safeguard provisions of § 959.54 and paragraph (g) of this section. The receiver shall furnish the committee with a report on the arrival condition of each shipment.

(ii) Upon approval of the committee, onions may be shipped for other experimental purposes exempt from regulations issued pursuant to §§ 959.42, 959.52 and 959.60, provided they are handled in accordance with safeguard provisions of § 959.54 and paragraph (g) of this section.

(iii) Upon approval of the committee, onions may be shipped for testing in types and sizes of containers other than those specified in paragraph (c), (f)(2) and (3) above. provided that the handling of onions in such experimental containers shall be under the supervision of the committee.

(5) *Export shipments.* (i) Upon approval of the committee, the prohibition against packaging or loading onions on any Sunday may be modified or suspended to permit the handling of onions for export provided such handling complies with the procedures and safeguards specified by the committee.

(ii) Following approval, if the handler grades, packages and ships onions for export on any Sunday, such handler shall on the first weekday following shipment, cease all grading, packaging and shipping operations for the same length of time as the handler operated on Sunday. Upon completion of such shipments, the handler shall report thereon as prescribed by the committee.

(iii) Export shipments shall also be exempt from all container requirements of this section.

(6) *Onions failing to meet requirements:* Onions failing to meet the grade, size and container requirements of this section, and not exempt under paragraph (e) or (f) of this section, may be handled only pursuant to § 959.126. Such onions not handled in accordance with paragraph (g) of this section shall be mechanically mutilated at the packing shed rendering them unsuitable for fresh market.

(g) *Safeguards.* Each handler making shipments of onions for relief, charity, canning, freezing or experimental purposes or onions packed in 50-pound cartons or 2, 3 or 5 pound containers customarily packed for the retail trade shall:

(1) Apply to the committee for and obtain a Certificate of Privilege to make such shipments:

(2) Furnish reports of each shipment made under the applicable Certificate of Privilege;

(3) Such reports, in accordance with § 959.80, shall be furnished to the committee in such manner, on such forms and at such times as it may prescribe. Each handler shall maintain records of such shipments pursuant to § 959.80(c), and the records shall be subject to review and audit by the committee to verify reports thereon.

In addition to the above, each handler making shipments for canning or freezing shall:

(4) Weigh or cause to be weighed each shipment prior to, or upon arrival at the canner or freezer.

(5) Attach a copy of the weight ticket to a completed copy of the Report of Special Purpose Onion Shipment and return both promptly to the committee office.

(6) Make each shipment directly to the applicable processor and attach a copy of the Report of Special Purpose Onion Shipment.

(7) Each canner or freezer who receives cull onions shall weigh the onions upon receipt, complete the Report of Special Purpose Onion Shipment which accompanies each load and mail it immediately to the committee office.

(8) Each canner or freezer who receives cull onions shall make available at its business office at any reasonable time during business hours, copies of all applicable purchase orders, sales contracts, or disposition documents for examination by the Department or by the committee. together with any other information which the committee or the Department may deem necessary to enable it to determine the disposition of the onions.

(h) *Definitions.* "U.S. onion standards" means the United States Standards for Grades of Bermuda-Granex-Grano Type Onions (7 CFR 2851.3195–2851.3209), or the United States Standards for Grades of Onions (Other Than Bermuda-Granex-Grano and Creole Types) (7 CFR 2851.2830–2851.2854), whichever is applicable to the particular variety, or variations thereof specified in this section. The term "U.S. No. 1" shall have the same meaning as set forth in these standards. All other terms used in this section shall have the same meaning as when used in Marketing Agreement No. 143, as amended, and this part.

(i) *Applicability to imports.* During the approximately mid-March through May period of each year, imported onions shall comply with the minimum grade, size, quality and maturity requirements imposed under this marketing order. The specific beginning and ending dates will be set forth in the summary of onion import regulation to be issued prior to the beginning of each seaon, after the Secretary determines when the imported onions are in most direct competition with regulated onions grown in South Texas. Therefore, under Section 8e of the act and Section 980.117 "Import regulations: onions" (7 CFR 980.117) such imported onions shall have not more than 20 percent defects of U.S. No. 1 grade and be at least 1 inch in diameter for white varieties and at least 1¾ inches in diameter for all other varieties. In percentage grade lots, tolerance for serious damage shall not exceed 10 percent including not more than 2 percent decay. Double the lot tolerance shall be permitted in individual packages in percentage grade lots. Applicants of tolerances in the U.S. onion standards shall apply to in-grade lots.

