The agency does not believe such additional measures are necessary. This CGMP provision does not stand alone but must be read in context with other CGMP regulations. Those regulations provide a variety of safeguards for different stages and aspects of the drug manufacturing process. It is the CGMP regulations, taken as a whole, that help ensure drug quality. Moreover, the consequences of widespread disclosure of problems with drug product quality resulting from a recall or other ameliorative action are sufficiently severe to provide most firms with a continuing incentive to maintain product quality. The agency has carefully reviewed this issue and believes that the final rule will not reduce drug product quality.

IV. Environmental Impact

The agency has determined under 21 CFR 25.24(a)(10) 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.

V. Analysis of Impacts

FDA has examined the impacts of the final rule under Executive Order 12866 and the Regulatory Flexibility Act (Pub. L. 96–354). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this rule is consistent with the regulatory philosophy and principles identified in the Executive Order. The amendments to the CGMP regulations are intended to allow drug manufacturers more flexibility and discretion in manufacturing drug products while maintaining those CGMP requirements necessary to ensure drug product quality. Because this may encourage innovation and the development of more efficient manufacturing procedures that should lead to cost savings for drug manufacturers. In addition, the rule is not a significant regulatory action as defined by the Executive Order and so is not subject to review under the Executive Order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. The agency certifies that the final rule will not have a significant economic impact on a substantial number of small entities. Therefore, under the Regulatory Flexibility Act, no further analysis is required.

List of Subjects in 21 CFR Part 211

Drugs, Labeling, Laboratories, Packaging and containers, Prescription drugs, Reporting and recordkeeping requirements, Warehouses.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 211 is amended as follows:

PART 211—CURRENT GOOD MANUFACTURING PRACTICE FOR FINISHED PHARMACEUTICALS

1. The authority citation for 21 CFR part 211 continues to read as follows:

Authority: Secs. 201, 501, 502, 505, 506, 507, 512, 701, 704 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 351, 352, 355, 356, 357, 360b, 371, 374).

2. Section 211.42 is amended in the introductory text of paragraph (c) by revising the second sentence to read as follows:

§ 211.42 Design and construction features.

* * * * *

(c) * * * There shall be separate or defined areas or such other control systems for the firm's operations as are necessary to prevent contamination or mixups during the course of the following procedures:

* * * * *

3. Section 211.68 is amended by adding a new sentence after the second sentence in paragraph (b) to read as follows:

§ 211.68 Automatic, mechanical, and electronic equipment.

* * * * *

(b) * * * The degree and frequency of input/output verification shall be based on the complexity and reliability of the computer or related system. * * *

4. Section 211.137 is amended by redesignating paragraph (g) as paragraph (h), and by adding new paragraph (g) to read as follows:

§ 211.137 Expiration dating.

* * * * *

(g) New drug products for investigational use are exempt from the requirements of this section, provided that they meet appropriate standards or specifications as demonstrated by stability studies during their use in clinical investigations. Where new drug products for investigational use are to be reconstituted at the time of dispensing, their labeling shall bear expiration information for the reconstituted drug product.

* * * * *

5. Section 211.170 is amended by revising the fourth sentence in the introductory text of paragraph (b) to read as follows:

§ 211.170 Reserve samples.

* * * * *

(b) * * * Except for those for drug products described in paragraph (b)(2) of this section, reserve samples from representative sample lots or batches selected by acceptable statistical procedures shall be examined visually at least once a year for evidence of deterioration unless visual examination would affect the integrity of the reserve sample. * * *

* * * * *

6. Section 211.180 is amended by revising paragraph (e)(1) to read as follows:

§ 211.180 General requirements.

* * * * *

(e) * * *

(1) A review of a representative number of batches, whether approved or rejected, and, where applicable, records associated with the batch.

* * * * *

Dated: January 11, 1995.

William K. Hubbard,

Interim Deputy Commissioner for Policy.

