

party listed in Appendix A to 31 CFR Chapter V with the bracketed suffix [NPWMD] of an item subject to the EAR. If OFAC authorizes an export from the United States or an export or reexport by a U.S. person to a party listed in Appendix A to 31 CFR Chapter V with the bracketed suffix [NPWMD], such authorization constitutes authorization for purposes of the EAR as well.

(ii) U.S. persons must seek authorization from BIS for the export or reexport to a party listed in Appendix A to 31 CFR Chapter V with the bracketed suffix [NPWMD] of any item subject to the EAR that is not subject to OFAC's regulatory authority pursuant to Executive Order 13382.

(iii) Non-U.S. persons must seek authorization from BIS for any export from abroad or reexport to a party listed in Appendix A to 31 CFR Chapter V with the bracketed suffix [NPWMD] of any item subject to the EAR.

(iv) Any export or reexport to a party listed in Appendix A to 31 CFR Chapter V with the bracketed suffix [NPWMD] of any item subject to the EAR and not authorized by OFAC is a violation of the EAR.

(v) Any export or reexport by a U.S. person to a party listed in Appendix A to 31 CFR Chapter V with the bracketed suffix [NPWMD] of any item subject to the EAR that is not subject to regulation by OFAC and not authorized by BIS is a violation of the EAR. Any export from abroad or reexport by a non-U.S. person to a party listed in Appendix A to 31 CFR Chapter V with the bracketed suffix [NPWMD] of any item subject to the EAR and not authorized by BIS is a violation of the EAR.

(3) *Relation to other EAR license requirements.* The license requirements in this section supplement any other requirements set forth elsewhere in the EAR.

(b) *License exceptions.* No license exceptions are available for the EAR license requirements imposed in this section.

(c) *Licensing policy.* Applications for EAR licenses required by this section generally will be denied. You should consult with OFAC concerning transactions subject to OFAC licensing requirements.

(d) *Contract sanctity.* Contract sanctity provisions are not available for license applications reviewed under this section.

## PART 746—[AMENDED]

■ 7. The authority citation for part 746 continues to read as follows:

**Authority:** 50 U.S.C. app. 2401 *et seq.*; 50 U.S.C. 1701 *et seq.*; 22 U.S.C. 287c; Sec 1503,

Public Law 108–11, 117 Stat. 559; 22 U.S.C. 6004; 22 U.S.C. 7201 *et seq.*; 22 U.S.C. 7210; E.O. 12854, 58 FR 36587, 3 CFR, 1993 Comp., p. 614; E.O. 12918, 59 FR 28205, 3 CFR, 1994 Comp., p. 899; E.O. 13222, 3 CFR, 2001 Comp., p. 783; Presidential Determination 2003–23 of May 7, 2003, 68 FR 26459, May 16, 2003; Presidential Determination 2007–7 of December 7, 2006, 72 FR 1899 (January 16, 2007); Notice of July 23, 2008, 73 FR 43603 (July 25, 2008).

■ 8. Revise § 746.7 to read as follows:

### § 746.7 Iran.

The Treasury Department's Office of Foreign Assets Control (OFAC) administers a comprehensive trade and investment embargo against Iran. This embargo includes prohibitions on exports and certain reexport transactions involving Iran, including transactions dealing with items subject to the EAR. These prohibitions are set forth in OFAC's Iranian Transactions Regulations (31 CFR part 560). In addition, BIS maintains licensing requirements on exports and reexports to Iran under the EAR as described in paragraph (a)(1) of this section or elsewhere in the EAR (*See, e.g.*, § 742.8—Anti-terrorism: Iran).

(a) *License requirements.*

(1) *EAR license requirements.* A license is required under the EAR to export or reexport to Iran any item on the CCL containing a CB Column 1, CB Column 2, CB Column 3, NP Column 1, NP Column 2, NS Column 1, NS Column 2, MT Column 1, RS Column 1, RS Column 2, CC Column 1, CC Column 2, CC Column 3, AT Column 1 or AT Column 2 in the Country Chart Column of the License Requirements section of an ECCN or classified under ECCNs 0A980, 0A982, 0A983, 0A985, 0E982, 1C355, 1C395, 1C980, 1C981, 1C982, 1C983, 1C984, 2A994, 2D994, 2E994, 5A980, 5D980, or 5E980.

(2) *BIS authorization.* To avoid duplication, exporters or reexporters are not required to seek separate authorization from BIS for an export or reexport subject both to the EAR and to OFAC's Iranian Transactions Regulations. Therefore, if OFAC authorizes an export or reexport, such authorization is considered authorization for purposes of the EAR as well. Transactions that are not subject to OFAC regulatory authority may require BIS authorization.

(b) *Licensing Policy.* Applications for licenses for transactions for humanitarian reasons or for the safety of civil aviation and safe operation of U.S.-origin aircraft will be considered on a case-by-case basis. Licenses for other purposes generally will be denied.

(c) *License Exceptions.* No license exceptions may be used for exports or reexports to Iran.

(d) *EAR Anti-terrorism controls.* The Secretary of State has designated Iran as a country that has repeatedly provided support for acts of international terrorism. Anti-terrorism license requirements and licensing policy regarding Iran are set forth in § 742.8 of the EAR.

(e) *Prohibition on exporting or reexporting EAR items without required OFAC authorization.* No person may export or reexport any item that is subject to the EAR if such transaction is prohibited by the Iranian Transactions Regulations (31 CFR part 560) and not authorized by OFAC. The prohibition of this paragraph (e) applies whether or not the EAR requires a license for the export or reexport.

Dated: January 9, 2009.

**Christopher R. Wall,**

*Assistant Secretary for Export Administration.*

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## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

#### 21 CFR Part 56

[Docket No. FDA–2004–N–0117] (formerly Docket No. 2004N–0242)

RIN 0910–AB88

#### Institutional Review Boards; Registration Requirements

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Final rule.

**SUMMARY:** The Food and Drug Administration (FDA, we) is issuing a final rule to require institutional review boards (IRBs) to register through a system maintained by the Department of Health and Human Services (HHS). The registration information includes contact information (such as addresses and telephone numbers), the number of active protocols involving FDA-regulated products reviewed during the preceding 12 months, and a description of the types of FDA-regulated products involved in the protocols reviewed. The IRB registration requirements will make it easier for FDA to inspect IRBs and to convey information to IRBs.

**DATES:** This rule is effective July 14, 2009. This effective date is necessary to allow refinement of the electronic

registration system so that it corresponds to this final rule. All IRBs must comply with the initial registration requirement and, if necessary, make required revisions to their registrations by September 14, 2009.

**FOR FURTHER INFORMATION CONTACT:** Erik Mettler, Office of Policy, Planning and Preparedness, Food and Drug Administration, WO1, rm. 4324, Silver Spring, MD 20993-0002, 301-796-4830.

**SUPPLEMENTARY INFORMATION:**

**I. Introduction**

**What Led Us to Issue This Rule?**

IRBs are “boards, committees, or groups formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of, biomedical research involving human subjects” (see 21 CFR 56.102(g)). An IRB’s primary purpose during such reviews is to assure the protection of the rights and welfare of human subjects (id.). FDA’s general regulations pertaining to IRBs are at part 56 (21 CFR part 56). (While section 520(g) of the Federal Food, Drug, and Cosmetic Act (“the act”) (21 U.S.C. 360j(g)) refers to “institutional review committees” rather than IRBs, FDA considers institutional review committees to be IRBs and to be subject to the IRB regulations.)

Even though IRBs play an important role in the conduct of clinical investigations regulated by FDA, we have never compiled a comprehensive list of IRBs involved in reviewing clinical investigations regulated by FDA. Existing FDA regulations have required some, but not all, clinical investigators or sponsors of clinical investigations to provide IRB names and addresses to FDA, and the requirements differ slightly among the different types of products regulated by FDA. For example, for human drug products, the sponsor must disclose the name and address of “each reviewing” IRB (see 21 CFR 312.23(a)(6)(iii)(b)). For medical devices, the sponsor must disclose the names and addresses of IRBs that “have been asked or will be asked” to review the investigation (see 21 CFR 812.20(b)(7)) (emphasis added). For other types of clinical investigations regulated by FDA (such as food additive studies involving human subjects), the regulations do not expressly require the sponsor or the clinical investigator to disclose or keep records showing an IRB’s name and address, and they make no distinction between “reviewing IRBs” and IRBs that have been asked or will be asked to review a study.

In 1998, the Department of Health and Human Services’ Office of the Inspector

General (OIG) issued several reports on IRBs. The OIG sought to identify the challenges facing IRBs and to make recommendations on improving Federal oversight of IRBs. One recommendation was that all IRBs should register with the Federal Government on a regular basis as part of an effort to develop more streamlined, coordinated, and probing means of assessing IRB performance and to enhance the Federal Government’s ability to identify and respond to emerging problems before they result in “serious transgressions” (see Office of the Inspector General, Department of Health and Human Services, *Institutional Review Boards: a Time for Reform*, pages 20 and 21, June 1998).

After reviewing the OIG’s recommendation, we concluded that IRB registration would serve several important goals. IRB registration would:

- Enable us to identify more precisely those IRBs reviewing clinical investigations regulated by FDA. At present, much of our knowledge about the identities and numbers of IRBs reviewing clinical investigations regulated by FDA is based on information from persons conducting or sponsoring clinical investigations rather than from IRBs themselves. This information may be obsolete (because there may be no obligation to update the information) or incomplete (because the requirements to report the names and addresses of IRBs are not uniform across all FDA-regulated products);
- Enable us to send educational information and other information to IRBs. Because we lack an accurate list of IRBs, our outreach and educational efforts are not as efficient as they might be. Changes in IRB addresses result in returned mail, and newly formed IRBs may not appear in FDA’s mailing lists; and
- Help us identify IRBs for inspection, because we would have a more accurate list of IRBs.

Consequently, FDA, in consultation with the Department of Health and Human Services, Office for Human Research Protections (OHRP), published a proposed rule in the **Federal Register** of July 6, 2004 (69 FR 40556), that would require IRB registration for IRBs reviewing clinical investigations involving FDA-regulated products. OHRP issued a companion proposed rule which appeared in the **Federal Register** of July 6, 2004 (69 FR 40584) that would require registration for IRBs reviewing federally supported research. The final OHRP IRB registration rule is published elsewhere in this issue of the **Federal Register**.

The goal of the two rules is to create a simple, electronic registration system

that all IRBs, regardless of whether they review clinical investigations regulated by FDA or federally supported research, can use.

**II. What Comments Did We Receive?**

*A. How Many Comments Did We Receive, and Who Submitted Comments?*

We received over 15 comments in response to the proposed rule. Individuals, IRB members, IRB associations, an IRB accreditation association, government, health, academic or trade associations, a university system, and drug companies submitted comments. In general, the comments supported IRB registration, although some disagreed with specific aspects of the proposal or with other issues that were discussed in the preamble to the proposed rule. To make it easier to identify comments and our responses, the word “Comment,” in parentheses, will appear before the comment’s description, and the word “Response,” in parentheses, will appear before our response. We have also numbered each comment to help distinguish between different comments. The number assigned to each comment is purely for organizational purposes and does not signify the comment’s value or importance or the order in which it was received.

*B. Who Must Register? (Section 56.106(a))*

Proposed § 56.106(a) would require the following IRBs to register:

- Each IRB in the United States that reviews clinical investigations regulated by FDA under sections 505(i) (21 U.S.C. 355(i)) or 520(g) of the act; and
- Each IRB in the United States that reviews clinical investigations that are intended to support applications for research or marketing permits for FDA-regulated products.

The preamble to the proposed rule invited comment on whether there are circumstances in which foreign IRBs should be required or invited to register (see 69 FR 40556 at 40558).

(Comment 1) One comment stated that foreign IRBs are not needed in America.

(Response) The comment may have misinterpreted the preamble. The issue is not whether foreign IRBs should or should not review studies, but rather whether foreign IRBs should be included in the IRB registration system.

(Comment 2) Several comments differed as to whether foreign IRBs should have to register. One comment would require foreign IRBs to register if they review research conducted in the

United States; the same comment would give foreign IRBs the option to register if they review research conducted outside the United States that may be used to support a future marketing application in the United States.

Several comments would allow for voluntary registration of foreign IRBs or ethical review committees. Two comments explained that registering foreign IRBs would enable them to have access to educational materials and other information. However, one comment would limit such registration to foreign IRBs reviewing research conducted in the United States, and another comment noted that local privacy laws in foreign countries might affect a foreign IRB's ability to provide certain registration information.

In contrast, one comment said that we should respect oversight of ethical review committees by foreign authorities and that we should not impose "additional bureaucracy." Similarly, another comment opposed registering foreign IRBs, stating that such registration could pose "significant difficulties" for clinical investigators and sponsors and that foreign laws and regulations might make it difficult for foreign IRBs to register.

(Response) We agree in part with the comments. We agree that foreign IRBs would benefit from educational and other materials that would be sent to registered IRBs. Therefore, we have revised § 56.106(a) to allow for voluntary registration by foreign IRBs and by any domestic IRB that is not otherwise required to register.

We decline to require registration by foreign IRBs that review research to be conducted in the United States. We do not believe a significant number of foreign IRBs review research that is to be conducted in the United States. Furthermore, requiring registration by foreign IRBs that review research conducted in the United States could lead to arguments over the validity of our regulatory authority when applied to actions occurring in a foreign country.

As for possible problems foreign IRBs might encounter in registering information due to foreign laws and regulations, the comments did not identify specific registration elements that would be a problem. Consequently, we lack sufficient information to determine whether we should modify certain IRB registration elements to accommodate foreign IRBs.

(Comment 3) One comment asked us to clarify whether the reference to section 520(g) of the act was limited to research done under an investigational device exemption (IDE) or encompassed

all investigational devices in a clinical investigation.

(Response) The reference to section 520(g) of the act encompasses all investigational devices in a clinical investigation, regardless of whether FDA approval of an IDE is needed in accordance with 21 CFR part 812 for the clinical investigation.

(Comment 4) One comment asked us to clarify whether the rule applied to "non-local" or "commercial" IRBs.

(Response) The comment did not explain what it meant by the terms "non-local" or "commercial" IRB. For purposes of this response, we will assume that a "non-local" IRB is one that is physically located away from the clinical trial site(s) and that a "commercial" IRB is one that is paid to review research.

If the "non-local" or "commercial" IRB is located in the United States and:

- Reviews clinical investigations regulated by FDA under sections 505(i) or 520(g) of the act; or
- Reviews clinical investigations that are intended to support applications for research or marketing permits for FDA-regulated products, then the non-local or commercial IRB must register under § 56.106(a). If the non-local or commercial IRB does not perform any of the reviews described immediately above or is outside the United States, then it may register voluntarily.

#### *C. What Information Must an IRB Register? (Section 56.106(b))*

Proposed § 56.106(b) would describe the information that IRBs would provide as part of the registration process. For example, proposed § 56.106(b)(1) would require the name and mailing address of the institution operating the IRB and the name, mailing address, phone number, facsimile number, and electronic mail address of the senior officer of that institution who is responsible for overseeing the IRB's activities. (A facsimile number also is known more commonly as a "fax number.")

(Comment 5) Several comments addressed the registration information in proposed § 56.106(b) generally. Two comments said that the registration information that OHRP and FDA would require should either be the same or that information required by OHRP, but not by FDA, should be clearly delineated and marked as optional for IRBs that are subject to FDA regulation. Similarly, one comment said that questions relating to research funded by HHS, which were part of OHRP's proposed registration system, should be identified clearly so IRBs that do not review HHS-funded research are not obliged to answer those questions.

Another comment said the proposed registration information is appropriate.

One comment urged us to reexamine the registration information to assure that the information is necessary to support the rule's stated goals.

(Response) We coordinated our rule with OHRP and tailored our respective registration information elements to be as consistent as possible and to use the same internet-based registration system.

