The storage tank proprietor shall maintain the plans and gauge tables for 3 years after discontinuing use of the storage tanks as bonded warehouses for the storage of imported petroleum or petroleum products.

(b) *Tags required on valves.* The inlet and outlet valves of each tank shall have tags of a permanent type affixed by the proprietor or lessee indicating the use of the valves.

(c) *Verification of gauge tables.* Whenever he has reason to suspect their reliability, the district director may require the measurement and calibrations shown on the gauge tables to be verified by a Customs officer. If no qualified Customs officer is available, the district director may accept an independent certification verifying the measurements and calibrations. The independent verification shall be performed at the expense of the storage tank proprietor.

§ 151.45 Storage tanks bonded as warehouses.

(a) *Application.* Tanks for the storage of imported petroleum or petroleum products in bulk may be bonded as warehouses of class 2 if to be used exclusively for the storage of petroleum or petroleum products belonging or consigned to the owner or lessee of the tank. In addition to the documents and bonds required to be filed with the application to bond (see section 19.2 of this chapter), the certified plans and gauge tables required by section 151.43 shall be filed.

(b) *Removal of nonbonded petroleum.* If a bonded tank is not empty at the time the first importation of bonded petroleum or petroleum products is to be stored therein, the amount of nonbonded petroleum or petroleum products in the tank shall be withdrawn by the proprietor as soon as possible. The request to withdraw shall be in the form of a letter and no formal withdrawal need be filed. Domestic or duty-paid petroleum or petroleum products shall not thereafter be stored in the tank as long as the tank remains bonded.

(c) *Information on warehouse withdrawal.* Warehouse withdrawals of petroleum or petroleum products from bonded tanks shall show the information specified in section 151.41, as well as the designation of the tank from which the merchandise is to be withdrawn. Such withdrawals may be made for "—— U.S. gallons, more or less", but in no case may the estimate vary by more than three percent from the gross quantity unladen.

§ 151.46 Allowance for excessive water and sediment.

Allowance for excessive moisture or other impurities in imported petroleum or petroleum products shall be made in accordance with section 158.13 of this chapter for the quantity of water and sediment, established to be in excess of that usually found in such merchandise, as set forth in the following table:

Merchandise	*Quantity (percent)*
Crude petroleum	0.3
Petroleum products having an API gravity at 60° or less than 22°	0.5
22° to 30°	0.3
More than 30°	0.0

§ 151.47 Entered quantities of petroleum or petroleum products released under entry or immediate delivery.

(a) *Optional entry of net quantity landed.* As an alternative to stating on the entry summary the gross quantity of petroleum or petroleum products released under the immediate delivery procedure in § 142.21 of this chapter, or under the entry documentation in § 142.3(a), the importer may file an entry summary for the net quantity of petroleum or petroleum products unladen. The net quantity shall be determined in accordance with section 158.13 of this chapter, with an allowance made for sediment and excessive water present, as prescribed in the table found in section 151.46, and reported in a laboratory test made by an independent commercial laboratory which has been approved by the Commissioner. The commercial laboratory report shall be filed with the entry summary.

(b) *Approval of independent commercial laboratories.* Applications of independent commercial laboratories for approval of the use of their tests in determining the net landed quantity of petroleum or petroleum products shall be sent to the Commissioner of Customs, Washington, D.C. 20229. For the purposes of this section, the approval of a public gauger by the Commissioner in accordance with § 151.43 shall constitute approval of the commercial laboratories operated by the public gauger as a part of the services rendered by him for his customers.

(c) *Use of Customs laboratory tests for liquidation.* Where there is a difference between the quantity reported by the Customs laboratory and the quantity reported by the approved independent commercial laboratory, the results of the Customs laboratory test shall be used in the liquidation of the entry and in determining the quantity chargeable against the importer's oil import license, unless the difference is within the limits set forth in paragraph (d) of this section.

(d) *Use of commercial laboratory tests for liquidation.* The quantity reported by the approved independent commercial laboratory shall be used in the liquidation of the entry and in determining the quantity chargeable against the importer's oil import license if the difference between the commercial laboratory test and the Customs laboratory test do not exceed the differences set forth in the following table (adapted from ASTM Designation D1796, Fig. 3):

Percentage of water and sediment found by Customs laboratory	Maximum percentage difference allowable
0.05 to 0.50	0.1
0.51 to 1.50	0.2
More than 1.50	0.3

(Sec. 507, 46 Stat. 732 (19 U.S.C. 1507)) (R.S. 251, as amended, sec. 624, 46 Stat. 759, 77A Stat. 14 (19 U.S.C. 66, 1202 (Gen. Hdntes. 11, 12), 1624))

PART 159—LIQUIDATION OF DUTIES

Section 159.21(a) is amended by changing the spelling of the word "gage" to "gauge" in the first sentence.

(R.S. 251, as amended, sec. 624, 46 Stat. 759 (19 U.S.C. 66, 1624))

[FR Doc. 80-16520 Filed 5-29-80; 8:45 am]

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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 Subjects in Research

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: This document establishes regulations to provide protection for prisoners involved in research activities that fall within the jurisdiction of the Food and Drug Administration (FDA). These regulations implement the recommendations of the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research (National Commission) on research involving prisoners. These regulations restrict the use of prisoners in research within the jurisdiction of FDA and establish requirements for the composition of and additional duties for institutional review boards when prisoners are involved in the research.

EFFECTIVE DATE: June 1, 1981.

FOR FURTHER INFORMATION CONTACT: Roger Barnes, Office of Health Affairs (HFV–2), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–443–1382.

SUPPLEMENTARY INFORMATION: Under the National Research Act (Pub. L. 93–348), the National Commission was charged with, among other duties, identifying the requirements for informed consent by prisoners for participation in biomedical and behavioral research. On the basis of its investigation and study of this issue (see paragraph 7), the National Commission identified the requirements for informed consent and made recommendations to the Secretary of Health and Human Services (HHS) about appropriate administrative actions to ensure that those requirements would be met in research subject to the Department's jurisdiction. The National Commission's recommendations covered research conducted or supported under programs administered by the Secretary and research reported to the Secretary in fulfillment of regulatory requirements (42 FR 3076, 3079, January 14, 1977).

Section 205 of the National Research Act, however, only required the Secretary to determine whether the National Commission's recommendations were appropriate to assure the protection of prisoners as subjects of biomedical or behavioral research conducted or supported under the programs the Secretary administered. (In the **Federal Register** of January 8, 1978 (43 FR 1050), the Secretary announced that the Department was adopting the National Commission's recommendations for such research and was proposing regulations implementing this determination. These regulations were adopted in final form on November 16, 1978 (43 FR 53652).) Section 205 did not explicitly impose an obligation on the Secretary to respond to the National Commission's recommendations with regard to research reported in fulfillment of regulatory requirements.

Nevertheless, the Secretary believed that a determination should be made as to whether the National Commission's recommendations should be adopted for non-HHS supported research that is submitted to FDA to satisfy its regulatory requirements. Because rulemaking authority with respect to FDA activities has been delegated to the Commissioner of Food and Drugs, the Secretary directed the Commissioner to take appropriate action on these recommendations (43 FR 1051).

In the **Federal Register** of May 5, 1978, the Commissioner announced the tentative decision to adopt the findings of both the National Commission and the Secretary regarding the inherently coercive nature of the prison environment and the need for special protections for prisoners involved as subjects of clinical research (43 FR 19417, 19418). Therefore, on the basis of the authority granted under the Federal Food, Drug, and Cosmetic Act (the act), the Commissioner proposed these regulations to establish those special protections.

FDA allowed 60 days for comment on the proposed regulations. The agency received more than 40 letters with comments directed to the proposal. These comments were from government officials, prisoners, clinical investigators, trade associations, professional societies, academic research institutions, drug companies, members of Congress on behalf of constituents, and other private citizens. The substantive comments received and the agency's conclusions about them are discussed below.

In addition, the reasoning in the preambles to HHS's proposed rulemaking (43 FR 1050) and rulemaking on adopting "Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects" (43 FR 53652) has been considered by FDA and is incorporated as part of this record.

Comments on the Advance Notice of Proposed Rulemaking and the Proposed Rule

1. Several comments challenged FDA's authority to issue these regulations.

A thorough discussion of FDA's authority was provided in the preamble to the proposed rule (see 43 FR 19419). FDA believes it is unnecessary to reproduce that discussion here. Some comments on the proposed regulations challenged the agency's analysis of its authority. FDA has studied them carefully, and FDA continues to believe that its assessment is accurate. However, in the interest of responsiveness, FDA will reply to each objection relating to its authority.

2. Two comments stated that FDA lacks authority to promulgate regulations concerning the validity of informed consent based on prisoner status.

FDA rejects these comments. As discussed in the preamble to the May 5, 1978 proposal, sections 505(i), 507(d), and 520(g) (21 U.S.C. 355(i), 357(d), and 360j(g)) of the act require that FDA promulgate regulations for the exemption of drugs and devices for investigational use. These sections of the act direct FDA to issue regulations that protect the public health in the course of clinical investigations and that provide that informed consent will be obtained from the human subjects of the investigations.The act also requires 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 devices, be consistent with ethical standards (21 U.S.C. 360j(g)(1)).

FDA believes that there is significant evidence that additional regulations are necessary to protect adequately the interests of prisoners who participate as human subjects of research within its jurisdiction. FDA notes that the legislative history of the National Research Act indicates that it was passed in reaction to abuses in the field of human experimentation, including prison research. See 1974 U.S. Code Cong. & Admin. News, 93rd Cong., 2d Sess., 3634, 3650 (S. Rep. 93–381). As at least one court has stated, a particular concern to the drafters of the National Research Act was that a subject's consent be based on full disclosure and be free of any form of coercion. *Clay* v. *Martin*, 509 F.2d 109, 173 (2d Cir. 1975), citing 1974 U.S. Code Cong. & Admin. News, *supra*, at 3657. Yet the National Commission found, which finding FDA has adopted, that the prison environment is inherently coercive.

Therefore, FDA has decided that due regard for the interests of prisoners as subject and for appropriate ethical standards, as well as for the protection of the public health and safety, requires that special protections be adopted for prisoners involved in clinical investigations. Under the authority granted to it in sections 505(i), 505(j), 507(d), 507(g), and 520(g) of the act FDA is promulgating these regulations that restrict the circumstances in which prisoners can be used as subjects in the research that is under the jurisdiction of FDA.

3. One comment stated that the act requires FDA to accept all clinical investigations that are submitted to the agency to support marketing of a new drug or device pursuant to sections 505(i), 507(d), and 520(g) of the act. The comment went on to suggest that FDA lacks the rulemaking authority to reject private scientific research on the basis that such research was conducted on prisioners.

FDA rejects this comment. No legal basis for the propositions asserted is cited in the comment, and none exists in the act. The agency's authority to define what clinical investigations it will eccept is well-established and is discussed at length in the preamble to

the proposed regulations (See 43 FR 19419).

4. Two comments argued that nothing in the act provides FDA with statutory authority to ban all privately supported and conducted scientific research involving prisoner volunteers.

These comments misconstrue the effect of these regulations. These reglations apply to all clinical investigations regulated by FDA under sections 505(i), 507(d), and 520(g) of the act, as well as clinical investigations that support applications for research or marketing permits for products regulated by FDA. However, the regulations do not affect privately supported and conducted scientific research on prisoner volunteers that is not subject to FDA jurisdiction.

5. One comment stated that the proposed regulations are an impermissible intrusion upon the rights of the States to manage their own prison systems. Two comments contended that FDA's regulations would vilolate a California law that permits prisoner research.

FDA disagrees with these comments. These regulations impose no obligations on State prison authorities. They state that except in limited circumstances, the agency will not permit the use of prisoners in the clinical investigations it regulates under sections 505(i), 507(d), and 520(g) of the act or accept clinical investigations that involved prisoner subjects in support of applications for research or marketing permits for products regulated by FDA.

6. Several comments stated that FDA was "taking away a prisoner right" to participate in research, and that these regulations denied equal protection of the law to prisoners by taking away that right.

FDA rejects these comments. Participation in research, which has been a source of income for prisoners, will be greatly restricted by these regulations. However, FDA believes that any deprivation to prisoners that results is clearly outweighed by the fact that these regulations are necessary to assure that the interests of prisoners who participate in research subject to FDA's jurisdiction are adequately protected (see also paragraph 12 of this preamble). It is relevant to point out, as noted in HHS's final rule published in the **Federal Register** of November 16, 1978 (43 FR 53652, 53654), that medical and medically related research involving prisoners: (1) has already been prohibited in all Federal prisons; (2) has been prohibited in eight States; and (3) is conducted only in about seven of the States that either permit it or do not regulate it. These prohibitions have been based on the demonstrable inequities of such research and on the questionable voluntariness of prisoner consent.