[FR Doc. 95–1361 Filed 1–19–95; 8:45 am]

BILLING CODE 4160–01–F

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[PP 1F4013/R2101; FRL–4930–9]

RIN 2070–AB78

Pesticide Tolerances for Imazethapyr

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This rule establishes tolerances for the sum of the residues of the herbicide imazethapyr, 2-[4,5-dihydro-4-methy1-4-(1-methylethyl)-5-oxo-1*H*-imidazo1-2-yl]-5-ethy1-3-pyridine carboxylic acid, as its ammonium salt and its metabolite, 2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1*H*-imidazol-2-yl]-5-(1-hydroxyethyl)-3-pyridine carboxylic acid, both free and conjugated, in or on

alfalfa, forage and hay at 3.0 parts per million (ppm). The American Cyanamid Co. requested this regulation that establishes the maximum permissible level for residues of the herbicide in or on alfalfa.

EFFECTIVE DATE: This regulation becomes effective January 20, 1995.

ADDRESSES: Written objections and hearing requests, identified by the document control number, [PP 1F4013/R2101], may be submitted to: Hearing Clerk (1900), Environmental Protection Agency, Rm. M3708, 401 M St., SW., Washington, DC 20460. A copy of objections and hearing requests filed with the Hearing Clerk should be identified by the document control number and submitted to: Public Response and Program Resources Branch, Field Operations Division (7506C), Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. In person, bring copy of objections and hearing request to: Rm. 1132, CM #2, 1921 Jefferson Davis Hwy., Arlington, VA 22202. Fees accompanying objections shall be labeled ''Tolerance Petition Fees'' and forwarded to: EPA Headquarters Accounting Operations Branch, OPP (Tolerance Fees), P.O. Box 36277M, Pittsburgh, PA 15251.

FOR FURTHER INFORMATION CONTACT: By mail: Robert J. Taylor, Product Manager (PM) 25, Registration Division (7505C), Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. Office location and telephone number: Rm. 245, CM #2, 1921 Jefferson Davis Hwy., Arlington, VA 22202, (703) 305–6800.

SUPPLEMENTARY INFORMATION: EPA issued a notice, published in the **Federal Register** of March 11, 1992 (57 FR 8658), which announced that the American Cyanamid Co., P.O. Box 400, Princeton, NJ 08540, had submitted pesticide petition (PP) 1F4013 to EPA proposing that 40 CFR part 180 be amended by establishing a tolerance under section 408 of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. 346a, for the combined residues of the herbicide imazethapyr, 2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1*H*-imidazo1-2-y1]-5-ethy1-3-pyridine-carboxylic acid, as its ammonium salt and the metabolite, 2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1*H*-imidazol-2-yl]-5-(1-hydroxyethyl)-3-pyridine carboxylic acid, both free and conjugated, in or on alfalfa, forage and hay at 3.0 ppm.

There were no comments or requests for referral to an advisory committee received in response to the notice of filing. The data submitted in the petition and other relevant material have been evaluated. The toxicology data listed below were considered in support of the tolerance.

1. Several acute toxicology studies placing technical-grade imazethapyr in Toxicity Category III.

2. An 18-month carcinogenicity study with mice fed diets containing 0, 1,000, 5,000, or 10,000 ppm with no carcinogenic effects observed under the conditions of the study at levels up to and including 10,000 ppm (1,500 mg/kg/day) (highest dose tested [HDT]), a systemic no-observed-effect level (NOEL) of 5,000 ppm (750 mg/kg/day), and a systemic LOEL of 10,000 ppm (1,500 mg/kg/day), based on decreased body weight gain in both sexes.

3. A 2-year chronic toxicity/carcinogenicity study in rats fed diets containing 0, 1,000, 5,000, or 10,000 ppm with no carcinogenic effects observed under the conditions of the study at levels up to and including 10,000 ppm (500 mg/kg/day [HDT]) and a systemic NOEL of 10,000 ppm (500 mg/kg/day [HDT]).

4. A l-year feeding study in dogs fed diets containing 0, 1,000, 5,000, or 10,000 ppm with a NOEL of 1,000 ppm (25 mg/kg/day and a LOEL of 5,000 ppm (125 mg/kg/day), based on decreased packed cell volume, hemoglobin, and erythrocytes in females.

5. A developmental toxicity study in rats fed dosage levels of 0, 125, 375, and 1,125 mg/kg/day, with a maternal toxicity NOEL of 375 mg/kg/day and a LOEL of 1,125 mg/kg/day (clinical signs of toxicity) and a developmental toxicity NOEL of greater than 1,125 mg/kg/day (HDT).

