Sunshine Act Meetings

Federal Register
Vol. 51, No. 242
Wednesday, December 17, 1986

This section of the FEDERAL REGISTER contains notices of meetings published under the "Government in the Sunshine Act" (Pub. L. 94-409) 5 U.S.C. 552b(e)(3).

BOARD FOR INTERNATIONAL BROADCASTING

TIME AND DATE: 9:00 a.m., January 12, 1987.

PLACE: Forbes, Inc., The Board Room, 60 Fifth Avenue, New York, New York 10011.

STATUS: Closed, pursuant to 5 U.S.C. 552(b)(c)(1) 22 CFR 1302.4(c) and (h) of the Board's rules (42 FR 9388, March 12, 1977).

MATTERS TO BE CONSIDERED: Matters concerning the broad foreign policy objectives of the United States Government.

CONTACT PERSON FOR ADDITIONAL INFORMATION: Bruce D. Porter, Executive Director, Board for International Broadcasting, Suite 400, 1201 Connecticut Ave., NW., Washington, DC 20036.

Bruce D. Porter,

Executive Director.

[FR Doc. 86-28369 Filed 12-15-86; 12:59 pm]

BILLING CODE 6155-01-M

FEDERAL RESERVE SYSTEM BOARD OF GOVERNORS

"FEDERAL REGISTER" CITATION OF PREVIOUS ANNOUNCEMENT: 51 FR 44565, December 10, 1986.

PREVIOUSLY ANNOUNCED TIME AND DATE OF THE MEETING: 12:00 Noon, Monday, December 15, 1986.

CHANGES IN THE MEETING: Addition of the following closed item(s) to the meeting:

Proposed amendments to the Board's Rules Regarding Delegation of Authority.

CONTACT PERSON FOR MORE INFORMATION: Mr. Joseph R. Coyne, Assistant to the Board; (202) 452-3204.

Dated: December 15, 1986.

James McAfee,

Associate Secretary of the Board.

[FR Doc. 86-28375 Filed 12-15-86; 2:22 pm]

BILLING CODE 6210-01-M

FEDERAL TRADE COMMISSION

"FEDERAL REGISTER" CITATION OF PREVIOUS ANNOUNCEMENT: 51 FR, December 12, 1986, Page No. 44861.

PREVIOUSLY ANNOUNCED TIME AND DATE OF THE MEETING: 2:00 p.m., Monday, December 15, 1986.

CHANGES IN THE AGENDA: The Federal Trade Commission has cancelled its previously announced oral argument at which it was to discuss R.J. Reynolds Tobacco Company, Inc., Docket No. 9206.

Emily H. Rock,

Secretary.

[FR Doc. 86-28405 Filed 12-15-86; 3:46 p.m.]

BILLING CODE 6750-01-M

Corrections

Federal Register
Vol. 51, No. 242
Wednesday, December 17, 1986

This section of the FEDERAL REGISTER contains editorial corrections of previously published Rule, Proposed Rule, and Notice documents. These corrections are prepared by the Office of the Federal Register. Agency prepared corrections are issued as signed documents and appear in the appropriate document categories elsewhere in the issue.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

48 CFR Parts PHS 315 and PHS 352

Acquisition Regulations; Acceptance of Late Proposals

Correction

In rule document 86–27050 beginning on page 43355 in the issue of Tuesday, December 2, 1986, make the following corrections:

1. On page 43356, in the first column, the **DATES** caption should read as follows:

DATES: Effective December 2, 1986.

Comment date: Comments must be received on or before February 2, 1987.

PHS 315.412 [Corrected]

2. On page 43357, in the first column, in paragraph (c)(1) of PHS 315.412, in the tenth line, "FAR 52.215.10" should read "FAR 52.215–10".

PHS 352.215–10 [Corrected]

3. On the same page, in the same column, in the 11th line from the bottom, in PHS 352.215–10, "1983" should read "1986".

BILLING CODE 1505-01-D

DEPARTMENT OF THE INTERIOR

Bureau of Land Management

43 CFR Public Land Order 6629

[ID–943–07–4220–11; I–7322]

Withdrawal of Public Lands for Protection of the Lower Salmon River, ID

Correction

In rule document 86–25653 beginning on page 41104 in the issue of Thursday, November 13, 1986, make the following corrections:

1. On page 41104, in the first column, under **Boise Meridian, Idaho**, the fourth and fifth lines should read "Sec. 10, lots 1, 2, 3, 4, 5, 7, 8, 10, NW¼SE¼;".

2. On the same page, in the second column, the 14th line should read "Sec. 35, W½NW¼.".

BILLING CODE 1505-01-D

Federal Register

Wednesday
December 17, 1986

Part II

Environmental Protection Agency

40 CFR Parts 430 and 431

Pulp, Paper, and Paperboard and the Board Mills Point Source Categories; Best Conventional Pollutant Control Effluent Limitations Guidelines; Final Rule

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Parts 430 and 431

[FRL-3074-7]

Pulp, Paper, and Paperboard and the Builders' Paper and Board Mills Point Source Categories; Best Conventional Pollutant Control Effluent Limitations Guidelines

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: EPA is establishing effluent limitations guidelines based on the "best conventional pollutant control technology" (BCT) for the pulp, paper, and paperboard and the builders' paper and board mills point source categories as required by the Clean Water Act. This final regulation controls the discharge of five-day biochemical oxygen demand (BOD5), total suspended solids (TSS), and pH into waters of the United States by existing sources that produce pulp, paper, and paperboard.

DATES: In accordance with 40 CFR Part 23 (50 FR 7268), this regulation shall be considered issued for purposes of judicial review at 1:00 p.m. Eastern time on January 2, 1987. These regulations shall become effective February 2, 1987.

Under section 509(b)(1) of the Clean Water Act, judicial review of this regulation can be made only by filing a petition for review in the United States Court of Appeals within 90 days after the regulation is considered issued for purposes of judicial review. Under section 509(b)(2) of the Clean Water Act, the requirements in this regulation may not be challenged later in civil or criminal proceedings brought by EPA to enforce these requirements.

ADDRESSES: On January 16, 1987, the complete public record for this rulemaking will be available for review in EPA's Public Information Reference Unit, Room 2404 (Rear) (EPA Library), 401 M Street, SW., Washington, DC. The EPA public information regulation (40 CFR Part 2) provides that a reasonable fee may be charged for copying.

FOR FURTHER INFORMATION CONTACT: Ms. Wendy D. Smith, Industrial Technology Division (WH-552), U.S. Environmental Protection Agency, 401 M Street, SW., Washington, DC 20460 (Phone: (202) 382-7184) or Ms. Debra Maness, Economic Analysis Division (WH-586), U.S. Environmental Protection Agency, 401 M Street, SW., Washington, DC 20460 (Phone: (202) 382-5385).

SUPPLEMENTARY INFORMATION:

I. Legal Authority

EPA is promulgating this regulation under the authority of sections 301, 304, 308, and 501 of the Clean Water Act (the Federal Water Pollution Control Act Amendments of 1972, 33 U.S.C. 1251 et seq., as amended by the Clean Water Act of 1977, Public Law 95-217; also called the "Act").

II. Scope of This Rulemaking

This final regulation applies to the pulp, paper, and paperboard and the builders' paper and board mills point source categories (hereafter known as the pulp, paper, and paperboard industry). These categories are included within the following: U.S. Department of Commerce, Bureau of the Census Standard Industrial Classifications (SIC): 2611 (pulp mills), 2621 (paper mills except building paper mills), 2631 (paperboard mills), and 2661 (building paper and building board mills).

Best conventional pollutant control technology limitations controlling BOD5, TSS, and pH are established for 23 subcategories of the pulp, paper, and paperboard industry which are as follows:

40 CFR Part 430

- Subpart A—unbleached kraft.
- Subpart B—semi-chemical.
- Subpart D—unbleached kraft-neutral-sulfite semi-chemical (cross recovery).
- Subpart E—paperboard from wastepaper.
- Subpart F—dissolving kraft.
- Subpart G—market bleached kraft.
- Subpart H—board, coarse, and tissue (BCT) bleached kraft.
- Subpart I—fine bleached kraft.
- Subpart J—papergrade sulfite (blow pit wash).
- Subpart K—dissolving sulfite pulp.
- Subpart N—groundwood-coarse, molded, and news (CMN) papers.
- Subpart O—groundwood-fine papers.
- Subpart P—soda.
- Subpart Q—deink.
- Subpart R—nonintegrated-fine papers.
- Subpart S—nonintegrated-tissue papers.
- Subpart T—tissue from wastepaper.
- Subpart U—papergrade sulfite (drum-wash).
- Subpart V—unbleached kraft and semi-chemical (BPT limitations for mills in this subcategory are included in subpart D—unbleached kraft-neutral sulfite semi-chemical (cross recovery)).
- Subpart W—wastepaper-molded products.
- Subpart X—nonintegrated-lightweight papers.
- Subpart Y—nonintegrated-filter and nonwoven papers, and,
- Subpart Z—nonintegrated-paperboard.

40 CFR Part 431

- Subpart A—builders' paper and roofing felt.

BCT limitations are not being established for Subpart L of 40 CFR Part 430, the groundwood-chemi-mechanical subcategory. When BAT regulations were promulgated for the pulp, paper, and paperboard industry, this subcategory was excluded from regulation under authority of paragraph 8(a)(iv) of the Revised Settlement Agreement in *NRDC* v. *Costle*, 12 ERC 1833 (1979). New source and pretreatment standards for this subcategory were also not established due to insufficient data. For the same reason, BCT effluent limitations are not being established at this time for this subcategory. (See 46 FR 1446, January 6, 1981).

BCT limitations are also not established for the groundwood-thermo-mechanical subcategory (Subpart M) because insufficient data are available to develop costs and pollutant removals for this subcategory.

III. Background

The Federal Water Pollution Control Act Amendments of 1972 established a comprehensive program to "restore and maintain the chemical, physical, and biological integrity of the Nation's waters." (Section 101(a).) To implement the Act, EPA was required to issue effluent limitations guidelines, pretreatment standards, and new source performance standards for industrial dischargers.

EPA promulgated effluent limitations guidelines based on best practicable control technology currently available and best available technology economically achievable and issued new source performance standards and pretreatment standards for existing and new sources for the pulp, paper, and paperboard industry on November 18, 1982 (47 FR 52006).

The 1977 amendments to the Clean Water Act added section 301(b)(2)(E) establishing "best conventional pollutant control technology" (BCT) for discharges of conventional pollutants from existing industrial point sources. BCT is not an additional limitation but replaces BAT for the control of conventional pollutants. Conventional pollutants are those defined in section 304(a)(4) [biochemical oxygen demand (BOD5), total suspended solids (TSS), fecal coliform, and pH], and any additional pollutants defined by the Administrator as "conventional" (oil and grease, 44 FR 44501, July 30, 1979).

EPA originally published a methodology for carrying out the BCT analysis on August 24, 1979 (44 FR 50732). The core of this methodology was a comparison of the costs of removing additional pounds of conventional pollutants for industry to the costs of removing conventional pollutants for an average-sized publicly owned treatment works (POTW). The 1979 methodology was challenged in the U.S. Court of Appeals for the Fourth Circuit, and on July 28, 1981, the Court issued its decision. *American Paper Institute* v. *EPA*, 660 F2d 954 (4th Cir. 1981). While upholding the methodology that EPA had developed for the POTW cost comparison test, the Court remanded the regulation to the Agency for two reasons. First, the Court held that the Clean Water Act requires EPA to consider two tests of "reasonableness" as part of the BCT methodology: A POTW cost-comparison test and an industry cost-effectiveness test. Since the 1979 methodology contained only the POTW cost test, the Court directed EPA to develop a separate industry cost-effectiveness test. If candidate BCT effluent limitations are not found "reasonable," after evaluation of both tests, then BCT limitations will be established equal to BPT. In no case may BCT be less stringent than BPT. Second, the Court remanded the regulation for EPA to correct certain statistical errors that had been made in calculating the POTW test.

The Agency proposed a revised methodology for the general development of BCT limitations on October 29, 1982 (47 FR 49176). EPA also published new cost information and announced that additional information on the development of the BCT methodology was available on September 20, 1984 (49 FR 37046). The Agency has recently finalized this methodology. Details of the methodology development are presented in the preamble discussing the final BCT methodology (see FR 24974, July 9, 1986).

On January 6, 1981, EPA proposed BCT limitations for the pulp, paper, and paperboard industry (46 FR 1430); these regulations were reproposed in 1982 when the revised BCT methodology was issued in response to the *American Pulp Institute* v. *EPA* decision above (47 FR 49176, October 29, 1982). The final BCT limitations for the pulp, paper, and paperboard industry promulgated today have been developed based on the recently promulgated BCT methodology.

IV. Methodology and Data Gathering Efforts

EPA first proposed BCT limitations for the pulp, paper, and paperboard industry on January 6, 1981. A great amount of technical information used to develop the final BCT limitations was collected prior to that proposal. The methodology and data gathering activities associated with the January 1981 rulemaking are detailed in sections III, IV, and V of the preamble to those proposed rules (46 FR 1430). Following this proposal, the Agency received numerous public comments. In order to respond fully to these comments, EPA engaged in additional data gathering activities. In particular, the Agency obtained discharge monitoring reports (DMR) from Regional and State permitting authorities and collected additional conventional pollutant data under the authority of Section 308 of the Clean Water Act to update its records and broaden the existing data base. These activities are explained in the preamble to the final BPT, BAT, PSES, PSNS, and NSPS regulations for the pulp, paper, and paperboard industry (47 FR 52006, November 18, 1982) and in section II of the *Development Document for Best Conventional Pollutant Control Technology Effluent Limitations Guidelines for the Pulp, Paper, and Paperboard and the Builders' Paper and Board Mills Point Source Categories*, U.S. EPA, Washington, DC August 1986 (hereafter referred to as the *Final Pulp and Paper BCT Development Document*).

The Agency has responded to the issues raised by public commenters, and a summary of these responses may be found in section XII of this preamble, "Public Participation and Responses to Major Comments." A more detailed presentation of comments and responses on the proposed BCT rules can be found in "Summary of Comments and Responses on the Proposed BCT Effluent Limitations Guidelines for the Pulp, Paper, and Paperboard Industry," which is part of the public record for this regulation.

V. Summary of Promulgated Regulations and Changes From Proposal

In reviewing comments on the proposed regulations, the Agency conducted extensive analyses of existing data, new data, and information submitted by the commenters. These analyses are listed in section XIII of this preamble. As a result of these analyses, the Agency made some changes in the control and treatment options considered for the basis of the BCT limitations and in the costs, energy, and non-water quality environmental impacts associated with each treatment option. These changes, including revisions to the cost of each treatment option, are explained in sections III and IV of the *Final Pulp and Paper BCT Development Document*.

In summary, when the BCT limitations were reproposed on October 29, 1982 (47 FR 49176), technology options for three subcategories passed the BCT cost test using the 1982 reproposed BCT methodology: The papergrade sulfite (drum wash), papergrade sulfite (blow pit wash), and the groundwood-thermo-mechanical subcategories. The BCT limitations for these subcategories were proposed based on BPT technology plus in-plant controls which is explained in section VI of this preamble. The remaining twenty-one subcategories failed the reproposed BCT cost test for all technology options; therefore, BCT limitations for these subcategories were proposed equal to BPT.

The final BCT effluent limitations guidelines issued today differ from the proposed regulations in several respects. After the Agency's review of all comments on the proposed rules and further analyses of additional data, EPA made all appropriate changes to the alternative technology options which could serve as the basis for the final limitations and to the costs for incremental conventional pollutant removal for each option. The Agency then applied these revised costs to the two-part BCT cost test that was recently promulgated. As a result, no option for any subcategory in the pulp, paper, and paperboard industry passes the BCT cost test. Therefore, BCT effluent limitations guidelines for each subcategory are set equal to BPT effluent limitations guidelines.

Second, on October 29, 1982, EPA proposed BCT limitations for the groundwood-thermo-mechanical subcategory (subpart M) which were more stringent than the BPT limitations for that subcategory. After proposal, EPA assessed the comments on these proposed effluent limitations guidelines and determined that insufficient data are available to calculate costs and pollutant removals for the four candidate BCT technology options. Therefore, the Agency is not issuing nationally-applicable BCT effluent limitations guidelines for the groundwood-thermo-mechanical subcategory at this time. The BCT effluent limitations guidelines were reserved for this subcategory when the final BPT, BAT, NSPS, PSES, and PSNS regulations were issued on November 18, 1982 and will remain reserved at this time. BCT effluent limitations will be developed on a case-by-case basis by Agency and State permit writers, as appropriate.

A minor change in the format of the originally proposed regulations (January 6, 1981) and reproposed BCT effluent limitations guidelines (October 29, 1982) was made when final BPT, BAT, NSPS, PSES, and PSNS were issued on November 18, 1982. This format change consisted of a reassignment of subpart letters and paragraph numerals; no substantive changes to the existing BPT effluent limitations were made (See 47 FR 52007). The subpart letters and paragraph numerals assigned to each subcategory in the final regulations issued on November 18, 1982 are the same used for the BCT effluent limitations promulgated today. These are listed in Section II of this preamble.

Another minor change involves language to clarify the relationship of 40 CFR Part 430, Subpart D and V. Pursuant to the November 18, 1982 final rule for certain effluent limitations guidelines for the pulp and paper industry, EPA determined that a new subcategory, the Unbleached Kraft and Semi-Chemical Subcategory (40 CFR Part 430, Subpart V), should be established to include all mills within the original unbleached kraft-neutral sulfite semi-chemical (cross recovery) subcategory (40 CFR Part 430, Subpart D) and those mills where both the unbleached kraft and another type of semi-chemical pulping process (i.e., green liquor) are used on site. Available data indicate that there are no significant differences in wastewater or conventional pollutant generation at mills where the neutral sulfite semi-chemical pulping process or any other semi-chemical process are used. See *Development Document for Effluent Limitations Guidelines and Standards for the Pulp, Paper, and Paperboard and the Builders' Paper and Board Mills Point Source Categories*, U.S. EPA, October 1982, pp. 90–92. Accordingly, all effluent limitations guidelines for Subpart D are identical to those in Subpart V.

EPA did not remove Subpart D from the Code of Federal Regulations because of the familiarity of permitting authorities and representatives of affected mills with that subpart. In today's final rule we are adding language in 40 CFR Part 430, Subpart D to clarify that the effluent limitations guidelines under Subpart D are entirely identical to those in Subpart V.

Another change involves the addition of language to five subparts so that all paragraphs in Parts 430 and 431 describing BCT effluent limitations are consistent. BPT regulations for the pulp, paper, and paperboard industry were issued in two phases. The phase II subcategories promulgated on January 6, 1977 (42 FR 1398) specifically addressed the application of BPT limitations to noncontinuous dischargers. The underlying standard for effluent discharges is the same for noncontinuous and continuous dischargers; however, noncontinuous dischargers are only required to meet annual average mass-based effluent limitations rather than be subject to the maximum day or average-of-30-consecutive-days mass-based limitations. The annual average limitations are determined by dividing the average of 30-consecutive-days limitations for BOD*5* and TSS by the appropriate variability factor for each pollutant in each subcategory. Language indicating this procedure is included in the BPT regulations for all Phase II subcategories.

The issue of applying BPT limitations to noncontinuous dischargers was not specifically addressed in the Phase I regulations. Accordingly, the BPT regulations for the Phase I subcategories do not contain language concerning noncontinuous dischargers. Nevertheless, the Agency considers the use of annual average effluent limitations to be the appropriate procedure for BPT/BCT limitations for noncontinuous dischargers in the Phase I subcategories, and in the October 29, 1982 reproposal of the BCT effluent limitations guidelines (47 FR 49176), language specifically addressing noncontinuous dischargers was added for 40 CFR Part 430, Subparts A, B, E, and V. Today's final rule promulgates this language for noncontinuous dischargers for these subparts of 40 CFR Part 430 and for Subpart A of 40 CFR Part 431. The Agency does not consider the new BCT effluent limitations to be different from the BPT effluent limitations that apply for these subcategories. The language simply codifies our procedure for applying BPT, and now BCT, limitations to noncontinuous dischargers.

VI. Control and Treatment Options and Technology Basis for the Final Regulation

A. Control and Treatment Technologies Applicable to the Pulp, Paper, and Paperboard Industry

In the development of effluent limitations guidelines and standards for the pulp, paper, and paperboard industry, EPA assessed various control and treatment technologies that may be employed to reduce pollutant discharges from this industry. An overview of applicable technologies is presented in section VII of the preamble to the proposed rules for the pulp, paper, and paperboard industry (46 FR 1430, January 6, 1981). Detailed descriptions of these technologies can be found in section VII of the development document supporting the proposed rules (*Development Document for Proposed Effluent Limitations Guidelines, New Source Performance Standards, and Pretreatment Standards for the Pulp, Paper, and the Builders' Paper and Board Mills Point Source Categories*, U.S. EPA, December, 1980).

B. Control and Treatment Technologies Considered

An extensive review of the control and treatment technology alternatives available for application in the pulp, paper, and paperboard industry resulted in the identification of several methods for the control of conventional pollutants beyond the level of control provided by the application of BPT effluent limitations guidelines. Four technology options were considered for the basis of the final BCT effluent limitations. Cost estimates for each option were developed by subcategory, and these cost estimates were assessed in light of the recently-promulgated BCT methodology to determine which options, if any, would pass the cost tests. The four options, which are discussed in detail in section III of the *Final Pulp and Paper BCT Development Document*, are summarized below:

- *Option 1*—Base effluent limitations on the model BPT technology for each subcategory plus additional in-plant production process controls. No additional end-of-pipe technology

beyond BPT is contemplated in this option. Effluent limitations would be based on specific controls that include segregation of non-contact cooling water, use of dry barking operations, collection of spills and leaks for reprocessing, increased efficiency of pulp washing, collection and reuse of paper machine spills, improvement in save-all operation, and effluent recycle-reuse. These controls primarily achieve reductions in water use, wastewater discharge, and BOD5 raw waste loading. Implementation of these process controls would improve performance of existing primary and secondary biological treatment systems due to the reductions of raw waste loadings.

- *Option 2*—Base effluent limitations on the addition of chemically-assisted clarification of the BPT final effluents for all integrated and secondary fiber subcategories and for the nonintegrated-fine subcategory (for these subcategories, BPT is based on biological treatment). EPA anticipates that additional solids-contact clarifier(s) would be added using alum as a coagulant and polymer as a flocculant aid. For the remaining nonintegrated subcategories, for which primary treatment was the basis of BPT, effluent limitations would be based on the addition of biological treatment.
- *Option 3*—Base effluent limitations on BCT Option 1 plus the addition of chemically-assisted clarification for all integrated and secondary fiber subcategories and for the nonintegrated-fine papers subcategory (for these subcategories BPT is based on biological treatment). EPA expects that additional solids-contact clarifier(s) would be added using alum as a coagulant and polymer as a flocculant aid. For the remaining nonintegrated subcategories, for which primary treatment was the basis of BPT, effluent limitations would be based on the application of Option 1 plus the addition of biological treatment.
- *Option 4*—Base effluent limitations on the levels attained by best performing mills in the respective subcategories. Best mill performance for a subcategory is generally the average performance at all mills where BPT effluent limitations are attained. The technologies for achieving Option 4 effluent limitations vary depending on the type of treatment systems that are employed at mills in each subcategory. Treatment systems commonly employed at mills in the integrated segment, nonintegrated-fine papers, and deink subcategories in which BPT was based on biological treatment include aerated stabilization basins, activated sludge systems, and oxidation ponds.