(Secs. 1–19, 48 Stat. 31, as amended; 7 U.S.C. 601–674)

Dated December 15, 1981.

D. S. Kuryloski,

Deputy Director, Fruit and Vegetable Division, Agricultural Marketing Service.

[FR Doc. 81–36209 Filed 12–17–81; 8:45 am]

BILLING CODE 3410–02–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 50

[Docket No. 78N–0049]

Protection of Human Subjects; Prisoners Used as Research Subjects; Reproposal of Regulations

AGENCY: Food and Drug Administration.

ACTION: Reproposal of rule.

SUMMARY: The Food and Drug Administration (FDA) is reproposing its regulations establishing conditions under which biomedical research on prisoners would be accepted in satisfaction of FDA's regulatory requirements. In the **Federal Register** of July 7, 1981 (46 FR 35085), FDA stayed indefinitely the effective date of the original regulations, pending final action on this reproposal. Under the reproposal, FDA would accept, in addition to the categories of research listed in the original regulation, the results of biomedical research on prisoners if the sponsor of the proposed research establishes that the conditions set forth by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research had been met.

DATES: Written comments by February 16, 1982. FDA intends that any final rule it may publish on this matter would

become effective 90 days after the date of its publication in the **Federal Register.**

ADDRESS: Written comments may be submitted to the Dockets Management Branch (formerly the Hearing Clerk's office) (HFA–305), Food and Drug Administration, Rm. 4–62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Halyna P. Breslawec, Office of Health Affairs (HFY–Z), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–443–1382.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of May 30, 1980 (45 FR 36386), FDA issued final regulations to provide protection for prisoners used as the subjects of biomedical research within the agency's jurisdiction. The regulations were promulgated to implement the recommendations of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (National Commission). The National Commission was created by Congress under the National Research Act of 1974 (Pub. L. 93–348) to investigate research on human subjects and to make recommendations to the Department of Health and Human Services (Department) on, among other things, the requirements for obtaining voluntary and informed consent, free from coercion. Section 205 of the National Research Act required the Secretary of the Department to respond to the National Commission's recommendations.

In a report on research on prisoners issued in 1977 (see the **Federal Register** of January 14, 1977; 42 FR 3076), the National Commission concluded that the prison environment is inherently coercive, diminishing the capacity of prisoners to give informed consent to participation in biomedical and behavioral research. Based on its investigation of the nature of research on prisoners, the conditions under which it is presently conducted, and the social, ethical, and legal questions raised by prison research, the National Commission recommended limitations on the types of research conducted on prisoners and recommended that the following conditions exist in prisons at which research is conducted to enable prisoners to give voluntary and informed consent.

1. *Standard of living.* Living conditions in the prison in which research will be conducted or from which subjects will be recruited are adequate as evidenced by all of the following standards:

(a) The prison population does not exceed designed capacity, and each prisoner has an adequate amount of living space;

(b) There are single occupancy cells available for those who desire them;

(c) There is segregation of offenders by age, degree of violence, prior criminal record, and physical and mental health requirements;

(d) There are operable cell doors, emergency exits and fire extinguishers, and compliance with state and local fire and safety codes is certified;

(e) There are operable toilets and wash basins in cells;

(f) There is regular access to clean and working showers;

(g) Articles of personal care and clean linen are regularly issued;

(h) There are adequate recreation facilities, and each prisoner is allowed an adequate amount of recreation;

(i) There are good quality medical facilities in the prison, adequately staffed and equipped, and approved by an outside medical accrediting organization such as the joint Commission on Accreditation of Hospitals or a state medical society;

(j) There are adequate mental health services and professional staff;

(k) There is adequate opportunity for prisoners who so desire to work for remuneration comparable to that received for participation in research;

(l) There is adequate opportunity for prisoners who so desire to receive education and vocational training;

(m) Prisoners are afforded opportunity to communicate privately with their visitors, and are permitted frequent visits;

(n) There is a sufficiently large and well-trained staff to provide assurance of prisoners' safety;

(o) The racial composition of the staff is reasonably concordant with that of the prisoners;

(p) To the extent that it is consistent with the security needs of the prison, there should be an opportunity for inmates to lock their own cells; and

(q) Conditions in the prison satisfy basic institutional environmental health, food service and nutritional standards.