7. Many comments objected to the recommendations of the National Commission. The comments argued that the National Commission had no basis to conclude that research conducted with prisoner subjects was unsafe or coercive. Several comments stated that the only rationale for the National Commission's recommendations was an emotional bias against research involving prisoners. These comments suggested that FDA reject the National Commission's recommendations and allow prisoners to continue to be subjects of clinical investigations subject to FDA's jurisdiction.

FDA rejects these comments. The National Commission's findings and recommendations were based on extensive research. The National Commission visited prison research facilities, interviewed many prisoners, and discussed prison procedures with prison officials. In addition, to ensure that viewpoints of minorities were heard, the National Commission contracted with the National Urban Coalition to organize a conference on human experimentation which was held in January 1977. The National Commission also conducted a public hearing on the issue of research involving prisoners and considered papers on the ethical issues involved in research with prisoners that were prepared for it. The National Commission used all of this information in its final report. FDA has not found any reason to alter its decision to adopt the findings and recommendations contained in that report.

8. One comment received by the Secretary after publication of the recommendations of the National Commission stated that the discontinuation of research currently in progress within one year following issuance of the regulations, might cause valid data to be lost or new studies to be jeopardized by sudden termination of the therapeutic regimen afforded by the study. The Secretary stated in response that the Commissioner would consider the effect of this matter on non-HHS supported research (43 FR 1052).

FDA believes that the one year interval strikes an appropriate balance between the need for prompt implementation of these protections for prisoners and the need of sponsors of ongoing clinical investigations involving prisoners as subjects to complete or discontinue the investigations or to bring them into compliance with these regulations without unduly jeopardizing valid data.

9. One comment suggested that regulations of HHS and FDA concerning use of prisoners in clinical investigations be uniform.

FDA agrees that, wherever possible, its regulations should be compatible with, if not identical to, those of the Department. A multiplicity of dissimilar and inconsistent Federal requirements is burdensome to institutions, institutional review boards, and the process of clinical investigation. These regulations closely follow and apply the principles set forth in the HHS regulations on prisoner research.

10. Several comments pointed out that FDA's regulations would prohibit prisoner participation in any research subject to FDA jurisdiction that is not related to the health or well-being of the subjects or is not on conditions particularly affecting prisoners as a class. These comments noted that under the National Commission's recommendations, reports on such research involving prisoners could be accepted in fulfillment of regulatory requirements, if certain conditions were met in the particular study. These comments argue that FDA's regulations consequently exceed the National Commission's recommendations.

FDA acknowledges that the National Commission did not explicitly recommend a prohibition on the use of prisoners in all research that is not related to the health or well-being of subjects or is not on conditions particularly affecting prisoners as a class. However, FDA believes that these regulations are authorized by the act and implement the thrust of the National Commission's recommendations.

The National Commission recommended that reports on research involving prisoners should be accepted in fulfillment of regulatory requirements only if three requirements are satisfied:

a. The type of research fulfills an important social or scientific need, and the reasons for involving prisoners in the type of research are compelling;

b. The involvement of prisoners in research satisfied "conditions of equity"; and

c. A high degree of voluntariness on the part of research subjects and openness on the part of the institutions characterized the conduct of the research (see 42 FR 3080; January 14, 1977).

FDA has reviewed all research subject to its jurisdiction that would not be permitted under § 50.44. Based on the act's requirements that subjects of clinical investigations be protected (see paragraph 2), on the National Commission's finding that the environment in prisons is inherently

coercive, and on the findings of the Secretary, FDA has concluded that there are no compelling reasons for involving prisoners in this research, and, consequently, that the first of the National Commission's requirements for the acceptance of reports on investigations cannot be satisfied for such research.

None of the comments submitted in response to the proposal suggested that a compelling reason for the agency to accept reports on this research could be asserted. For example, several comments pointed to problems that might develop in Phase I testing if prisoners could not be used, but no comment suggested that alternate subjects for Phase I testing could not be found. Significantly, other nations active in biomedical research have been able to conduct investigations without involving prisoners.

In addition, FDA has incorporated the reasoning of HHS for restricting the use of prisoners as subjects, which is set forth in the preambles to the proposed and final rulemaking of the Department (see 43 FR 1050–1051 and 43 FR 53652, 53654).