EPA expects that aerated stabilization basin treatment systems would be upgraded through the addition of spill prevent and control systems, by increasing aeration capacity, and by providing additional settling capacity. For the nonintegrated-fine papers subcategory, the Agency anticipates that equalization would also be provided. Conversion to the extended aeration activated sludge process was considered to be the probable method of upgrading the performance of aerated stabilization basins located in colder climates.

Activated sludge systems would most likely be upgraded through the addition of spill prevention and control systems, by providing equalization, by increasing the capacity of aeration basins and by providing for operation in the contact stabilization mode, and by increasing the size of clarification and sludge-handling equipment. Ponds would probably be upgraded through the addition of rapid sand filtration to remove algae that can contribute to the discharge of large levels of suspended solids.

At mills in the nonintegrated subcategories in which BPT is based or assumed to be based on primary treatment, EPA assumes that existing primary treatment systems would be upgraded by reducing clarifier overflow rates to provide for better settling, by adding chemical coagulants, and by increasing sludge-handling capability.

At best performing mills in the remaining subcategories (paperboard from wastepaper, tissue from wastepaper, wastepaper-molded products, and builders' paper and roofing felt), extensive use is made of production process controls to reduce wastewater discharge. Therefore, Option 4 for these subcategories is based on the application of the same technologies as discussed in BCT Option 1: the technology on which BPT is based plus the application of additional production process controls.

C. Technology Option Costs and Application to the BCT Methodology

For each subcategory, EPA estimated the costs for each of the four alternative technology options. The development of these costs is detailed in section IV of the *Final Pulp and Paper BCT Development Document*. The actual cost estimates for each candidate technology are also presented.

The costs for each technology option are used to determine if the candidate technology option passes the BCT cost test. EPA evaluated the four technology options considered for the pulp, paper, and paperboard industry by applying the recently promulgated BCT cost test, which consists of two parts: the POTW test and the industry cost-effectiveness test. This methodology is detailed in section II of the BCT Methodology preamble (51 FR 24974).

POTW Test. In general, to "pass" the POTW test, the cost per pound of conventional pollutants removed by industrial dischargers in upgrading from BPT to the candidate BCT level must be less than the cost per pound of conventional pollutants removed in upgrading POTWs from secondary treatment to advanced secondary treatment. For the pulp, paper, and paperboard industry, this upgrade cost must be less than the POTW benchmark of $0.28 per pound (in first quarter 1978 dollars) based on long-term performance data. (See 51 FR 24974 for a description of the use of long-term performance data where available.)

As discussed in section III, conventional pollutants are defined by the Act to include BOD5, TSS, fecal coliform, pH and any additional pollutants defined by the Administrator as "conventional" (oil and grease, 44 FR 44501, July 30, 1979). The pollutants included in calculating the POTW pollutant removal are BOD5 and TSS. These pollutants were also used to calculate the pollutant removal for candidate BCT technology options in the pulp and paper industry. Oil and grease was not included since this conventional pollutant is not generally a concern in the pulp, paper, and paperboard industry. Fecal coliform is also not a general concern for the pulp, paper, and paperboard industries. The pollutant parameter pH is not included in the calculations because control of this pollutant is not measurable as "pounds removed." An acceptable interval for controlling pH is evaluated with respect to the particular processes of a candidate technology. Generally, the acceptable pH interval for BCT will be the same as that for BPT.

Industry Test. Generally, candidate technologies must also "pass" the industry cost-effectiveness test. For each industry subcategory, EPA computes a ratio which is a comparison of two incremental costs. The first is the cost per pound removed by the BCT candidate technology relative to BPT; the second is the cost per pound removed by BPT relative to no treatment (i.e., raw wasteload).

The ratio of the first cost divided by the second is a measure of the candidate technology's cost-effectiveness. The ratio is compared to an industry cost benchmark, which is based on POTW cost and pollutant removal data. If the

industry ratio is lower than the benchmark, the candidate technology passes the industry cost test. The benchmark for the pulp, paper, and paperboard industry, whose ratio is based on long-term performance data, is 1.29.

Application of BCT POTW and Industry Cost Tests. For each subcategory in the pulp, paper, and paperboard industry, EPA applied the costs calculated for each option to the BCT POTW and industry cost test. Results are presented in Table 1.

As shown in Table 1, none of the subcategories in the pulp, paper, and paperboard industry pass both parts of the BCT cost test at any of the four alternative treatment options. Therefore, BCT limitations for each subcategory are set equal to the BPT limitations.

TABLE 1.—SUMMARY OF BCT COST TEST CALCULATIONS FOR PULP, PAPER, AND PAPERBOARD INDUSTRY

[1st Quarter 1978 Dollars]

Subcategory (subpart)	POTW test [1]	Industry cost test [2]
Unbleached Kraft (A):		
BPT	0.24	
Option 1	0.98	4.10
Option 2	1.33	5.57
Option 3	1.31	5.51
Option 4	1.38	5.79
Semi-Chemical (B):		
BPT	0.32	
Option 1	0.66	2.06
Option 2	1.56	4.88
Option 3	1.44	4.52
Option 4	1.43	4.49
Paperboard from Wastepaper (E):		
BPT	0.12	
Option 1	1.22	10.50
Option 2	4.42	38.22
Option 3	2.25	19.42
Option 4	1.22	10.50
Dissolving Kraft (F):		
BPT	0.11	
Option 1	2.07	19.28
Option 2	1.32	12.33
Option 3	1.39	12.98
Option 4	0.63	5.90
Market Bleached Kraft (G):		
BPT	0.18	
Option 1	0.66	3.71
Option 2	1.50	8.41
Option 3	1.45	8.10
Option 4	1.00	5.59
BCT Bleached Kraft (H):		
BPT	0.11	
Option 1	1.39	12.75
Option 2	1.51	13.88
Option 3	1.41	12.99
Option 4	1.04	9.51
Alkaline Fine [3] (I,P):		
BPT	0.14	
Option 1	1.85	13.71
Option 2	1.66	12.29
Option 3	1.52	11.27
Option 4	0.86	6.39
Papergrade Sulfite [4] (J,U):		
BPT	0.26	
Option 1	0.51	1.96
Option 2	1.75	6.67
Option 3	1.40	5.39
Option 4	0.71	2.74
Dissolving Sulfite Pulp (K):		
BPT	0.14	
Option 1	0.70	4.99
Option 2	1.07	7.64
Option 3	1.22	8.69
Option 4	0.64	4.61
Groundwood-CMN Papers (N):		
BPT	0.15	
Option 1	0.59	3.88
Option 2	2.79	18.47
Option 3	1.63	10.78
Option 4	1.02	6.73
Groundwood-Fine Papers (O):		
BPT	0.15	
Option 1	1.05	7.12
Option 2	3.01	20.33
Option 3	1.86	12.58
Option 4	0.99	6.66
Deink (Q):		
BPT	0.09	
Option 1	0.25	2.78
Option 2	1.22	13.83
Option 3	0.72	8.17
Option 4	0.71	8.07
Nonintegrated Fine Papers (R):		
BPT	0.22	
Option 1	0.35	1.62
Option 2	1.95	9.01
Option 3	1.23	5.67
Option 4	0.77	3.57
Nonintegrated Tissue Papers (S):		
BPT	0.28	
Option 1	0.86	3.06
Option 2	3.09	11.02
Option 3	2.80	9.97
Option 4	4.03	14.37
Tissue from Wastepaper (T):		
BPT	0.32	
Option 1	0.74	2.28
Option 2	4.44	13.75
Option 3	3.01	9.32
Option 4	0.74	2.28
Unbleached Kraft and Semi-Chemical (V):		
BPT	0.17	
Option 1	0.63	3.73
Option 2	1.68	9.99
Option 3	1.35	8.02
Option 4	0.94	5.59
Wastepaper Molded Products (W):		
BPT	1.04	
Option 1	1.45	1.40
Option 2	9.21	8.88
Option 3	2.86	2.75
Option 4	1.45	1.40
Nonintegrated Lightweight Papers (X):		
BPT	0.34	
Option 1	0.98	2.91
Option 2	3.16	9.38
Option 3	2.81	8.33
Option 4	4.12	12.21
Nonintegrated Filter and Nonwoven Papers (Y):		
BPT	1.80	
Option 1	1.41	0.78
Option 2	4.47	2.48
Option 3	3.97	2.20
Option 4	5.69	3.16
Nonintegrated Paperboard (Z):		
BPT	0.35	
Option 1	1.79	5.09
Option 2	6.83	19.41
Option 3	6.17	17.56
Option 4	10.09	28.71
Builders' Paper and Roofing Felt (Part 431 Subpart A):		
BPT	0.13	
Option 1	0.86	6.47
Option 2	23.16	173.63
Option 3	1.90	14.25
Option 4	0.86	6.47

[1] POTW test: Total annual cost per pound removed (BPT to BCT).

Candidate technology passes if POTW test is less than $0.28 in 1st Quarter 1978 dollars.

[2] Industry cost test: Total annual cost per pound removed (BPT to BCT) divided by total annual cost per pound removed (raw wasteload to BPT).

Candidate technology passes if industry cost test is less than 1.29.

[3] Includes fine bleached kraft (Subpart I) and soda (Subpart P) subcategories.

[4] Includes blow pit wash (Subpart J) and drum wash (Subpart U) subcategories.

VII. Economic Considerations

A. Costs and Economic Impact

As shown in section VI above, none of the candidate technologies considered as a basis for BCT effluent limitations guidelines for the pulp, paper, and paperboard industry pass the BCT cost test. Since the BCT effluent limitations guidelines are being set equal to the BPT effluent limitations guidelines for each subcategory, there are no incremental costs associated with these BCT regulations, and no adverse economic impacts will occur.

B. Executive Order 12291

Executive Order 12291 requires EPA and other agencies to perform regulatory impact analyses of major regulations. Major rules are those which impose an annual cost on the economy of $100 million or more or have certain other economic impacts. This regulation is not considered a major rule because no incremental costs are associated with attainment of BCT limitations and the regulation meets none of the other criteria specified in section I, paragraph (b) of the Executive Order.

C. Regulatory Flexibility Analysis

Pub. L. 96–354 requires EPA to prepare a Regulatory Flexibility Analysis for all regulations that have a significant impact on a substantial number of small entities. Since no economic impacts are anticipated to result from the final BCT effluent limitations, a formal Regulatory Flexibility Analysis is not required.

VIII. Non-Water Quality Environmental Impacts

Eliminating or reducing one form of pollution may cause other environmental problems. Section 304(b) and 306 of the Act require EPA to consider the non-water quality environmental impacts (including energy requirements) of certain regulations. Since the final BCT effluent limitations promulgated today for the pulp, paper, and paperboard industry to not require any incremental conventional pollutant removal beyond the BPT level, no additional non-water quality impacts (including air pollution, solid waste generation, and energy requirements) are expected.

IX. Upset and Bypass Provisions

A recurring issue of concern has been whether industry guidelines should include provisions authorizing noncompliance with effluent limitations guidelines and standards during periods of "upset" or "bypass." An upset, sometimes called an "excursion," is an unintentional noncompliance occurring for reasons beyond the reasonable control of the permittee. Industry argues that an upset provision in EPA's effluent limitations guidelines is necessary because such upsets inevitably occur even in properly operated control equipment. Because technology-based effluent limitations guidelines require only what technology can achieve, they claim that liability for such situations is improper. When confronted with this issue, courts have been divided on the question of whether an explicit upset or excursion incident may be handled through EPA's exercise of enforcement discretion. Compare, *Marathon Oil Co.* v. *EPA*, 564 F.2d 1253 (9th Cir. 1977) with *Weyerhaeuser Co.* v. *Costle*, 590 F.2d 1011 (D.C. Cir. 1978) and *Corn Refiners Association, Inc.* v. *Costle*, 594 F.2d 1223 (8th Cir. 1979.) See also, *American Petroleum Institute* v. *EPA*, 540 F.2d 1023 (10th Cir. 1976); *CPC International, Inc.* v. *Train*, 540 F.2d 1320 (8th Cir. 1976); *FMC Corp.* v. *Train*, 539 F.2d 973 (4th Cir. 1976).

While an upset is an unintentional episode during which effluent limitations are exceeded, a bypass is an act of intentional noncompliance during which waste treatment facilities are circumvented in emergency situations. Bypass provisions have, in the past, been included in NPDES permits.

EPA has determined that both upset and by-pass provisions should be included in NPDES permits and has promulgated NPDES regulations that include such permit provisions (40 CFR 122.41). The upset provision establishes an upset as an affirmative defense to prosecution for violation of technology-based effluent limitations guidelines. The bypass provision authorizes bypassing to prevent loss of life, personal injury or severe property damage. Permittees in the pulp, paper, and paperboard industry are entitled to upset and bypass provisions in NPDES permits, and this final regulation does not affect the applicability of such provisions.

X. Variances and Modifications

These BCT effluent limitations guidelines must generally be applied in all Federal and State NPDES permits issued to direct dischargers in the pulp, paper, and paperboard industry.

The only exception to the binding limitations is EPA's "fundamentally different factors" variance (see *E.I. duPont de Nemours and Co.* v. *Train*, 430 U.S. 112 (1977); *Weyerhaeuser Co.* v. *Costle*, supra). This variance recognizes factors concerning a particular discharger that are fundamentally different from the factors considered in this rulemaking. This variance clause is included in the NPDES regulations and is cross referenced in the specific pulp, paper, and paperboard industry regulations (see the NPDES regulations at 40 CFR Part 125, Subpart D).

XI. Relationship to NPDES Permits

This regulation does not restrict the power of any permit-issuing authority to act in a manner that is consistent with EPA regulations, guidelines, or policy. For example, the fact that this regulation does not control a particular pollutant does not preclude the permit issuer from limiting such pollutants on a case-by-case basis when necessary to carry out the purposes of the Act. In addition, to the extent that state water quality standards or other provisions of state or Federal law require limitation of pollutants not covered by this regulation (or require more stringent effluent limitations on covered pollutants), the permit-issuing authority must apply such effluent limitations.

One additional topic that warrants discussion is the operation of EPA's NPDES enforcement program, many aspects of which have been considered in developing this regulation. The Agency wishes to emphasize that, although the Clean Water Act is a strict liability statute, the initiation of enforcement proceedings by EPA is discretionary (*Sierra Club* v. *Train*, 557 F.2d 485 (5th Cir. 1977)). EPA has exercised and intends to exercise that discretion in a manner that recognizes and promotes good faith compliance efforts.

XII. Public Participation and Response to Major Comments

Individual pulp, paper, and paperboard facilities and trade associations have participated in the development of this regulation. Following the publication of proposed rules on January 6, 1981 and October 29, 1982 in the **Federal Register**, the technical Development Document, the economic impact analysis, and supporting record materials were made available for public review.

Since proposal, the Agency has received many comments on its technical analysis for BCT effluent limitations in this industry. All comments received have been considered carefully, and appropriate changes in the regulations have been made where data and information supported those changes. All comments received are included in the public record for this rulemaking. A summary of the comments and the responses to these comments is presented in a document entitled "Summary of

Comments and Responses on the Proposed BCT Effluent Limitation Guidelines for the Pulp, Paper, and Paperboard Industry" hereafter referred to as the "Comments and Responses" document. A summary of the Agency's responses to major comments not covered in other sections of this preamble appears below.

1. *Comment:* Permit writers should continue to have maximum flexibility to: (1) Account for site specific conditions, (2) assure water quality protection, and (3) avoid excessively stringent permit conditions.

Response: As explained in Sections XI and XII of this preamble, the promulgated limitations will be applied to individual pulp, paper, and paperboard facilities through NPDES permits issued by EPA or approved State agencies. However, the promulgation of these limitations does not prevent the permitting authority from imposing more stringent limitations on a case-by-case basis using best professional judgment when such limitations are necessary to protect water quality and carry out the purposes of the Clean Water Act.

2. *Comment:* In its cost analyses, EPA should have used actual mill costs for BPT. The industry cost ratio is incorrect if the BPT cost is understated.

Response: EPA obtained some actual cost information as part of its 308 questionnaire data gathering activities in 1976. However, in many cases, the data were not complete, were estimates only, or were unsupported. Therefore, to develop representative costs for the whole industry, EPA used a model mill approach which is explained in Section IV of the *Final Pulp and Paper BCT Development Document.*

3. *Comment:* EPA's general methodology for determining costs is flawed. Specific examples given include: (1) Basing costs on a facility constructed in a moderate climate only, (2) not incorporating geographical cost adjustment factors, and (3) underestimating energy costs. Also, EPA fails to state the acceptable confidence interval for BCT costs.

Response: EPA reviewed all comments on the cost methodology and made all appropriate changes. In response to the specific comments listed above: (1) EPA assessed costs associated with various climates and determined that the costs estimated for moderate climates can be appropriately applied in the BCT costing methodology. Climate is a factor only in the initial choice of the type of biological treatment system, and the BCT option costs are based only on upgrading the existing biological treatment systems. (2) EPA has determined that geographical cost adjustment factors do not significantly impact the total cost; however, cost adjustment factors are presented in the *Final Pulp and Paper BCT Development Document* for informational purposes; (3) EPA has reviewed national energy costs and has determined that the energy cost of $0.0325/kwH is an appropriate estimate for us in the BCT costing methodology. Finally, EPA's costs are pre-engineering cost estimates and are expected to have a variability on the order of plus or minus 30 percent when applied to individual mill situations.

4. *Comment:* Raw waste loads for the unbleached kraft and semi-chemical, dissolving sulfite pulp, papergrade sulfite, nonintegrated segment, and secondary fibers segment subcategories are incorrect.

Response: EPA reviewed all comments on raw waste loads and reassessed its analysis before promulgation of the BCT effluent limitations. All appropriate changes were made and are specifically explained in the "Comments and Responses" document.

5. *Comment:* Raw waste load control measures can not be applied in a universal manner nor can they achieve the same reductions at different mills. Reuse and recycle of process streams may be constrained because of materials of construction, heat buildup, inherent process configuration and capacity, and existing load reduction practices. Specific examples are given to substantiate claims that EPA has overestimated the flow and raw waste load reduction from BPT to BCT Option 1: (1) Reusing relief and flow condensates will not destroy BOD*5*, but would require steam distillation at a considerable cost; (2) TSS is a function of BOD*5* reduction, not BOD*5* influent levels. Thus, at a constant BOD*5* reduction, final TSS levels should not change.

Response: The Agency recognizes the difficulty in predicting the benefits derived from individual process controls, and, for this reason, based BCT Option 1 raw waste loads on actual mill data whenever sufficient data were available. Sufficient data were not available for the dissolving kraft, dissolving sulfite, and groundwood CMN subcategories, however, and, as a result, Option 1 raw waste loads were based on the reductions in flow and BOD*5* that were predicted from the application of the BCT Option 1 process controls.

The Agency has completed an extensive review of mill data to ensure that the estimated effluent reductions from each process control for each subcategory were reasonable. In addition, the Agency reviewed available sources of information to assure that the process controls were suitable for use in the various subcategories and that the combination of controls would obtain the reductions in waste loads predicted for each subcategory. Revisions in the applicability of the process controls and the resulting effluent reductions were made as required. As shown in the Record, EPA performed mass balance calculations to show that if all controls were employed, a mill could meet the reduced levels.

The Agency has compared the raw waste loads determined by the general methodology (average of flows less than the BPT flow and average of BOD*5* levels less than BPT raw waste BOD*5* for most subcategories) with the raw waste loads predicted from the application of BCT Option 1 process controls. The raw waste loads determined by these two methods are comparable in all cases.

The Agency has reviewed BPT and suggested BCT Option 1 process controls, and believes that, if the Option 1 controls are added to a mill that has BPT controls and has a well-operated BCT treatment system in place, the mill can attain the BPT Option 1 effluent levels. The costs of attaining BCT Option 1 limitations are based on model mills for each subcategory assuming that all mills are now meeting BPT limitations.

As explained above, the estimated reductions that can be obtained for each internal control have been reviewed and corrected as necessary. Some examples of EPA's reassessment are:

(1) The reuse of relief and blow condensates has been deleted as an Option 1 internal process control because its use may lead to air quality problems.

(2) The TSS final effluent regression equation is an empirical relationship between influent BOD*5* concentration and TSS final effluent concentration. Although the percentage BOD*5* reduction remains nearly constant in a biosystem after application of flow and BOD*5* reducing process controls, the pounds of BOD*5* removed per ton are decreased by the process controls and the TSS is therefore reduced. The regression equation correctly predicts this within a reasonable degree of certainty.

6. *Comment:* EPA's cost estimates for Option 1 internal controls are underestimated for: (1) Deink mills, (2) unbleached kraft and semi-chemical

mills, and (3) papergrade sulfite pulp mills.

Response: EPA has reviewed the cost estimates for all Option 1 internal controls. In response to the above comments:

(1) EPA has revised the costs for Option 1 controls for deink mills. The Agency added recycle as an Option 1 control for this subcategory and made corresponding changes to the attainable BCT Option 1 final effluent levels.

(2) EPA has reviewed the process controls applicable to the unbleached kraft, semi-chemical, and the unbleached kraft and semi-chemical subcategories. Reuse of condensates has been deleted, the costs of additional brown stock washers have been recalculated, and the costs of buildings and other ancillary equipment have been included.

(3) EPA has derived equations for BPT effluent levels based on the percent sulfite pulp produced at each mill and has determined mill specific levels representative of BPT. BCT Option 1 costs were revised as appropriate.

7. *Comment:* Chemically assisted clarification (CAC) is not an acceptably demonstrated technology nor can it be achieved at the stated costs. Further, the estimated TSS performance levels for Options 2 and 3 are unrealistic. Bench scale tests indicate that CAC will not achieve 15 mg/1 TSS.

Response: EPA has revised its assessment of CAC based on additional data submitted by commenters. On the basis of these new data, long-term average TSS performance levels for Options 2 and 3 have been revised from 15 to 25 mg/1.

8. *Comment:* EPA's use of the BOD5 reduction equation (derived when BPT effluent limitations were developed) to determine best performers in the unbleached kraft, semi-chemical, and unbleached kraft and semi-chemical subcategories is invalid.

Response: EPA reviewed all claims made by commenters concerning the BOD5 reduction equation used for these subcategories. Using additional data representative of these subcategories yields a reduction equation very similar to the one derived at BPT promulgation. The Agency has determined that this equation is applicable to these subcategories and that its use is appropriate to determine the comparison effluent levels (used in place of BPT effluent levels) to identify best performers in these subcategories. Details of the Agency's analysis are explained in the "Comments and Responses" document.

9. *Comment:* EPA should base BCT Option 4 performance on the Discharge Monitoring Report (DMR) data used in the development of final BPT and NSPS issued in November 1982. Deletions of data should be explained.

Response: EPA is basing the BCT Option 4 technology on the most recent and complete DMR data available. The rationale for all data deletions is presented in the administrative record.

10. *Comment:* EPA's approach for establishing BCT Option 4 performance levels for the dissolving sulfite pulp subcategory is incorrect because the Agency transferred technology from the papergrade sulfite pulp subcategory. BCT Option 4 costs for these subcategories are understated.

Response: EPA assessed the claims made by commenters and determined that it is appropriate to transfer technology from the best performing mills in the papergrade sulfite pulp subcategory. There are no data available for mills in the dissolving sulfite pulp subcategory employing treatment systems representative of BPT, the technologies used in the papergrade sulfite pulp subcategory are similar to those that would be employed in the dissolving sulfite pulp subcategory, and the technologies can be readily transferred from the papergrade sulfite pulp subcategory to the dissolving sulfite pulp subcategory because both subcategories have similar processes and products. Therefore, the Agency determined that it is appropriate to use data from mills in the papergrade sulfite pulp subcategory employing BPT treatment systems to develop performance levels for the dissolving sulfite pulp subcategory (see *Tanners' Council of America* v. *Train*, 540 F.2d 1188, Fourth Circuit, 1976). EPA reviewed the BCT Option 4 cost analysis for these subcategories and altered its methodology. As a result, the cost effectiveness ratio is similar to that predicted by the commenter. Details of the Agency's analysis are explained in the "Comments and Responses" document.