2. *Provisions for effective redress of grievance.* A grievance committee exists composed of elected prisoner representatives, prisoner advocates, and representatives of the community. The committee should enable prisoners to obtain effective redress of their grievances (including grievances concerning the existence of conditions established in (a)(2)). The committee should also facilitate inspections and monitoring by the accrediting agency to assure continuing compliance with requirement (a)(2)(C).

3. *Separation of research participation from parole considerations.* Effective procedures exist to assure that parole boards cannot take into account prisoners' participation in research and that prisoners are clearly informed that there is absolutely no relationship between research participation and determinations by their parole boards.

4. *Public scrutiny.* Prisoners are able to communicate, without censorship, with persons outside the prison, and, on a privileged, confidential basis, with attorneys, legal organizations that assist prisoners, the accrediting agency, the grievance committee referred to in this section, and the institutional review board. Each of these persons or organizations must be able to conduct private interviews with any prisoner who so desires. The accrediting agency, Administration, grievance committee, and institutional review board must be allowed free access to the prison. 42 FR 3080.

In accordance with its findings, the National Commission recommended that the Department support or accept research on prisoners if: (1) The research is intended and is reasonably likely to improve the health and well-being of prisoners individually or as a class (42 FR 3079, 3080), or (2) the research fulfills an important scientific need, and there is a compelling need to use prisoners and a determination by the agency head that the conditions for informed consent identified by the National Commission exist at the prison in question (42 FR 3080).

In the **Federal Register** of January 5, 1978 (43 FR 1050), the Department proposed regulations adopting the National Commission's findings and implementing its recommendations. The Department concluded, however, that the requirements for informed consent established by the National Commission for any research other than that benefitting prisoners individually or as a class (nonbeneficial research) were so stringent that it was doubtful that any existing prison and few research projects could meet them. Moreover, the Department found that it did not have the administrative capability to determine whether a prison or research project met the National Commission's criteria for informed consent (43 FR 1050, 1051). The proposed regulations therefore permitted only research that had the intent and reasonable probability of benefitting prisoners individually or as a class. The Department's final regulations were published in the **Federal Register** of November 16, 1978 (43 FR 53652).

The National Research Act did not impose an express obligation on the Department to respond to the National Commission's recommendations with respect to research regulated by or submitted in satisfaction of FDA's regulatory requirements. The Department concluded, however, that because the legislative history of the National Research Act reveals that Congress was also concerned with FDA-regulated research, FDA should consider whether to apply the National Commission's recommendations to research within FDA's jurisdiction (43 FR 1051).

FDA concluded that it had authority under the Federal Food, Drug, and Cosmetic Act (the act) to promulgate regulations protecting the interests of prisoners used as research subjects in clinical investigations submitted to FDA. Therefore, in the **Federal Register** of May 5, 1978 (43 FR 19417), FDA issued its proposal and in the **Federal Register** of May 30, 1980 issued final rules modeled after those of the Department, establishing criteria for acceptance of the results of research on prisoners.

FDA's regulations, codified in Subpart C of 21 CFR Part 50, permitted research on prisoners only when the research had the intent or reasonable probability of benefitting prisoners individually or as a class. FDA's regulations, like those of the Department, did not provide an exception for other types of research that might meet the National Commission's requirements for research not directly beneficial to prisoners. FDA concluded that in view of the National Commission's finding that prisons are inherently coercive and of the lack of evidence that other groups of potential research subjects could not be found, the need to protect prisoners outweighed any need to use prisoners that had yet been presented to FDA (45 FR 36388, 36389). Thus, it appeared to the agency that sponsors of research could never establish a compelling need to use prisoners, FDA therefore did not provide sponsors of research an opportunity to prove the existence of the conditions under which the National Commission concluded that prisoners could give informed consent to participation in nonbeneficial research.

