 1, 1976, (3) any loan or loans, which in the aggregate do not exceed $5,000, to finance improvements to or rehabilitation of a building or structure occupied as a residence prior to January 1, 1976, or (4) any loan or loans, which in the aggregate do not exceed an amount prescribed by the Director, to finance nonresidential additions or improvements to be used solely for agricultural purposes on a farm.

This 30 day period does not supersede the statutory requirement that a community, whether or not participating in the program, be given the opportunity for a period of six months to establish that it is not seriously flood prone or that such flood hazards as may have existed have been corrected by floodworks or other flood control methods. The six months period shall be considered to begin 30 days after the date of publication in the **Federal Register** or the effective date of the Flood Hazard Boundary Map, whichever is later. Similarly, the one year period a community has to enter the program under section 201(d) of the Flood Disaster Protection Act of 1973 shall be considered to begin 30 days after publication in the **Federal Register** or the effective date of the Flood Hazard Boundary Map, whichever is later.

This identification is made in accordance with Part 64 or Title 44 of the Code of Federal Regulations as authorized by the National Flood Insurance Program (42 U.S.C. 4001–4128).

Section 65.3 is amended by adding in alphabetical sequence a new entry to the table: