The cost impact figures discussed above are based on assumptions that no operator has yet accomplished any of the proposed requirements of this AD action, and that no operator would accomplish those actions in the future if this proposed AD were not adopted. The cost impact figures discussed in AD rulemaking actions represent only the time necessary to perform the specific actions actually required by the AD. These figures typically do not include incidental costs, such as the time required to gain access and close up, planning time, or time necessitated by other administrative actions.

Regulatory Impact

The regulations proposed herein would not have a substantial direct effect on the States, on the relationship between the national Government and the States, or on the distribution of power and responsibilities among the various levels of government. Therefore, it is determined that this proposal would not have federalism implications under Executive Order 13132.

For the reasons discussed above, I certify that this proposed regulation (1) is not a ''significant regulatory action'' under Executive Order 12866; (2) is not a ''significant rule'' under the DOT Regulatory Policies and Procedures (44 FR 11034, February 26, 1979); and (3) if promulgated, will not have a significant economic impact, positive or negative, on a substantial number of small entities under the criteria of the Regulatory Flexibility Act. A copy of the draft regulatory evaluation prepared for this action is contained in the Rules Docket. A copy of it may be obtained by contacting the Rules Docket at the location provided under the caption **ADDRESSES.**

List of Subjects in 14 CFR Part 39

Air transportation, Aircraft, Aviation safety, Safety.

The Proposed Amendment

Accordingly, pursuant to the authority delegated to me by the Administrator, the Federal Aviation Administration proposes to amend part 39 of the Federal Aviation Regulations (14 CFR part 39) as follows:

PART 39—AIRWORTHINESS DIRECTIVES

1. The authority citation for part 39 continues to read as follows:

Authority: 49 U.S.C. 106(g), 40113, 44701.

§ 39.13 [Amended]

2. Section 39.13 is amended by adding the following new airworthiness directive:

Boeing: Docket 2000–NM–134–AD.

Applicability: Model 747 series airplanes, as listed in Boeing Alert Service Bulletin 747–57A2311, dated January 27, 2000; certificated in any category.

Note 1: This AD applies to each airplane identified in the preceding applicability provision, regardless of whether it has been modified, altered, or repaired in the area subject to the requirements of this AD. For airplanes that have been modified, altered, or repaired so that the performance of the requirements of this AD is affected, the owner/operator must request approval for an alternative method of compliance in accordance with paragraph (c) of this AD. The request should include an assessment of the effect of the modification, alteration, or repair on the unsafe condition addressed by this AD; and, if the unsafe condition has not been eliminated, the request should include specific proposed actions to address it.

Compliance: Required as indicated, unless accomplished previously.

To detect and correct fatigue cracking of the front spar web of the wing, which could result in fuel leaking onto an engine and a consequent fire, accomplish the following:

Repetitive Inspections

(a) At the later of the times specified in paragraphs (a)(1) and (a)(2) of this AD, perform the Part 1 external web inspection—including detailed visual, ultrasonic, and high frequency eddy current (HFEC) inspections—to detect cracking of the front spar web of the wing, in accordance with Boeing Alert Service Bulletin 747–57A2311, dated January 27, 2000. In lieu of the Part 1 external web inspection, accomplishment of the Part 2 optional web inspection to detect cracking—which also includes detailed visual, ultrasonic, and HFEC inspections—in accordance with Boeing Alert Service Bulletin 747–57A2311, dated January 27, 2000, is acceptable for compliance with this paragraph. Repeat the inspections thereafter at intervals not to exceed 2,000 flight cycles.

Note 2: For the purposes of this AD, a detailed visual inspection is defined as: ''An intensive visual examination of a specific structural area, system, installation, or assembly to detect damage, failure, or irregularity. Available lighting is normally supplemented with a direct source of good lighting at intensity deemed appropriate by the inspector. Inspection aids such as mirror, magnifying lenses, etc., may be used. Surface cleaning and elaborate access procedures may be required.''

(1) Prior to the accumulation of 13,000 total flight cycles or 30,000 total flight hours, whichever occurs first.

(2) Within 18 months after the effective date of this AD.