11. *Comment:* Costs calculated for BCT Option 4 are understated for: (1) Dissolving kraft mills due to underestimated energy costs and the omission of foam control costs; (2) unbleached kraft and semi-chemical mills because EPA did not consider all factors; (3) paperboard from wastepaper mills; and (4) dissolving sulfite pulp and papergrade sulfite pulp mills due to underestimated sludge disposal costs.

Response: EPA reviewed all BCT Option 4 costs and made all appropriate revisions. Details are presented in the "Comments and Repsonses" document and in the administrative record. In response to specific comments: (1) EPA reviewed energy costs for the dissolving kraft subcategory and determined that these costs are correct. EPA agrees with the commenter that foam control costs for this subcategory were not included in the BCT Option 4 costs. These costs have been considered in the final rulemaking; (2) Each factor cited by the commenters as having been ignored by EPA in developing BCT Option 4 costs for the unbleached kraft and semi-chemical subcategories was included in EPA's cost development, as shown in the administrative record; (3) EPA altered its BCT Option 4 methodology for the paperboard from wastepaper subcategory and used the BCT Option 1 methodology. Also, EPA reviewed the record for the BPT rulemaking and determined that the costs of BPT were overstated. The Agency reassessed its methodology and lowered the BPT costs because too many internal controls were included. These controls are now considered BCT technologies, therefore the costs of these controls were added to the previous BPT estimates. As a result, the costs for BCT Option 4 for this subcategory increased; and (4) The Agency reassessed its sludge disposal costs and made all appropriate revisions based on available data. However, no sludge dewatering or sludge disposal cost information was submitted by the commenters to support the claims that dissolving sulfite pulp and papergrade sulfite pulp Option 4 costs were underestimated.

12. *Comment:* EPA should clarify the definition of each subcategory in the appropriate subpart of the regulations so that permit writers and industry will not be confused in later years when supporting material is unavailable.

Response: The Agency believes that the definition of each subcategory as defined in the November 1982 final rules and in the development document supporting that rule adequately characterizes each subcategory in the pulp, paper, and paperboard industry. It is unnecessary to include any more specific definition in the regulation because permit writers will continue to use the supporting materials in the future when making permit decisions. All development documents supporting pulp, paper, and paperboard industry regulations are important tools for both permit writers and industry representatives and will be available at all times.

13. *Comment:* EPA neglected to incorporate the Fundamentally Different Factors (FDF) variance citation, 40 CFR 125.30–125.32, in the BCT guidelines published on October 29, 1982 for Subparts J, M, U, V, and W. Since EPA

has acknowledged that the FDF variance is available for all limits under sections 301 and 304 of the Clean Water Act, reference to §§ 125.30–125.32 must be included in the BCT regulations for the subparts mentioned above.

Response: The fundamentally different factors variance is independently available to all facilities covered by effluent guidelines by the terms of the regulations at 40 CFR 125.30–125.32. However, to avoid any confusion, EPA has made the appropriate changes to the pulp and paper BCT effluent guidelines.

14. *Comment:* Option 4 costs are underestimated for the papergrade sulfite subcategories because the BPT starting point levels were overestimated. The Agency used the flow versus percent sulfite equation; however, the correct starting point is the Option 4 formula where BOD5 and TSS are related to percent sulfite produced on-site.

Response: The Agency has reviewed and altered its methodology for the papergrade sulfite subcategories. As a result, EPA used the formula relating BOD5 and TSS to percent sulfite produced on-site to identify the best performers in the papergrade sulfite pulp subcategory. EPA also determined the BPT starting point levels as a function of percent sulfite produced on-site. The Agency has now correctly determined the Option 4 removals. The current BCT cost effectiveness ratio is similar to that predicted by the commenter.

XIII. Availability of Technical Information

The major documents on which this regulation is based are: (1) *Development Document for Best Conventional Pollutant Control Technology Effluent Limitations Guidelines for the Pulp, Paper, and Paperboard and the Builders' Paper and Board Mills Point Source Categories* (U.S. EPA, Washington, DC, August 1986), and (2) *Summary of Comments and Responses on the Proposed BCT Effluent Limitations Guidelines for the Pulp, Paper, and Paperboard Industry.*

On January 16, 1987, (30 days after publication in the **Federal Register**), copies of the technical Development Document will be available for public review in EPA's Public Information Reference Unit, Room 2404 (Rear) (EPA Library), 401 M Street, SW., Washington, DC. On January 16, 1987 (30 days after publication in the **Federal Register**), the complete Record, including the Agency's responses to comments on the proposed regulation, will be available for review at the Public Information Reference Unit. The EPA information regulation (40 CFR Part 2) allows the Agency to charge a reasonable fee for copying.

Copies of the technical Development Document may also be obtained from the National Technical Information Service (NTIS), Springfield, Virginia 22161 (703/487–6000). A notice will be published in the **Federal Register** announcing the availability of these documents from NTIS. (This should occur within 60 days of publication of this regulation.)

XIV. Office of Management and Budget (OMB) Review

This regulation was submitted to the Office of Management and Budget (OMB) for review as required by Executive Order 12291. Written comments made by OMB are in the record for this final rulemaking.

List of Subjects in 40 CFR Parts 430 and 431

Paper and paper products industry, Water pollution control, Waste treatment and disposal.

Dated: December 5, 1986.

Lee M. Thomas,

Administrator.

XV—Appendix A

Abbreviations, Acronyms, and Other Terms Used in this Notice

Act—The Clean Water Act.

Agency—The U.S. Environmental Protection Agency.

BAT—The best available technology economically achievable, under section 304(b)(2)(B) of the Act.

BCT—The best conventional pollutant control technology, under section 304(b)(4) of the Act.

BPT—The best practicable control technology currently available, under section 304(b)(1) of the Act.

Clean Water Act—The Federal Water Pollution Control Act Amendments of 1972 (33 U.S.C. 1251 et seq.), as amended by the Clean Water Act of 1977 (Public Law 95–217).

Direct Discharger—A facility where wastewaters are discharged or may be discharged into waters of the United States.

Indirect Discharger—A facility where wastewaters are discharged or may be discharged into a publicly owned treatment works.

New Sources—Industrial facilities which are "new sources" under the definition in section 306 of the Act.

NPDES Permit—A National Pollutant Discharge Elimination System permit issued under section 402 of the Act.

NSPS—New source performance standards, under section 306 of the Act.

POTW or POTWs—Publicly owned treatment works.

PSES—Pretreatment standards for existing sources of indirect discharges, under section 307(b) of the Act.

PSNS—Pretreatment standards for new sources of indirect discharges, under section 307(c) of the Act.

RCRA—Resource Conservation and Recovery Act (Public Law 94–580) of 1976, as amended, 42 U.S.C. 6901 et seq.

For the reasons set out in the preamble, 40 CFR Part 430 is amended as follows:

PART 430—PULP, PAPER, AND PAPERBOARD POINT SOURCE CATEGORY

1. The authority citation for Part 430 continues to read as follows:

Authority: Secs. 301, 304 (b), (c), (e), and (g), 306 (b) and (c), 307 (b) and (c) and 501 of the Clean Water Act (the Federal Water Pollution Control Act Amendments of 1972, as amended by the Clean Water Act of 1977) or the "Act"; 33 U.S.C., 1311, 1314 (b), (c), (e), and (g), 1316 (b) and (c), 1317 (b) and (c) and 1361; 86 Stat. 816, Pub. L. 92–500; 91 Stat. 1567, Pub. L. 95–217.

2. Sections 430.63, 430.73, 430.83, 430.93, 430.103, 430.113, 430.143, 430.153, 430.163, 430.173, 430.183, 430.193, 430.203, 430.213, 430.233, 430.243, 430.253, and 430.263 are revised. The text of each section is identical except for the section number in the heading and the section number referenced at the end of the section. The text of the sections is set out only once. Within the text are two blank spaces, one designated (a) and one designated (b). In the table preceding the text, column (a) indicates the section number to be added to the section heading for the respective subparts of Part 430. Column (b) indicates the section number to be added to the text of the section indicated in column (a).

Subpart	Section Number to be added to section heading (a)	Section Number to be added to text of the section in (a) (b)
F—Dissolving Kraft Subcategory	430.63	430.62
G—Market Bleach Kraft Subcategory	430.73	430.72
H—BCT Bleached Kraft Subcategory	430.83	430.82
I—Fine Bleached Kraft Subcategory	430.93	430.92
J—Papergrade Sulfite (Blow Pit Wash) Subcategory	430.103	430.102
K—Dissolving Sulfite Pulp Subcategory	430.113	430.112
N—Groundwood—CMN Papers Subcategory	430.143	430.142
O—Groundwood—Fine Papers Subcategory	430.153	430.152

Subpart	Section Number to be added to section heading (a)	Section Number to be added to text of the section in (a) (b)
P—Soda Subcategory	430.163	430.162
Q—Deink Subcategory	430.173	430.172
R—Nonintegrated—Fine Papers Subcategory	430.183	430.182
S—Nonintegrated—Tissue Papers Subcategory	430.193	430.192
T—Tissue froom Wastepaper Subcategory	430.203	430.202
U—Papergrade Sulfite (Drum Wash) Subcategory	430.213	430.212
W—Wastepaper—Molded Products Subcategory	430.233	430.232
X—Nonintegrated—Lightweight Papers Subcategory	430.243	430.242
Y—Nonintegrated Filter and Nonwoven Papers Subcategory	430.253	430.252
Z—Nonintegrated—Paperboard Subcategory	430.263	430.262

§ __(a) *Effluent limitations guidelines representing the degree of effluent reduction attainable by the application of the best conventional pollutant control technology (BCT).*

Except as provided in §§ 125.30 through 125.32, any existing point source subject to this subpart shall achieve the following effluent limitations representing the degree of effluent reduction attainable by the application of the best conventional pollutant control technology (BCT): The limitations shall be the same as those specified for conventional pollutants (which are defined in § 401.16) in § __(b) of this subpart for the best practicable control technology currently available (BPT).

3. Section 430.13 is amended by adding text to read as follows:

§ 430.13 Effluent limitations guidelines representing the degree of effluent reduction attainable by the application of the best conventional pollutant control technology (BCT).

Except as provided in §§ 125.30 through 125.32, any existing point source subject to this subpart shall achieve the following effluent limitations representing the degree of effluent reduction attainable by the application of the best conventional pollutant control technology (BCT): The limitations shall be the same as those specified for conventional pollutants (which are defined in § 401.16) in § 430.12 of this subpart for the best practicable control technology currently available (BPT), except that non-continuous dischargers shall not be subject to the maximum day and average-of-30-consecutive-days limitations, but shall be subject to annual average effluent limitations determined by dividing the average-of-30-consecutive-days limitations for BOD*5* by 1.50 and TSS by 1.67.

4. Section 430.23 is amended by adding text to read as follows:

§ 430.23 Effluent limitations guidelines representing the degree of effluent reduction attainable by the application of the best conventional pollutant control technology (BCT).

Except as provided in §§ 125.30 through 125.32, any existing point source subject to this subpart shall achieve the following effluent limitations representing the degree of effluent reduction attainable by the application of the best conventional pollutant control technology (BCT): The limitations shall be the same as those specified for conventional pollutants (which are defined in § 401.16) in § 430.22 of this subpart for the best practicable control technology currently available (BPT), except that non-continuous dischargers shall not be subject to the maximum day and average-of-30-consecutive-days limitations, but shall be subject to annual average effluent limitations determined by dividing the average-of-30-consecutive-days limitations for BOD*5* by 1.36 and TSS by 1.36.

5. Section 430.43 is amended by adding text to read as follows:

§ 430.43 Effluent limitations guidelines representing the degree of effluent reduction attainable by the application of the best conventional pollutant control technology (BCT).

BCT effluent limitations for unbleached kraft-neutral sulfite semi-chemical (cross recovery) mills are presented in Subpart V.

6. Section 430.53 is amended by adding text to read as follows:

§ 430.53 Effluent limitations guidelines representing the degree of effluent reduction attainable by the application of the best conventional pollutant control technology (BCT).

Except as provided in §§ 125.30 through 125.32, any existing point source subject to this subpart shall achieve the following effluent limitations representing the degree of effluent reduction attainable by the application of the best conventional pollutant control technology (BCT): The limitations shall be the same as those specified for conventional pollutants (which are defined in § 401.16) in § 430.52 of this subpart for the best practicable control technology currently available (BPT), except that non-continuous dischargers shall not be subject to the maximum day and average-of-30-consecutive-days limitations, but shall be subject to annual average effluent limitations determined by dividing the average-of-30-consecutive-days limitations for BOD*5* by 1.77 and TSS by 2.18.

7. Section 430.223 is amended by adding text to read as follows:

§ 430.223 Effluent limitations guidelines representing the degree of effluent reduction attainable by the application of the best conventional pollutant control technology (BCT).

Except as provided in §§ 125.30 through 125.32, any existing point source subject to this subpart shall achieve the following effluent limitations representing the degree of effluent reduction attainable by the application of the best conventional pollutant control technology (BCT):

Pollutant or pollutant property	Maximum for any one day [1]	Average of daily values for 30 consecutive days
BOD*5*	8.0	4.0
TSS	12.5	6.25
pH	([2])	([2])

[1] Kg/kkg (or pounds per 1,000 lb of product).
[2] Within the range of 6.0 to 9.0 at all times.

Non-continuous dischargers shall not be subject to the maximum day and average-of-30-consecutive-days limitations, but shall be subject to annual average effluent limitations determined by dividing the average-of-30-consecutive-days limitations for BOD*5* by 1.36 and TSS by 1.75.

For the reasons set out in the preamble, 40 CFR Part 431 is amended as follows:

PART 431—THE BUILDERS' PAPER AND BOARD MILLS POINT SOURCE CATEGORY

1. The authority citation for part 431 continues to read as follows:

Authority: Secs. 301, 304(b), (c), (e), and (g), 306(b) and (c), 307(b) and (c) and 501 of the Clean Water Act (the Federal Water Pollution Control Act Amendments of 1972, as amended by the Clean Water Act of 1977) or the "Act", 33 U.S.C., 1311, 1314(b), (c), (e), and (g), 1316(b) and (c), 1317(b) and (c); and 1361; 86 Stat. 816, Pub. L. 92–500; 91 Stat. 1567, Pub. L. 95–217.

2. Section 431.13 is amended by adding text to read as follows:

§ 431.13 Effluent limitations guidelines representing the degree of effluent reduction attainable by the application of the best conventional pollutant control technology (BCT).

Except as provided in § 125.30–32, any existing point source subject to this subpart shall achieve the following effluent limitations representing the degree of effluent reduction attainable by the application of the best conventional pollutant control technology (BCT): The limitations shall be the same as those specified for conventional pollutants (which are defined in § 401.16) in § 431.12 of this subpart for the best practicable control technology currently available (BPT), except that noncontinuous dischargers shall not be subject to the maximum day and average-of-30-consecutive-days limitations, but shall be subject to annual average effluent limitations determined by dividing the average-of-30-consecutive-days limitations for BOD*5* by 1.90 and TSS by 1.90.

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December 17, 1986

Part III

Department of Health and Human Services

Food and Drug Administration

Dimetridazole; Opportunity for Hearing; Notice

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 86N-0438]

Dimetridazole; Opportunity for Hearing

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA), Center for Veterinary Medicine (Center), is proposing to withdraw approval of new animal drug applications for dimetridazole, and antiprotozoal agent approved for use in turkeys. This action is based on the Center's determination that the drug is not shown to be safe for use (1) because new evidence provides a reasonable basis from which serious questions about the ultimate safety of dimetridazole and the residues that may result from its use may be inferred, (2) because new evidence shows that dimetridazole is no longer shown to be safe by adequate tests by all methods reasonably applicable, and (3) because new evidence shows that the labeled directions for use have not been followed in practice and are not likely to be followed in the future.

DATES: A written appearance requesting a hearing by January 16, 1987; data and analysis on which the request for hearing relies by February 17, 1987.

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

FOR FURTHER INFORMATION CONTACT: Philip J. Frappaolo, Center for Veterinary Medicine (HFV-240), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-4940.

SUPPLEMENTARY INFORMATION:

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I. Introduction

FDA's Center for Veterinary Medicine is providing an opportunity for hearing on a proposal to withdraw approval of the new animal drug applications (NADA's) for dimetridazole and to revoke the new animal drug regulations reflecting approval of the NADA's (21 CFR 520.680, 556.210, and 558.240). Dimetridazole belongs to a class of compounds called 5-nitroimidazoles, some of which are used to treat protozoal diseases in man and other animals. Dimetridazole is approved for use in turkeys (1) for the prevention and treatment and as an aid in the control of blackhead (histomoniasis, infectious enterohepatitis), (2) for growth promotion, and (3) for improved feed efficiency (21 CFR 558.240 and 520.680). Section 558.240 provides for continuous use at 0.015 to 0.02 percent (136 to 182 grams per ton) in feed and for use for not more than 7 days at 0.06 to 0.08 percent (544 to 725 grams per ton) in feed. Section 520.680a provides for continuous use at 0.01 or 0.02 percent in drinking water and for use for 5 days only at 0.04 percent in drinking water. Section 520.680b provides for the use of one 125-milligram tablet for 1 to 10 pound birds and for the use of two 125-milligram tablets for birds weighing more than 10 pounds. The regulations specify a 5-day withdrawal period. In the Federal Register of November 13, 1964 (29 FR 15255), FDA established a tolerance of zero for residues of dimetridazole in the uncooked edible tissues and eggs of turkeys (current 21 CFR 556.210).

This action is being taken in accordance with section 512(e)(1)(B) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360b(e)(1)(B)). That section requires FDA to withdraw approval of an NADA if the agency finds:

> * * * that new evidence not contained in such application or not available to the [FDA] until after such application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the [FDA] when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved * * *.

As discussed in Section III of this notice, the Center has determined that dimetridazole is not shown to be safe for use within the meaning of section 512(e)(1)(B) of the act because new evidence provides a reasonable basis from which serious questions about the ultimate safety of the drug and the residues that may result from its use may be inferred, because new evidence shows that the drug is no longer shown to be safe by adequate tests by all methods reasonably applicable, and because new evidence shows that the labeled directions for use have not been followed in practice and are not likely to be followed in the future. Dimetridazole has been used widely for the treatment and prevention of dysentery in swine, a species in which use of the drug has not been approved. Unless the approvals are withdrawn, the misuse in swine is likely to continue.

II. Relevant NADA'S

A. Affected NADA's

The NADA's for dimetridazole known to the Center and affected by this notice are:

Firm	NADA No.	Date approved
Salsbury Laboratories, Inc.	14-145	Jan. 21, 1964.
Salsbury Laboratories, Inc.	14-345	Nov. 13, 1964.
Salsbury Laboratories, Inc.	14-613	Mar. 19, 1965.

The approval of NADA 36-826 for dimetridazole, held by Albers Milling Co. (a Division of Carnation Co.), was voluntarily withdrawn in response to a letter dated March 6, 1986, from the Center's Associate Director for Surveillance and Compliance (see 51 FR 28764; August 11, 1986). The Associate Director pointed out that § 514.115(d) of FDA's regulations governing administrative actions on applications (21 CFR 514.115(d)) provides for the withdrawal of approval of an NADA upon the written request of the sponsor if the drug that is the subject of the application is no longer being marketed, and suggested that Albers, whose dimetridazole product was not being marketed, might want to withdraw its approval voluntarily under § 514.115(d).

By letter dated March 6, 1986 (Ref.1), the Center's Associate Director for Surveillance and Compliance informed Salsbury Laboratories, Inc. (Robert R. Baron, Director, Regulatory Affairs), 2000 Rockford Rd., Charles City, IA 50616, that the Center had initiated a causal review of the firm's NADA's for dimetridiazole and requested Salsbury to submit to the Center any additional data the firm had pertaining to the drug. Salsbury indicated (Refs. 2 and 3) that it would submit additional data in response to the March 6 letter. It did not do so, however.

By letter dated August 18, 1986 (Ref. 4), the Center's Associate Director for Surveillance and Compliance informed Salsbury that the Center had completed its causal review of the firm's NADA's for dimetridazole. The letter stated that the Center had concluded (1) that new evidence evaluated together with the evidence available when the NADA's were approved shows that the drug is not shown to be safe, and (2) that dimetridazole is not longer shown to be safe by adequate tests by all methods reasonably applicable. (The new evidence and the data required to support continued approval of the applications were summarized in an enclosure accompanying the letter (Ref. 5).) For these reasons, and because of the amount and nature of the scientific studies necessary to establish the safety of dimetridazole, the Associate Director advised Salsbury that, unless it voluntarily withdrew the NADA's within 30 days of receipt of the letter, the Center intended to publish a notice of opportuntiy for hearing on a proposal to withdraw approval of the applications.

Salsbury neither withdrew the NADA's nor responded to the August 18 letter.

B. Other NADA's

In 1973 and 1974, Salsbury submitted supplements to its NADA's 14-345 and 14-613 requesting approval for the use of dimetridazole in the prevention and treatment of swine dysentery. By letters dated June 8, 1973 (Ref. 6) and February 7, 1974 (Ref. 7), Hess & Clark, Inc., which had also submitted NADA's (93-534, 93-535, and 96-406) requesting such approval, authorized FDA to refer to the data in those NADA's and any supplements thereto in the agency's consideration of Salsbury's supplemental applications. Neither Hess & Clark's NADA's nor Salsbury's supplemental NADA's were approved, but some of Hess & Clark's data are relevant to the Salsbury NADA's affected by this notice, as Salsbury recognized (Ref. 2). The data in question are summarized and discussed in Sections III.A(1)(b)(*i*), (2)(b), (3)(a)(*ii*), and III.B(1)(a) and (b) of this notice. Disclosure of those data in such summary form has been authorized by the Director of the Center for Veterinary Medicine pursuant to § 514.11(d) of FDA's regulations governing NADA's (21 CFR 514.11(d)), under the authority delegated to the Director by 21 CFR 5.23.

III. Withdrawal Under Section 512(e)(1)(B) of The Act (The Safety Clause)

A. New Evidence Shows That Dimetridazole is not Shown to be Safe

Under the Safety Clause, "the [Center] must provide a reasonable basis from which serious questions about the ultimate safety of [dimetridazole] and the residues that may result from its use may be inferred." (Diethylstilbestrol; Withdrawal of Approval of New Animal Drug Applications; Commissioner's Decision, 44 FR 54842, 54861; September 21, 1979, *Aff'd, Rhone-Poulenc, Inc., Hess & Clark Div.* v. *FDA*, 636 F.2d 750 (D.C. Cir. 1980).) "Serious questions" can be raised where the evidence is not conclusive, but merely suggestive of an adverse effect. The "serious questions" can relate to adverse effects such as carcinogenicity, tumorigenicity, or another toxicological endpoint. Assuming the Center does provide a basis for questioning dimetridazole's safety, the sponsor will have the ultimate burden of showing the drug's safety (44 FR 54861).

The necessary "serious questions" about dimetridazole's safety can be raised from evidence about either the parent drug or its metabolites. A metabolite is a compound formed in a living organism from the parent drug by chemical or biological mechanisms. Residues of an animal drug in edible tissues will, therefore, be made up not only of the parent drug, but also of its metabolites. Moreover, metabolites can be more toxic than the parent drug and may be responsible for toxic effects seen after its administration. Accordingly, when considering the safety of a new animal drug, all drug-related residues, including metabolites, are to be taken into account. This principle complies with the requirement in section 512(d)(2)(A) of the act that FDA, before approving a new animal drug, evaluate the safety of both the parent drug and "any substance formed in or on food" because of the use of the drug.