FDA's regulations also included provisions establishing the composition and duties of institutional review boards where prisoners are involved (§§ 50.46 and 50.48). With the provisions for prison research, FDA also promulgated provisions that set out the scope and definitions used in Part 50, FDA's general regulations on protection of human subjects (§§ 50.1 and 50.3).

FDA's regulations were scheduled to become effective June 1, 1981. Shortly after the final regulations were published, however, a lawsuit was filed challenging the regulations. In the **Federal Register** of March 27, 1981 (46 FR 18951), the effective date of the regulations was deferred until 5 months after resolution of the lawsuit. FDA delayed the effective date in part for the purpose of reviewing the regulations under Executive Order 12291.

In the **Federal Register** of July 7, 1981 (46 FR 350850, FDA announced that it had reconsidered the regulations' utility and costs, and that it intended to repropose Subpart C of Part 50 and invite public comment on the reproposal. The notice stayed the effective date of the regulations until final action is taken on the reproposal. At the time the stay was imposed, the regulations had never been put into effect. (The stay did not affect, however, § 50.1 *Scope* and § 50.3 *Definitions.)* In a separate notice published in the **Federal Register** of July 7, 1981 (46 FR 35084), the agency announced that these sections would go into effect on July 27, 1981, with FDA's general informed consent and institutional review board regulations (46 FR 35084; July 7, 1981).

Reproposal

FDA's regulations, as published on May 30, 1980, were premised on a conclusive presumption that sponsors could not establish that research projects not directly beneficial to prisoners satisfied the conditions recommended by the National Commission for such research. FDA has reconsidered its decision to establish broader prohibitions on prisoner research than were recommended by the National Commission. FDA has not altered its belief that it has both the authority and the obligation to ensure the voluntary consent of prisoners used as the subjects of research within FDA's jurisdiction. It is, however, within the expertise of the National Commission to identify the safeguards needed to protect voluntary and informed consent among prisoners. Given that expertise, FDA should, whenever it is practicable, adopt the National Commission's recommendations.

Practicability

FDA possesses the inspectional resources necessary to permit a determination whether conditions at a particular prison meet the National Commission's requirements. FDA has an existing staff of trained investigators responsible for conducting inspections to ensure compliance with the act. Furthermore, the number of prison research projects within FDA's jurisdiction is very small, and the variety of research is limited. The expenditure of resources necessary for FDA to implement an exception procedure for research that does not directly benefit prisoners would thus be minimal.

Accordingly, FDA is reproposing Subpart C of 21 CFR part 50. The reproposal amends § 50.44 (21 CFR 50.44) to include an exception procedure for research that does not directly benefit prisoners. The exception closely follows the recommendations of the National Commission. Sponsors of proposed research will be required to establish (1) that the research serves an important social or scientific need and the reasons for using prisoners are compelling, (2) that the involvement of prisoners in this type of research satisfies conditions of equity, and (3) that prison conditions permit voluntary and informed consent. Sponsors of proposed research will have the burden of establishing that the research meets each, of these conditions. FDA investigators may, however, be sent to the sites of proposed research to assist the IRB in determining whether the National Commission's requirements have been met.

The IRB will make the determination whether the regulations' requirements have been met, after consulting with the Research Involving Human Subjects Committee, an ethical review committee established by the agency (see FDA Staff Manual Guide, 2111.3), whose members include agency officials and members of the public.

Minor revisions have been made in §§ 50.44(a) (1) and (2) and 50.48. The reproposal eliminates the requirements that the agency consult with appropriate experts and publish a **Federal Register** notice announcing its intention to approve research under § 50.44(a) (1) and (2) because FDA believes these requirements were unnecessary and excessively burdensome. The reproposal also eliminates the requirements in § 50.48(a)(7) that research sponsors provide followup examinations of participants. The National Commission did not recommend followup examinations for prisoners, nor does FDA require followup examinations for nonprisoner research subjects. FDA believes that it is not appropriate in this instance to impose additional requirements on research involving prisoners.