Repair

(b) If any cracking is detected during any inspection required by paragraph (a) of this AD, prior to further flight, repair in accordance with a method approved by the Manager, Seattle Aircraft Certification Office (ACO), FAA; or in accordance with data meeting the type certification basis of the airplane approved by a Boeing Company Designated Engineering Representative who has been authorized by the Manager, Seattle ACO, to make such findings. For a repair method to be approved by the Manager, Seattle ACO, as required by this paragraph, the approval letter must specifically reference this AD.

Alternative Methods of Compliance

(c) An alternative method of compliance or adjustment of the compliance time that provides an acceptable level of safety may be used if approved by the Manager, Seattle ACO. Operators shall submit their requests through an appropriate FAA Principal Maintenance Inspector, who may add comments and then send it to the Manager, Seattle ACO.

Note 3: Information concerning the existence of approved alternative methods of compliance with this AD, if any, may be obtained from the Seattle ACO.

Special Flight Permits

(d) Special flight permits may be issued in accordance with sections 21.197 and 21.199 of the Federal Aviation Regulations (14 CFR 21.197 and 21.199) to operate the airplane to a location where the requirements of this AD can be accomplished.

Issued in Renton, Washington, on July 25, 2000.

Donald L. Riggin,

Acting Manager, Transport Airplane Directorate, Aircraft Certification Service.

[FR Doc. 00–19267 Filed 7–28–00; 8:45 am]

BILLING CODE 4910–13–U

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 315 and 601

[Docket No. 98D–0785]

Revised Draft Guidance for Industry on Developing Medical Imaging Drugs and Biologics; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Availability of guidance.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a revised draft guidance for industry entitled ''Developing Medical Imaging Drugs and Biological Products.'' FDA has revised the draft guidance issued on October 14, 1998, in response to comments from industry and other interested persons. The revised draft guidance is intended to assist developers of drug and biological products used for medical imaging in conducting the clinical investigations of, and submitting various types of applications for, such products. The revised draft guidance also provides

information on how the agency will interpret and apply provisions in FDA's final rule on in vivo radiopharmaceuticals used for diagnosis and monitoring.

DATES: Submit written comments on the revised draft guidance by September 29, 2000. General comments on agency guidance documents are welcome at any time.

ADDRESSES: Submit written requests for single copies of the revised draft guidance to the Drug Information Branch (HFD–210), Center for Drug Evaluation and Research (CDER), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, or the Office of Communication, Training, and Manufacturers Assistance (HFM–40), Center for Biologics Evaluation and Research (CBER), 1401 Rockville Pike, Rockville, MD 20852–1448, FAX 888–CBERFAX or 301–827–3844. Send two self-addressed adhesive labels to assist either office in processing your request. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the revised draft guidance. Submit written comments to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Requests and comments should be identified with the docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT:

Robert K. Leedham, Jr., Center for Drug Evaluation and Research (HFD–160), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–7510, or

George Q. Mills, Center for Biologics Evaluation and Research (HFM–573), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852–1448, 301–827–5097.

SUPPLEMENTARY INFORMATION:

I. Description of the Guidance

In the **Federal Register** of October 14, 1998 (63 FR 55067), FDA published a notice announcing the availability of a draft guidance for industry entitled ''Developing Medical Imaging Drugs and Biological Products.'' The draft guidance is intended to assist developers of drug and biological products used for medical imaging in planning and coordinating the clinical investigations of, and submitting various types of applications for, such products. The draft guidance also provides information on how the agency will interpret and apply provisions in the final rule, published in the **Federal Register** of May 17, 1999 (64 FR 26657), on the evaluation and approval of in vivo radiopharmaceuticals used in the diagnosis and monitoring of diseases. The final rule describes certain types of indications for which FDA will approve diagnostic radiopharmaceuticals and lists factors that the agency will consider in evaluating the safety and effectiveness of a diagnostic radiopharmaceutical drug or biological product under the Federal Food, Drug, and Cosmetic Act (the act) or the Public Health Service Act (the PHS Act), respectively.

The draft guidance applies to medical imaging agents that are used for diagnosis and monitoring and that are administered in vivo. Such agents include contrast agents used with medical imaging techniques such as radiography, computed tomography, ultrasonography, and magnetic resonance imaging, as well as radiopharmaceuticals used with imaging procedures such as single-photon emission computed tomography and positron emission tomography. The draft guidance is not intended to apply to possible therapeutic uses of these agents or to in vitro diagnostic products.