For new animal drugs used in food-producing animals, the Center is concerned with intermittent and chronic exposure of people to relatively low concentrations of residues. The Center tailors the type of toxicological testing needed for a showing of safety for a specific drug by considering its proposed use in the animals whose tissues we eat, the probable exposure of people to the parent drug and its metabolites (residues) under its conditions of use, their possible biological effects as deduced by structure-activity relationships, and their effects as observed in biological systems. (See section 512(d)(2) of the act; 21 CFR 514.1(b)(8)(iii); and FDA guidelines concerning "General Principles for Evaluating the Safety of Compounds used in Food-Producing Animals" (Ref. 8), the availability of which was announced in a notice published in the Federal Register of October 31, 1985 (50 FR 45556).)

The purpose of the toxicological studies is to define the biological effects of the sponsored drug. An important part of that definition is the relationship between the amount of the test substance and the observed biological effect. The Center always requires testing of the sponsored xenobiotic drug. The Center may also require separate testing of a metabolite when such testing is necessary to define adequately the biological effect of the sponsored drug. For a carcinogen, the Center calculates the safe concentration for residues from the tumor data using a statistical extrapolation procedure; for other toxicological endpoints, the Center calculates the safe concentration for residues from the no-observed-effect-level using a safety factor approach.

In this case, the Center has concluded that new evidence requires that Salsbury conduct chronic bioassays to resolve questions about the carcinogenicity of dimetridazole (see Sections III.A(1) and B(1)(a) of this notice). Without the results of such studies, it is impossible to establish a safe concentration for the drug.

(1) New evidence of toxicity

(a) *Genetic toxicity.* There is an extensive data base on the correlation between the results in bacterial mutagenicity assays and carcinogenicity as determined by long-term whole animal studies (Refs. 9, 10, and 11). These data demonstrate that mutagenicity in bacteria is a reliable indication that a chemical is likely to be carcinogenic. In addition, correlative studies for the oncogenic potential of 60 chemicals have demonstrated that the sex-linked recessive lethal test in *Drosophila melanogaster* has a high degree of detection capability both for direct-acting carcinogens and procarcinogens (Refs. 12 through 15).

Dimetridazole has been shown to be mutagenic in a variety of in vitro bacterial tests including (1) *Salmonella typhimurium* (tester strains TA100, TA100–FR$_1$, TA1530, his G46, TA1531, TA1532, TA1534) (Ames test) (Refs. 16 through 19), (2) *Klebsiella pneumoniae* (Refs. 18 and 20), (3) *Escherichia coli* (Ref. 20), and (4) *Citrobacter freundii* (Refs. 18 and 20).

Genotoxic activity associated with dimetridazole has also been demonstrated in the sex-linked recessive lethal test using *Drosophila melanogaster* (Ref. 21). Significant dose-dependent dimetridazole-induced enhancements of sex-linked recessive lethality were observed in a feeding study in larvae.

As a class of compounds, 5-nitroimidazoles are mutagenic in a number of different assay systems (Refs. 9 through 33). At least 20 5-nitroimidazoles have been demonstrated to be mutagenic to *S. typhimurium* tester strain TA100 (Refs. 22 and 23). Included among these are several 5-nitroimidazoles that are structural analogs of dimetridazole, i.e., ipronidazole, ronidazole, metronidazole, 2-methyl-5-nitroimidazole, ornidazole, nimorazole, tinidazole, carnidazole, and azanidazole. These data indicate that any 5-nitroimidazole, whether a parent compound or a metabolite, could be carcinogenic.

Metronidazole and ipronidazole are mutagenic in the same bacterial assay systems as dimetridazole (Refs. 20 and 24). These systems include several tester strains of *S. typhimurium, E. coli, K. pneumoniae,* and *C. freundii.* The fact that all three compounds are mutagenic in the same test systems is especially noteworthy because metronidazole and ipronidazole have each been shown to be carcinogenic in mice (see Section III.A(1)(b) of this notice).

Numerous reports describe the mutagenic activity of metronidazole in the Ames test (Refs. 16, 17, and 25 through 28). Potent mutagenic activity resulting from metronidazole treatment has been observed in the eukaryotic microorganism *Neurospora crassa* as well (Refs. 29 and 30).

Metabolites of metronidazole have also been reported to be mutagenic in the Ames test (Refs. 27, 31, and 32). Mutagenic activity in the Ames test was found in the urine of 10 patients given therapeutic doses of metronidazole orally or per vagina and was associated with parent drug and metabolites (Refs. 31). In another study, also using the Ames test, significant mutagenic activity was detected in the urine of six female patients taking metronidazole (Ref. 27). In a third study, the urine of two patients receiving therapeutic doses of metronidazole was found to have mutagenic activity in the Ames test (Ref. 32).

Ronidazole, another structural analog of dimetridazole, is also mutagenic in *S. typhimurium* tester strains his G46, TA1530, TA1531, TA1532, TA1534, TA1535, TA98, and TA100, *K. pneumoniae, E. coli,* and *C. freundii* (Refs. 9, 20, and 33). In addition, ronidazole caused sex-linked recessive lethal mutations in *Drosophila melanogaster* (Ref. 21).

The fact that dimetridazole in particular and 5-nitroimidazoles in general are mutagenic in bacterial and *Drosophila* systems raises serious questions about the carcinogenicity of dimetridazole and its metabolites. In addition, the fact that the metabolites of a closely related compound, metronidazole, are mutagenic raises serious questions about the safety of the metabolites of dimetridazole.

(b) *Tumorigenicity.* Dimetridazole and metronidazole have been shown to cause an increase in mammary tumors in rats. In addition, ipronidazole and metronidazole are both demonstrated carcinogens in mice. The fact that dimetridazole is a tumorigen in rats and that dimetridazole is structurally closely related to two demonstrated carcinogens raises serious questions about the carcinogenicity of dimetridazole. Indeed, dimetridazole has been predicted to be a carcinogen on the basis of computer-assisted structure activity relationship studies, using pattern recognition methods (Ref. 34).

(*i*) *Dimetridazole causes a significant increase in tumors in rats.* In a feeding study in female Sprague-Dawley rats, dimetridazole caused a significant increase ($P<0.001$) in adenofibromas of the mammary gland (Ref. 35). Thirty-five rats were fed dimetridazole at a concentration of 0.2 percent in the diet for 46 weeks, followed by a control diet for an additional 20 weeks. Adenofibromas were present in 25 of the treated rats but in only 4 of the control rats at the end of the study. Dimetridazole also increased the multiplicity of mammary tumors in experimental animals (mean=1.7 tumors per tumor-bearing rat in the dosed group versus 1.0 tumor per tumor-bearing rat in the control group). Mammary adenocarcinomas were not seen in the control or in the treated rats.

In 1976, Hess & Clark, Inc., submitted a long-term (122 week) feeding study in Carworth CFY rats entitled "Dimetridazole (Emtryl): Tumorigenicity in Rats," which was conducted by May & Baker, LTD (Ref. 86). Groups of 50 male and 50 female rats received 0, 100, 400, or 2,000 parts per million (ppm) dimetridazole in the diet for 122 weeks. All surviving animals were sacrificed during the 123rd week of dosing. In the study, dimetridazole caused a dose-related increase in mammary adenofibromas in male and female rats in the two highest dose groups. This increase was evidenced both by an increase in the number of rats with tumors and in the number of tumors per tumor-bearing rat.

The Center has concluded that each of these feeding studies demonstrates that dimetridazole is tumorigenic in rats and raises serious questions about the carcinogenicity of the drug. The studies cannot answer those questions because they are inadequate to assess the cumulative effects of exposure to dimetridazole and its metabolites. The flaws in each study are in Section III.B(1)(a) of this notice.

The occurrence of benign tumors raises the strong possibility that the agent in question is also carcinogenic because compounds that induce benign neoplasms frequently induce malignant neoplasms (Ref. 36). In addition, benign neoplasms may be an early stage in a multi-step carcinogenic process and they may progress to malignant neoplasms; moreover, benign neoplasms themselves may jeopardize the health and life of the host. For these reasons, if a substance is found to induce benign neoplasms in experimental animals it should be regarded as a potential hazard to human health requiring further evaluation (Ref. 36). Indeed, the results of a bioassay

provide "some evidence of carcinogenicity" when the study exhibits a chemically related increased incidence of benign neoplasms, even when those tumors may not progress to malignant neoplasms (51 FR 11843, 11844; April 7, 1986).

(*ii*) *Dimetridazole is structurally related to demonstrated carcinogens.* Ipronidazole and metronidazole, which are structurally related to dimetridazole, have been shown to be carcinogenic in mice. The fact that two structurally related compounds are demonstrated carcinogens strengthens the Center's concerns about the carcinogenicity of dimetridazole.

Ipronidazole was administered to Charles River CD–1 mice orally in their diet at a concentration of 0, 20, 200, and 1,000 ppm (Ref. 37). This study, which was conducted between 1977 and 1979, was designed to end at 104 weeks or at 20 percent survival, whichever occurred first. It ended at week 89 for the males and at week 100 for the females. Ipronidazole caused a significant increase in adenomas and adenomas plus carcinomas of the lung in male and female mice. Based upon these data, the Center has concluded that ipronidazole is a carcinogen.

BALB/c/Cb/Se mice (33 males and 34 females) were administered 66 milligrams per kilogram per day metronidazole in an aqueous solution by a stomach tube for 100 days (Ref. 38). Animals were sacrificed at the 80th week after the start of treatment (earlier if moribund). Metronidazole caused a significant increase ($P<0.001$) in lung tumors in males and a significant increase ($P<0.001$) in lymphocytic lymphomas in females.

In a study by Rustia and Shubik (Ref. 39), metronidazole again significantly increased the incidence of lung tumors in mice. Swiss mice were divided into five groups and given metronidazole in their diet for up to 120 weeks as follows: Group 1, 36 males and 36 females, 0.5 percent metronidazole; Group 2, 20 males and 20 females, 0.3 percent metronidazole; Group 3, 20 males and 20 females, 0.15 percent metronidazole; Group 4, 10 males and 10 females, 0.06 percent metronidazole; Group 5, 70 males and 70 females, 0.0 percent metronidazole. Metronidazole caused significant increases in the incidence of lung tumors in both male and female mice in the three highest dose groups when compared to controls. (For the 0.5 percent group, $P<.001$ in males and $P<0.01$ in females; for the 0.3 percent group, $P<0.001$ in both males and females; for the 0.15 percent group, $P<0.005$ in males and $P<0.025$ in females.) In addition, the drug caused significant increases ($P<0.010$ for the 0.5 percent group; $P<0.050$ for the 0.3 percent group) in the incidence of malignant lymphomas in female animals when compared to controls.

Rust (Ref. 40) also reported a dose-related increase in lung tumors in both male and female CF_1 albino mice fed 0, 75, 150, or 600 milligrams per kilogram per day metronidazole for 92 weeks and then sacrificed. Sixty males and 60 females were in the control group and 40 males and 40 females were in each of the treatment groups. The incidence of lung tumors increased with increased dietary exposure to metronidazole in both male and female mice.

Two papers (Refs. 41 and 42) describe chronic feeding studies in rats using metronidazole. Both studies demonstrate that, when fed to rats, metronidazole is tumorigenic.

Sas:MRC(WI)BR rats received metronidazole at 0, 0.06, 0.3, and 0.6 percent of their diet for up to 150 weeks. Each treatment group contained 30 males and 30 females; the control group had 100 males and 100 females. Metronidazole caused a significant incidence ($P<0.020$) of mammary fibroadenomas in females given the highest dose; animals given the two lower doses developed an increased but not statistically significant incidence of these tumors when compared to controls. The multiplicity of fibroadenomas was also increased significantly ($P<0.010$) in animals given the highest dose. The multiplicity of fibroadenomas increased with increasing dose. The number of mammary tumors in male rats was increased, but the increase was not statistically significant. In addition, the drug caused a significant increase (23.3 percent in the 0.6 percent group versus 0 percent in the controls) in hepatic tumors in high-dose females when compared to controls (Ref. 41).

A second study in rats gave similar results (Ref. 42). Fifty male and 50 female Sprague-Dawley rats were administered 30 milligrams per kilogram metronidazole in aqueous solution by stomach tube daily for 100 days; the control group also contained 50 males and 50 females. Rats were sacrificed after a long latency period (>120 weeks). Metronidazole caused a significant increase ($P<0.001$) in mammary tumors in female rats treated with metronidazole when compared to controls. Thirty-six (72 percent) of the 50 treated female rats had a total of 62 mammary tumors (1.72 tumors per tumor-bearing rat). There were 28 fibroadenomas, 18 adenomas, 11 fibromas, and 5 carcinomas. Fifteen (30 percent) of the female control rats had a total of 17 mammary tumors (1.13 tumors per tumor-bearing rate. There were nine fibroadenomas and eight adenomas.

(c) *Toxicity of metabolites.* As discussed in Section III.A(2) of this notice, the Center has concluded that several pathways account for the metabolism of dimetridazole in turkeys. Some of the metabolites and their toxicity are discussed below.

(*i*) *Metabolites containing a nitro group.* Reduction of the nitro group is a major step in the metabolism of nitroheterocyclic compounds (Refs. 43 and 44). The nitro group is believed to be reduced stepwise via nitroso and hydroxylamino intermediates to the amine. These intermediates, particularly the hydroxylamino, can covalently bind to protein or deoxyribonucleic acid (DNA). Binding of chemical electrophiles to cellular macromolecules is accepted as the mechanism by which most chemical carcinogens initiate the neoplastic process (Refs. 45 and 46). The carcinogenic activity of many nitroheterocyclic compounds such as the 5-nitroimidazoles may be associated, in part, with the presence of the 5-nitro group (Refs. 43, 47, and 48).

Several metabolites of dimetridazole in turkeys retain a nitro group. These metabolites are 2-hydroxymethyl-1-methyl-5-nitroimidazole (HMMNI), 1-methyl-5-nitroimidazole-2-carboxylic acid (MNICA), 2-hydroxymethyl-1-methyl-5-nitro-imidazole sulfate, and 2-hydroxymethyl-1-methyl-5-nitroimidazole glucuronide (see Section III.A(2) of this notice). Given the toxicity of nitro-containing compounds, the Center regards as a suspect carcinogen any metabolite of dimetridazole that retains a nitro group.

(*ii*) *2-Hydroxymethyl-1-methyl-5-nitroimidazole (HMMNI) and 1-methyl-5-nitroimidazole-2-carboxylic acid (MNICA).* A demonstrated metabolite of dimetridazole is HMMNI, which results from oxidation at the 2-methyl group of dimetridazole (see Section III.A(2)(a) of this notice). When tested in vitro with TA1535, the analogous 2-hydroxymethyl metabolite of metronidazole was some 5 to 10 times more mutagenically active than parent drug metronidazole (Ref. 32). Similar mutagenic activity would be expected for HMMNI.

Metabolites of metronidazole in the urine of patients receiving therapeutic doses of the drug were found to be mutagenic when tested in vitro with TA1535 (Ref. 31). Metabolites were separated prior to mutagenicity testing, and each was identified by its R_f value. Mutagenic activity was associated with the areas where 1-(hydroxyethyl)-5-nitroimidazole-2-carboxylic acid and 1-

(2-hydroxyethyl)-2-hydroxymethyl-5-nitroimidazole would be expected to migrate. Based upon this study, the Center believes that HMMNI and MNICA, the structural analogs of the mutagenic metabolites of metronidazole, would be mutagens and therefore suspect carcinogens.

The Center's concern about the mutagenicity of HMMNI and MNICA are supported by the fact that both of these compounds retain a nitro group, which is associated with mutagenic activity (Refs. 43, 47, and 48).

(*iii*) *Acetamide.* One postulated metabolite of dimetridazole is acetamide, which results from ring scission. In each of two feeding studies in rats, acetamide was shown to cause hepatic tumors (Refs. 49 and 50). In one experiment (Ref. 49), 4 groups of 25 1-month old male Wistar rats were fed a diet containing 0, 1.25, 2.5, or 5 percent acetamide for 1 year. One rat per group was sacrificed each month; the remaining rats were sacrificed after 1 year. Liver tumors (most of them described as trabecular carcinomas and some as adenocarcinomas with lung metastases) were seen in 4/24, 6/22, and 1/18 rats available for examination from the low-, medium-, and high-dose groups, respectively. The first liver tumor was seen after 16 weeks. No liver tumors occurred in any of the 25 controls. Another group of 50 male Wistar rats was fed 5 percent acetamide continuously in the diet. For the first 26 weeks of the experiment, a rat was sacrificed each week; for the remainder of the experiment, one rat was sacrificed every other week. Liver tumors (described as being trabecular carcinomas and some as adenocarcinomas with lung metastases) were observed in 4/48 rats treated for 38 to 52 weeks, compared with 0/43 in controls. In another 52-week experiment (Ref. 49), acetamide was administered at a concentration of 5 percent in the diet to 99 male Wistar rats. Each week, the treatment of two rats was stopped and they were returned to a control diet for the remainder of the year. Liver tumors were found in 22/81 rats autopsied.

In another study (Ref. 50), 2 groups of 40 male Wistar rats were fed diets containing 2.5 percent acetamide or 2.5 percent acetamide plus 5.6 percent L-arginine-L-glutamate, and 2 groups of 15 male Wistar rats were fed a diet containing 5.6 percent of the dipeptide or a control diet for 1 year. In 2/8 rats fed acetamide and available for examination after 1 year, hepatomas were observed; 7/16 rats fed acetamide for 1 year and maintained on a control diet for an additional 3 months developed liver tumors. By contrast, 1/11 rats that received acetamide plus the dipeptide for 1 year and that were available for examination developed a hepatoma, and 1/19 rats receiving such a diet for 1 year and the control diet for 3 months had hyperplastic liver nodules. No liver tumors occurred in the control group or in rats fed 5.6 percent of the dipeptide alone.

The International Agency for Research on Cancer (Ref. 51) concluded that these studies show that acetamide is carcinogenic in rats. The Center agrees.

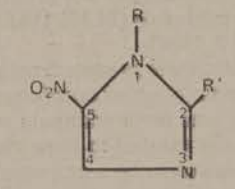
(*iv*) *Other metabolites.* The Center has identified several other possible metabolites of dimetridazole (see Section II.A(2) of this notice). The safety of these metabolites, including the covalently bound residues of dimetridazole, has not been established.

(d) *Center's conclusions.* The Center has concluded that there are serious questions about the carcinogenicity of dimetridazole and its metabolites. As discussed above, this conclusion is based on the results of feeding studies with dimetridazole, with structurally related compounds, and with acetamide. The Center's conclusion is also based on the results of genetic toxicity tests with dimetridazole and structurally related compounds. Because the Center has concluded that both of the existing feeding studies with dimetridazole in rats are seriously flawed (see Section III.B(1)(a) of this notice), neither is suitable for calculating a safe concentration for the total residue of dimetridazole (see Section III.B(1)(a) of this notice). The questions about the carcinogenicity of dimetridazole can only be answered by adequate chronic bioassays in two rodent species.

(2) The Metabolism of Dimetridazole

The 5-nitroimidazoles undergo extensive metabolism. The biotransformations generally include or are postulated to include (1) changes (oxidation or reduction) with the ring structure remaining intact and (2) scission of the ring. In order to describe as fully as possible the metabolic pathways open to dimetridazole, the Center has summarized research on the metabolism of ornidazole, metronidazole, and ronidazole in addition to data on the metabolism of dimetridazole in turkeys and swine. Structually, ornidazole and metronidazole differ from dimetridazole only in the substituent on the 1-nitrogen; ronidazole differs from dimetridazole by having a methyl carbamate rather than a methyl group at the 2-position of the ring (see Figure 1).

Figure 1



Dimetridazole, $R=CH_3$, $R'=CH_3$

Ronidazole, $R=CH_3$, $R'=CH_2OCNH_2$ (O)

Ornidazole, $R=CH_2CH(OH)CH_2Cl$, $R'=CH_3$

Metronidazole, $R=CH_2CH_2OH$, $R'=CH_3$

Based on the information summarized below with respect to the metabolism of 5-nitroimidazoles, the Center has reached the following conclusions about the metabolism of dimetridazole:

1. Dimetridazole in turkeys likely undergoes extensive metabolism.

2. Ring intact metabolites result mainly from oxidation at the 2-methyl group.

3. Ring scission can take place, leading to acetamide. In addition, some radioactivity probably becomes incorporated into natural components via fragments from dimetridazole.

4. Dimetridazole would be expected to yield covalently bound residues, based on research demonstrating the ability of ronidazole to bind covalently with amino acids and proteins.

(a) *Dimetridazole in turkeys.* The basic metabolic routes for dimetridazole in turkeys are shown in Figure 2. The study on which this Figure is based is discussed in detail in Sections III.B(1)(b) and (c) of this notice (Ref. 85). Paper chromatographic examination of urine and water soluble extracts of feces revealed dimetridazole, HMMNI, MNICA, and the sulfate conjugate of HMMNI. A fifth metabolite was postulated to be the glucuronide of HMMNI. Two other metabolites were detected but not identified.

(b) *Dimetridazole in swine.* Dimetridazole, labeled with ^{14}C in the N-methyl group, was administered orally to two pigs in a single dose of 29.8 milligrams per kilogram or 16.6 milligram per kilogram; the animals were sacrificed 6 or 17 hours after dosing, respectively (Ref. 52). Samples of urine and tissues taken at sacrifice were examined by several techniques, including paper and thin layer

chromatography, electrophoresis, and automatic amino acid analysis, for isotopically labeled products.

In the tissues of the pig sacrificed at 6 hours after dosing, three residues were identified: Dimetridazole, HMMNI, and MNICA. The results of analyses for these compounds are given in Table 1. These data show that a large portion of the residue remains uncharacterized, particularly in liver.

TABLE 1

Compound	Amount of compound present					
	As percent of total ^{14}C in specified tissue			In ppm		
	Muscle	Kidney	Liver	Muscle	Kidney	Liver
Dimetridazole	0.5	0.5	0.07	0.04	0.18	0.01
HMMNI	40.2	25.7	0.5	3.56	10.31	0.09
MNICA	13.8	3.6	(1)	1.33	1.55	(1)
Total	54.5	29.8	0.57	4.93	12.04	0.10

[1] Not detected.

Based on the data for turkeys and swine, the Center believes that the pathways shown in Figures 2, 3, and 4 account for the metabolism for dimetridazole in both species.