We agree that the IRB registration system should specify whether certain registration information is optional or not required for IRBs subject only to our jurisdiction. The preamble to the proposed rule stated that, "In those instances where the Internet registration site would seek more information than FDA would require under this proposal, the site would clarify that IRBs regulated solely by FDA may, but are not required to, provide the additional information" (69 FR 40556 at 40558). The Internet registration site will be structured so that required information will be identified or marked as such, and IRBs indicating that they are registering pursuant to FDA's regulation also will be directed to questions requesting information required only under FDA's regulation.

(Comment 6) Proposed § 56.106(b)(1) would require IRBs to provide the name and mailing address of the institution operating the IRB and the name, mailing address, phone number, facsimile number, and electronic mail address of the "senior officer of that institution who is responsible for overseeing activities performed by the IRB." The preamble to the proposed rule explained that the senior officer "must not be an IRB member, IRB staff, or a sponsor or investigator participating in an investigation under review by that IRB" (see 69 FR 40556 at 40558).

Several comments addressed this provision. Two comments supported the proposed requirement, but two other comments stated that our interpretation of "senior officer" was too prohibitive or too restrictive. These comments said that if a senior officer is on the IRB, his or her membership should not invalidate registration or subject the IRB to enforcement action.

Another comment questioned what we meant when we referred to "IRB staff." The comment said that some IRBs distinguish staff from IRB members to ensure the IRB's integrity and independence. The comment suggested that we list persons who cannot be a "senior officer" and that we delete "IRB staff" from that list.

(Response) We agree, in part, with the comments. We recognize that, in some cases, it may not be feasible to identify

a “senior officer” who is not also an IRB member or IRB staff. However, our experience indicates that IRBs sometimes form subcommittees or other groups and that the institutions overseeing the IRBs may not be aware of these subcommittees or other groups. Thus, when we said that the “senior officer” should not be an IRB member or IRB staffer, our goal was to ensure that the institution overseeing the IRB’s activities is truly aware of those activities. For these reasons, where feasible, we recommend that the senior officer not be an IRB member or an IRB staffer.

Additionally, as the preamble to the proposed rule stated, information regarding the institution will enable us to identify the institution and to determine whether problems that might exist for one IRB at that institution exist at other IRBs affiliated with that institution (see 69 FR 40556 at 40558).

Additionally, on our own initiative, we have revised § 56.106(b)(1) to require the street address for the institution if the street address is different from the institution’s mailing address.

(Comment 7) One comment said we should ensure that any addresses and telephone numbers are current and are kept current. The comment suggested that we issue fines and penalties if IRBs fail to keep such information current.

(Response) Section 56.106(e) requires IRBs to revise their registration information within 90 days if a contact person or chairperson information changes; this would encompass changes in the contact person’s or chairperson’s telephone number.

As for the comment’s suggestion of imposing fines and penalties, we do not have legal authority to impose fines for failure to maintain IRB registration information. As for other penalties, we discuss the consequences of failing to register in comment 24 of this document.

(Comment 8) Proposed § 56.106(b)(2) would require IRBs to provide the IRB’s name, the names of each IRB chair person and each contact person (if one exists) for the IRB, and the IRB’s mailing address, street address (if different from the mailing address), phone number, facsimile number, and electronic mail address.

One comment supported the proposal. However, another comment noted that the OHRP proposal would require IRBs to provide the name, gender, degree, scientific or nonscientific specialty, and affiliation of each IRB member and suggested that we revise our rule to require the same information as the OHRP rule.

(Response) We agree, in part, and disagree, in part, with the comment’s suggestion that we require the same information as OHRP’s rule. We decline to revise the rule as requested by the comment. Unlike OHRP, we have never required IRBs to give us the names, educational background, and qualifications of all IRB members. Our rule does not include this information because our regulatory emphasis has been on the IRB’s overall composition. Consequently, our final rule does not require such information about individual IRB members.

We have, however, revised § 56.106(b)(2) to replace “chair person” with “chairperson.” This change reflects the common spelling for this noun and does not alter the application or interpretation of § 56.106(b)(2). Additionally, we have revised § 56.106(b)(2) to require the phone number and electronic mail address for the IRB chairperson; this will enable us to communicate with the IRB chairperson quickly if such a need arises.

On our own initiative, we have revised § 56.106(b)(2) to delete the parenthetical of “(if one exists)” after “the contact person’s name” and to require and the name, mailing address, phone number, facsimile number, and electronic mail address of the contact person providing the registration information. This information will enable us to communicate with the contact person if any questions arise regarding the IRB or its registration information, and the information now required is similar to that required for the contact person under OHRP’s rule. We also have reorganized the provision to make it easier to understand what information is required.

(Comment 9) Proposed § 56.106(b)(3) would require IRBs to provide the “number of active protocols (small, medium, or large) involving FDA-regulated products reviewed.” The proposal explained that a “small” number of protocols is 1 to 25 protocols; “medium” is 26 to 499 protocols, and “large” is 500 protocols or more.

Several comments interpreted this provision in different ways or sought clarification as to its meaning. In brief:

- One comment asked us to define “protocol” because it said questions would arise regarding multi-site studies involving a single protocol.

- Another comment would redefine the numerical ranges so that “small” would be 1 to 99 protocols, “medium” would be 100 to 499 protocols, “large” would be 500 to 1,999 protocols, and “very large,” a new category, would be 2,000 protocols or more. The comment

explained that a “substantial number” of organizations oversee thousands of protocols and that these organizations operate differently compared to those that review 500 protocols.

- Another comment expressed concern about the protocol numbers, stating that it was unclear how useful or accurate the data would be due to complexities in IRB review and “protocol driven research activities,” the level of IRB review (such as full IRB review or expedited review), and frequent or daily changes in protocol review numbers.

Similarly, another comment stated that protocols are neither uniform nor uniformly complex, so that protocol activity is not a reasonable basis for determining IRB activity. A third comment said that we should consider the protocol ranges to be only approximations of IRB workloads and use the information carefully and cautiously in evaluating or characterizing IRBs.

- Another comment disputed the need for protocol review information, arguing that compliance with regulatory requirements is an issue regardless of the number of protocols reviewed by an IRB.

(Response) The preamble to the proposed rule explained that information regarding the number of protocols reviewed would enable us to determine how active an IRB is and to assign our inspection resources based on IRB activity levels (see 69 FR 40556 at 40558). Our intent was not to get an exact or precise figure, and the proposal’s use of “small,” “medium,” and “large” protocol ranges reflected that intent.

Consequently, we decline to revise the rule to define “protocol” in the final rule. *Webster’s II—New Riverside University Dictionary* defines “protocol,” in relevant part, as “the plan for a scientific experiment or treatment” (see *Webster’s II—New Riverside University Dictionary* at page 947 (1988)). Thus, in the comment’s scenario, if an IRB conducts one review for a multi-site study, that single review could be considered as one “protocol.” If an IRB conducts separate reviews for individual study sites, then it conceivably could have reviewed multiple “protocols” notwithstanding the fact that the study plan remains essentially the same for all sites.

However, on our own initiative, we have amended § 56.106(b)(3) to define what the term “active protocol” means. The final rule defines “active protocol” as “any protocol for which an IRB conducted an initial review or a continuing review at a convened

meeting or under an expedited review procedure during the preceding 12 months." We have made this change to be consistent with changes made by OHRP in its final rule.

With respect to the proposal's numerical ranges and their usefulness to us, we reiterate that our intent was to get a general—rather than a precise—sense of how active IRBs are and to assign our limited inspectional resources more efficiently and effectively. We recognize that there are different types of IRB review and that changes in an IRB's workload could make an IRB's protocol estimate outdated or obsolete at a later point in time. However, given the protocol ranges were created simply to give us an idea about an IRB's activity, we have revised the rule to eliminate the "small," "medium," and "large" ranges. Instead, the final rule requires an approximate number of active protocols reviewed, but we neither expect nor want IRBs to constantly change or update their protocol numbers whenever their protocol numbers fluctuate. If the approximate number of protocols changes after initial IRB registration, the IRB should report the new protocol number as part of the re-registration process which takes place every 3 years.