Aside from these substantive factors, FDA decided to prohibit the use of prisoners in research subject to its jurisdiction that is not related to the health or well-being of the subjects or to conditions particularly affecting prisoners as a class because this prohibition is consistent with the regulations adopted by HHS. As discussed in paragraph 9 of this preamble, the agency believes that, when appropriate, there is significant value in FDA adopting regulations compatible with, if not identical to, those of HHS.

11. One comment suggested that a prisoner population is needed to maintain a well-controlled testing atmosphere. The comment pointed out that many activities of prisoners are monitored, and that there is less control over those same activities in nonprisoner populations. Therefore, the comment asserted, drug studies can be more effectively done in prisons.

While it is true that many activities of prisoners are monitored that are not monitored in nonprisoner populations, FDA disagrees with the conclusion and rejects the comment. No data showing that prisoners are necessary to conduct well-controlled research, and that no reasonable alternative is available, have ever been presented to FDA, nor is the existence of such data indicated in the National Commission's report. In addition, FDA has found that in certain circumstances, prisoners are actually an unsuitable population for drug testing. See, e.g., Warner-Lambert/Parke-Davis & Co.; Benylin; Final Decision (44 FR 51512, 51524, August 31, 1979).

12. Several comments stated that research was a good way for prisoners to earn money while incarcerated. Comments also suggested that prisoners receive other benefits from participation in the studies and are motivated by a desire to help the public.

In its report, the National Commission stated that in its interviews with prisoners involved in Phase I drug studies, participants gave many reasons for volunteering for research, "but it was clear that the overriding motivation was the money they received for participating. In fact, their strongest objection was that the pay for participation in research was held down to levels comparable to prison industries" (42 FR 3083). The National Commission found, however, that "although prisoners who participate in research affirm that they do so freely, the conditions of social and economic deprivation in which they live compromise their freedom" (42 FR 3078). The National Commission believed that the availability of a population living in conditions of social and economic deprivation makes it possible for researchers to bring to this population types of research which persons better situated would ordinarily refuse. The National Commission concluded that "prisoners are, as a consequence of being prisoners, more subject to coerced choice and more readily available for the imposition of burdens which others will not willingly bear" (42 FR 3078). FDA adopts these findings by the National Commission.

13. Several comments stated that research involving prisoners is safe, and that prisoners do not need special protections. These comments asserted that prisoners are now free from any outside influence in choosing to participate in studies, and therefore, these regulations are unnecessary.

FDA rejects these comments for the reasons that are set forth in paragraph 12 of this preamble.

14. One comment suggested that FDA prohibit the use of prisoners in any research that is subject to FDA jurisdiction.

FDA rejects this comment. One of the specific recommendations of the National Commission was that "[r]esearch on practices both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the individual prisoner may be conducted or supported * * *." (42 FR 3080). The National Commission believed, and FDA agrees, that a research subject should not be deprived of health benefits (even experimental ones) simply because the subject is a prisoner. Section 50.44(b)(2) and (3) (21 CFR 50.44 (b)(2) and (3)) allows submission of research that will benefit the prisoner subjects involved.

15. One comment suggested that psychiatric patients should not be used in drug studies that will not directly benefit their health. The comment stated that because of the nature of their illness, they may not be able to give effective informed consent to participate in a drug study.

FDA agrees with this comment, and except in limited circumstances, psychiatric patients in prisons, like other prisoners, cannot be used as subjects in studies subject to FDA's jurisdiction. The National Commission issued its report concerning the institutionalized mentally disabled patients in the **Federal Register** of March 17, 1978 (43 FR 11328). HHS has issued proposed regulations governing the use of mentally disabled patients as subjects in clinical investigations, and FDA is considering the need to publish similar regulations.

16. One comment questioned the scope of these regulations. The comment stated that it was unclear whether all clinical investigations, including those involving cosmetics, OTC drugs, and low-risk medical devices were covered by these regulations.

The scope of these regulations pertains to those clincial investigations regulated by FDA under sections 505(i), 507(d), or 520(g) of the act, as well as clinical investigations that support applications for research or marketing permits for products regulated by the agency. Therefore, the regulations would be applicable to clinical investigations involving OTC drug products and any medical devices, whether or not the devices are significant risk devices as defined in 21 CFR Part 812, if reports of those investigations are to be submitted to FDA. Cosmetic products are not included among the types of products to which the regulation applies.