Figure 2. Oxidative and Reductive Pathways for 1,2-Disubstituted-5-Nitroimidazoles

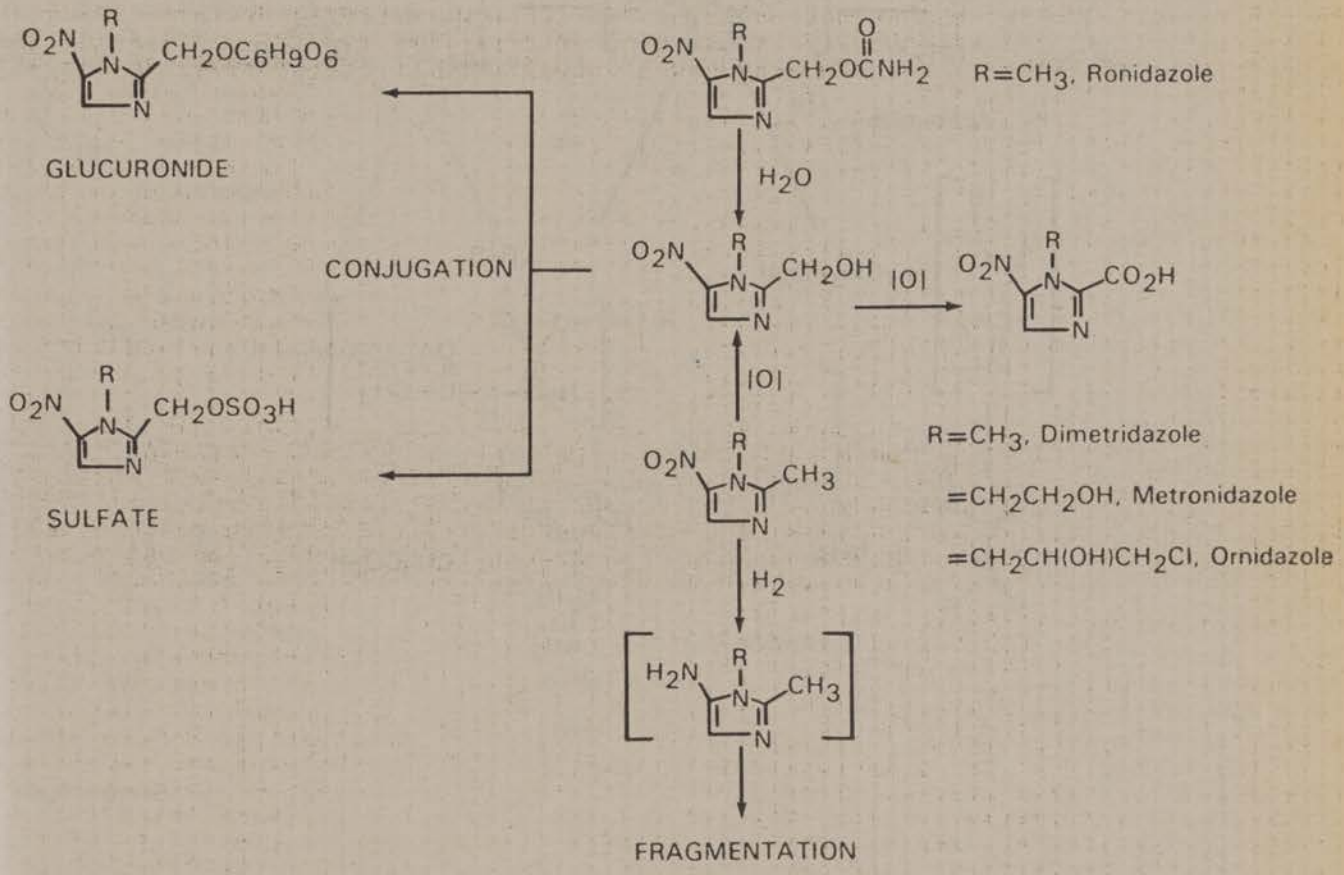


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Figure 3. Possible Fragmentation Patterns through Parent Drug

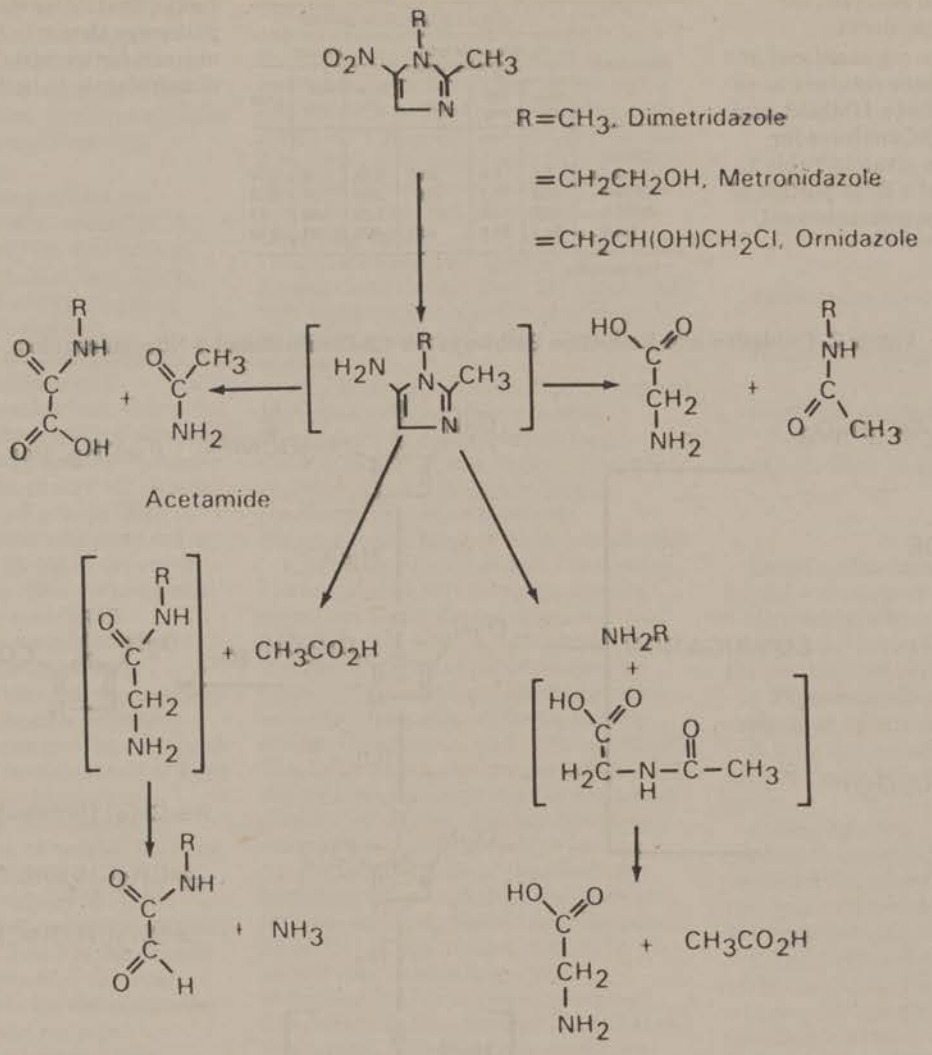
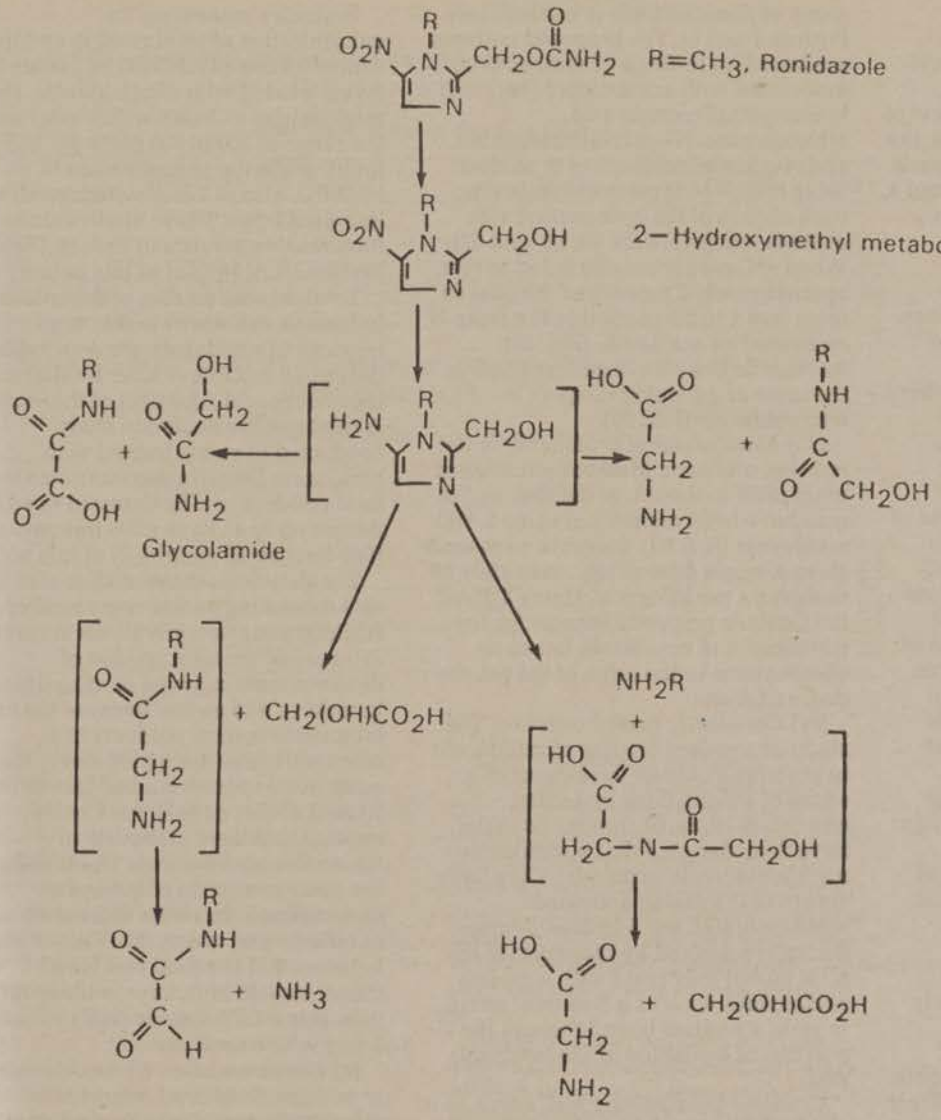


Figure 4. Possible Fragmentation Patterns through 2-Hydroxymethyl Metabolite



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(*i*) *Oxidation.* Dimetridazole is first oxidized to HMMNI, which in turn oxidizes to MNICA. See Figure 2.

(*ii*) *Reduction.* The nitro group of dimetridazole or the 2-hydroxymethyl derivative is reduced to the 5-aminoimidazole. See Figure 2. In view of the instability of 5-aminoimidazoles, the molecule would be expected to degrade to simple fragments. See Figures 3 and 4.

(*iii*) *Ring scission.* Figures 3 and 4 present possible pathways for the scission of the imidazole ring of dimetridazole and of HMMNI.

In addition to the degradative routes, the Center believes that some of the label would be incorporated into endogenous compounds via biosynthetic pathways. Covalent binding of ring intact metabolites could also occur.

(c) *Metabolism of other 5-nitroimidazoles—(i) Ronidazole in turkeys.* In a study of the metabolism of ronidazole in turkeys (Ref. 53), birds were administered 0.006 percent ^{14}C-ronidazole (labeled in the C–2 position of the ring or in the N-methyl group) through the feed for 3 days. Samples of tissues were analyzed for metabolites using paper electrophoresis and thin layer chromatography. This analysis revealed the presence of only parent ronidazole and HMMNI at zero withdrawal. Analysis of the aqueous soluble extracts of liver, which contain up to 80 percent of the total tissue radioactivity, showed the presence of ^{14}C-N-methylglycolamide, ^{14}C-oxalic acid (from birds dosed with 2-^{14}C-ronidazole), and ^{14}C-methylamine. These products all demonstrate the degradation of ronidazole, most likely via HMMNI, through ring scission. HMMNI is a common metabolite of ronidazle and dimetridazole (see Figure 2). Therefore, although there is no direct evidence of ring scission of dimetridazole in turkey tissue, the data on the metabolism of ronidazole provide an adequate basis to anticipate similar biotransformations for dimetridazole.

(*ii*) *Metronidazole in mammalian and bacterial systems.* The metabolism of metronidazole has been studied in a number of systems including rats (Ref. 54) and bacteria (Refs. 55, 56, and 57).

Figure 2 shows the ring-intact excretion products identified in the urine of rats dosed once at 10 milligrams per kilogram with 2-^{14}C-metronidazole. The products of the pathway labeled "oxidation," the 2-hydroxymethyl derivative and the 2-carboxylic acid, are analogous to those observed for dimetridazole in turkeys. Using xanthine oxidase and bacteria, several researchers demonstrated the extensive fragmentation of metronidazole (Ref. 58). Based on this research, the Center believes that similar fragmentation could occur in the turkey if the nitro group of dimetridazole is reduced (see Figures 3 and 4). The proposed patterns are based on findings of radioactivity associated with acetamide, N-(2-hydroxyethyl)oxamic acid, ethanolamine, N-acetylethanolamine, and N-glycolethanolamine in studies using [1',2',-^{14}C2] metronidazole (i.e., each carbon of the hydroxethyl side chain is labeled) (Refs. 54, 56, and 57). When ^{14}C-metronidazole is fed to rats, approximately 2 percent of the dose in urine and 1 to 2.5 percent in the feces is recovered as acetamide (Ref. 56). Acetamide has also been identified in the urine of patients taking metronidazole (Ref. 59).

(*iii*) *Metabolism of ornidazole in the rat, dog, and man.* Metabolic studies of ornidazole in the rat, in the dog, and in man have been carried out using 2-^{14}C-ornidazole (Ref. 60). Subjects were each given a single dose of approximately 10 milligrams per kilogram. Figure 2 gives the Center's proposed scheme for the metabolism of ornidazole based on observations in the urine of the rat, the dog, and man.

(*iv*) *Covalently bound residues.* The study of covalent binding of ronidazole to proteins has been the subject of a series of publications by Lu and coworkers (Refs. 61 through 68), who have demonstrated that a ronidazole metabolite binds to protein. They have shown that suitably activated ronidazole (i.e., the 5-hydroxyamino derivative derived by reduction of the nitro group) may react with a protein nucleophile, such as a free thiol group, to yield a product bound through the 2'-position of 4-position of the imidazole ring.

Covalent binding may well occur as a result of the use of dimetridazole in turkeys. Binding could be expected to take place via HMMNI. Although the carbamate group of ronidazole is better leaving group than the hydroxyl of dimetridazole, the in vitro data show that HMMNI binds to protein (Refs. 61 and 62). These covalently bound residues would persist in turkey tissues.

(3) Evidence of Residues

Salsbury conducted studies measuring the depletion of dimetridazole in turkeys (see Section III.A(3)(a)(*i*) of this notice). The analytical method used by Salsbury does not detect dimetridazole (<2/.0 parts per billion (ppb)) at short withdrawal times.

However, radiotracer studies used to detect residues of dimetridazole in swine and residues of ronidazole in turkeys and swine show that large quantities of total residue of dimetridazole are probably present in tissue.

In studies measuring the concentration of total residue and the concentration of HMMNI in tissues from swine treated with dimetridazole, the total residue at 7-day withdrawal was in the range of 300 to 900 parts per billion (ppb), while the concentration of HMMNI, also at 7-day withdrawal, was less than 2 ppb. These studies show that total residue persists in tissues. (See Section III.A(3)(a)(ii) of this notice.)

Total residue studies with ronidazole in turkeys demonstrate that total residues of ronidazole are detectable in tissues up to 21 days after treatment. (See Section III.A(3)(b)(*i*) of this notice.) A total residue depletion study conducted in swine treated with ronidazole likewise demonstrates that total residues can be detected in edible tissues up to 42 days after treatment. (See Section III.A(3)(b)(*ii*) of this notice.)

The data from these studies also show that measuring parent compound or HMMNI does not provide an accurate estimate of the total residue of dimetridazole in swine or of ronidazole in turkeys and swine. Because the major biotransformation products of 5-nitroimidazoles are qualitatively the same in all species studied (see Section III.A(2) of this notice), the Center expects that the metabolism of dimetridazole in turkeys would follow the same metabolic pathways as dimetridazole in swine and ronidazole in turkeys and swine. The Center also believes that the total residue of dimetridazole in turkeys is likely to persist in edible tissues well beyond the 5-day withdrawal period.

(a) *Dimetridazole—(i) Residue studies in turkeys.* Salsbury Laboratories submitted several residue depletion studies in turkeys treated with dimetridazole. The two studies in which dimetridazole was measured with the method with the lowest limit of detection are discussed below (Ref. 69); the other studies are discussed in Section III.B(1)(b) of this notice.

A group of 20-week old turkeys was treated with 0.08 percent dimetridazole in the feed (therapeutic dose) for 7 days. A group of 10-week old turkeys was treated with 0.02 percent dimetridazole in the feed (prophylactic dose) for 10 weeks. At the end of the dosing period for each group, six birds were sacrificed at each of the following withdrawal times: 0, 1, 3, 5, 7, 10, and 14 days. Muscle, liver, kidney, and skin were collected from each bird at the time of sacrifice.

Tissues samples were assayed for dimetridazole by using a gas

chromatographic method with a limit of detection of 2 ppb.

Tables 2 and 3 present the residue data obtained from the studies conducted by Salsbury.

TABLE 2.—DIMETRIDAZOLE IN TISSUES OF TURKEYS TREATED WITH 0.08 PERCENT DIMETRIDAZOLE IN THE FEED

(Mean residue levels expressed as ppb)

Withdrawal time (days)	Muscle	Liver	Kidney	Skin
0	168	9.2	<2	170.0
1	<2	<2	<2	4.3
3	<2	<2	<2	<2.0
5	<2	<2	<2	<2.0

TABLE 3.—DIMETRIDAZOLE IN TISSUES OF TURKEYS TREATED WITH 0.02 PERCENT DIMETRIDAZOLE IN THE FEED

(Mean residue levels expressed as ppb)

Withdrawal time (days)	Muscle	Liver	Kidney	Skin
0	112	<2	<2	144.0
1	<2	<2	<2	2.5
2	<2	<2	<2	3.7
3	<2	<2	<2	3.0
5	<2	<2	<2	2.5
7	(1)	(1)	(1)	2.6

[1] Samples not analyzed.

Salsbury concluded that the dimetridazole in the skin of turkeys treated at the 0.02 percent level was due to contamination. Therefore, the firm measured dimetridazole in skin in two additional studies, one using 0.08 percent dimetridazole in feed (Ref. 70) and another using 0.02 percent (Ref. 69). At the 0.08 percent level, the mean concentration of dimetridazole in skin was 227 ppb at zero withdrawal, 32.2 ppb after 1-day withdrawal, and <2 ppb at all remaining withdrawal periods. At the 0.02 percent level, the mean concentrations of dimetridazole in skin were 105 ppb at zero withdrawal and <2 ppb at all other withdrawal periods.

(*ii*) *Residue studies in swine.* Hess & Clark conducted a study under NADA 93–535 to determine the total residue of dimetridazole in the edible tissues of swine (Ref. 71). Pigs were treated with a single dose of approximately 25 milligrams per kilogram (range 19 to 37 milligrams per kilogram) of dimetridazole-N-methyl-^{14}C. Muscle biopsies were taken from three pigs at 24 and 48 hours after treatment and from one pig at 72 hours after treatment. Animals were slaughtered 7 days after administration of ^{14}C-dimetridazole, and samples of muscle, liver, kidney, and fat were analyzed.

The mean concentrations of total residue of dimetridazole measured in the muscle biopsies at 24, 48, and 72 hours after treatment were 665 ppb, 270 ppb, and 400 ppb, respectively. The mean concentration of total residue of dimetridazole found in edible tissues at slaughter (7 days after treatment) was as follows: 318 ppb in muscle, 908 ppb in liver, 805 ppb in kidney, and 370 ppb in fat.

Based on the results of a study to quantify dimetridazole, HMMNI, and MNICA in two pigs dosed with ^{14}C-dimetridazole (Ref. 52), Hess & Clark concluded that parent compound was not adequate for monitoring the total residue of dimetridazole and therefore developed a method to measure HMMNI (Ref. 72). Using that method, HMMI was measured in the tissues of swine treated with unlabeled dimetridazole in the drinking water (Ref. 73). Fifteen pigs were treated with dimetridazole in the drinking water at a level of 200 milligrams per liter for 5 days (approximately 10 milligrams per kilogram per day). Three pigs were slaughtered at 0, 3, 5, 6, and 7 days after withdrawal from medication. Tissue samples of muscle, liver, kidney, fat, and skin were taken at the time of slaughter and analyzed for levels of HMMNI. The results are given in Table 4.

TABLE 4.—HMMNI IN SWINE TREATED WITH 10 MILLIGRAMS PER KILOGRAM DIMETRIDAZOLE IN THE DRINKING WATER FOR 5 DAYS

[Mean residues expressed as ppb]

Withdrawal time (days)	Muscle	Liver	Kidney	Skin	Fat
0	301	<2	235	123	25
3	<2	(1)	<2	(1)	(1)
5	<2	(1)	<2	(1)	(1)
6	<2	<2	<2	<2	<2
7	<2	(1)	<2	(1)	(1)

[1] Samples not analyzed.

These studies demonstrate that the total residue of dimetridazole in swine at 7-day withrawal ranges from 300 to 900 ppb while the concentration of HMMNI is less than 2 ppb. Thus, total residue persists in edible tissues and the measurement of HMMNI is inadequate to monitor the total residue of dimetridazole in swine.

(b) *Ronidazole—(i) Residue studies in turkeys.* In a study by Rosenblum (Ref. 74), the amount of total radioactivity detected in tissues of turkeys treated with 0.006 percent ^{14}C-ronidazole in feed was far greater than assay values for ronidazole and HMMNI, as shown in Table 5.

TABLE 5.—CONCENTRATION OF TOTAL RESIDUE, RONIDAZOLE, AND HMMNI IN TURKEY TISSUE AT ZERO WITHDRAWAL

Treatment	Tissue	Total residue (ppm)	(Residue (ppm)	
			Ronidazole	HMMNI
Three days on drug (ring - 2-^{14}C).	Kidney	4.43	0.09	0.0
	Liver	3.77	0.01	0.0
	Muscle	2.05	1.6	0.03
Three days on drug (N-$^{14}CH_3$).	Kidney	4.00	<0.03	0.0
	Liver	4.15	<0.02	0.0
	Muscle	2.58	1.5	0.1

In another study, the concentration of total residue of ronidazole was measured, at various withdrawal times, in turkeys treated for 4 days with ^{14}C-ronidazole administered in feed containing 0.006 percent of drug (Ref. 53). The results are given in Table 6. The time for depletion of radioactivity from tissues to background levels varied depending on the tissue, with residues in muscle detectable up to 21 days after withdrawal. Based on these data, the Center concludes that the total residue of dimetridazole, for which the maximum approved dose is 13 times higher than the dose of ronidazole used in this study, would likewise persist beyond the 5-day withdrawal period.

TABLE 6.—CONCENTRATION OF TOTAL RESIDUE IN TISSUES OF TURKEYS TREATED WITH 0.006 PERCENT RONIDAZOLE IN THE DIET

[Mean values expressed as ppm]

Withdrawal time (days)	Muscle	Liver	Kidney	Fat
0	3.0	4.5	4.7	—
2	0.275	0.500	0.725	0.370
5	0.085	0.180	0.400	—
10	0.260	0.045	0.135	—
14	0.025	0	0.070	—
21	0.004	0	0	—

(ii) Residue studies in swine. Swine were treated with ^{14}C-ronidazole administered once daily for 3 days. The dose was 7 milligrams per kilogram per day. Total radioactivity in tissues was determined at withdrawal times of 6 hours and 3, 7, 14, 28, and 42 days after treatment (Ref. 75). Concentrations of total residue in muscle, liver, kidney, and fat are given in Table 7.

TABLE 7.—TOTAL RESIDUE IN TISSUES OF SWINE TREATED WITH ^{14}C-LABELED RONIDAZOLE

[Mean residues expressed as ppm]

Withdrawal time (days)	Muscle	Liver	Kidney	Fat
0	6.47	10.63	9.37	1.46
3	0.49	1.53	1.22	0.30
7	0.52	1.15	0.85	0.25
14	0.35	0.44	0.27	0.15
28	0.18	0.10	0.09	0.06
42	0.13	0.06	0.05	0.05

In another study (Ref. 76), four groups of pigs (three per group) were treated with unlabeled ronidazole in the drinking water (0.012 percent, corresponding to 15 milligrams per kilogram per day) for 7 days. Three pigs were slaughtered at 0, 1, 3, and 5 days after discontinuation of medication. Samples of muscle, liver, kidney, and fat were taken at slaughter and analyzed for the parent compound by using a differential pulse polarographic method with a limit of detection of 2 ppb. Residue values are given in Table 8.