As for compliance activities, we believe the comment may have misinterpreted the preamble to the proposed rule. We did not state that we would base inspections solely on an IRB's self-reported level of "small," "medium," or "large" numbers of protocols reviewed. We simply said that the information would help us assign inspection resources based on IRB activity levels.

To put it another way, we have limited inspectional resources, and our field staffs that inspect IRBs are also responsible for many other types of inspections and activities. We must prioritize our routine IRB inspections in some manner to make the most efficient use of our resources. Such prioritization of IRB inspections is not tantamount to declaring, as the comment suggests, that IRBs reviewing "small" or "medium" numbers of protocols do not have to comply with FDA regulations or that we enforce our requirements differently depending on whether an IRB reviews a "small," "medium," or "large" number of protocols. Nevertheless, given that the final rule does not contain the "small," "medium," or "large" protocol ranges, the issue is largely moot.

(Comment 10) Proposed § 56.106(b)(4) would require IRBs to describe the types of FDA-regulated products, such as biological products, color additives,

food additives, human drugs, or medical devices, involved in the protocols that they review.

Two comments addressed this provision. One comment stated that it had no objection to the requirement provided that the description could be simple or generic without numerical ranges associated with each product type. Another comment said the descriptions would be appropriate only if we used the information for purposes of sending useful and targeted information to IRBs. The comment also said that the description should be generic and without numerical ranges associated with product types.

(Response) We agree with the comments. Section 56.106(b)(4) merely seeks a generic description of the FDA-regulated products in the protocols reviewed by the IRB. So, for example, if the IRB reviews protocols for human drug studies, the description, to satisfy § 56.106(b)(4), could simply be "human drugs." If the IRB reviews protocols for human drug and medical device studies, the description would be "human drugs" and "medical devices." We also note that the electronic registration system will list the types of FDA-regulated products and allow individuals to check the appropriate boxes relating to those products and to check "other" and explain what the "other" FDA-regulated products are.

Furthermore, § 56.106(b)(4) does not require IRBs to assign numerical values to the FDA-regulated product types. As the comments noted, our intent is to use this information to send product-specific information to IRBs, and we can do so with a simple description of product types.

(Comment 11) Proposed § 56.106(b)(5) would require an indication whether the IRB is accredited and, if so, the date of the last accreditation and the name of the accrediting body or organization. The preamble to the proposed rule stated that we recognized that IRB accreditation is a developing concept and invited comment on "the perceived value of collecting information on the accreditation status of IRBs" (see 69 FR 40556 at 40558).

We received more than 10 comments on IRB accreditation issues, and the comments reflected a considerable difference of opinion regarding IRB accreditation and whether we should require information about such accreditation. In brief, the comments stated:

- IRB accreditation information may give FDA useful information in deciding which IRBs to inspect and may help us decide whether to focus educational activities on certain areas. One comment

added that accreditation information would help us evaluate the value of IRB accreditation. In contrast, one comment said that IRB accreditation information will not give FDA new information that will be useful in assessing accreditation's value;

- FDA should refer to accreditation of human research protection programs rather than accreditation of IRBs;

- FDA should require information about the name of the accrediting organization under which the IRB functions or collect information about accreditation type or level. One comment explained that one body has two different accreditation categories;

- The additional reporting burden should not be passed on to the institution;

- FDA should delete the provision because accreditation information can be collected without the need for a regulation or is publicly available from accrediting organizations. One comment added that accreditation information, if it were part of the IRB registration requirement, might be unreliable because our rule would require re-registration every 3 years; and

- Accreditation does not accurately represent a measure of compliance with human subject protection requirements. Similarly, an IRB's lack of accreditation could be misconstrued as reflecting on the quality of the IRB's human subject protection program. In contrast, one comment strongly encouraged IRBs to become accredited, and another comment said that accreditation implies that a certain standard has been achieved.

(Response) The final rule omits accreditation information from the IRB registration requirements. We agree that, if necessary, we can obtain accreditation information from the accreditation organizations themselves and that the resulting information may be more reliable or accurate, given that the rule does not require certain registration information to be updated until re-registration. We also agree that, as a general matter, accreditation does not ensure or demonstrate that a particular action was done correctly; instead, accreditation may increase one's confidence that the accredited body is capable of performing a particular action correctly.

Furthermore, we continue to believe that accreditation, insofar as human subject protection is concerned, is still a developing concept. Consequently, we will continue to follow such accreditation activities, but will not require accreditation information as part of IRB registration.

Finally, because the final rule does not require accreditation information, the comment regarding reporting burdens is moot.

*D. When Must an IRB Register? (Section 56.106(c))*

Proposed § 56.106(c) would have IRBs register once and to renew their registrations every 3 years. Initial IRB registration would occur within 30 days before the date when the IRB intends to review clinical investigations regulated by FDA. IRB registration would become effective upon HHS posting of the registration information on its Web site.

(Comment 12) One comment would have us consider IRBs to be registered as soon as they complete submitting the registration information regardless of whether the IRB submitted the information electronically or in writing. Another comment suggested that the electronic registration system acknowledge or document that the IRB has registered. Another comment stated that, if IRB registration is to identify IRBs for future inspections, there is no need for a 30-day "waiting" period.

A different comment said that the 30-day time period might interfere with IRB review, particularly expedited reviews and full IRB reviews that take less than 30 days. The comment suggested that we revise the rule so that IRBs may not issue a determination on FDA-regulated research until they have registered.

Another comment asked us to clarify when IRBs must register. The comment explained that the codified provision directed IRBs to submit an initial registration within 30 days before the date when the IRB intends to review clinical investigations regulated by FDA. The comment said that the word "within" could mean that an IRB could register "anytime between one and 30 days before reviewing a protocol," but that the preamble to the proposed rule interpreted proposed § 56.106(c) as requiring registration at least 30 days before reviewing the protocol. The comment preferred giving IRBs the ability to register any time between 1 and 30 days before reviewing protocols in FDA-regulated research.

(Response) We agree, in part, with the comments. For IRBs that register electronically, the registration system will notify them that they are registered. This notification will be sent to the electronic mail address that the IRB provides as part of the registration process. The IRB's registration will be effective after review and acceptance by HHS. We have amended § 56.106(c) regarding the time at which IRB registration becomes effective to

correspond to changes made by OHRP in its final rule which is published elsewhere in this issue of the **Federal Register**. OHRP revised a comparable provision in its rule to clarify when IRB registration would become effective.

For IRBs that submit their registration information in writing, our experience with written forms in other contexts suggests that some individuals will not complete the forms or omit required information. As a result, we may need to contact individuals to obtain the missing information. Therefore, it would be more practical for us to consider IRBs who submit their registration information in writing to be registered only after they have submitted all required registration information, we have entered that information into the electronic registration system, and the information is reviewed and accepted by HHS.

As for the comments concerning the 30-day timeframe and the suggestion that we amend the rule so that IRBs cannot issue decisions on FDA-regulated research until they have registered, we have decided to eliminate the 30-day timeframe from the final rule. We note that IRB registration, alone, does not address issues regarding an IRB's competence or expertise, nor does it require IRBs to meet a particular standard in order to conduct a review. However, because it is important to FDA to assemble an accurate IRB database, we have revised § 56.106(c) to state that: "Each IRB must submit an initial registration. The initial registration must occur before the IRB begins to review a clinical investigation described in paragraph (a) of this section. Each IRB must renew its registration every 3 years. IRB registration becomes effective after review and acceptance by HHS."

(Comment 13) One comment would require IRBs to renew their registration every year instead of every 3 years. The comment said that 3 years would be too long a time period.

(Response) We decline to revise the rule as suggested by the comment. IRB registration does not confer any particular status on IRBs, nor does registration, alone, reflect upon an IRB's competence or capabilities. Moreover, given that the information we seek through IRB registration is quite basic (as in names and addresses) and that § 56.106(e) describes how and when IRBs are to revise their registration information, annual registration would not appear to confer any advantages or make registration information more accurate or reliable. Consequently, we decline to require IRBs to register annually.