In a document published in the **Federal Register** of January 5, 1999 (64 FR 457), FDA reopened the comment period on the draft guidance until February 12, 1999. In another document published in the **Federal Register** of February 16, 1999 (64 FR 7561), FDA extended the comment period until April 14, 1999.

FDA received numerous written comments on the medical imaging draft guidance. In addition, the agency held public meetings on January 25 and March 26, 1999, to discuss various issues concerning the draft guidance.

II. Revisions to the Draft Guidance

In response to comments and on its own initiative, FDA has made several revisions to the medical imaging draft guidance. The revisions include substantive changes as well as relatively minor clarifications of terms and provisions. Following is a brief summary of the most significant revisions that FDA has made to the draft guidance.

A. Clinical Safety Assessments: Group 1 and Group 2 Agents

In accordance with several comments, FDA has redefined the category of medical imaging agents—Group 1 agents—that may be able to undergo a more focused clinical safety evaluation during development (i.e., a complete standard clinical safety evaluation may not be necessary). The revisions make it possible for more medical imaging agents to be eligible for Group 1 status than under the previous definition.

A principal change in Group 1 criteria is substitution of a no-observed-adverse-effect level (NOAEL) in place of a no-observed-effect-level (NOEL) in evaluations of the safety margin. An applicant will not be asked to demonstrate a NOEL that is at least 1,000 times greater than the maximal dose and dosage to be used in human studies, as stated in the original draft guidance. Instead, the NOAEL in expanded-acute, single-dose toxicity studies and safety pharmacology studies in suitable animal species should be at least 100 times greater than the maximal dose and dosage to be used in human studies. The NOAEL in short-term, repeated-dose toxicity studies should be at least 25 times greater than the maximal dose and dosage for humans.

The revised draft guidance also specifies when FDA will make Group 1 designations. Group 1 designations based on the safety margin will be made at the end of phase 1, after animal studies and initial human trials have been completed. Group 1 designations based on documented history of extensive clinical use without observed safety issues may occur at any time during drug development.

B. Blinded Imaging Evaluations

In response to concerns raised about blinding procedures discussed in the original draft guidance, FDA has substantially revised the recommendations on blinded imaging evaluations. The revised draft guidance states that either a fully blinded image evaluation or an image evaluation blinded to outcome by independent readers generally should serve as the principal image evaluation for demonstration of efficacy to support approval of a medical imaging agent. The revised draft guidance also notes that such image evaluations may be performed through sequential unblinding.

C. Endpoints in Trials of Medical Imaging Agents

The revised draft guidance includes a more detailed discussion of the use of primary endpoints in clinical trials designed to establish or support the efficacy of a medical imaging agent. The revised draft guidance clarifies that such primary endpoints usually should be related directly to clinically meaningful objectives. The revised draft guidance notes that image interpretations often have clinical implications that may be incorporated into the primary endpoint in clinical trials on the efficacy of a medical imaging agent. The revised

draft guidance also explains when objective imaging features, subjective image assessments, and clinical outcomes may be appropriate for use as primary imaging endpoints.

D. Other Issues on Imaging Conditions and Image Evaluations

FDA has made several other changes to the provisions in the original draft guidance on special considerations in the clinical evaluation of efficacy. These include the following: (1) Clarifying the steps in the evaluation of medical images (distinguishing between the assessment of objective image features and the interpretation of findings on an image); (2) providing a revised explanation of independent image evaluations; (3) suggesting when offsite and onsite image evaluations may be appropriate; (4) adding a discussion of the use of protocol and nonprotocol images in evaluating efficacy; and (5) clarifying the recommendations on separate or combined image evaluations.

E. Clinical Usefulness

FDA has revised the discussion of demonstrating the effectiveness of a medical imaging agent by evaluating its ability to provide useful clinical information related to its proposed indication. The revised draft guidance clarifies the ways in which a sponsor may establish the clinical usefulness of its product, depending on the specific indication. The agency also has provided several examples of how clinical usefulness should be established for different types of indications and under different circumstances.

III. Statement of Guidance Practices

This Level 1 draft guidance is being issued consistent with FDA's good guidance practices (62 FR 8961, February 27, 1997). It represents the agency's current thinking on the development of medical imaging drugs and biological products. The revised draft guidance does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes, regulations, or both.