TABLE 8.—RONIDAZOLE IN TISSUES OF SWINE TREATED WITH 0.012 PERCENT RONIDAZOLE IN THE DRINKING WATER FOR 7 DAYS

[Mean residues expressed as ppm]

Withdrawal time (days)	Muscle	Liver	Kidney	Fat
0	3.00	ND	0.014	0.058
1	0.08	ND	ND	ND
3	ND	ND	ND	ND
5	ND	ND	ND	ND

ND=No detectable residue.

The results presented in Tables 7 and 8 demonstrate that the total residue of ronidazole in swine persists in tissues up to 42 days after treatment and that, by contrast, no ronidazole is detectable after 1-day withdrawal.

(4) An Adequate Method To Monitor for Total Residue of Dimetridazole Does Not Exist.

Section 512(b)(7) of the act and § 514.1(b)(7) of FDA's regulations require that the sponsor develop a reliable and practical regulatory method to be used in monitoring compliance with a drug's conditions of use. In contrast to the radiotracer procedures used in total residue and metabolism studies, the regulatory method must use procedures that can measure the residue in animals that are slaughtered for food.

To provide a means of developing a method to monitor the total residue in all edible tissues of a treated animal, the Center selects a target tissue and a marker residue. The target tissue is the edible tissue selected to monitor for the total residue in the target animal. The target tissue is usually, but not necessarily, the last tissue in which residues deplete to the permitted concentration. A maker residue is a residue the concentration of which is in a known relationship to the concentration of the total residue in the target tissue. The marker residue can be the sponsored compound, any of its metabolites, or a combination of the residues for which a common assay can be developed. The target tissue and marker residue are selected so that the absence of marker residue above a designated concentration (R_m) will confirm that each edible tissue has a concentration of total residue at or below its permitted concentration.

Application of the concepts of marker residue and target tissue requires an experimental determination of the quantitative relationships among the residues that might serve as the marker residue in each of the various edible tissues that might serve as the target tissue in each of the species for which approval of the drug is sought. Because these relationships may change with

time, the Center requires that the sponsor measure the depletion of potential marker residues in potential target tissues starting just after the last treatment with the sponsored compound and continuing until the total residue has depleted to the permitted concentration for that tissue.

Salsbury has developed two methods to measure dimetridazole in the edible tissues of turkeys. One is a differential polarographic method with a limit of detection of 0.05 to 0.1 ppm depending on the size of the tissue sample used for analysis (Ref. 77). This method measures parent dimetridazole and any nitro-containing metabolites that can be efficiently extracted from tissue. Salsbury has not demonstrated the extent of recovery for any metabolites from turkey tissues with the assay extraction procedures. The other method is a gas liquid chromatographic method with a limit of detection of 2 ppb (Ref. 78). This latter method measures only parent compound. Salsbury has not demonstrated that parent dimetridazole is an adequate marker residue because it has not determined the relationship between parent drug and total residues at any time after treatment is discontinued. Therefore, neither method is adequate for monitoring the total residue of dimetridazole in tissues of turkeys.

B. New Evidence Shows That Dimetridazole is no Longer Shown to be Safe by Adequate Tests by All Methods Reasonably Applicable

Section 512(d)(1)(A) of the act requires FDA to refuse to approve an NADA if the agency finds that:

> * * * the investigations, reports of which are required to be submitted to the [FDA] pursuant to subsection (b) [21 U.S.C. 360b(b)], do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof * * *.

The analog of section 512(d)(1)(A) is section 512(e)(1)(B), which requires withdrawal of approval of an NADA where "* * * tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the [FDA] when the application was approved, shows that such drug is not shown to be safe * * *."

The Center can satisfy its burden under the safety clause by citing (1) progress in scientific standards (new evidence) such that new tests are needed for a safety evaluation under current scientific standards, and (2) a failure by the sponsor to do such tests. Section 512(e)(1)(B) of the act is not as explicit as section 512(d)(1)(A) in imposing on the sponsor the duty to conduct tests and submit the results. But the general philosophy of section 512 (as of sections 505, 409, and 706 of the act (21 U.S.C. 355, 348, and 376)) is that testing shall be the responsibility of the firm, and not the agency. That philosophy is explicitly reflected in section 512(b)(1) and (d)(1)(A). There is no reason to interpret section 512(e)(1)(B) differently.

Section 512(d)(1)(A) of the act uses the phrase "adequate tests," but section 512(e)(1)(B) does not. Nevertheless, it would be absurd to interpret "tests" in section 512(e)(1)(B) as possibly including inadequate tests. Therefore, it is appropriate to read "tests" in section 512(e)(1)(B) as "adequate tests." It is also appropriate to read the general "new evidence" provision of section 512(e)(1)(B) as incorporating the standard of "adequate tests by all methods reasonably applicable," which appears in section 512(d)(1)(A) of the act. Thus, if new evidence of scientific progress shows that the data supporting an NADA no longer constitute adequate tests by all methods reasonably applicable to a determination of safety, that new evidence warrants withdrawal under section 512(e)(1)(B). *Cf. United States* v. *Western Serum Co., Inc.*, 666 F.2d 335 (9th Cir. 1982) (absent current general recognition of the safety of an animal drug, that drug is a new animal drug and must have an approved NADA).

(1) The Data in the NADA's Are Inadequate

Salsbury's NADA's for dimetridazole were approved in 1964 and 1965. At that time, the Center required less toxicological testing to demonstrate safety than it does today. The Center generally relied upon the results of 90-day toxicity studies and a demonstration with a chemical assay that the concentration of the parent drug was below 0.1 ppm in the edible tissues at the time the animals were slaughtered for food. Thus, the studies in laboratory animals conducted by Salsbury and submitted to its NADA's consisted only of (1) a 90-day oral toxicity study in rats (Ref. 79), (2) a 90-day oral toxicity study in dogs (Ref. 81), and (3) a 30-day dose-range finding toxicity study in dogs (Ref. 82). In 1973, Hess & Clark submitted (1) a 90-day oral toxicity study in rats (Ref. 80), (2) a 90-day oral toxicity study in dogs (Ref. 80), (3) a 30-day intermittent oral dose toxicity study in dogs (Ref. 83), and (4) a 30-day oral toxicity study in rats (Ref. 83). (The Hess & Clark studies are included in Salsbury's NADA's by virtue of an authorization from Hess & Clark (see Section II.B. of this notice).) Salsbury's NADA's also included a residue depletion study to measure dimetridazole in the tissues of treated turkeys (Ref. 84), and a study on the absorption, excretion, and metabolism of dimetridazole in turkeys (Ref. 85). Each of these studies is discussed below.

These data no longer constitute adequate tests by all methods reasonably applicable to show whether or not dimetridazole is safe. In the last 25 years, there has been considerable progress in the field of regulatory toxicology. Based on the increased knowledge of chemical toxicity, there is now greater concern about the public health significance of chronic, low level exposure to residues of an animal drug. As a result, toxicological testing standards are more rigorous and test endpoints are more sensitively measured today than was the case in the early 1960's. A number of factors are responsible for these changes. The factors include the increase in the number of animals used at each dose, an increase in the number of tissues examined for toxic lesions, and improvements in animal husbandry and general laboratory techniques. These and other improvements have contributed to the increased reliability and statistical sensitivity of the classical toxicological feeding study. In addition, new tests such as tests for genetic toxicity, for reproductive toxicity, and for teratogenicity are routinely required prior to approval of a new animal drug. Furthermore, as the toxicological data base has expanded, scientists are better able to make predictions about potential toxicity based on structure-activity relationships. In light of the changes in regulatory toxicology and the data discussed in Section III.A. of this notice, chronic bioassays in two rodent species are required to determine the carcinogenicity of dimetridazole. None of the NADA's includes data from an adequate bioassay in any such species. Each NADA is also lacking the results of an adequate 90-day or longer feeding study in a nonrodent mammalian species.

None of the toxicity studies in the applications is adequate to establish a no-observed-effect-level because (1) the lowest dose caused testicular atrophy in rats and testicular and renal degenerative changes in dogs; (2) the number of animals per dose was not sufficient in any of the studies; or (3) hematology, blood chemistry, organ weight, or histopathology data were

lacking or inadequate in each of the studies.

The total residue and metabolism data contained in the study on the absorption, excretion, and metabolism of dimetridazole in turkeys are inadequate primarily bacause they do not provide reliable information of the total residue remaining in the edible tissues of treated turkeys. In addition, the NADA's do not contain metabolism data in the species used for toxicological testing. Thus, it is impossible to determine if the metabolites present in the edible tissues of turkeys have been adequately tested for toxicity.

a. *Toxicity data.* Salsbury conducted a 90-day study in rats (Ref. 79). The doses used were 0, 2,000, 4,000, 6,000, 8,000 and 10,000 ppm in the diet. Each dose group consisted of 10 male and 10 female rats. A no-observed-effect-level cannot be established from this study because testicular atrophy was observed at all doses ($P=0.01$ at the lowest dose). In addition, insufficient numbers of animals were used at each dose and blood chemistry and hematology data were not reported.

Hess & Clark submitted another 90-day study in rats (Ref. 80). The study used doses of 0, 50, and 100 milligrams per kilogram body weight per day with five male and five female rats in each dose group. A no-observed-effect-level cannot be established from this study because insufficient numbers of animals were used at each dose and clinical chemistry, hematology, and organ weight data were not reported.

Salsbury conducted a 90-day study in dogs (Ref. 81). The doses used were 0, 16, 33, 66, and 132 milligrams per kilogram body weight per day and were administered in gelatin capsules. The lowest dose group consisted of four male dogs; each of the other dose groups consisted of two male and two female dogs. A no-observed-effect-level cannot be established from this study because, at the lowest dose tested, all dogs showed mild cortical nephrosis and one dog showed renal necrosis, and because dose-related testicular degenerative changes were observed in all dose groups. In addition, there were no female dogs in the lowest dose group, insufficient numbers of animals were used in the remaining dose groups, and blood chemistry (except blood urea nitrogen), urinalysis, and organ weight data were not reported.

Hess & Clark submitted another 90-day study in dogs (Ref. 80). The study used doses of 12.5 and 50 milligrams per kilogram body weight per day with one male and one famale dog at each dose. A no-observed-effect-level cannot be established from this study because all dogs showed hyperexcitability and distension of irises. In addition, a concurrent control group was not used, insufficient numbers of animals were used at each dose, and organ weight data were not reported.

Salsbury also conducted a 30-day dose-range finding toxicity study in dogs (Ref. 82). Hess & Clark also submitted a 30-day intermittent oral dose toxicity study in dogs (Ref. 83), and a 30-day oral toxicity study in rats (Ref. 83). None of these studies can be used to establish a no-observed-effect-level because of their short duration.

In 1976, Hess & Clark submitted a 122-week feeding study in Carworth CFY rats using dimetridazole (Ref. 86). (This study is also discussed in Section III.A(1)(b)(*i*) of this notice.) Groups of 50 male and 50 female rats received 0, 100, 400, or 2,000 ppm dimetridazole in the diet for 122 weeks. All surviving animals were sacrificed during the 123rd week of dosing.

Because of the way in which the histopathological examination was conducted, the Center has concluded that this study is seriously flawed and is not suitable for any quantitative evaluation of the potential carcinogenicity of dimetridazole.

In the control and 100 ppm dose groups, only those rats that died or were sacrificed at the end of the study (the last 20 rats) received complete histological examinations for the 32 tissues listed on page 296 of the study report. The remainder of the rats had only gross lesions examined histologically. An addendum to the report dated April 1976 included data from histopathological examinations of 20 males and 20 females from the 2,000 ppm group. Mammary glands, however, were not included in the additional tissues examined. Therefore, no additional information concerning mammary gland tumors was obtained from those histopathological examinations.

Table 9 gives the number of rats in each dose group that did not have a histopathological examination of mammary tissue.

TABLE 9

	Dose—ppm							
	Males				Females			
	0	100	400	2,000	0	100	400	2,000
Number of rats with no tissue preserved	5	5	3	6	6	10	4	2
Number of rats not examined	15	22	42	22	5	6	3	5
Total number of rats not evaluated	20	27	45	28	11	16	7	7
Percent of rats not evaluated	40	54	90	56	22	32	14	14

As can be seen from Table 9, more than 50 percent of the male rats were not examined histopathologically for mammary tumors. This is especially important because 20 to 25 percent of the mammary tumors were not detected by palpation but only upon histopathological examination. Therefore, it is very likely that more tumors were present but not detected, especially in the 400 ppm dose group. Although not as extensive as for the males, a similar problem exists for the female rats.

The Center has also concluded that the feeding study discussed in Section III. A(1)(b)(*i*) of this notice is inadequate for any quantitative evaluation of the carcinogenicity of dimetridazole because the study was not of sufficient duration, too few animals were used, only female animals were used, and only one dose of dimetridazole was tested.

(b) *Residue data.* Salsbury conducted a residue depletion study to measure the concentration of dimetridazole in tissues of treated turkeys (Ref. 84). Turkeys were treated with 0.025 percent (n=70), 0.05 percent (n=70), 0.1 percent (n=110), or 0.2 percent (n=110) dimetridazole in the feed until they were 24 weeks of age. For the 0.025 percent and 0.05 percent groups, an unspecified number of birds were sacrificed at 0, 3, 6, 12, 24, and 48 hours after withdrawal of medicated feed. For the 0.1 percent and 0.2 percent groups, an unspecified number of birds were sacrificed at 0, 3, 6, 12, 24, 48, 72, and 96 hours. Tissue samples of breast muscle, liver, kidney, fat, and thigh skin were taken at sacrifice. The concentration of dimetridazole in tissues was measured using a polarographic method with a claimed limit of detection of 0.05 ppm. The results of this study are given in Tables 10 and 11.

TABLE 10.—CONCENTRATION OF DIMETRIDAZOLE (PPM)

Tissue	Drug level	Withdrawal time (hours)					
		0	3	6	12	24	48
Muscle	0.05	3.44	1.98	0.71	0.92	ND.	<.05
	0.025	0.10	0.09	0.08	ND	<.05	ND
Liver	0.05	6.67	1.17	2.34	0.10	<.05	ND
	0.025	0.12	<.05	0.12	<.05	<.05	ND
Kidney	0.05	0.64	0.11	0.06	0.08	<.05	ND
	0.025	0.15	0.05	<.05	<.05	<.05	ND
Fat	0.05	2.27	1.31	0.75	0.89	0.08	<.05
	0.025	0.12	<.05	0.05	<.05	0.05	<.05
Skin	0.05	3.28	1.29	1.10	0.78	0.06	ND
	0.025	0.06	0.08	0.12	<.05	<.05	ND

ND=No detectable residue.

TABLE 11—CONCENTRATION OF DIMETRIDAZOLE (PPM)

	Tissue Drug level (percent)	Withdrawal time (hours)			12				
		0	3	6	24	48	72	96	
Muscle	0.1	11.56	5.75	5.24	3.31	0.22	0.08	0.05	0.06
	0.2	12.72	12.40	8.66	(a)0.29	1.04	0.23	(b)	(a)0.06
Liver	0.1	15.20	6.52	6.96	4.75	0.48	<.05	<.05	0.06
	0.2	14.88	14.68	8.50	(a)0.21	1.07	0.24	(b)	(a)0.16
Kidney	0.1	6.80	0.88	1.65	1.42	0.10	<.05	<.05	<.05
	0.2	17.76	12.44	6.75	(a)0.90	0.14	0.14	(b)	(a)0.08
Fat	0.1	7.40	3.41	2.99	1.81	0.10	<.05	0.08	<.05
	0.2	(c)	0.03	2.69	(c)	0.69	0.29	(b)	(a)0.11
Skin	0.1	7.40	3.90	3.84	3.12	0.26	0.10	0.07	0.06
	0.2	15.68	6.60	6.67	0.27	0.75	0.22	(b)	(a)0.10

(a)=Value calculated from 1 bird.
(b)=Birds not available at this withdrawal period.
(c)=Insufficient sample for analysis.

Salsbury submitted a study on the absorption, excretion, and metabolism of dimetridazole in turkeys (Ref. 85). For the metabolism and recovery experiments, turkeys weighing approximately 3 kilograms received by a crop tube a single dose of 100 milligrams per kilogram unlabeled dimetridazole (one turkey), 300 milligrams per kilogram unlabeled dimetridazole (two turkeys), or 32 milligrams per kilogram (equivalent to 0.05 percent in the drinking water) dimetridazole labeled with ^{14}C in the 2-position of the ring and 2-methyl group (seven turkeys). For the residue experiments in tissue, turkeys were given free access to medicated water (0.05 percent) for 6 days (five turkeys) or were administered a single dose of labeled dimetridazole at 32 milligrams per kilogram as specified above (two turkeys). Samples of excreted material, tissues, and expired air were assayed by colorimetric, polarographic, or radiochemical procedures.

Dimetridazole was measured by a polarographic method with a limit of detection of 0.1 ppm. These results are given in Table 12.

TABLE 12.—CONCENTRATION OF DIMETRIDAZOLE IN TISSUES OF TURKEYS TREATED FOR 6 DAYS WITH 0.05 PERCENT DIMETRIDAZOLE IN THE DRINKING WATER

[Mean values expressed in ppm]

Withdrawal time (days)	Muscle	Liver	Kidney	Skin
0	0.92	0.66	<0.1	0.38
1	0.04	0.22	<0.1	<0.1
2	<0.1	<0.1	<0.1	<0.1

The residue in tissues of turkeys treated with a single dose of ^{14}C-labeled dimetridazole was determined by both a radiochemical and polarographic method, 72 hours after treatment. These results are given in Table 13.

TABLE 13.—CONCENTRATION OF RESIDUE IN TISSUES OF TURKEYS TREATED WITH A SINGLE DOSE OF ^{14}C-LABELED DIMETRIDAZOLE

[32 milligrams per kilogram (ppm)]

Tissue	Polarographic	Radiochemical
Muscle	<0.05	
Liver	<0.05	<0.03
Kidney	<0.1	<0.05
Skin	<0.05	

For the samples analyzed, residue concentrations were below the limit of detection of the assays.

The studies, the results of which are given in Tables 11, 12, and 13, do not and cannot provide an adequate determination of total residue in turkey tissues. As discussed in Section III.A(4) of this notice, the Center applies a marker residue approach (i.e., analyzing for a residue whose relationship to the total residue is known) to monitor the total residue in edible tissues. In the case of dimetridazole, the relationship between the concentration of dimetridazole and the concentration of total residue in turkey tissues has not been established. Without such information, the results of studies measuring the concentration of dimetridazole in turkey tissues (see Tables 11 and 12) cannot be regarded as reflecting the total residue.

The results of the radiotracer study (see Table 13) cannot be used to derive the relationship between the concentration of dimetridazole and the concentration of total residue for several reasons. First, the turkeys were treated with only a single dose of dimetridazole, and not according to label directions. Multiple dosing with labeled drug would give higher total residue values than those reported in the study. Second, the total residue values reported for tissues in Table 13 were obtained by assaying a benzene extract of the tissues, not by assaying whole tissue samples. Thus, the amount of radioactivity that was nonextractable was not determined. Radioassay of whole tissue samples would also give higher total residue values than those reported. Finally, it is impossible to establish the relationship between total residue measured by the radiochemical method and residue measured by the polarographic method because all residue values reported were below the limit of detection of the assay.

In 1973 Salsbury submitted the residue depletion studies described in Section III.A(3)(a)(*i*) of this notice. For the reasons stated in that Section, the studies are not adequate to determine the total residue of dimetridazole in, or

the depletion of that residue from, the tissues of treated turkeys. Based on the residue data summarized in Tables 10 and 12 of this notice, which show that liver and muscle from birds sacrificed at zero withdrawal (6 hours) contain dimetridazole in the range of 1 to 2 ppm, the Center concludes that the total residue in those tissues would be considerably higher.

(c) *Metabolism data.* In the study on the absorption, excretion, and metabolism of dimetridazole in turkeys (Ref. 85) discussed in Section III.B(1)(b) of this notice, examination by ultraviolet light of a paper chromatogram of urine collected at 24 hours post dosing revealed six spots following treatment at the 32 milligrams per kilogram, 100 milligrams per kilogram, and 300 milligrams per kilogram levels. In addition, a seventh spot was found using autoradiography of a sample of urine of birds treated with labeled dimetridazole. Four of the metabolites were identified by comparison of chromatograms for unknowns versus standards using several solvent systems. The four metabolites and the percentage of the total radioactivity excreted were: unchanged dimetridazole (3.4 percent), HMMNI (9.4 percent), 1-methyl-5-nitroimidazole-2-ylmethyl hydrogen sulfate (44.4 percent), and MNICA (25.8 percent). Another metabolite, representing 8.8 percent of the excreted dose, was identified by color reactions as a conjugated glucuronide of a nitroimidazole. The glucuronide was thought to be that of HMMNI but positive identification was not made because a reference standard was not used. The remaining two metabolites, comprising 10.9 percent of the excreted drug, were shown to be non-nitro containing compounds. One of these two compounds did not absorb ultraviolet light and was presumed to be a ring-degraded metabolite, because absorbing ultraviolet light is characteristic of ring-intact imidazoles. Salsbury concluded that almost all the excreted drug is metabolized and that the basic metabolic pathway involves oxidation of the 2-methyl group to 2-hydroxymethyl. In addition, Salsbury found the nitro group to be resistant to reduction in the turkey, with approximately 90 percent of the excreted drug in the form of a nitroimidazole.

Salsbury found that, 3 days after a single oral dose of labeled dimetridazole to turkeys at 32 milligrams per kilogram, an average of 79.6 percent of the radioactivity was recovered in the urine, 7.7 percent in the feces, and 1.2 percent in the expired air. About 90 percent of the administered drug, therefore, can be accounted for in the 3-day period after dosing; 80 percent of the drug is excreted within 48 hours post-dosing. Examination of the urine-fecal extracts with polarographic and colorimetric methods (methods which would detect nitro-containing metabolites) evidenced 66.1 percent and 63 percent recovery, respectively, during the 3-day period after dosing.

The Center has concluded that these studies are inadequate to characterize the metabolism of dimetridazole in turkeys for several reasons. First, Salsbury did not present a metabolic profile for any of the edible tissues. Second, the results for urine actually reflect those for urine and water soluble extracts of feces. In the study, excreta were combined and centrifuged, with the supernatant designated urine, and the pellet designated feces. Third, the turkeys should have been dosed with labeled drug at the maximum use level approved (i.e, 7 days' dosing with labeled dimetridazole at 32 milligrams per kilogram), because underdosing may not permit full characterization of the metabolites present in tissue.

The data on the metabolism of dimetridazole in swine submitted by Hess & Clark in the 1970's and relied upon by Salsbury (see Section II.B. of this notice) are summarized in Section III.A(2)(b) of this notice. Those data are useful in providing an understanding of the possible metabolism of the drug in turkeys, but they do not and cannot provide definitive information on the metabolism of dimetridazole in turkey tissues.

(2) Salsbury Has Not Submitted the Additional Residue, Metabolism, or Toxicological Data Required To Support Continued Approval of its NADA's

Since approval of the NADA's for dimetridazole, the Center has advised Salsbury on numerous occasions that additional residue, metabolism, and toxicological data are required to support continued approval of the applications. Salsbury has not submitted any of the requisite data.