Legal Authority

FDA's legal authority to adopt regulations protecting prisoners used as

the subjects of research submitted to was discussed at length in the preamble to the May 5, 1976 proposal end in the preamble to the May 30, 1980 final rule. FDA receives hundreds of reports of clinical investigations each year by those seeking approval by the agency of research and marketing application. FDA must evaluate these reports to determine, among other things, their scientific validity and ethical acceptability. To use its limited resources efficiently, and to guide persons involved with biomedical research within the jurisdiction of the agency, FDA needs standards to screen out clinical investigations that are not acceptable and thus should not be authorized, or warrant no further evaluation in support of a product application. The promulgation of regulations establishing ethical standards for research on prisoners serves this goal.

Specific authority to establish ethical standards for clinical investigations, including requirements governing informed consent, derives from several sections of the act. Sections 505(i), 507(d), and 520(g) of the act (21 U.S.C. 355(i), 357(d), 360j(g)) require that the agency issue regulations that establish the conditions under which drugs and medical devices will be available for investigational use. Those sections of the act direct the agency to issue regulations to protect the public health in clinical investigations and to provide that informed consent will be obtained from the human subjects of the investigations. The act also requires that these regulations, in the case of drugs, have due regard for the interests of patients (21 U.S.C. 355(j)(1) and 21 U.S.C. 357(g)(1)), or, in the case of medical devices, be consistent with ethical standards (21 U.S.C. 360j(g)(1).

Finally, section 701(a) of the act (21 U.S.C. 371(a)) empowers the agency to issue regulations for the efficient enforcement of the act. The Supreme Court has upheld FDA's authority under section 701(a) of the act to promulgate analogous standards for determining whether clinical investigations of drugs intended for human use, submitted to FDA, were scientifically reliable. See *Weinberger* v. *Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609 (1973). To assess the validity of regulations issued under section 701(a) of the act, the issue is whether the statutory scheme as a whole justifies promulgation of the regulation. *National Confectioners Ass'n* v. *Califano*. 569 F. 2d 690, 693 (D.C. Cir. 1978). As explained in the preamble to the May 30, 1980 final rule, FDA believes that ensuring informed consent as well as due regard for the interests of prisoners as research subjects and for consistency with ethical standards requires that special protections be adopted for prisoners involved in clinical investigations. Therefore, the agency believes these regulations are essential to enforcement of the agency's responsibilities under sections 505(i), 505(j), 507(d), 507(g), and 520(g) of the act.

Request for Comments

The agency invites comments on this proposal and specifically requests information and views on the following issues: (1) The reproposed regulations do not set forth the National Commission's detailed criteria for assuring that prisons' conditions are such that informed consent is possible. Should the agency incorporate any or all of these criteria in the regulations? Which of the criteria, if any, would be excessively burdensome for sponsors to establish or beyond FDA's capacity to evaluate? (2) The reproposal imposes on research sponsors the burden of establishing that the requirements for informed consent are met and provides an opportunity to respond if a proposed research project is disapproved. The agency recognizes that due process requires the agency to provide procedural protections appropriate under the circumstances. *See Mathews* v. *Eldridge*, 424 U.S. 319 (1976). What procedures would be appropriate in light of the interests at stake and the issues to be resolved in establishing whether proposed research satisfies ethical requirements?

The agency has prepared a threshold assessment of this proposed regulation and has determined that the economic effects of this regulation do not warrant a regulatory flexibility analysis or regulatory impact analysis. If promulgated, the regulation would not have a significant economic impact on a substantial number of small entities as determined by the Regulatory Flexibility Act. The agency has also determined that the rule does not involve major economic consequences as defined by Executive Order 12291. The threshold assessment has been placed on file in the Dockets Management Branch for public review.