IV. Request for Comments

Interested persons may submit to the Dockets Management Branch (address above) written comments on the revised draft guidance document by September 29, 2000. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments should be identified with the docket number found in brackets in the heading of this document. The revised draft guidance document and received comments may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

V. Electronic Access

Persons with access to the Internet may obtain the revised draft guidance at http://www.fda.gov/cder/ guidance/ index.htm or http://www.fda.gov/cber/ guidelines/ index.htm.

VI. The Paperwork Reduction Act of 1995

This draft guidance contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (the PRA) (44 U.S.C. 3501–3520). A description of these provisions is provided in the following paragraphs with an estimate of the annual reporting burden. Included in the estimate is the time for reviewing the instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing each collection of information.

FDA invites comment on the following: (1) Whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Title: Draft Guidance for Industry on Developing Medical Imaging Drugs and Biological Products.

Description: FDA is issuing a revised draft guidance on the development of medical imaging drugs and biological products. The draft guidance is intended to assist developers of drug and biological products used for medical imaging in planning and coordinating the clinical investigations of, and submitting various types of applications for, such products. The draft guidance provides information on how the agency will interpret and apply provisions of the existing regulations regarding the content and format of an application for approval of a new drug (21 CFR 314.50) and the content of a biological product application (21 CFR 601.25). The draft guidance also provides information on how the agency will interpret and apply the final rule on the evaluation and approval of in vivo radiopharmaceuticals used for diagnosis and monitoring (64 FR 26657). The final rule, by adding part 315 (21 CFR part 315), clarifies requirements for the evaluation and approval of drug and biological radiopharmaceuticals under the authority of the act and the PHS Act.

Existing regulations, which appear primarily in parts 314 and 601 (21 CFR parts 314 and 601), specify the information that manufacturers must submit so that FDA may properly evaluate the safety and effectiveness of new drugs and biological products. This information is usually submitted as part of a new drug application (NDA) or a biologics license application, or as a supplement to an approved application. Part 315 contains regulations that clarify what information is relevant for diagnostic radiopharmaceuticals. This revised draft guidance supplements these regulations. Under part 315 and the revised draft guidance, information required under the act and the PHS Act to establish safety and effectiveness would still have to be reported.

Description of Respondents: Manufacturers of medical imaging drugs and biological products, including contrast drug products and diagnostic radiopharmaceuticals.

Burden Estimate: The final rule on in vivo radiopharmaceuticals used for diagnosis and monitoring set forth an estimated annual reporting burden on the industry that would result from that rulemaking (64 FR 26657 at 26667). OMB has approved this collection of information until July 31, 2002, under OMB control number 0910–0409. This revised draft guidance on the development of medical imaging drugs and biological products is in part intended to explain how FDA will interpret and apply the final rule. Thus, the estimated annual reporting burden of the draft guidance is the same as that of the final rule, with one change. In addition to the diagnostic radiopharmaceuticals that are the subject of the final rule, the revised draft guidance also addresses the development of contrast drug products, which FDA evaluates and approves under part 314, but which are not affected by the final rule.

Table 1 provides an estimate of the annual reporting burden for contrast drug products. FDA estimates that the potential number of respondents who would submit applications or supplements for contrast drug products would be one. Although FDA did not approve any NDA's for contrast drugs

(there are no biological contrast drug products) in fiscal year 1999, for purposes of estimating the annual reporting burden, the agency assumes that it will approve one contrast drug each fiscal year. The annual frequency of responses for contrast drugs is estimated to be one response per application or supplement. The hours per response, which is the estimated number of hours that an applicant would spend preparing the information to be submitted for a contrast drug in accordance with this draft guidance, is estimated to be approximately 2,000 hours.

The revised draft guidance would not impose any additional reporting burden because safety and effectiveness information is already required by existing regulations. In fact, clarification by the revised draft guidance of FDA's standards for evaluation of medical imaging drugs and biological products is expected to reduce the overall burden of information collection. FDA received no comments on the analysis of information collection burdens stated in the notice of availability of the original draft guidance published on October 14, 1998. FDA invites comments on this revised analysis of information collection burdens.