By letter dated March 1, 1977 (Ref. 87), the Center requested that Salsbury submit a chronic feeding study in a rodent species other than the rat to support the firm's then pending supplemental NADA's for the use of dimetridazole in swine. The letter stated that the data from the study in rats submitted by Hess & Clark in support of its NADA's (see Sections III.A(1)(b)(*i*) and III.B(1)(a) of this notice) indicated that dimetridazole is a tumorigen and possibly a weak carcinogen. The Center's March 1 request, taken together with the information in FDA's (1) final rule governing chemical compounds in food-producing animals; criteria and procedures for evaluating assays for carcinogenic residues in edible products of animals (42 FR 10412, 10429; February 22, 1977), (2) proposed rule governing chemical compounds in food-producing animals; criteria and procedures for evaluating assays for carcinogenic residues (44 FR 17070, 17104; March 20, 1979), and (3) reproposed rule governing sponsored compounds in food-producing animals; criteria and procedures for evaluating the safety of carcinogenic residues (50 FR 45530, 45550; October 31, 1985), provided Salsbury notice that the Center also required such a study to support the continued approvability of the firm's NADA's for the use of dimetridazole in turkeys. By letter dated August 18, 1986 (Ref. 4), the Center requested that Salsbury submit a chronic feeding study in rats and a chronic feeding study in mice to support the continued approvability of those NADA's.

Salsbury did not submit such studies in response to any of the Center's requests, nor did the firm indicate that it would conduct them (see Section II.A. of this notice).

By letter dated October 2, 1973 (Ref. 88), the Center requested Salsbury to determine in turkey tissue the depletion of HMMNI, 1-methyl-5-nitroimidazole-2-ylmethyl hydrogen sulfate, and MNICA. The Center's request was the subject of a conference with Salsbury on December 13, 1973 (Ref. 89). By letter dated December 21, 1973 (Ref. 90), Salsbury proposed that it be allowed (1) to rely on information on the metabolism of dimetridazole, ipronidazole, and ronidazole; and (2) to develop a chemical assay for HMMNI and measure its depletion in turkey tissues instead of conducting a qualitative radiotracer metabolism study. By letter dated May 29, 1974 (Ref. 91), the Center rejected Salsbury's proposal and requested a metabolism study in turkey tissue using radiotracer methods sensitive to 2 ppb. By letter dated August 18, 1986 (Ref. 4), the Center again asked Salsbury for total residue depletion and metabolism studies in turkeys.

Salsbury did not submit any data in response to any of these numerous requests.

Plainly, new tests are needed for a safety evaluation of dimetridazole; the data supporting Salsbury's NADA's no longer constitute adequate tests by all methods reasonably applicable to a determination of the safety of the drug. And despite repeated requests, Salsbury

has not conducted the requisite new tests. Accordingly, withdrawal of approval of the NADA's is warranted under section 512(e)(1)(B) of the act on the ground that dimetridazole is not shown to be safe for use because new evidence shows that the drug is no longer shown to be safe by adequate tests by all methods reasonably applicable.

C. New Evidence Shows That Dimetridazole Is Not Shown To Be Safe by Virtue of Misuse

Section 512(d)(2)(D) of the act provides that in determining whether a drug is safe for use under the conditions prescribed, recommended, or suggested in the labeling, the agency is to consider, among other factors, whether those conditions of use are reasonably certain to be followed in practice. Accordingly, where labeled indications for use of an approved new animal drug have not been followed, and are not reasonably likely to be followed in practice, the drug is not shown to be safe for use and therefore its approval is subject to withdrawal under section 512(e)(1)(B) of the act. Furthermore, the use or intended use of an approved new animal drug in a manner that is inconsistent with the conditions of its approval causes the drug to be unsafe and thereby adulterated under sections 512(a)(1) (A) and (B) and 501(a)(5) of the act. The approval of such an adulterated drug is also subject to withdrawal under section 512(e)(1)(b) of the act. See "Chloramphenicol Oral Solution; Opportunity for Hearing" (50 FR 27059; July 1, 1985).

The Center has, in the past, exercised its regulatory discretion through a policy permitting "extra-label" use of approved new animal drugs in certain circumstances. Until recently, the policy permitted extra-label use of drugs in food-producing animals unless residues occurred in edible products. Because of evidence increasing misuse of chloramphenicol and other drugs, the Center revised the policy to provide that extra-label use of new animal drugs in food-producing animals is permitted only in very limited instances. The policy is stated in Compliance Policy Guide 7125.06 (see 49 FR 20915, May 17, 1984; and 49 FR 45930, November 21, 1984). In August and November 1986, the Center revised the policy to clarify that it does not apply to drugs added to medicated feeds intended for extra-label use or to dimetridazole for use in swine (see 51 FR 42656; November 25, 1986).

Even before the 1986 revisions, the policy was inapplicable to the use of dimetridazole in swine. First, several new animal drugs, e.g., carbadox, lincomycin, virginiamycin, gentamicin, and tiamulin, are approved for use in the treatment and prevention of swine dysentery (see 21 CFR 558.115, 558.325, 558.635, 520.1044, 520.1263, 520.2455). Second, a safe concentration of residues of dimetridazole in the edible tissues of swine has not been established (see Sections III.A., A(1)(c)(*ii*), and III.B(1) of this notice), and there is no approved method to monitor the total residue of the drug in swine.

The sections below document evidence available to the Center establishing that dimetridazole medicated premix and dimetridazole soluble powder have been used widely for the treatment and prevention of swine dysentery and that such use is likely to continue.

Treponema hyodysenteriae, an anaerobic spirochete, has been identified as the primary etiologic agent in swine dysentery (Refs. 92, 93, and 94). Swine dysentery, a severe mucohemorrhagic diarrheal disease, affects pigs primarily during the growing-finishing period and is most commonly observed in 15- to 70-kilogram pigs (Refs. 93 and 94). It is reported that morbidity of swine dysentery is usually over 90 percent and that the mortality can be as high as 30 percent (Refs. 93 and 94). Estimates place the infection rate at more than 10 percent of the swine herds in the United States (Ref. 92). When swine herds in Iowa, Illinois, and Missouri were surveyed, an average of 39.5 percent of them were found to be infected with *T. hyodysenteriae* (Ref. 95).

Nitroimidazole compounds are said to be effective in the prevention and treatment of swine dysentery (Refs. 93 through 98). In one study (Ref. 98), dimetridazole and ronidazole reportedly were effective not only in treating swine dysentery, but also in eliminating *T. hyodysenteriae* from carrier pigs. This latter effect of dimetridazole is reported elsewhere in the literature (Refs. 95 and 97). For example, one publication, "Swine Dysentery-Practitioner Planning Guide For Herd Elimination Programs" (Ref. 97), claims that dimetridazole is effective in eliminating *T. hyodysenteriae* in pigs at a dose of 36.4 grams per 50 gallons of water (0.04 percent) for 3 to 4 weeks. For the prevention of swine dysentery, dimetridazole is recommended at a level of 100 or 182 grams per ton of feed (Refs 92, 93, 94, and 97). For the treatment of swine dysentery, dimetridazole is recommended at a level of 0.025 percent in the water for 5 days (Refs. 92, 93, and 94).

Although dimetridazole has apparently been administered to swine in the United States for a number of years, the Center's increased concern over the drug's use has resulted from new information about its toxicity (see Section III.A(1) of this notice). Furthermore, there is neither a safe concentration for residues of dimetridazole in the edible tissues of swine, nor is there an approved method to monitor the total residue of the drug in swine.

(1) Evidence of Misuse

Results of more than 20 inspections of swine producers, veterinarians, feed mills, and distributors conducted by FDA since 1984 show that dimetridazole premix and soluble powder are used extensively for swine dysentery, also known as bloody scours. The inspections have documented the illegal use of dimetridazole premix and soluble powder in Arkansas, Illinois, Iowa, Minnesota, Missouri, Tennessee, and Texas.

In some cases, feed mills purchased the premix for sale to hog producers or to veterinarians prescribing it for swine dysentery. In other cases, distributors sold the dimetridazole premix to persons who then added it to hog feed or sold it to others for eventual use in such feed. For example, in 1984, a routine FDA inspection of a feed mill in Minnesota revealed that the mill received from a hog producer 1 and 2 pound bags of dimetridazole premix to be mixed in hog feed. The producer admitted to receiving the repackaged dimetridazole premix from a local veterinary clinc, which had repacked the premix into the 1 and 2 pound bags. The hog producer admitted that the premix was sold to him by the clinic for the treatment and prevention of bloody scours in his hogs. The veterinarian at the clinic admitted to having sold dimetridazole premix to 10 to 15 hog producers for the prevention and treatment of swine dysentery.

Dimetridazole soluble powder is an over-the-counter drug. Evidence obtained during FDA inspections shows that the powder is frequently sold to hog producers to be added to the feed or drinking water for the treatment of swine dysentery. For example, in Illinois, which was the second highest State in percent of total pig crop in 1985 (Ref. 99), FDA observed dimetridazole soluble powder in nearly every feed mill and farm supply store. Moreover, producers, veterinarians, and distributors report that the use of dimetridazole for the treatment and prevention of swine dysentery is

widespread. In one case, a veterinarian in Illinois purchased 194 50-pound bags of dimetridazole premix and 2,000 units of dimetridazole soluble powder over a 1-year period. He admitted that although some of each product was sold to turkey producers, the rest was sold to other veterinarians, or prescribed by him, for use in the prevention or treatment of swine dysentery. The veterinarian admitted to prescribing dimetridazole for the disease for more than 15 years.

Textbooks now used in schools of veterinary medicine throughout the United States refer to the use of dimetridazole in the treatment of swine dysentery (Refs. 92, 93, and 94). Although the references are accompanied by footnotes explaining or suggesting that the drug is not approved for use in swine dysentery in this country, the fact that dimetridazole is cited as a treatment for the disease encourages use of the drug. Such use is also encouraged by the veterinary and trade literature (Refs. 95 through 98), which recommend dimetridazole for the prevention and treatment of swine dysentery.

For all these reasons, the Center concludes that the use of dimetridazole for the treatment and prevention of swine dysentery is widespread.

(2) Likelihood of Misuse in the Future

Based on the current attitude among hog producers and veterinarians, the Center believes that the use of dimetridazole for the treatment and prevention of swine dysentery will continue if approval of Salsbury's NADA's is not withdrawn. The misuse is not localized but has a broad geographic distribution in predominant hog-rearing areas. Producers and veterinarians engaged in swine management admit that dimetridazole is widely used in the treatment and prevention of swine dysentery. In many instances, veterinarians and hog producers report that they believe that dimetridazole is effective in preventing and treating swine dysentery, and that they will continue to use dimetridazole for the disease. Many veterinarians, producers, and feed mill operators report that dimetridazole is commonly prescribed and used in their area for swine dysentery. As a veterinarian in Indiana commented in a letter to FDA, there is widespread belief on the part of producers that dimetridazole is effective against swine dysentery. Indeed, in one case, a producer stated that although he would discontinue the extra-label use of other animal drugs, he would continue to use dimetridazole in swine. The likelihood of misuse in the future is also substantial because of the extent to which the product is promoted through agriculture extension meetings, local feed supply houses, veterinary clinics, the veterinary literature, and by word of mouth (Refs. 95 and 97).

IV. Environmental Economic Impact

The Center has carefully considered the potential environmental effects of this action and has concluded that the action will not have a significant impact on the human environment and that an environmental impact statement therefore will not be prepared. The Center's finding of no significant impact and the evidence supporting this finding, contained in an environmental assessment under 21 CFR 25.31, may be seen in the Dockets Management Branch, Food and Drug Administration (address above), between 9 a.m. and 4 p.m., Monday through Friday.

The economic consequences of the withdrawal of dimetridazole are expected to be minimal. Salsbury is the only firm that holds approved NADA's for the drug, and a substitute product approved for the same claims in turkeys is readily available at competitive prices.

V. References

In addition to the Salsbury and Hess & Clark NADA's identified in Section II of this notice, copies of the references and other documents cited or referred to in Section II, III, and IV of this notice have been placed on display in the Dockets Management Branch (address above). Except for data and information prohibited from public disclosure under section 301(j) of the act (21 U.S.C. 331(j)), § 20.61 of FDA's regulations governing public information (21 CFR 20.61), § 514.11 of FDA's regulations governing NADA's (21 CFR 514.11), or 18 U.S.C. 1905, and data and information exempt from public disclosure under § 20.64, copies of the NADA's, the references, and the other documents may be examined in the Dockets Management Branch by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Letter from William B. Bixler, FDA, to Robert R. Baron, Salsbury Laboratories, Inc., dated March 6, 1986.

2. Letter from Robert R. Baron, Salsbury Laboratories, Inc., to Andrew J. Beaulieu, FDA, dated April 9, 1986.

3. Letter from Robert R. Baron, Salsbury Laboratories, to Andrew J. Beaulieu, FDA, dated July 7, 1986.

4. Letter from William B. Bixler, FDA, to Robert R. Baron, Salsbury Laboratories, Inc., dated August 18, 1986.

5. Summary of Causal Review on Dimetridazole.

6. Letter from Vincent E. DeFelice, Hess & Clark Division of Rhodia, Inc., to Bureau of Veterinary Medicine, FDA, dated June 8, 1973.

7. Letter from Vincent E. DeFelice, Hess & Clark Division of Rhodia, Inc., to Bureau of Veterinary Medicine, FDA, dated February 7, 1974.

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VI. Notice of Opportunity for Hearing

Therefore, notice is given to the sponsors listed in Section II of this notice, and to all other interested persons, that the Center proposes, under section 512(e) of the act, to withdraw approval of the NADA's for dimetridazole. This action is based on section 512(e)(1)(B) of the act in that the drug is not shown to be safe for use (1) because new evidence provides a reasonable basis from which serious questions about the ultimate safety of dimetridazole and the residues that may result from its use may be inferred, (2) because new evidence shows that dimetridazole is no longer shown to be safe by adequate tests by all methods reasonably applicable, and (3) because new evidence shows that the labeled directions for use have not been followed in practice and are not likely to be followed in the future. Upon finalization of the withdrawal of approvals of the applications identified in Section II of this notice, the corresponding regulations shall be revoked as provided in section 512(i) of the act (21 U.S.C. 360b(i)) (21 CFR 514.115(e)).

In accordance with provisions of section 512 of the act (21 U.S.C. 360b) and regulations promulgated under it (21 CFR Part 514) and under authority delegated to the Director of the Center for Veterinary Medicine (21 CFR 5.84), the Center hereby provides an opportunity for hearing to show why approval of the new animal drug applications listed in Section II.A of this notice, and all supplements thereto, should not be withdawn. Any hearing would be subject to the provisions of 21 CFR Part 12.

If a sponsor decides to seek a hearing, the sponsor shall file (1) on or before January 16, 1987 a written notice of appearance and request for a hearing, and (2) on or before February 17, 1987 the data, information, and analyses relied on to justify a hearing, as specified in 21 CFR 514.200.

Any other interested person may also submit comments on this notice. Procedures and requirements governing this notice of opportunity for hearing, a notice of appearance and request for hearing, submission of data, information, and analyses to justify a hearing, other comments, and a grant or denial of hearing, are contained in 212 CFR 514.200.

The failure of the sponsor to file timely written appearance and request for hearing as required by 21 CFR 514.200 constitutes an election by the sponsor not to avail itself of the opportunity for a hearing. The Center will summarily enter a final order withdrawing approval of the application.

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 there is no genuine and substantial issue of fact that precludes the withdrawal of approval of the application(s), or that the 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 under this notice shall be filed in four copies. All submissions under this notice, except as provided in 21 CFR 10.20(j), may be seen in the Dockets Management Branch (address above) between 9 a.m. and 4 p.m., Monday through Friday.

This notice is issued under the Federal Food, Drug, and Cosmetic Act (sec. 512, 82 Stat. 343-351 (21 U.S.C. 360b)) and under authority delegated to the Director of the Center for Veterinary Medicine (21 CFR 5.84).

Dated: December 11, 1986.

Gerald B. Guest,

Director, Center for Veterinary Medicine.

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Federal Register

Wednesday
December 17, 1986

Part IV

Department of Housing and Urban Development

Office of the Assistant Secretary for Fair Housing and Equal Opportunity

24 CFR Part 146

Nondiscrimination on the Basis of Age in Programs Receiving Federal Financial Assistance; Final Rule

Guidelines for Application of Standards for Determining Age Discrimination; Notice

DEPARTMENT OF HOUSING AND URBAN DEVELOPMENT

Office of the Assistant Secretary for Fair Housing and Equal Opportunity

24 CFR Part 146

[Docket No. R-86-876; FR-1161]

Nondiscrimination on the Basis of Age in Programs or Activities Receiving Federal Financial Assistance

AGENCY: Office of the Assistant Secretary for Fair Housing and Equal Opportunity, HUD.

ACTION: Final rule.

SUMMARY: This final rule implements the Age Discrimination Act of 1975 in connection with programs and activities carried out by HUD. The Act generally prohibits discrimination on the basis of age in HUD programs and activities receiving Federal financial assistance. This final regulation is designed to guide the actions of recipients of financial assistance from HUD.

EFFECTIVE DATE: Under section 7(o)(3) of the Department of Housing and Urban Development Act (42 U.S.C. 3535(o)(3)), this final rule cannot become effective until after the first period of 30 calendar days of continuous session of Congress which occurs after the date of the rule's publication. HUD will publish a notice of the effective date of this rule following expiration of the 30-session-day waiting period. Whether or not the statutory waiting period has expired, this rule will *not* become effective until HUD's separate notice is published announcing a specific effective date.

FOR FURTHER INFORMATION CONTACT: Mrs. Myra Kennedy, Office of Fair Housing and Equal Opportunity, U.S. Department of Housing and Urban Development, 451 7th Street, SW., Room 5230, Washington, DC 20410 (202) 755-5904 (This is not a toll-free number).

SUPPLEMENTARY INFORMATION:

Background and Responses to Public Comments

The Age Discrimination Act of 1975 (the Act), 42 U.S.C. 6101-6107, prohibits any person from being excluded from participation in, denied the benefits of, or subjected to discrimination under, any program or activity receiving Federal financial assistance. The Act does not apply to any age distinction established under authority of any law which provides benefits or establishes criteria for participation on the basis of age or in age-related terms, nor does it apply when an explicit age distinction is necessary to the normal operation of a program or to the achievement of the statutory objective of a program.

The Act mandated that the Department of Health and Human Services (HHS) publish a general regulation to guide the development of specific regulations by each Federal agency that administers programs of financial assistance. HHS published a final general regulation on June 12, 1979 (44 FR 33768).

In compliance with the Act and in keeping with the HHS general regulation, on November 4, 1980, HUD published in the **Federal Register** (45 FR 73454) a notice of proposed rulemaking proposing to add to Title 24 of the Code of Federal Regulations a new Part 146, Nondiscrimination on the Basis of Age in HUD Programs or Activities Receiving Federal Financial Assistance. Interested parties were given until January 5, 1981 to submit comments. Comments were received from five entities: a children's interest fund, an elderly interest association, a county association, and two private individuals. All comments have been carefully reviewed and considered in the adoption of this final rule. The following is a summary of the comments received and the Department's responses to those comments.

1. All five commenters requested clarification of the four-part test contained in § 146.12(b) which was proposed to be used to determine when an age distinction is necessary to the normal operation of a program or to the achievement of a statutory objective of a program (thus providing an exception to the rule). All four parts of the test must be met. The discussion below following each of the four described parts of the test responds to the questions about the test raised by the commenters by clarifying the intent of each part. (The example and analysis under comment 2 will further illustrate application of the four-part test.) Note that § 146.12 is redesignated as § 146.13 in the final rule.

a. *Age is used as a measure or approximation of one or more other characteristics.* This refers to a situation in which an *age distinction is used as an indicator* of some other (non-age) characteristic. If age is not being used as an indicator or measure of some other (non-age) characteristic, it is unnecessary to apply the four-part test.

b. *The other characteristics must be measured or approximated in order for the normal operation of the program to continue, or to achieve any statutory objective of the program.* The test asks whether the other (non-age) characteristic that is being measured by the use of an age distinction is a characteristic that *must be measured* in order for the normal operation of the program or activity to continue, or to achieve any statutory objective of the program or activity.

c. *The other characteristics can be reasonably measured or approximated by the use of age.* The test asks whether the non-age characteristic is *capable of being reasonably approximated by age.* Hence, the test requires the agency to determine how accurate a measure the age distinction is of the non-age characteristic; i.e., whether there is a sufficiently high correlation between the age distinction being used and the non-age characteristic that is being measured to warrant the use of age.

d. *The other characteristics are impractical to measure directly on an individual basis.* Even though a non-age characteristic is capable of being reasonably approximated through the use of an age distinction, the test requires that the characteristic be measured without the use of an age distinction *unless it would be impractical to do so.* In other words, the four-part test permits the use of age distinctions only when no other practical alternative exists.

2. Several commenters requested that examples appear in the final rule to demonstrate how the four-part test should be applied. HUD will soon publish an Age Discrimination Act handbook which will provide detailed guidance and specific examples. However, below is one example of how the four-part test should be applied.

Example: A project providing housing for the elderly or handicapped under Section 202 of the Housing Act of 1959, 12 U.S.C. 1701q, refuses to accept as tenants persons over 66 years of age. The stated reason for this age distinction is that Section 202 of the Housing Act of 1959 was generally designed to provide housing for elderly and handicapped individuals capable of "independent living." In addition, the project in question does not provide services for those unable to live independently. The project sponsor asserts that persons over a certain age (66 years) are not likely to be capable of living independently.

Analysis: Section 146.13 of the final rule provides that no person in the United States shall, on the basis of age, be excluded from participation in, be denied the benefits of, or be subjected to discrimination under, any program or activity receiving Federal financial assistance. Section 202 projects receive Federal financial assistance as defined in Section 146.7. Persons over 66 years of age are excluded from the project

because of their age. However, under § 146.13(b), a recipient is permitted to take an action otherwise prohibited by § 146.13(a) if the action reasonably takes into account age as a factor necessary to the normal operation or achievement of any statutory objective of a program or activity. An action reasonably takes into account age as a factor necessary to the normal operation or the achievement of any statutory objective of a program or activity if it satisfies the four-part test:

(1) *Is age used as a measure or approximation of one or more other characteristics? Yes.* In this hypothetical instance, age is used as a measure or approximation of prospective tenants' ability to live independently.

(2) *Must the other (i.e., non-age) characteristics be measured or approximated in order for the normal operation of the program or activity to continue, or to achieve any statutory objective of the program or activity? Yes.* In this case, the non-age characteristic (the ability to live independently) must be measured in order for the normal operation of the program or activity to continue. The Section 202 project in question is designed for independent living. Persons not capable of independent living would not be able to reside successfully in the project.

(3) *Can the other (i.e., non-age) characteristic be reasonably measured or approximated by the use of age? No.* While there may be a correlation between age and the ability to live independently, there are many people well over the age of 66 who are fully capable of independent living. In addition, there are many people under the age of 66 who are not capable of independent living. Therefore, the non-age characteristic cannot *reasonably* be measured or approximated by the use of age.

(4) *Is it impractical to measure the other characteristic directly on an individual basis? No.* Project management can, through individual interviews and other means, determine, without bearing an impractical burden, whether an individual applicant is capable of living independently. In most cases, a face-to-face interview will suffice to make this determination. Therefore, age is an inaccurate and unnecessary way of determining an applicant's ability to live independently.

In order to qualify for the exemption contained in § 146.12(b), the age distinction must satisfy *all four parts* of the test. In this case, the age distinction failed to satisfy two parts of the test. Therefore, it violates the Act.

In today's issue of the **Federal Register**, HUD is publishing additional guidelines for the application of standards for determining whether prohibited age discrimination is being practiced.