6. A developmental toxicity study in rabbits fed dosage levels of 0, 100, 300, and 1,000 mg/kg/day with a maternal toxicity NOEL of 300 mg/kg/day and a LOEL of 1,000 mg/kg/day (death) and a developmental toxicity NOEL of greater than 1,000 mg/kg/day (HDT).

7. A two-generation reproduction study in rats fed dietary levels of 0, 1,000, 5,000, or 10,000 ppm with a NOEL for systemic and reproductive effects of 10,000 ppm (500 mg/kg/day [HDT]).

8. A mutagenic test with *Salmonella typhimurium* (negative); an *in vitro* chromosomal aberration test in Chinese hamster ovary cells (positive without metabolic activation but at dose levels that were toxic to the cells and negative with metabolic activation); an *in vivo* chromosomal aberration test in rat bone marrow cells (negative); an unscheduled DNA synthesis study in rat hepatocytes (negative).

Based on the NOEL of 25 mg/kg bwt/day in the 1-year dog feeding study, and using a hundredfold uncertainty factor, the acceptable daily intake (ADI) for imazethapyr is calculated to be 0.25 mg/kg bwt/day. The theoretical maximum residue contrbution (TMRC) is 0.000100 mg/kg bwt/day for existing tolerances for the overall U.S. population. The current action will not increase the TMRC since no finite residues of imazethapyr are expected from meat and milk derived from animals consuming treated alfalfa. This tolerance and previously established tolerances utilize a total of 0.05 percent of the ADI for the overall U.S. population. For U.S. subgroup populations, nonnursing infants and children aged 1 to 6, the previously established tolerances utilize a total of 0.16 percent of the ADI.

A maximum Tolerated Dose (MTD) or Limit Dose (20,000 ppm) was not evaluated in the chronic toxicity/carcinogenicity study with rats. However, the highest dose tested was within 50 percent of the dose level necessary for an adequate carcinogenicity study in rats (20,000 ppm or 1,000 mg/kg/day); this chemical is structurally similar to two other pesticides (Scepter and Assert) that were not carcinogenic in rats or mice, and the genetic toxicity studies were negative for imazethapyr. For these reasons, no further carcinogenicity testing is required.

Although an analytical method is available for imazethapyr on alfalfa (confirmed by EPA), the Agency has requested that the petitioner rewrite the primary enforcement procedure to include an alternate CE buffer system as the confirmatory step and the petitioner has agreed. This pesticide is useful for the purposes for which the tolerances are sought. The nature of the residues is adequately understood for the purposes of establishing these tolerances. Adequate analytical methodology, capillary electrophoresis, is available for enforcement purposes. Because of the long lead time from establishing this tolerance to publication, enforcement methodology is being made available in the interim to anyone interested in pesticide enforcement when requested by mail from: Calvin Furlow, Public Response and Program Resources Branch, Field Operations Division (7506C), Office Pesticide Programs, Environmental Protection Agency, 401 St., SW., Washington, DC 20460. Office location and telephone number: Rm. 1130A, CM #2, 1921 Jefferson Davis Hwy., Arlington, 22202.

There are currently no actions pending against the registration of this chemical. There is no expectation of residue occurring in meat, milk, poultry,

or eggs from this tolerance. Based on the data and information submitted above, the Agency has determined that the establishment of tolerances by amending 40 CFR part 180 will protect the public health. Therefore, EPA is establishing the tolerance as described 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, Environmental Protection Agency, at the address given above. 40 CFR 178.20. A copy of the objections and/or hearing requests filed with the Hearing Clerk should be submitted to the OPP docket for this rulemaking. The obctions submitted must specify the provisions of the regulation deemed objectionable and the grounds for the objection. 40 CFR 178.25. Each objection must be accompanied by the fee prescribed by 40 CFR 180.33(i). If a hearing is requested, the objections must include a statement of the factual sue(s) on which a hearing is requested, the requestor's intentions on each issue, and a summary of any evidence relied upon by the objector. 40 CFR 178.27. A request for hearing will be granted if the Administrator determines at the material submitted shows the following: There is a genuine and substantial issue of fact; there is a reasonable possibility that available evidence identified by the requestor would, if established, resolve one or more of such issues in favor of the requestor, taking into account uncontested aims or facts to the contrary; and resolution of the factual issue(s) in the manner sought by the requestor would be adequate to justify the action requested. 40 CFR 178.32.