The agency has determined pursuant to 21 CFR 25.24(b)(12) (proposed December 11, 1979; 44 FR 71742) that this action is of a type that does not individually or cumulatively have a significant impact on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

Therefore, under the Federal Food, Drug and Cosmetic Act (secs. 406, 409, 502, 503, 505, 506, 507, 510, 513–516, 518–520, 70l(a), 706, 801, 52 Stat. 1049–1054 as amended, 1055, 1058 as amended, 55 Stat. 851 as amended, 59 Stat. 463 as amended, 72 Stat. 1785–1788 as amended, 74 Stat. 399–407 as amended 76 Stat. 794–795 as amended, 90 Stat. 540–560, 562–574 (21 U.S.C. 346, 348, 352, 353, 355, 356, 357, 360, 360c–360f, 360h–360j, 371(a), 376, 381)), and the Public Health Service Act (secs. 215, 351, 354–360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173–1188 as amended (42 U.S.C. 216, 262, 263b–263n)) and under 21 CFR 5.11 (see 46 FR 26052; May 11, 1981). It is proposed that Chapter 1 of Title 21 of the Code of Federal Regulations be amended in Part 50 by revising Subpart C to read as follows:

PART 50—PROTECTION OF HUMAN SUBJECTS

* * * * *

Subpart C—Protections Pertaining to Clinical Investigations Involving Prisoners as Subjects

Sec.

Subpart C—Protections Pertaining to Clinical Investigations Involving Prisoners as Subjects

§ 50.40 Applicability.

(a) The regulations in this subpart apply to any clinical investigation involving prisoners as subjects that is regulated by the Food and Drug Administration under section 505(i), 507(d), or 520(g) of the act, as well as any clinical investigation involving prisoners that supports any application for a research or marketing permit as defined by § 50.3(b).

(b) Nothing in this subpart shall be construed as indicating that compliance with the procedures set forth herein will authorize research involving prisoners as subjects to the extent such research is limited or barred by applicable State or local law.

§ 50.42 Purpose.

Because prisoners may be under constraints because of their incarceration which could affect their ability to make a truly voluntary and uncoerced decision whether or not to

participate as subjects in research, it is the purpose of this subpart to provide additional safeguards for the protection of prisoners involved in research to which this part is applicable.

§ 50.44 Restrictions on clinical investigations involving prisoners.

(a) Any clinical investigation that is regulated by the Food and Drug Administration under section 505(i), 507(d), or 520(g) of the act, as well as any clinical investigation that supports an application for research or marketing permit as defined by § 50.3(b), may involve prisoners as subjects only if the institution responsible for the conduct of the clinical investigation has certified to the Food and Drug Administration that the institutional review board has approved the clinical investigation under § 50.48; and

(1) The proposed clinical investigation involves solely research on practices that have the intent and reasonable probability of improving the health and well-being of the particular prisoners chosen. Subject to the approval of the institutional review board, prisoners may be assigned to control groups; or

(2) The institutional review board determines, after consultation with the Research Involving Human Subjects Committee, that the proposed clinical investigation involves research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis, which is much more prevalent in prisons than elsewhere). Subject to the approval of the institutional review board, prisoners may be assigned to control groups: or

(3) If the proposed clinical investigation involves research other than that described in paragraph (a) (1) or (2) of this section, the institutional review board determines, after consultation with the Research Involving Human Subjects Committee, that the following requirements are satisfied:

(i) The type of research fulfills an important social or scientific need, and the reasons for involving prisoners are compelling:

(ii) The involvement of prisoners in the type of research satisfies conditions of equity; and

(iii) A high degree of voluntariness on the part of the prospective participants and of accessibility on the part of the penal institution(s) to be involved characterizes the conduct of the research.

(b) A sponsor that seeks approval of any clinical investigation that is regulated by the Food and Drug Administration under section 505(i), 507(d), or 520(g) of the act as well as any clinical investigation that supports a research or marketing permit as defined by § 50.3(b) shall present evidence to the institutional review board establishing that the proposed research meets the requirements of paragraph (a) (1), (2), or (3) of this section.

(c) Authorized representatives of the Food and Drug Administration may inspect at reasonable times and in a reasonable manner, any prison at which a research activity has been proposed or is being conducted, to assist the institutional review board in determining whether the requirements of this section are met.

(d) The institutional review board shall determine whether the requirements of this section have been met, and shall notify the sponsor of the decision to approve or disapprove the proposed research activity. If the institutional review board disapproves a proposed research activity, it shall include in its written notification to the research sponsor and the agency a statement of the reasons for the disapproval. The sponsor shall be given an opportunity to respond.