*E. Where Can an IRB Register? (Section 56.106(e))*

Proposed § 56.106(e) would direct IRBs to register at a specific Internet address or, if an IRB lacked the ability to register electronically, to send its registration information to a specific mail address. We indicated that we would provide the Internet address and mail address in the final rule. We also invited comment on whether we should discontinue written IRB registration procedures after some time period has elapsed, because we did not know how widespread Internet access is among IRBs (see 69 FR 40556 at 40558).

(Comment 14) Several comments pertained to the registration site(s). One comment said we should maintain one common registration site with OHRP and that the registration system should automatically include currently registered IRBs. The comment said the registration system should also allow such IRBs to retain their assigned numbers. The comment acknowledged the intent to create a single registration site, but implied that the proposed rule's omission of a specific Internet address created concern. Another comment supported creation of a simple, electronic registration system.

(Response) We agree that a single Internet registration site should be used for electronic registrations and have always worked with OHRP towards that end. We were unable to provide a specific Internet address at the time of the proposed rule because the electronic registration system was still under development. The final rule now states that the Internet registration address is <http://ohrp.cit.nih.gov/efile>.

Additionally, as we stated in the preamble to the proposed rule, OHRP will continue to recognize previous IRB registrations (see 69 FR 40556 at 40558).

(Comment 15) One comment asked whether entities that have more than one IRB at the same location need to register more than once or whether they could register once and provide multiple pieces of information in connection with a single registration.

(Response) The electronic registration system will assign an organization number to each entity, and this will enable the entity to register several IRBs without having to enter the same data repeatedly for each IRB.

(Comment 16) Two comments encouraged us to have the electronic registration system consider IRBs to be registered automatically once an IRB completes the electronic registration process or to send acknowledgements to the IRBs once they complete the electronic registration process.

(Response) As we stated in our response to comment 12 of this document, when an IRB completes the electronic registration process and HHS has reviewed and accepted the information, the electronic registration system will notify IRBs that they are registered.

(Comment 17) Several comments responded to our question whether we should discontinue written IRB registrations after some time period has elapsed. One comment supported conversion to electronic registration as soon as possible, but said it is important to allow small organizations the time to acquire the necessary technology. The comment agreed that not all institutions have electronic capabilities or Internet access.

Another comment supported giving IRBs the option to submit registration information in writing for a predetermined period of time, but did not suggest any time period. A different comment also supported the written registration option, but suggested that it be available only for 2 years.

Another comment opposed discontinuing written IRB registration. The comment said that there are adverse consequences to both the IRB and any sponsor or investigator that might use an unregistered IRB (which appeared to be a reference to a later discussion, in the preamble to the proposed rule, about "What Happens if an IRB Does Not Register?" (see 69 FR 40556 at 40559)), so we should continue to make written IRB registration possible.

(Response) While we continue to believe that most IRBs will use the electronic registration system, we do not know how many IRBs will use the written registration option, and the administrative record for this rulemaking does not give us sufficient basis to set a deadline at which we would end the written registration option. (We realize that one comment suggested a 2-year period, but, given that IRBs have 3 years to renew registrations, discontinuing written registrations after 2 years would not give IRBs the opportunity to renew their registrations in writing.) Consequently, until we become more experienced with IRB registrations, we will continue to offer written registration as an alternative to electronic registration, and the final rule states that IRBs that lack the ability to register electronically must send their registration information, in writing, to the Good Clinical Practice Program (HF-34), Office of Science and Health Coordination, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

#### *F. How Does an IRB Revise Its Registration Information? (Section 56.106(e))*

Proposed § 56.106(e) would have IRBs revise their registration information within specific timeframes if certain changes occurred. For example, if the IRB's contact or chair person information changes, proposed § 56.106(e) would require the IRB to change its registration information within 90 days of the change. If the IRB decided to disband or to discontinue reviewing FDA-regulated clinical investigations, it would report that change within 30 days. All other information changes would be reported when the IRB renews its registration.

(Comment 18) Two comments pointed out a discrepancy between the proposed rule and its preamble. The comments noted that the preamble to the proposed rule said that if an IRB reviews new types of FDA-regulated products, it would revise its registration information within 30 days (see 69 FR 40556 at 40559), yet proposed § 56.106(e) was silent regarding such changes. The comments suggested that we reconcile the codified text with the preamble.

(Response) The comments were correct. We inadvertently omitted changes in the IRB's review of FDA-regulated research from proposed § 56.106(e), and we have revised the rule so that IRBs must revise their registration information within 30 days if they review new types of FDA-regulated products. Additionally, on our own initiative, we have added a parenthetical phrase to clarify that a decision to review "new types of FDA-regulated products" should be interpreted as a decision to review a different category of FDA-regulated products, such as a decision to review studies pertaining to food additives when the IRB previously reviewed studies pertaining to drug products. We do not want IRBs to revise their registration information if they decide to review studies pertaining to subcategories within the same class of FDA-regulated products; for example, if an IRB previously reviewed studies pertaining to drugs intended to treat cardiac conditions and then decided to review studies pertaining to drugs intended to treat cancer, both types of studies would still pertain to drug products, so there would be no "new type" of FDA-regulated product within § 56.106(e).

(Comment 19) One comment addressed IRBs that have decided to disband. The comment said that the process of closing an IRB may take longer than 30 days, so requiring IRBs

to revise their registration information within 30 days of a decision to disband would put an "undue burden" on IRBs and the institutions responsible for the IRBs.

(Response) We agree in part, and disagree in part with the comment. We agree that, in some cases, closing an IRB may take more than 30 days, but, in other cases, the process may take less time. In other words, IRBs vary in size, resources, organization, and complexity, and, as a result, different IRBs will take different amounts of time to perform the same or similar functions.

The comment also may have misinterpreted the proposed rule. Proposed § 56.106(e) stated that an IRB's decision to disband or to discontinue reviewing FDA-regulated clinical investigations is a change that must be reported within 30 days of that change; thus, the proposal would begin the time period when IRB decides to close, not when the IRB finally closes. Nevertheless, for consistency with OHRP's final rule (which appears elsewhere in this issue of the **Federal Register**), we have revised § 56.106(e) to state that an IRB's decision to disband is a change that must be reported "within 30 days of permanent cessation of the IRB's review of research." In the preamble to the OHRP final rule, OHRP states that "the date of permanent cessation of the IRB's review of \* \* \* research would occur on or after the IRB's decision to disband, but not before the IRB's decision to disband was made."

Furthermore, given the simplicity of the electronic registration system, we do not believe that IRBs or their institutions will find it "unduly" burdensome to report the IRB's decision to disband.

(Comment 20) One comment would shorten the time period for reporting changes in the IRB's contact or chair person information from 90 days to 60 days.

(Response) We decline to revise the rule as suggested by the comment. The comment did not identify any advantage in shortening the timeframe, and we do not believe that reducing the timeframe by 30 days will confer any significant benefit.

#### *G. What Other Comments Did We Receive?*

##### *1. What Information Will Be Publicly Available?*

The preamble to the proposed rule referred to the OHRP proposal for information regarding public disclosure of IRB registration information, the Freedom of Information Act (FOIA), and

the Privacy Act of 1974 (see 69 FR 40556 at 40557). It also stated that, insofar as FDA's registration system was concerned, the name of the institution operating the IRB and the IRB's name will be publicly accessible, and all other IRB registration information would be subject to public disclosure under FOIA and our public information regulations at part 20 (21 CFR part 20) (see *id.*).

(Comment 21) One comment said that, in addition to the institution's name and the IRB's name, we should make the following information publicly available:

- The name, address, and telephone number of the IRB contact; and
- For accredited IRBs, information relating to that accreditation.

Another comment asked us to clarify what information would be publicly available under FOIA.

(Response) All registration information required under this rule will be subject to FOIA and any other applicable statutes and regulations pertaining to public disclosure. Please note that certain information may be withheld from public disclosure or may require an individual's consent to public disclosure (see, e.g., § 20.63(e) (stating that a request for all records relating to a specific individual will be denied as a clearly unwarranted invasion of personal privacy unless accompanied by the written consent of the individual named)).

As for accreditation information, accreditation status is not required under the final rule, so that information will not be publicly available from us or from OHRP.