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN [1]

	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
Contrast Drugs	1	1	1	2,000	2,000
Total					2,000

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.

In compliance with section 3507(d) of the PRA (44 U.S.C. 3507(d)), the agency has submitted the information collection provisions of this revised draft guidance to OMB for review. Interested persons are requested to send comments on this information collection by August 30, 2000, to the Office of Information and Regulatory Affairs, OMB, New Executive Office Bldg., 725 17th St. NW., rm. 10235, Washington, DC 20503, Attn: Wendy Taylor, Desk Officer for FDA.

Dated: July 20, 2000.

Margaret M. Dotzel,

Associate Commissioner for Policy.

[FR Doc. 00–19176 Filed 7–28–00; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF THE TREASURY

Internal Revenue Service

26 CFR Part 1

[REG–116495–99]

RIN 1545–AX68

Loans From a Qualified Employer Plan to Plan Participants or Beneficiaries

AGENCY: Internal Revenue Service (IRS), Treasury.

ACTION: Notice of proposed rulemaking.

SUMMARY: This document contains proposed Income Tax Regulations relating to loans made from a qualified employer plan to plan participants or beneficiaries. These regulations affect administrators of, participants in, and beneficiaries of qualified employer plans that permit participants or beneficiaries to receive loans from the plan, including loans from section 403(b) contracts and other contracts issued under qualified employer plans.

DATES: Written and electronic comments and requests for a public hearing must be received by October 30, 2000.

ADDRESSES: Send submissions to: CC:MSP:RU (REG–116495–99), room 5226, Internal Revenue Service, POB 7604, Ben Franklin Station, Washington, DC 20044. Submissions may be hand delivered Monday through Friday between the hours of 8 a.m. and 5 p.m. to: CC:MSP:RU (REG–116495–99), Courier's Desk, Internal Revenue Service, 1111 Constitution Avenue, NW., Washington, DC. Alternatively, taxpayers may submit comments electronically via the Internet by selecting the ''Tax Regs'' option on the IRS Home Page, or by submitting comments directly to the IRS Internet site at http://www.irs.gov/tax_regs/regslist.html.

FOR FURTHER INFORMATION CONTACT: Concerning the regulations, Vernon S. Carter, (202) 622–6070; concerning submissions Sonya Cruse (202) 622–7180 (not toll-free numbers).

SUPPLEMENTARY INFORMATION:

Background

This document contains proposed amendments to the Income Tax Regulations (26 CFR Part 1) under section 72 of the Internal Revenue Code of 1986 (Code).

Explanation of Provisions

Section 72(p)(1)(A) provides that a loan from a qualified employer plan (including a contract purchased under a qualified employer plan) by a participant or beneficiary is treated as received as a distribution from the plan for purposes of section 72 (a deemed distribution). Section 72(p)(1)(B) provides that an assignment or pledge of (or an agreement to assign or pledge) any portion of a participant's or beneficiary's interest in a qualified employer plan is treated as a loan from the plan.

Section 72(p)(2) provides that section 72(p)(1) does not apply to the extent certain conditions are satisfied. Specifically, under section 72(p)(2), a loan from a qualified employer plan to a participant or beneficiary is not treated as a distribution from the plan if the loan satisfies requirements relating to the term of the loan and the repayment schedule, and to the extent the loan satisfies certain limitations on the amount loaned.

Section 1704(n) of the Small Business Job Protection Act of 1996, Public Law 104–188 (110 Stat. 1755), added section 414(u) of the Code. Section 414(u)(4) provides that if a plan suspends the obligation to repay a loan made to an employee from the plan for any part of a period during which the employee is performing service in the uniformed services, that suspension is not to be taken into account for purposes of section 72(p).[1] The proposed regulations provide a rule clarifying that, under section 414(u)(4), if a plan provides for the suspension of a participant's obligation to repay a loan for any part of any leave of absence for a period of military service (as defined in chapter 43 of title 38, United States Code), the suspension will not cause the loan to be deemed distributed, even if the leave exceeds one year, as long as loan repayments resume upon the completion of the military service, the amount then remaining due on the loan

[1] Rev. Proc. 96–49 (1996–2 C.B. 369), includes a model amendment that may be used to reflect section 414(u)(4).