(e) Except as provided in paragraph (a) (1), (2), or (3) of this section, any clinical investigation regulated by the Food and Drug Administration under section 505(i), 507(d), or 520(g) of the act, as well as any clinical investigation that supports an application for a research or marketing permit as defined by § 50.3(b), may not involve prisoners as subjects.

§ 50.46 Composition of institutional review boards where prisoners are involved.

In addition to satisfying any other requirements governing institutional review boards set forth in this chapter, an institutional review board, in carrying out responsibilities under this part with respect to research covered by this subpart, shall also meet the following specific requirements:

(a) A majority of the institutional review board (exclusive of prisoner members) may not be associated with the prison(s) involved, apart from their membership on the institutional review board.

(b) At least one member of the institutional review board shall be a prisoner, or a prisoner advocate with appropriate background and experience to serve in that capacity, except that if a particular research project is reviewed by more than one institutional review board only one institutional review board need satisfy this requirement.

§ 50.48 Additional duties of the institutional review boards where prisoners are involved.

(a) In addition to all other responsibilities prescribed for institutional review boards under this chapter, the institutional review board shall review each clinical investigation covered by this subpart and approve such clinical investigation only if it finds that:

(1) The research under review represents one of the categories of research permitted under § 50.44(a) (1), (2), or (3);

(2) Any possible advantages accruing to the prisoner through his or her participation in the clinical investigation, when compared to the general living conditions, medical care, quality of food, amenities, and opportunity for earnings in prison, are not of such a magnitude that his or her ability to weigh the risks of the clinical investigation against the value of such advantages in the limited-choice environment of the prison is impaired;

(3) The risks involved in the clinical investigation are commensurate with risks that would be accepted by nonprisoner volunteers;

(4) Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners; unless the principal investigator provides to the institutional review board justification in writing for following some other procedures, control subjects shall be selected randomly from the group of available prisoners who meet the characteristics needed for that research project;

(5) Any information given to subjects is presented in language which is appropriate for the subject population;

(6) Adequate assurance exists that parole boards will not take into account a prisoner's participation in the clinical investigation in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the clinical investigation will have no effect on his or her parole; and

(b) The institutional review board shall carry out such other duties as may be assigned by the Food and Drug Administration.

(c) The institution shall certify to the Food and Drug Administration, in such form and manner as the Food and Drug Administration may require, that the duties of the institutional review board under this subpart have been fulfilled.

Interested persons, may, on or before February 16, 1982, submit to the Dockets Management Branch (HFA–305), Food

and Drug Administration, Rm. 4–62, 5600 Fishers Lane, Rockville, MD 20857 written comments regarding this proposal. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

Dated: September 17, 1981.

Arthur Hull Hayes, Jr.,

Commissioner of Food and Drug.

Dated November 25, 1981.

Richard S. Schweiker,

Secretary of Health and Human Services.

[FR Doc. 81–36120 Filed 12–17–81; 8:45 am]

BILLING CODE 4160–01–M

DEPARTMENT OF LABOR

Occupational Safety and Health Administration

29 CFR Part 1910

[Docket No. H–111]

Occupational Exposure to Ethylene Dibromide

AGENCY: Occupational Safety and Health Administration (OSHA), Labor.

ACTION: Advance notice of proposed rulemaking.

SUMMARY: The Occupational Safety and Health Administration is considering revising the present occupational health standard regulating employee exposure to ethylene dibromide (EDB), 29 CFR 1910.1000. Table Z–2. Recent scientific studies have reported that EDB caused cancer when administered either orally, by inhalation, or by skin application in 3 strains of rats and 3 strains of mice. In addition, other studies have shown EDB to be a mutagen, teratogen, and testicular toxin in experimental animals. The results of these studies indicate that the present permissible exposure level, for EDB of 20 parts per million (ppm) as an 8-hour time weighted average (TWA) exposure does not provide exposed workers adequate protection against cancer and other adverse health effects. This notice summarizes the potential health effects associated with exposure to EDB and invites interested parties to submit comments, suggestions, and information on several important issues.

DATES: Comments in response to this advance notice of proposed rulemaking should be submitted on or before March 1, 1982.