(Comment 22) One comment suggested that sponsors and investigators have access to the IRB registration database. The comment said that sponsors and investigators currently have access to Federal-wide assurances data and suggested that, if sponsors and investigators could not have access to the IRB registration database, we or OHRP should issue a report of IRB registrations or issue certificates to individual IRBs.

(Response) OHRP currently posts all registered IRBs on its Web site, including the name and location of the organization operating the IRB(s) and the name and location of each IRB.

We decline to issue reports on IRB registration or certificates to show that an IRB is registered. As we stated in our response to comment 12 of this document, IRB registration, alone, does not address issues regarding an IRB's competence or expertise, nor does it require IRBs to meet a particular standard in order to conduct a review.

(Comment 23) One comment said we should establish a link to the publicly available IRB registration information from the portion of our own Web site that pertains to "Good Clinical Practices in FDA-Regulated Clinical Trials," located at <http://www.fda.gov/oc/gcp/default.htm>.

(Response) We agree with the comment and have modified our Web site accordingly.

## 2. What Happens if an IRB Does Not Register?

The preamble to the proposed rule stated that sponsors and investigators who used unregistered IRBs might be using IRBs that "would not have had the benefit of receiving educational materials from FDA and would not have been identified on an FDA IRB registration list for future inspection" (see 69 FR 40556 at 40559). Thus, the preamble to the proposed rule added that, "to the extent that any existing FDA regulation requires a sponsor or investigator to comply with [part 56] or to use an IRB that complies with part 56, FDA will consider sponsors and investigators using an unregistered IRB to be in conflict with their regulatory obligations" (*id.*).

The preamble to the proposed rule also noted how we considered other options to require sponsors and investigators to use only registered IRBs, such as refusing to consider information from an application for a research permit for a clinical investigation that is reviewed or is to be reviewed by an unregistered IRB (*id.*). The preamble to the proposed rule also invited comment on what sanctions or administrative mechanisms, if any, should or might be used against sponsors and investigators who use unregistered IRBs and whether any additional changes to our regulations were necessary.

(Comment 24) We received many comments relating to sanctions, other regulatory changes, and ensuring that sponsors and investigators use only registered IRBs. The comments reflected a considerable difference of opinion. For example:

- One comment said we should impose and enforce "high fines" for failure to follow human subject protection regulations;
- Several comments said that the forms investigators currently use (Form FDA 1572) could be used to reinforce or otherwise highlight the need to use only registered IRBs, but the comments differed as to whether investigators should be subject to any sanctions if they use an unregistered IRB. For example, one comment said failure to use a registered IRB should be treated

the same as any other breach of an investigator's responsibilities, but others said that IRBs, rather than sponsors or investigators, should be responsible for any failure to register. One comment also opposed placing an investigation on clinical hold because, the comment argued, clinical holds are appropriate when the rights and/or safety of human subjects are in jeopardy or other material, noncompliance concerns are evident; the comment said that failure to register does not mean improper oversight by the IRB or by the sponsor. Some comments argued that sponsors and investigators should not be obliged to monitor an IRB's registration status. In contrast, one comment would have us amend the investigational new drug (IND) application regulations to authorize us to place a study on clinical hold if the sponsor or investigator uses an unregistered IRB. The same comment suggested that we consider additional enforcement options, such as "refusing to consider information from an application for a research permit for a clinical investigation that is reviewed or is to be reviewed by an unregistered IRB."

- Several comments, mostly from pharmaceutical firms or trade associations, opposed any changes outside the IRB regulations. The comments, in general, felt that the existing IND regulations were sufficient and clear regarding a sponsor's or investigator's obligation to use IRBs that comply with part 56. Some comments said we should not expend resources on revising the IND regulations but should promote awareness of the IRB registration requirements instead. Another comment, from an association of medical colleges, also opposed revisions to the IND regulations, stating that clinical holds would be unworkable because, if an unregistered IRB had reviewed a clinical study and the clinical study had proceeded, retroactive review of the study would be impermissible. The comment said we should refuse to consider information from an application for a research permit that is reviewed or is to be reviewed by an unregistered IRB.

- One comment suggested a "flexible" approach whereby we would start by sending a certified letter to an unregistered IRB regarding its failure to register and include registration instructions. If the IRB remained unregistered, the comment suggested that we inspect the IRB. The comment said that this approach would allow us to take appropriate action against unregistered IRBs without "unnecessarily penalizing" sponsors and investigators who have attempted to



follow our regulations in good faith. Similarly, another comment advocated sending letters to IRBs or notices to sponsors rather than imposing sanctions.

- One comment agreed with us that an IRB's failure to register would not justify disqualification of the IRB under § 56.121 absent the extreme circumstances described in § 56.121(b)(1) (the IRB has refused or repeatedly failed to comply with regulatory requirements) or § 56.121(b)(2) (the noncompliance adversely affects the rights or welfare of the human subjects in a clinical investigation).

(Response) We agree in part and disagree in part with the comments. We agree that the existing IND regulations, as well as the IDE regulations, are sufficient and clear regarding a sponsor's or investigator's obligation to use IRBs that comply with part 56. We also agree that an IRB's failure to register, alone, should not lead to disqualification proceedings under § 56.121 absent extreme circumstances. We intend to educate IRBs, sponsors, and investigators about the IRB registration requirements and to encourage sponsors and investigators to use registered IRBs for the same reasons we stated in the preamble to the proposed rule.

Given the existing IND and IDE regulations and our intent to pursue educational efforts, we disagree with those comments that would have us impose fines or place clinical investigations on clinical hold if the sponsor or investigator used an unregistered IRB. We believe that it would be premature for us to consider the use of such sanctions before we and the regulated community have gained sufficient experience with the IRB registration program.

### 3. What Other Issues Did the Comments Raise?

Several comments addressed issues that were either not part of the rulemaking or not material to the proposed codified text.

(Comment 25) One comment disagreed with the preamble to the proposed rule when we stated that our knowledge about the identities and numbers of IRBs reviewing FDA-regulated clinical research is obsolete or incomplete (see 69 FR 40556 at 40557). The comment said that we require sponsors to identify IRBs and that, for 20 years, OHRP has maintained a list of IRBs that have filed assurances (under 45 CFR part 46). The comment said that such past practices were apparently

sufficient for purposes of conducting inspections.

(Response) We disagree with the comment. As we stated in the preamble to the proposed rule, existing FDA regulations have required some, but not all, clinical investigators and sponsors to provide IRB names and addresses to us, and those regulatory requirements differ slightly (see 69 FR 40556 at 40557). Consequently, because of differences within our own regulations, we do not have a comprehensive list of IRBs that review FDA-regulated research. Additionally, because our pre-existing regulations do not require sponsors and investigators to revise or update IRB information if and when the IRB changes its address, contact person, or chair person, or even, in some cases, to provide addresses, contact information, or chair person information to us, the IRB information we do have is not as detailed as the information we seek under this rule.

As for institutions that have filed assurances with OHRP under 45 CFR part 46, the IRBs associated with such institutions are not necessarily identical to those that review FDA-regulated research. OHRP's regulations apply to institutions that are engaged in human subjects research conducted or supported by HHS. In contrast, our IRB regulations apply to clinical investigations regulated by us, regardless of whether those investigations are conducted or supported by HHS. Thus, the fact that OHRP has operated an assurance system for decades does not necessarily mean that the OHRP list of institutions that have filed assurances can serve as a list of IRBs that review FDA-regulated research.

(Comment 26) One comment said that registration and re-registration fees should be set at \$5,000 to cover costs. The comment said that taxpayers should not have to pay the fees or fund the costs of "profiteers," and that pharmaceutical companies should not "get away" with low fees when "they can pay their executives \$150,000,000 at retirement."

(Response) We decline to revise the rule as suggested by the comment. We have no express authority to impose registration or re-registration fees on IRBs. Additionally, the rule is directed at IRBs themselves rather than pharmaceutical firms, so issues relating to pharmaceutical executives' salaries are not relevant to this rulemaking.

(Comment 27) One comment asked us to confirm that our IRB inspections will adhere to the guidelines described in the "Guidance for Institutional Review Boards and Clinical Investigators."