17. Several comments raised questions about specific definitions in proposed § 50.3 (21 CFR 50.3). Other comments suggested alternative definitions to those contained in that section.

With one exception, proposed § 50.3 has been reproposed by the agency in its proposed standards for informed consent, published in the **Federal Register** of August 14, 1979 (44 FR 47713). Comments on the proposed standards for informed consent, including reproposed § 50.3, are on file in the Hearing Clerk's office (HFA–305), Rm. 4–62, 5600 Fishers Lane, Rockville,

MD 20857, under Docket No. 78N-0400. Those comments on the prisoner research regulations that contained questions or suggestions about definitions in proposed § 50.3 have been included in Docket No. 78N-0400 and will be addressed when the final regulations governing informed consent are published.

FDA is adopting at this time the definition of the term "Application for research or marketing permit," § 50.3(b) (21 CFR 50.3(b)). The agency has decided to do so to ensure that the meaning of this phrase, which is used to define the scope of these regulations, is clear.

18. Several comments urged that the regulations should permit prisoners to receive placebos as a control group. A few comments stated that the validity of any research done would be questionable unless there was a placebo control group. One comment suggested that the regulationd does not clearly state whether prisoners would be able to act as placebo controls in otherwise permissible prisoner research.

To be consistent with the HHS regulations, FDA has revised § 50.44 (21 CFR 50.44) to permit certain research on conditions particularly affecting prisoners as a class, in addition to research on practices that have the intent and reasonable probability of improving the health and well-being of the subjects. FDA has also decided to permit prisoners to participate in these types of research as members of a control group, including a placebo control group, even though as members of a control group they may not benefit directly from the research. These changes were based on comments received by FDA and the Department. However, to be consistent with the recommendations of the National Commission, FDA has required that prisoner participation in research on conditions affecting prisoners as a class and in research as control subjects be approved by the agency on a study by study basis.

19. One comment noted that the preamble to the proposal stated that the agency has concluded that an environmental impact statement is not required for this regulation, but that an environmental impact assessment was on file with the FDA Hearing Clerk. The comment pointed out that, in fact, no environmental impact assessment had been filed.

The notice of proposed rulemaking did inadvertently refer to an environmental impact assessment (43 FR 19419). However, this proposed action did not require the preparation of an environmental impact assessment under 21 CFR 25.1(b) and (h). An environmental impact assessment also is not required under FDA's proposed new environmental regulations (44 FR 71742; December 11, 1979). The agency has determined pursuant to proposed 21 CFR 25.24(b)(12) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental impact assessment nor an environmental impact statement is required.

20. One comment asserted that a proper economic assessment of the impact of this regulation had not been prepared by FDA. The comment stated that the document FDA prepared did not adequately describe the proposed regulations and was not prepared under the appropriate Executive Order.

FDA agrees with the comment concerning the reference to the appropriate Executive Order. The original economic impact assessment concluded that the proposed regulations would not have a major economic impact as defined by Executive Order 11821, as amended by Executive Order 11949. During the period from January 1, 1978 to March 22, 1978, when Executive Order 12044 was issued, no Executive Order was in effect, although FDA continued to prepare economic impact assessments under the expired order. This process continued until August, 1978, when FDA prepared "Interim Regulatory Analysis Guidelines" for use by the agency in implementing Executive Order 12044. Because the proposed regulations were published during the period of transition from the standards of Executive Order 11821, as amended, to those of Executive Order 12044, the technically appropriate reference was not made. However, the specific relevant standard for assessing whether the action would have a major economic impact was the same.

FDA also agrees in part with the comment that the original economic impact assessment did not adequately describe the proposed regulations. FDA therefore has reassessed the economic impact of this regulation under the standards established in Executive Order 12044. This assessment has confirmed that the regulation will not have a major economic impact as defined by that order.

A copy of the amended regulatory analysis assessment is on file with the Hearing Clerk, Food and Drug Administration.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 406, 409, 502, 503, 505, 506, 507, 510, 513–516, 518–520, 701(a), 706, and 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, and 381)) and the Public Health Service Act (secs. 215, 351, 354–360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173–1186 as amended (42 U.S.C. 216, 262, 263b–263n)) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.1), Subchapter A of Chapter I of Title 21 of the Code of Federal Regulations is amended by adding new Part 50, to read as follows:

PART 50—PROTECTION OF HUMAN SUBJECTS

Subpart A—General Provisions

Sec.
50.1 Scope.
50.3 Definitions.