3. Several commenters questioned HUD's authority to conduct compliance reviews and terminate funds of recipients. Response: HUD has the authority to conduct compliance reviews of recipients under Title VI of the Civil Rights Act of 1964, 42 U.S.C. 2000d–1; Sections 104(d) and 109 of the Housing and Community Development Act of 1974, 42 U.S.C. 5304, 5309; and under the Age Discrimination Act of 1975 that will enable it to investigate and correct violations of the above authorities. HUD may conduct these reviews even in the absence of a complaint against a recipient. The review may be as comprehensive as necessary to determine whether a violation has occurred. If a compliance review under the Act indicates a violation of this part, HUD will attempt to achieve voluntary compliance. If voluntary compliance cannot be achieved, HUD will arrange for enforcement as described in § 146.35 of this part. The determination of the recipient's violation may be made only after a recipient has had an opportunity for a hearing on the record before an administrative law judge. Therefore, cases that are settled in mediation, or before a hearing, will not involve termination of a recipient's Federal financial assistance from HUD.

4. One commenter suggested that HUD withdraw the proposed rule pending further study of the impact that the Act and the proposed regulation would have on certain groups; i.e., the elderly, families with children, and persons under 18 years of age. Response: A HUD recipient, in furtherance of statutory objectives and normal program objectives, may administer a program or activity which is designed only for a particular age group, so no adverse impact on special age groups that HUD seeks to serve is anticipated.

5. Another commenter requested clarification as to whether the proposed regulation allowed certain housing sites to be designated only for elderly (over age 62) tenants. Response: The Section 202 program (12 U.S.C. 1701q) contains a minimum age requirement of 62 years for non-handicapped persons. This statutory requirement constitutes an exception to the Age Discrimination Act. In the absence of a statutory requirement of this kind, age distinctions involving limits on access to housing would have to be subjected to the four-part test described previously.

Discussion of Changes in Final Rule

The final rule incorporates the basic standards for defining age discrimination that were set forth in the proposed rule. It also sets forth the responsibilities of HUD recipients and the investigation, settlement, and enforcement procedures that HUD will use to ensure compliance with the Act.

The self-evaluation requirement has been revised from the provision contained in the proposed rule. The proposed rule provision required all recipients employing 15 or more employees to complete a written self-evaluation. Section 146.25 now states that such recipients *may* be required to undertake a self-evaluation as part of a compliance review or complaint investigation conducted by HUD. The change is made to be consistent with the requirements of the Paperwork Reduction Act of 1980. The paperwork burden associated with the self-evaluation will apply only to recipients where circumstances indicate the need for the self-evaluation in connection with a compliance review or complaint investigation.

Other Matters

This rule does not constitute a "major rule" as that term is defined in section 1(b) of the Executive Order on Federal Regulation issued by the President on February 17, 1981. Analysis of the rule indicates that it does not (1) have an annual effect on the economy of $100 million or more; (2) cause a major increase in costs or prices for consumers, individual industries, Federal, State or local government agencies, or geographic regions; or (3) have a significant adverse effect on competition, employment, investment, productivity, innovation, or on the ability of United States-based enterprises to compete with foreign-based enterprises in domestic or export markets.

A Finding of No Significant Impact with respect to the environment has been made in accordance with 24 CFR Part 50, which implements section 102(2)(C) of the National Environmental Policy Act of 1969, 42 U.S.C. 4332. The Finding of No Significant Impact is available for public inspection during regular business hours in the Office of the Rules Docket Clerk, Room 10278, 451 Seventh Street, SW., Washington, DC 20410.

Under 5 U.S.C. 605(b) (the Regulatory Flexibility Act), the Undersigned hereby certifies that this rule does not have a significant economic impact on a substantial number of small entities

because it primarily concerns the investigation, settlement, and enforcement procedure that HUD will use to ensure compliance with each recipient's statutory responsibility under the Age Discrimination Act of 1975. It is not expected to cause any significant impact on small entities.

This rule is listed in 51 FR 38463 as item number 939 in the Department's Semiannual Agenda of Regulations published on October 27, 1986, pursuant to Executive Order 12291 and the Regulatory Flexibility Act.

The Catalog of Federal Domestic Assistance title and program number is Nondiscrimination in Federally-Assisted Programs (on the Basis of Age), 14.402.

In accordance with the Paperwork Reduction Act of 1980 (Pub. L. 96–511), the reporting or recordkeeping provisions that are included in this regulation have been submitted for approval to the Office of Management and Budget (OMB). They are not effective until OMB approval has been obtained and the public notified to that effect through a technical amendment to this regulation.

List of Subjects in 24 CFR Part 146

Discrimination against the aged, Civil rights, Grant programs: Housing and community development, Administrative practice and procedures, Loan programs: Housing and community development, Reporting and recordkeeping requirements.

Accordingly, Title 24 of the Code of Federal Regulations, Subtitle B, Chapter I, is amended by adding a new Part 146, to read as follows:

PART 146—NONDISCRIMINATION ON THE BASIS OF AGE IN HUD PROGRAMS OR ACTIVITIES RECEIVING FEDERAL FINANCIAL ASSISTANCE

Subpart A—General

Sec.

Subpart B—Standards for Determining Age Discrimination

Subpart C—Duties of HUD Recipients

Subpart D—Investigation, Settlement, and Enforcement Procedures

Authority: Age Discrimination Act of 1975 (42 U.S.C. 6103); sec. 7(d), Department of Housing and Urban Development Act (42 U.S.C. 3535(d)).

Subpart A—General

§ 146.1 Purpose of the Age Discrimination Act of 1975.

The Age Discrimination Act of 1975 (the Act) prohibits discrimination on the basis of age in programs or activities receiving Federal financial assistance. The Act, however, permits federally assisted programs and activities and recipients of Federal funds to continue to use certain age distinctions and factors other than age which meet the requirements of the Act and this part.

§ 146.3 Purpose of HUD's age discrimination regulation.

The purpose of this part is to state HUD's policies and procedures under the Age Discrimination Act of 1975, consistent with the government-wide age discrimination regulation contained at 45 CFR Part 90.

§ 146.5 Applicability of part.

This part applies to each program or activity that receives Federal financial assistance provided by HUD.

§ 146.7 Definitions.

As used in this part, the term:

"Act" means the Age Discrimination Act of 1975, 42 U.S.C. 6101–07.

"Action" means any act, activity, policy, rule, standard, or method of administration or the use of any policy, rule, standard, or method of administration.

"Age" means how old a person is, or the number of elapsed years from the date of a person's birth.

"Age distinction" means any action using age or an age-related term.

"Age-related term" means a word or words which necessarily imply a particular age or range of ages (for example, "children", "adult", "older persons", but not "student").

"Federal financial assistance" means any grant, entitlement, loan, cooperative agreement, contract (other than a procurement contract or a contract of insurance or guaranty), or any other arrangement by which HUD provides or otherwise makes available assistance in the form of:

(a) Funds;

(b) Service of Federal personnel; or

(c) Real or personal property or any interest in or use of property, including:

(1) Transfers or leases of property for less than fair market value or for reduced consideration; and

(2) Proceeds from a subsequent transfer or lease of property if the Federal share of its fair market value is not returned to the Federal government.

"HUD" means the United States Department of Housing and Human Development.

"Recipient" means any State or its political subdivisions; any instrumentality of a State or its political subdivisions; any public or private agency; any Indian tribe or Alaskan Native Village, institution, organization, or other entity; or any person to which Federal financial assistance is extended, directly or through another recipient. Recipient includes any successor, assignee, or transferee, but does not include the ultimate beneficiary of the assistance.

"Secretary" means the Secretary of HUD or his or her designee.

"Subrecipient" means any of the entities in the definition of "recipient" to which a recipient extends or passes on Federal financial assistance. A subrecipient is regarded as a recipient of Federal financial assistance and has all the duties of a recipient set out in this part.

"United States" means the several States, the District of Columbia, Puerto Rico, the Virgin Islands, American Samoa, Guam, Wake Island, the Canal Zone, the Trust Territory of the Pacific Islands, the Northern Marianas, and the territories and possessions of the United States.

Subpart B—Standards for Determining Age Discrimination

§ 146.11 Scope of subpart.

This subpart contains the standards that HUD will use to determine whether an age distinction, or a factor other than age that may have a disproportionate effect on persons of different ages, is prohibited.

§ 146.13 Rules against age discrimination.

(a) The rules stated in this paragraph are limited by the exceptions contained in paragraphs (b) and (c) of this section.

(1) *General rule.* No person in the United States shall, on the basis of age, be excluded from participation in, be denied the benefits of, or be subjected to discrimination under, any program or activity receiving Federal financial assistance.

(2) *Specific rules.* A recipient may not, in any program or activity receiving Federal financial assistance, directly or through contracting, licensing, or other arrangements, use age distinctions or take any other actions that have the effect, on the basis of age, of:

(i) Excluding individuals from, denying them the benefits of, or subjecting them to discrimination under, a program or activity receiving Federal financial assistance; or

(ii) Denying or limiting individuals in their opportunity to participate in any program or activity receiving Federal financial assistance.

(3) The specific forms of age discrimination listed in paragraph (2) of this paragraph (a) do not necessarily constitute a complete list.

(b) *Exceptions for normal operation or statutory objective of any program or activity.* A recipient is permitted to take an action otherwise prohibited by paragraph (a) of this section if the action reasonably takes into account age as a factor necessary to the normal operation or the achievement of any statutory objective of a program or activity. An action reasonably takes into account age as a factor necessary to the normal operation or the achievement of any statutory objective of a program or activity, if:

(1) Age is used as a measure or approximation of one or more other characteristics; and

(2) The other characteristics must be measured or approximated in order for the normal operation of the program or activity to continue, or to achieve any statutory objective of the program or activity; and

(3) The other characteristics can be reasonably measured or approximated by the use of age; and

(4) The other characteristics are impractical to measure directly on an individual basis.

(c) *Exceptions for reasonable factors other than age.* A recipient is permitted to take action otherwise prohibited by paragraph (a) of this section if the action is based on a factor other than age, even though that action may have a disproportionate effect on persons of different ages. An action may be based on a factor other than age only if the factor bears a direct and substantial relationship to the normal operation of the program or activity or the achievement of a statutory objective.

(d) *Burden of proof.* The burden of proving that an age distinction or other action falls within an exception described in paragraph (b) or (c) of this section is on the recipient of Federal financial assistance.

(e) For the purposes of paragraphs (b) and (c), "normal operation" means the operation of a program or activity without significant changes that would impair its ability to meet its statutory objectives. "Statutory objectives" means any purpose of a program or activity expressly stated in any Federal, State, or local statute adopted by an elected, general purpose legislative body.

(f) Notwithstanding paragraph (b) of this section, if a recipient operating a program provides special benefits to the elderly or to children, such use of age distinctions shall be presumed to be necessary to the normal operation of the program.

Subpart C—Duties of HUD Recipients

§ 146.21 General responsibilities.

Each recipient has primary responsibility to ensure that its programs and activities that receive Federal financial assistance from HUD comply with the provisions of the Act, the government-wide regulation, and this part, and shall take steps to eliminate violations of the Act. A recipient also has responsibility to maintain records, provide information, and to afford HUD access to its records to the extent HUD finds necessary to determine whether a program or activity receiving Federal financial assistance from HUD is in compliance with the Act and this part.

§ 146.23 Notice of subrecipients.

Whenever a recipient passes Federal financial assistance from HUD to subrecipients, the recipient shall provide the subrecipient with written notice of its obligations under this part and the recipient will remain responsible for the subrecipient's compliance with respect to programs and activities receiving Federal financial assistance from HUD.

§ 146.25 Assurance of compliance and recipient assessment of age distinctions.

(a) Each recipient of Federal financial assistance from HUD shall sign a written assurance as specified by HUD that it will comply with the Act and this part with respect to programs and activities receiving Federal financial assistance from HUD.

(b) As part of a compliance review under § 146.31 or an investigation under § 146.37, HUD may require a recipient employing the equivalent of 15 or more employees to complete, in a manner specified by the Secretary or Secretary's designee, a written self-evaluation of an age distinction imposed in its program or activity receiving Federal financial assistance from HUD, so that HUD may have to assess the recipient's compliance with the Act. Whenever an assessment indicates a violation of the Act or this part, the recipient shall take corrective action to remedy the violation.

§ 146.27 Information requirements.

In order to make it possible for HUD to determine whether recipients are in compliance with the Act and this part, each recipient shall:

(a) Keep records in a form and containing information that HUD determines is necessary;

(b) Make information available to HUD upon request;

(c) Permit reasonable access by HUD to the books, records, accounts and other recipient facilities and sources of information.

Subpart D—Investigation, Settlement, and Enforcement Procedures

§ 146.31 Compliance reviews.

(a) HUD may conduct pre-award reviews to determine whether programs or activities submitted for HUD assistance are consistent with the age distinctions set forth at § 146.13(b).

(b) If a pre-award review indicates that the proposed programs or activities are not consistent with the age distinctions set forth at § 146.13(b), the application will be returned to the applicant for additional information or clarification or for correction consistent with this part.

(c) HUD may conduct compliance reviews of recipients that will enable it to investigate and correct violations of this part. HUD may conduct these reviews even in the absence of a complaint against a recipient. The review may be as comprehensive as necessary for HUD to determine whether a violation has occurred.

(d) If a compliance review indicates a violation, HUD will attempt to achieve voluntary compliance. If voluntary compliance cannot be achieved, HUD may begin enforcement procedures as provided in § 146.39.

§ 146.33 Complaints.

(a) Any person, individually or as a member of a class or on behalf of others, may file a complaint with HUD alleging discrimination prohibited by the Act. A complainant shall file a complaint within 180 days from the date the complainant first had knowledge of the alleged act of discrimination. However, for good cause, HUD may extend this

time limit. The filing date for a complaint will be the date upon which the complaint is deemed sufficient to be processed.

(b) HUD shall facilitate the filing of complaints and shall take the following measures:

(1) Accept as a sufficient complaint any written legible statement which is signed by the complainant and which identifies the parties involved, the date the complainant first had knowledge of the alleged violation, and describes generally the alleged prohibited action or practice;

(2) Freely permit a complainant to add information to the complaint to meet the requirements of a sufficient complaint;

(3) Widely disseminate information regarding the obligations of recipients under the Act and this part;

(4) Notify the complainant and the recipient of their rights under the complaint process, including the right to have a representative at all stages of the complaint process; and

(5) Notify the complainant and the recipient of their right to contact HUD for information and assistance regarding the complaint resolution process.

(c) HUD will return to the complainant any complaint determined to be outside the coverage of this part, and shall state the reasons why it is outside the coverage.

§ 146.35 Mediation.

(a) HUD shall refer to the Federal Mediation and Conciliation Service, a mediation agency designated by the Secretary of Health and Human Services, all complaints that:

(1) Fall within the coverage of this part, unless the age distinction complained of is clearly with an exeption; and

(2) Contain all information necessary for further processing.

(b) Both the complainant and the recipient shall participate in the mediation process to the extent necessary to reach an agreement or make an informal judgment that an agreement is not possible. There should be at least one meeting by each party with the mediator during the mediation process. However, the recipient and the complainant need not meet with the mediator at the same time.

(c) If the complainant and the recipient reach an agreement, the mediator shall prepare a written statement of the agreement and have the complainant and recipient sign it. The mediator shall send a copy of the agreement to HUD. HUD will take no further action on the complaint unless the complainant or the recipient fails to comply with the agreement.

(d) The mediator shall protect the confidentiality of information obtained in the course of the mediation process. No mediator shall testify in any adjudicative proceeding, produce any document, or othewise disclose any information obtained in the course of the mediation process without the prior approval of the head of the mediation agency.

(e) HUD shall use the mediation process for a maximum of 60 days after receiving a complaint. Mediation ends if:

(1) 60 days elapse from the time HUD receives the complaint; or

(2) Before the end of the 60-day period, an agreement is reached; or

(3) Before the end of the 60-day period, the mediator determines that an agreement cannot be reached.

This 60-day period may be extended by the mediator, with the concurrence of HUD, for not more than an additional 30 days if the mediator determines that it is likely that an agreement will be reached during such extended period.

§ 146.37 Investigation.

(a) *Investigation and settlement following mediation.*

(1) HUD shall investigate complaints that are unresolved after mediation or are reopened because of an alleged violation of a mediation agreement.

(2) In the investigation of complaints filed under this part, HUD will establish facts through such methods as discussion with the complainant and recipient and the review of documents in the possession of either party. HUD may also seek the assistance of any applicable State agency. Where possible, HUD will settle the complaint on terms that are mutually agreeable to the parties.

(3) Settlements shall be in writing and signed by the parties and by an authorized HUD official.

(4) A settlement shall not affect the initiation or continuation of any other enforcement effort of HUD, including compliance reviews or investigation of other complaints involving the recipient.

(5) A settlement reached under this paragraph (a) is an agreement to resolve an alleged violation of the Act to the satisfaction of the parties involved, and does not constitute a finding of discrimination against the recipient.

(b) *Failure of settlement.* If HUD cannot resolve the complaint through settlement, it may make a formal determination that the Act or this part has been violated and begin enforcement procedures, as provided in § 146.39. HUD shall inform the recipient and complainant in writing that the matter cannot be resolved through settlement.

§ 146.39 Enforcement procedures.

(a) HUD may enforce the Act this regulation by:

(1) Termination of a recipient's financial assistance from HUD under the program or activity involved, if the recipient has violated the Act or this part. The determination of the recipient's violation may be made only after a recipient has had an opportunity for a hearing on the record before an Administrative Law Judge. If the financial assistance consists of a Community Development Block Grant, the requirements of section 109(b) of the Housing and Community Development Act of 1974, 42 U.S.C. 5309, must also be satisfied before the termination of financial assistance. Cases settled in mediation or before hearing will not involve termination of a recipient's Federal financial assistance from HUD.

(2) Any other means authorized by law, including, but not limited to:

(i) Referral to the Department of Justice for proceedings to enforec any rights of the United States or obligations of the recipient created by the Act or this part;

(ii) Use of any requirement of, or referral to, any Federal, State or local government agency that will have the effect of correcting a violation of the Act or this part.

(b) Whenever the Secretary determines that a State or unit of general local government which is a recipient of Federal financial assistance under Title I of the Housing and Community Development Act of 1974, 42 U.S.C. 5301–5317, has failed to comply with requirements of the Age Discrimination Act or this part with respect to a program or activity funded in whole or in part with such assistance, he or she shall notify the Governor of such State or the chief executive officer of such unit of general local government of the noncompliance and shall request the Governor or chief executive officer to secure compliance. If within a reasonable period of time, not to exceed 60 days, the Governor or chief executive officer fails or refuses to secure compliance, the Secretary is authorized to take the action specified in (a) of this section, exercise the powers and functions provided for in section 111(a) of the Housing and Community Act of 1974, 42 U.S.C. 5311(a), or take such other action as may be provided by law.

(c) HUD shall limit any termination under § 146.35 to the particular recipient and particular program or activity HUD finds to be in violation of this part. HUD shall not base any part of a termination on a finding with respect to any program or activity of the recipient which does

not receive Federal financial assistance from HUD.

(d) HUD shall take no action under paragraph (a) of this section until:

(1) The Secretary has advised the recipient of its failure to comply with the Act or this part and has determined that voluntary compliance cannot be achieved.

(2) Thirty days have have elapsed after the Secretary has submitted a written report of the circumstances and grounds of the action to the committees of the Congress having legislative jurisdiction over the Federal program or activity involved. A report shall be filed whenever any action is taken under paragraph (a) of this section.

(e) (1) The Secretary may defer the provision of new Federal financial assistance to a recipient when termination proceedings under this section are initiated.

(2) New financial assistance from HUD includes all assistance for which HUD requires an application, approval, or submissions under the Community Development Block Grant program including renewal or continuation of existing activities, or authorization of new activities, during the deferral period. New financial assistance from HUD does not include increases in funding as a result of changed computation for formula awards or assistance approved before the beginning of a hearing under this section.

(3) HUD shall not impose a deferral until the recipient has received a notice of an opportunity for a hearing under this section. HUD shall not continue a deferral for more than 60 days unless a hearing has begun within that time or the time for beginning the hearing has been extended by mutual consent of the recipient and the Secretary. HUD shall not continue a deferral for more than 30 days after the close of the hearing, unless the hearing results in a finding that the recipient has violated that Act or this part.

§ 146.41 Prohibition against intimidation or retaliation.

A recipient may not engage in acts of intimidation or retaliation against any person who:

(a) Attempts to assert a right protected by this part; or

(b) Cooperates in any mediation, investigation, hearing, or other part of HUD's investigation, settlement, and enforcement process.

§ 146.43 Hearing, decisions, post-termination proceedings.

Certain HUD procedural provisions applicable to the enforcement of Title VI of the Civil Rights Act of 1964, 42 U.S.C. 2000d–1 shall apply to HUD enforcement of this part. These provisions are contained in 24 CFR 1.9 through 1.12 and 24 CFR Part 2.

§ 146.45 Exhaustion of administrative remedies.

(a) A complainant may file a civil action following the exhaustion of administrative remedies under the Act. Administrative remedies are exhausted if:

(1) 180 days have elapsed since the complainant filed the complaint and HUD had made no finding with regard to the complaint; or

(2) HUD issues any finding in favor of the recipient.

(b) If HUD fails to make a finding within 180 days or issues a finding in favor of the recipient, HUD shall:

(1) Promptly advise the complainant of this fact;

(2) Advise the complainant of his or her right to bring a civil action for injunctive relief; and

(3) Inform the complainant:

(i) That he or she may bring a civil action only in a United States District Court for the district in which the recipient is located or transacts business;

(ii) That a complianant prevailing in a civil action has the right to be awarded the costs of the action, including reasonable attorney's fees, but that the complainant must demand these costs in the complaint;

(iii) That before commencing the action, the complainant must give 30 days' notice by registered mail to the Secretary of HUD, the Secretary of Health and Human Services, the Attorney General of the United States, and the recipient;

(iv) That the notice must state: the alleged violation of the Act, the relief requested, the court in which the complainant is bringing the action, and whether or not attorney's fees are demanded in the event the complainant prevails; and

(v) That the complainant may not bring an action if the same alleged violation of the Act by the same recipient is the subject of a pending action in any court of the United States.

§ 146.47 Remedial and affirmative action by recipients.

(a) Where the Secretary finds that a recipient has unlawfully discriminated on the basis of age, the recipient shall take any action that the Secretary may require to overcome the effects of the discrimination. If another recipient exercises control over a subrecipient that has unlawfully discriminated, the Secretary may require both recipients to take remedial action.

(b) Even in the absence of a finding of discrimination, a recipient may take affirmative action to overcome the effects of conditions that resulted in limited participation in the recipient's program or activity on the basis of age.

(c) If a recipient operating a program which serves the elderly or children in addition to persons of other ages provides special benefits to the elderly or children, the provision of those benefits shall be presumed to be voluntary affirmative action, provided that it does not have the effect of excluding otherwise eligible persons from participation in the program.

§ 146.49 Alternate funds disbursal procedure.

(a) Except as otherwise provided in this paragraph and to the extent authorized by law, the Secretary may redisburse funds withheld or terminated under this part directly to an alternate recipient, including any public or non-profit private organization or agency, State or political subdivision of the State. Under Title I of the Housing and Community Development Act of 1974, 42 U.S.C. 5301, funds withheld because of a reduction or withdrawal of a recipient's Community Development Block Grant must be reallocated in the succeeding fiscal year, in accordance with the applicable regulations governing that program.

(b) The Secretary shall require the alternate recipient to demonstrate:

(1) The ability to comply with the regulations; and

(2) The ability to achieve the goals of the Federal statute authorizing the program or activity.

Dated: July 31, 1986.

William E. Wynn,

Acting General Deputy Assistant Secretary For Fair Housing and Equal Opportunity.

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