(Response) This rulemaking does not affect how we conduct IRB inspections. We may, however, use IRB registration information to help us prioritize inspections. Additionally, our receipt of more accurate IRB addresses and contact information due to IRB registration should make it easier and more efficient to schedule IRB inspections.

### H. What Other Amendment Did We Propose?

The proposal would also make a non-substantive amendment to part 56. The proposal would revise the definition of "An Application for an Investigational Device Exemption," at § 56.102(b)(12), to eliminate its reference to 21 CFR part 813. The preamble to the proposed rule explained that this change is necessary because we removed the regulations at part 813 (which had pertained to intraocular lenses) in 1997 (see 62 FR 4164, January 29, 1997).

We received no comments on this aspect of the proposal. Consequently, the final rule deletes a reference to part 813.

## III. Implementation

This rule is effective July 14, 2009. This protracted effective date is necessary to allow refinement of the electronic registration system so that it corresponds to this final rule and to OHRP's final rule.

## IV. Legal Authority

In general, the act authorizes us to issue regulations pertaining to investigational uses of FDA-regulated products (see, e.g., sections 409(j) (21 U.S.C. 348(j)) (investigations involving food additives); 505(i) (investigations involving human drugs); 520(g) (investigations involving devices); and 721(f) (21 U.S.C. 379e(f)) of the act (investigations involving color additives)).

The act also requires the submission of a petition or application to FDA (see, e.g., sections 409(b) (food additive petitions); 505(b) (new drug applications); 505(j) (abbreviated new drug applications); 513(f) (premarket notification for devices); 515(c) (premarket approval applications for devices); 520(m) (humanitarian device exemption applications); and 721(b) of the act (color additive petitions)) before marketing begins.

To implement these provisions of the act, section 701(a) of the act gives us the authority to issue regulations for the efficient enforcement of the act. By requiring IRB registration, the final rule will aid in the efficient enforcement of the act's provisions regarding the

investigational use of various FDA-regulated products (because then we would be able to conduct IRB inspections more efficiently) as well as those provisions regarding marketing applications (because marketing applications usually depend on clinical investigations involving human subjects, and IRBs are supposed to provide protections for the rights and welfare of such human subjects). Moreover, by requiring IRBs to register, the final rule will enable FDA to contact IRBs more quickly and efficiently on various issues, such as adverse reactions that may be attributed to a particular product, new regulatory requirements or policies, or problems associated with a particular protocol or clinical investigator. Consequently, we conclude that we have sufficient legal authority to issue the final rule.

### V. Economic Impact Analysis

We have examined the impacts of the final rule under Executive Order 12866, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this final rule is not a significant regulatory action as defined by the Executive Order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because the required registration information is minimal and the costs associated with registration are low, the agency certifies that the final rule will not have a significant economic impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement, which includes an

assessment of anticipated costs and benefits, before proposing “any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100,000,000 or more (adjusted annually for inflation) in any one year.” The current threshold after adjustment for inflation is \$127 million, using the most current (2006) Implicit Price Deflator for the Gross Domestic Product. FDA does not expect this final rule to result in any 1-year expenditure that would meet or exceed this amount.

The final rule requires most IRBs to register with FDA. The information sought through the registration process is minimal, consisting largely of names and addresses for a contact person, the institution operating the IRB (if an institution exists), the head of the institution, the IRB, and the IRB chairperson. The registration would also indicate the approximate number of active protocols reviewed and the types of FDA-regulated products involved. We estimate that initial IRB registration may require 1 hour. The average loaded wage rate for administrators at public institutions is about \$44 per hour.<sup>1</sup> This means that each IRB would spend \$44 for an initial registration (\$44 per hour x 1 hour per initial registration).

We estimate that re-registration would require less time, especially if the IRB verifies existing information. If re-registration requires 30 minutes, then the cost of re-registration to each IRB would be approximately \$22 (\$44 per hour x 0.5 hours per re-registration).

Revising an IRB’s registration information would probably involve costs similar to re-registration costs. If the revision requires 30 minutes, then the cost of revising an IRB’s registration information would be approximately \$22 per IRB.

Given the minimal registration information that would be required and the low costs associated with registration, this final rule is not a significant regulatory action, and we certify that the final rule does not have a significant economic impact on a

substantial number of small entities. Therefore, the rule is not a “significant regulatory action” under Executive Order 12866 and does not require a Regulatory Flexibility Act analysis.

Additionally, assuming that an estimated 5,000 IRBs would register, the final rule will result in a 1-year expenditure of \$220,000 (5,000 IRBs x \$44 registration wage costs per IRB). Because the total expenditure under the rule will not result in a 1-year expenditure of \$100 million or more, we are not required to perform a cost-benefit analysis under the Unfunded Mandates Reform Act.

### VI. Environmental Impact

We have determined under 21 CFR 25.30(h) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

### VII. Paperwork Reduction Act of 1990

This rule contains information collection requirements that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501–3520). The title, description, and respondent description of the information collection provisions are shown below with an estimate of the annual reporting and recordkeeping burden. Included in the estimate is the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing each collection of information.

*Title:* Institutional Review Boards: Registration Requirements.

*Description:* The final rule requires IRBs to register with FDA.

*Description of Respondents:* Businesses and individuals.

The estimated burden associated with the information collection requirements of this rule is 8,750 hours.

We estimate the burden of this collection of information as follows:

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN<sup>1</sup>

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
56.106(c) (initial registration)	5,000	1	5,000	1	5,000
56.106(c) (re-registration)	2,500	1	2,500	0.5	1,250

<sup>1</sup> Source: United States Department of Labor, Bureau of Labor Statistics; National Compensation Survey, June 2005. Overall hourly rate in the United

States for administrators and officials, public administration, is \$31.54. To account for benefits, the hourly rate was increased by 40 percent and

rounded to the nearest whole dollar. Data accessed on August 31, 2006, at <http://data.bls.gov>.

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN<sup>1</sup>—Continued

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
56.106(e)	5,000	1	5,000	0.5	2,500
Total					8,750

<sup>1</sup> There are no capital costs or operating and maintenance costs associated with this collection of information.

Our estimates are based on the following considerations. According to a 1998 OIG report, there are 3,000 to 5,000 IRBs in the United States, and most are associated with hospitals and academic centers (see Department of Health and Human Services, Office of the Inspector General, *Institutional Review Boards: A Time for Reform*, page 3, June 8, 1998). While not all IRBs are involved in clinical investigations regulated by FDA, for purposes of the PRA, we will use 5,000 as the maximum number of IRBs subject to the final rule.

Additionally, because the final rule requires basic information about an IRB (such as names and addresses) and because registration would, in most cases, be done electronically, we will assume that registration will take only 1 hour per IRB. Thus, the total burden hours would be 5,000 hours (5,000 IRBs x 1 hour per IRB).

Re-registration and revisions to existing registration information should require less time than initial registration. We will assume that re-registration and revisions will take only 30 minutes per IRB. We will also assume, based on OHRP's experience with its IRB registration program, that 50 percent of IRBs (2,500) will re-register and that all (5,000) will revise their registration information. Therefore, the total burden hours for re-registration will be 1,250 hours (2,500 IRBs x 0.5 hours per IRB), and the total burden hours for revisions will be 2,500 hours (5,000 IRBs x 0.5 hours per IRB).

Prior to the effective date of this final rule, FDA will publish a notice in the **Federal Register** announcing OMB's decision to approve, modify, or disapprove the information collection provisions in this final rule. In compliance with the PRA (44 U.S.C. 3507(d)), we have submitted the information collection requirements of this rule to OMB for review. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

### VIII. Federalism

We have analyzed this final rule in accordance with the principles set forth

in Executive Order 13132. We have determined that the rule does not contain policies that have substantial direct effects 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. Accordingly, we have concluded that the rule does not contain policies that have federalism implications as defined in the order and, consequently, a federalism summary impact statement is not required.

#### List of Subjects in 21 CFR Part 56

Human research subjects, Reporting and recordkeeping requirements, Safety.

■ Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner, part 56 is amended as follows:

#### PART 56—INSTITUTIONAL REVIEW BOARDS

■ 1. The authority citation for 21 CFR part 10 continues to read as follows:

**Authority:** 21 U.S.C. 321, 343, 346, 346a, 348, 350a, 350b, 351, 352, 353, 355, 360, 360c–360f, 360h–360j, 371, 379e, 381; 42 U.S.C. 216, 241, 262, 263b–263n.

#### § 56.102 [Amended]

■ 2. Amend § 56.102 in paragraph (b)(12) by removing the phrase “parts 812 and 813” and by adding in its place the phrase “part 812”.

■ 3. Add § 56.106 to subpart A to read as follows:

#### § 56.106 Registration.

(a) *Who must register?* Each IRB in the United States that reviews clinical investigations regulated by FDA under sections 505(i) or 520(g) of the act and each IRB in the United States that reviews clinical investigations that are intended to support applications for research or marketing permits for FDA-regulated products must register at a site maintained by the Department of Health and Human Services (HHS). (A research permit under section 505(i) of the act is usually known as an investigational new drug application (IND), while a research permit under section 520(g) of

the act is usually known as an investigational device exemption (IDE).) An individual authorized to act on the IRB's behalf must submit the registration information. All other IRBs may register voluntarily.

(b) *What information must an IRB register?* Each IRB must provide the following information:

(1) The name, mailing address, and street address (if different from the mailing address) of the institution operating the IRB and the name, mailing address, phone number, facsimile number, and electronic mail address of the senior officer of that institution who is responsible for overseeing activities performed by the IRB;

(2) The IRB's name, mailing address, street address (if different from the mailing address), phone number, facsimile number, and electronic mail address; each IRB chairperson's name, phone number, and electronic mail address; and the name, mailing address, phone number, facsimile number, and electronic mail address of the contact person providing the registration information.

(3) The approximate number of active protocols involving FDA-regulated products reviewed. For purposes of this rule, an “active protocol” is any protocol for which an IRB conducted an initial review or a continuing review at a convened meeting or under an expedited review procedure during the preceding 12 months; and

(4) A description of the types of FDA-regulated products (such as biological products, color additives, food additives, human drugs, or medical devices) involved in the protocols that the IRB reviews.

(c) *When must an IRB register?* Each IRB must submit an initial registration. The initial registration must occur before the IRB begins to review a clinical investigation described in paragraph (a) of this section. Each IRB must renew its registration every 3 years. IRB registration becomes effective after review and acceptance by HHS.

(d) *Where can an IRB register?* Each IRB may register electronically through <http://ohrp.cit.nih.gov/efile>. If an IRB lacks the ability to register electronically, it must send its

registration information, in writing, to the Good Clinical Practice Program (HF-34), Office of Science and Health Coordination, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

(e) *How does an IRB revise its registration information?* If an IRB's contact or chair person information changes, the IRB must revise its registration information by submitting any changes in that information within 90 days of the change. An IRB's decision to review new types of FDA-regulated products (such as a decision to review studies pertaining to food additives whereas the IRB previously reviewed studies pertaining to drug products), or to discontinue reviewing clinical investigations regulated by FDA is a change that must be reported within 30 days of the change. An IRB's decision to disband is a change that must be reported within 30 days of permanent cessation of the IRB's review of research. All other information changes may be reported when the IRB renews its registration. The revised information must be sent to FDA either electronically or in writing in accordance with paragraph (d) of this section.

Dated: January 7, 2009.

**Jeffrey Shuren,**

*Associate Commissioner for Policy and Planning.*

[FR Doc. E9-682 Filed 1-14-09; 8:45 am]

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## DEPARTMENT OF STATE

### 22 CFR Part 42

[Public Notice: 6457]

RIN 1400-AB84

#### **Visas: Documentation of Immigrants Under the Immigration and Nationality Act, as Amended: Electronic Petition for Diversity Immigrant Status**

**AGENCY:** State Department.

**ACTION:** Final rule.

**SUMMARY:** This rule makes final an interim rule published in the **Federal Register** on August 18, 2003, amending the Department's regulations pertaining to the manner in which aliens may petition for the opportunity to participate in the Diversity Visa Program. The rule changed the standard mail-in system previously used to an entirely electronic system for the purpose of making the process less prone to fraud, improve efficiency and significantly reduce the processing costs to the Government.

**DATES: Effective Date:** This rule is effective on January 15, 2009.

**FOR FURTHER INFORMATION CONTACT:** Lauren Prosnik, Legislation and Regulations Division, Visa Services, Department of State, Washington, DC 20520-0106, (202) 663-1202, e-mail ([prosnikla@state.gov](mailto:prosnikla@state.gov)).

#### **SUPPLEMENTARY INFORMATION:**

#### **Why is the Department promulgating this rule?**

The Department published an interim rule, Public Notice 4446 at 68 FR 49353, Aug. 18, 2003, with a request for comments. The comment period expired on October 17, 2003. No public comments were received during the comment period.

#### **What did the rule do?**

The rule amended the Department's regulations at 22 CFR 42.33 to establish an entirely electronic system utilizing a specifically designated Internet Web site, by which aliens can petition for the opportunity to participate in the Diversity Visa Program.

#### **Why was the petitioning process changed?**

There are three main benefits to changing the mail-in process to an electronic format. First, it helps eliminate multiple applications, prohibited under INA Section 204(a)(1)(I). Secondly, it greatly reduces the cost of administering the system. Finally, it benefits the petitioners by immediately notifying them of the receipt of the petition, impossible under the mail-in system.

#### **PART 42—VISAS: DOCUMENTATION OF IMMIGRANTS UNDER THE IMMIGRATION AND NATIONALITY ACT, AS AMENDED**

■ Accordingly, the interim rule amending 22 CFR part 42 which was published at 68 FR 49353 on August 18, 2003, is adopted as final without change.

Dated: January 2, 2009.

**Janice L. Jacobs,**

*Assistant Secretary for Consular Affairs, Department of State.*

[FR Doc. E9-698 Filed 1-14-09; 8:45 am]

**BILLING CODE 4710-06-P**

## DEPARTMENT OF HOUSING AND URBAN DEVELOPMENT

### 24 CFR Parts 203 and 3500

[Docket No. FR-5180-F-04]

RIN 2502-AI61

#### **Real Estate Settlement Procedures Act (RESPA): Rule To Simplify and Improve the Process of Obtaining Mortgages and Reduce Consumer Settlement Costs; Deferred Applicability Date for the Revised Definition of "Required Use"**

**AGENCY:** Office of the Assistant Secretary for Housing-Federal Housing Commissioner, HUD.

**ACTION:** Final rule.

**SUMMARY:** This final rule delays the effective date of the definition of "required use" as revised by HUD's November 17, 2008, final rule amending its RESPA regulations. The November 17, 2008, final rule provides that the revised definition is applicable commencing January 16, 2009, the effective date of the final rule. As a result of recently initiated litigation, HUD has determined to delay the effective date of the revised definition of "Required use" until April 16, 2009.

**DATES:** This correction is effective January 16, 2009. The definition of "Required use" in § 3500.2, as revised by HUD's final rule published on November 17, 2008, at 73 FR 68204, is delayed until April 16, 2009.

**FOR FURTHER INFORMATION CONTACT:** Ivy Jackson, Director, or Barton Shapiro, Deputy Director, Office of RESPA and Interstate Land Sales, Office of Housing, Department of Housing and Urban Development, 451 7th Street, SW., Room 9158, Washington, DC 20410-8000; telephone 202-708-0502 (this is not a toll-free telephone number). Persons with hearing or speech impairments may access this number through TTY by calling the toll-free Federal Information Relay Service at 800-877-8339.

**SUPPLEMENTARY INFORMATION:** On November 17, 2008 (73 FR 68204), HUD published a final rule amending its regulations to further the purposes of the Real Estate Settlement Procedures Act (12 U.S.C. 2601-2617) by requiring more timely and effective disclosures related to mortgage settlement costs for federally related mortgage loans to consumers. The final rule followed publication of a March 14, 2008, proposed rule (73 FR 14030) and made changes in response to public comment and in further consideration of certain issues by HUD. Additional information