Subpart B—[Reserved]

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

50.40 Applicability.
50.42 Purpose.
50.44 Restrictions on clinical investigations involving prisoners.
50.46 Composition of institutional review boards where prisoners are involved.
50.48 Additional duties of the institutional review boards where prisoners are involved.

Authority: Secs. 406, 409, 502, 503, 505, 506, 507, 510, 513–516, 518–520, 701(a), 706, and 801, Pub. L. 717, 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, and 381); secs. 215, 351, 354–360F, Pub. L. 410, 58 Stat. 690, 702 as amended, 82 Stat. 1173–1186 as amended (42 U.S.C. 216, 262, 263b–263n)

Subpart A—General Provisions

§ 50.1 Scope.

(a) This part applies to all clinical investigations regulated by the Food and Drug Administration under sections 505(i), 507(d), and 520(g) of the Federal Food, Drug, and Cosmetic Act, as well as clinical investigations that support applications for research or marketing permits for products regulated by the Food and Drug Administration, including food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products. Additional specific obligations and commitments of, and standards of conduct for, persons who sponsor or

monitor clinical investigations involving particular test articles may also be found in other parts (e.g., Parts 312 and 812). Compliance with these parts is intended to protect the rights and safety of prisoner subjects involved in investigations filed with the Food and Drug Administration pursuant to sections 406, 409, 502, 503, 505, 506, 507, 510, 513–516, 518–520, 706, and 801 of the Federal Food, Drug, and Cosmetic Act and sections 351 and 354–360F of the Public Health Service Act.

(b) References in this part to regulatory sections of the Code of Federal Regulations are to Chapter I of Title 21, unless otherwise noted.

§ 50.3 Definitions.

As used in this part:

(a) [Reserved]

(b) "Application for research or marketing permit" includes:

(1) A color additive petition, described in Part 71.

(2) A food additive petition, described in Parts 171 and 571.

(3) Data and information about a substance submitted as part of the procedures for establishing that the substance is generally recognized as safe for use that results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food, described in §§ 170.30 and 570.30.

(4) Data and information about a food additive submitted as part of the procedures for food additives permitted to be used on an interim basis pending additional study, described in § 180.1.

(5) Data and information about a substance submitted as part of the procedures for establishing a tolerance for unavoidable contaminants in food and food-packaging materials, described in section 406 of the act.

(6) A "Notice of Claimed Investigational Exemption for a New Drug," described in Part 312.

(7) A new drug application, described in Part 314.

(8) Data and information about the bioavailability or bioequivalence of drugs for human use submitted as part of the procedures for issuing, amending, or repealing a bioequivalence requirement, described in Part 320.

(9) Data and information about an over-the-counter drug for human use submitted as part of the procedures for classifying these drugs as generally recognized as safe and effective and not misbranded, described in Part 330.

(10) Data and information about a prescription drug for human use submitted as part of the procedures for classifying these drugs as generally recognized as safe and effective and not misbranded, described in this chapter.

(11) Data and information about an antibiotic drug submitted as part of the procedures for issuing, amending, or repealing regulations for these drugs, described in Part 430.

(12) An application for a biological product license, described in Part 601.

(13) Data and information about a biological product submitted as part of the procedures for determining that licensed biological products are safe and effective and not misbranded, described in Part 601.

(14) Data and information about an in vitro diagnostic product submitted as part of the procedures for establishing, amending, or repealing a standard for these products, described in Part 809.

(15) An "Application for an Investigational Device Exemption," described in Part 812.

(16) Data and information about a medical device submitted as part of the procedures for classifying these devices, described in section 513.

(17) Data and information about a medical device submitted as part of the procedures for establishing, amending, or repealing a standard for these devices, described in section 514.

(18) An application for premarket approval of a medical device, described in section 515.

(19) A product development protocol for a medical device, described in section 515.

(20) Data and information about an electronic product submitted as part of the procedures for establishing, amending, or repealing a standard for these products, described in section 358 of the Public Health Service Act.

(21) Data and information about an electronic product submitted as part of the procedures for obtaining a variance from any electronic product performance standard, as described in § 1010.4.

(22) Data and information about an electronic product submitted as part of the procedures for granting, amending, or extending an exemption from a radiation safety performance standard, as described in § 1010.5.

Subpart B—[Reserved]

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

§ 50.40 Applicability.