ADDRESS: Comments, in quadruplicate, should be mailed to Docket Officer, Occupational Safety and Health Administration, Docket No. H–111, Room S–6212, U.S. Department of Labor, 200 Constitution Avenue, NW., Washington, D.C., 20210, telephone 202–523–7894. All material submitted will be available for inspection and copying at this address.

FOR FURTHER INFORMATION CONTACT: Mr. James F. Foster, Office of Information and Consumer Affairs, Room N–3637, Occupational Safety and Health Administration, U.S. Department of Labor, 200 Constitution Avenue, NW., Washington, D.C. 20210, telephone (202) 523–8151.

SUPPLEMENTARY INFORMATION:

1. Background

a. Chemical Identification

Ethylene dibromide (Chem. Abstr. Services Reg. No.: 106–93–4) is a colorless, non-flammable liquid at room temperature with a distinctive, mildly sweet odor detectable in air at levels ranging from 10 to 25 parts per million *(1)* Synonyms for ethylene dibromide include EDB, 1,2-dibromoethane, ethylene bromide, sym-dibromoethane and glycol bromide. It has a chemical formula of $C_2H_4Br_2$, with a molecular weight of 187.9.

b. Production, Use, and Exposure

Ethylene dibromide is produced commercially by reacting ethylene with liquid bromine. The Environmental Protection Agency estimated that about 340 to 360 million pounds of EDB are produced annually in the United States. *(1)* According to EPA's estimates, the major use of EDB (about 230 million pounds per year) is as an anti-knock compound in gasoline. A second major use of EDB (about 13 to 15 million pounds per year) is as an ingredient in pesticides. In addition, EDB is used as an intermediate in the synthesis of dyes and pharmaceuticals, and as a solvent for resins, gums, and waxes.

It is estimated that 12,500 employeee may be exposed to EDB in its manufacture or use in gasoline blending and pesticide formulation. In addition, several hundred thousand workers are potentially exposed to EDB while working with leaded gasoline, but information submitted to OSHA suggests that exposures resulting from the use of EDB in leaded gasoline are relatively low. *(2)*

The limited EDB sampling data available indicates that the potential for the highest worker exposure levels for EDB result from its use as a post-harvest fumigant for grain and citrus. Secondary exposure may occur among an estimated 1,000 packers, warehouse and dock workers, and an undetermined number of truckers who handle fruit fumigated with EDB. An additional l0,000 employees in approximately 400 flour mills may have potential for exposure from spot fumigation of milling machinery. The State of California estimated that more than 12,000 workers state-wide are exposed to EDB as a result of post-harvest fumigation to control the recent infestation by the Mediterranean fruit fly. *(3)*

c. Present Standard

The permissible exposure level for occupational exposure to ethylene dibromide is found in Table Z–2 of 29 CFR 1910.1000. The standard provides that an employee's airborne exposure to ethylene dibromide, in any 8-hour workshift of a 40-hour workweek, shall not exceed an 8-hour time weighted average (TWA) limit of 20 parts per million (ppm). Further, an employee's exposure to ethylene dibromide shall not exceed a ceiling concentration of 30 ppm at any time during an 8-hour shift, except for a very brief time period (maximum duration of 5 minutes), when the "acceptable maximum peak" concentration shall not exceed 50 ppm, The standard provides that administrative or engineering controls must be implemented to reduce exposures to within the PEL whenever feasible. When such controls are not feasible to achieve full compliance, protective equipment or any other protective measure shall be used to keep the exposure of employees to EDB within the limits prescribed.

The current standard for EDB was adopted in 1971 as a national consensus standard, under Section 6(a) of the Occupational Safety and Health Act of 1970 (84 Stat. 1593; 29 U.S.C. 655). The source of the standard was the American National Standards Institute (ANSI) 1970 recommendation for acceptable concentrations of ethylene dibromide (ANSIZ37.31–1970). The ANSI exposure limits were intended to protect workers from injury to the lungs, liver, and the kidneys which had been observed from excessive, acute, or chronic exposures to EDB in humans and experimental animals. The potential for EDB to cause cancer or reproductive damage was not a basis for the establishment of the current exposure limits for EDB.

d. Actions by Other Groups

On December 14, 1977, EPA issued a notice of Rebuttable Presumption Against Registration and Continued