Under Executive Order 12866 (58 FR 51735, Oct. 4, 1993), the Agency must determine whether the regulatory action is ''significant'' and therefore subject to review by the Office of Management and Budget (OMB) and the requirements of the Executive Order. Under section 3(f), the order defines a ''significant regulatory action'' as an action that is likely to result in a rule (1) having an annual effect on the economy of $100 million or more, or adversely and materially affecting a sector the economy, productivity, competition, jobs, the environment, public health or safety, or State, local, or tribal governments or communities (also referred to as ''economically significant''); (2) creating serious inconsistency or otherwise interfering with action taken or planned by another Agency; (3) materially altering the budgetary impacts of entitlement, grants, user fees, or loan programs or the rights and obligations of recipients thereof; or (4) raising novel legal or policy issues arising out of legal mandates, the President's priorities, or the principles set forth in this Executive Order.

Pursuant to the terms of the Executive Order, EPA has determined that this rule is not ''significant'' and is therefore not subject to OMB review. 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 small entities. A certification statement to this effect was published in the **Federal Register** of May 4, 1981 (46 FR 24950).

List of Subjects in 40 CFR Part 180

Environmental protection, Administrative practice and procedure, Agricultural commodities, Pesticides and pests, Reporting and recordkeeping requirements.

Dated: January 9, 1995.

Stephen L. Johnson,

Director, Registration Division, Office of Pesticide Programs.

Therefore, 40 CFR part 180 is amended as follows:

PART 180—[AMENDED]

1. The authority citation for part 180 continues to read as follows:

Authority: 21 U.S.C. 346a and 371.

2. In § 180.447, paragraph (b) is amended by revising the table therein, to read as follows:

§ 180.447 Imazethapyr, ammonium salt; tolerances for residues.

* * * * *

(b) * * *

Commodity	Parts per million
Alfalfa, forage	3.0
Alfalfa, hay	3.0
Peanuts	0.1
Peanuts, hulls	0.1

* * * * *

[FR Doc. 95–1498 Filed 1–19–95; 8:45 am]

BILLING CODE 6560–50–F

40 CFR Part 180

[PP 1F3991/R2102; FRL–4931–1]

RIN 2070–AB78

Pesticide Tolerances for Triclopyr

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This rule establishes a tolerance for residues of the herbicide triclopyr [(3,5,6-trichloro-2-pyridinyl)oxyacetic acid) and its metabolites 3,5,6-trichloro-2-pyridinol and 2-methoxy-3,5,6-trichloropyridine in or on the raw agricultural commodities (RACs) rice grain at 0.3 part per million (ppm) and rice straw at 10.0 ppm, and for triclopyr in poultry meat, poultry fat, and meat byproducts (except kidney) at 0.1 ppm, and eggs at 0.05 ppm. DowElanco requested this regulation that establishes the maximum permissible level for residues of the herbicide in or on the commodities.

EFFECTIVE DATE: This regulation becomes effective January 20, 1995.

ADDRESSES: Written objections and hearing requests, identified by the document control number, [PP 1F3991/R2102], may be submitted to: Hearing Clerk (1900), Environmental Protection Agency, Rm. M3708, 401 M St., SW., Washington, DC 20460. A copy of any objections and hearing request filed with the Hearing Clerk should be identified by the document control number and submitted to: Public Response and Program Resources Branch, Field Operations Division (7506C), Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW, Washington, DC 20460. In person, bring copy of objections and hearing request to: Rm 1132, CM #2, 1921 Jefferson Davis Hwy., Arlington, VA 22202. Fees accompanying objections shall be labeled ''Tolerance Petition Fees'' and forwarded to: EPA Headquarters Accounting Operations Branch, OPP (Tolerance Fees), P.O. Box 36277M, Pittsburgh, PA 15251.

FOR FURTHER INFORMATION CONTACT: By mail: Robert J. Taylor, Product Manager (PM) 25, Registration Division (7505C), Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. Office location and telephone number: Rm. 245, CM #2, 1921 Jefferson Davis Hwy., Arlington, VA 22202, (703) 305–6800.

SUPPLEMENTARY INFORMATION: EPA issued a notice, published in the **Federal Register** of December 13, 1991 (56 FR 65080), which announced that DowElanco, 9330 Zionsville Rd.,