(a) The regulations in this subpart apply to all clinical investigations involving prisoners as subjects that are regulated by the Food and Drug Administration under sections 505(i), 507(d), or 520(g) of the Federal Food, Drug, and Cosmetic Act, as well as clinical investigations involving prisoners that support applications for research or marketing permits for products regulated by the Food and Drug Administration.

(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.

Inasmuch as 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 activities to which this subpart is applicable.

§ 50.44 Restrictions on clinical investigations involving prisoners.

(a) Except as provided in § 50.44(b), clinical investigations regulated by the Food and Drug Administration under sections 505(i), 507(d), and 505(g) of the Federal Food, Drug, and Cosmetic Act, as well as clinical investigations that support applications for research or marketing permits for products regulated by the Food and Drug Administration may not involve prisoners as subjects.

(b) Clinical investigations that are regulated by the Food and Drug Administration under sections 505(i), 507(d), or 520(g) of the Federal Food, Drug, and Cosmetic Act, as well as clinical investigations that support applications for research or marketing permits for products regulated by the Food and Drug Administration, 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)(i) In the judgment of the Food and Drug Administration, the proposed clinical investigation involves solely research on practices both innovative and accepted, which have the intent and reasonable probability of improving, the health and well-being of the subjects;

(ii) In cases in which these studies require the assignment of prisoners in a manner consistent with protocols approved by the institutional review board to control groups that may not benefit from the research, the study may proceed only after the Food and Drug

Administration has consulted with appropriate experts, including experts in penology, medicine, and ethics, and has published notice in the **Federal Register** of its intent to approve such research; or

(2) 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) provided that the Food and Drug Administration has consulted with appropriate experts, including experts in penology, medicine, and ethics, and has published notice in the **Federal Register** of its intent to approve such research; subject to the approval of the Food and Drug Administration, prisoners may participate in the research even though they are assigned, in a manner consistent with protocols approved by the institutional review board, to control groups that may not benefit from the research.

§ 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) shall have no association 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 clinical investigations covered by this subpart and approve such clinical investigations only if it finds that:

(1) The research under review represents one of the categories of research permitted under § 50.44(b) (1) and (2);

(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 must 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

(7) Where the institutional review board finds there may be need for followup examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact.

(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 section have been fulfilled.

Effective date. This regulation shall become effective June 1, 1981.

Dated: May 27, 1980.

Jere E. Goyan,

Commissioner of Food and Drugs.

[FR Doc. 80-16578 Filed 5-29-80; 8:45 am]

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DEPARTMENT OF HOUSING AND URBAN DEVELOPMENT

Office of Assistant Secretary for Housing—Federal Housing Commissioner

24 CFR Part 201

[Docket No. R-80-817]

Mortgage Insurance and Home Improvement Loans; Changes in Interest Rates

AGENCY: Department of Housing and Urban Development.

ACTION: Final rule.

SUMMARY: The change in the regulations decreases the HUD/FHA maximum allowable finance charge on Title I property improvement, mobile home loans, and combination and mobile home lot loans. This action by HUD is designed to bring the maximum interest rate and financing charges on HUD/FHA-insured loans into line with market rates and help assure an adequate supply of and demand for FHA financing.

EFFECTIVE DATE: May 19, 1980.

FOR FURTHER INFORMATION CONTACT: John N. Dickie, Director, Financial Analysis Division, Office of Financial Management, Department of Housing and Urban Development, 451 7th Street, S.W., Washington, D.C. 20410 (202–426–4667).

SUPPLEMENTARY INFORMATION: The following miscellaneous amendments have been made to this chapter to decrease the maximum interest rate which may be charged on loans insured by this Department. Maximum finance charges on mobile home loans and the property improvement loans have been lowered from 18.00 percent to 16.50 percent and the finance charges on combination loans for the purchase of a mobile home and a developed or undeveloped lot has been lowered from 17.50 percent to 16.00 percent.

The Secretary has determined that such changes are immediately necessary to meet the needs of the market and to prevent speculation in anticipation of a change, in accordance with his authority contained in 12 U.S.C. 1709–1, as amended. The Secretary has, therefore, determined that advance notice and public comment procedures are unnecessary and that good cause exists for making this amendment effective immediately.

A Finding of Inapplicability respecting the National Environmental Policy Act of 1969 has been made in accordance with HUD's environmental procedures.