the approval must specifically reference this AD.

Note 3: There is no terminating action currently available for the repetitive inspections required by 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 4: Information concerning the existence of approved alternative methods of compliance with this AD, if any, may be obtained from the Seattle ACO.

Special Flight Permit

(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 June 12, 2002.

Ali Bahrami,

Acting Manager, Transport Airplane Directorate, Aircraft Certification Service.

[FR Doc. 02–15368 Filed 6–18–02; 8:45 am]

BILLING CODE 4910–13–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 312

[Docket No. 00N–1663]

RIN 0910–AA61

Investigational New Drugs: Export Requirements for Unapproved New Drug Products

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to amend its regulations on the exportation of investigational new drugs, including biological products. The proposed rule would provide four different mechanisms for exporting an investigational new drug product. These provisions would implement changes in FDA's export authority resulting from the FDA Export Reform and Enhancement Act of 1996, and they would also simplify the existing requirements for exports of investigational new drugs.

DATES: Submit written or electronic comments by September 17, 2002. Submit written comments on the information collection requirements by July 19, 2002.

ADDRESSES: Submit written comments to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to *http://www.fda.gov/dockets/ecomments.* Submit written comments on the information collection requirements to the Office of Information and Regulatory Affairs, OMB, New Executive Office Bldg., 725 17th St. NW., rm. 10235, Washington, DC 20502, Attn: Stuart Shapiro.

FOR FURTHER INFORMATION CONTACT: Philip L. Chao, Office of Policy, Planning, and Legislation (HF–23), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–3380.

SUPPLEMENTARY INFORMATION:

I. Background

Current FDA regulations at § 312.110 (21 CFR 312.110) require any person who intends to export an unapproved new drug product for use in a clinical investigation either to have an investigational new drug application (IND) or to submit a written request to FDA. The written request must provide sufficient information about the drug to satisfy FDA that the drug is appropriate for investigational use in humans, that the drug will be used for investigational purposes only, and that the drug may be legally used by the consignee in the importing country for the proposed investigational use (see § 312.110(b)(2)(i)). The request must also specify the quantity of the drug to be shipped and the frequency of expected shipments (§ 312.110(b)(2)(i)). If FDA authorizes exportation of the drug, it notifies the government of the importing country (§ 312.110(b)(2)(i)). Similar procedures exist for export requests made by foreign governments (see § 312.110(b)(2)(ii)). Section 312.110(b)(3) states that the requirements in paragraph (b) apply only where the drug is to be used for the purpose of a clinical investigation. Section 312.110(b)(4) states that the requirements in paragraph (b) do not apply to the exports of new drugs approved or authorized for export under section 802 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 382) or section 351(h)(1)(A) of the Public Health Service Act.

The program for exporting investigational new drugs is commonly known as the ''312 program'' because the regulation pertaining to the program is located in part 312 (21 CFR part 312). Between fiscal years 1994 and 1997, FDA received nearly 1,800 export requests under the 312 program. Very few requests (less than 1 percent) presented any safety, quality, or other public health concerns.

In 1996, the President signed into law amendments to the act that changed the export requirements for certain drugs, biologics, and devices that may not be marketed or sold in the United States. These amendments, known as the FDA Export Reform and Enhancement Act of 1996 (Public Law 104–134, amended by Public Law 104–180), created, among other things, two new provisions that affect the exportation of investigational drug products. One provision, now section 802(b)(1)(A) of the act, authorizes exportation of an unapproved new drug to any country if that drug has valid marketing authorization by the appropriate authority in Australia, Canada, Israel, Japan, New Zealand, Switzerland, South Africa, the European Union (EU), or a country in the European Economic Area (EEA) and certain other requirements are met. These countries are listed in section 802(b)(1)(A)(i) and (b)(1)(A)(ii) of the act and are sometimes referred to as the ''listed countries.'' Currently, the EU countries are Austria, Belgium, Denmark, Germany, Greece, Finland, France, Ireland, Italy, Luxembourg, the Netherlands, Portugal, Spain, Sweden, and the United Kingdom. The EEA countries are the EU countries, and Iceland, Liechtenstein, and Norway. The list of countries in section 802(b)(1)(A)(i) of the act will expand automatically if any country accedes to the EU or becomes a member of the EEA. Exports under section 802(b)(1)(A) of the act can encompass exportation of an unapproved new drug product for investigational use in a foreign country if the exported drug product has marketing authorization in any listed country and the relevant statutory requirements are met. Exports under section 802(b)(1)(A) of the act do not require prior FDA authorization.

The second provision, now section 802(c) of the act, permits exportation of unapproved new drugs (including biological products) intended for investigational use to any listed country in accordance with the laws of that country. Exports of drugs to the listed countries under section 802(c) of the act do not require prior FDA authorization and are exempt from regulation under section 505(i) of the act (21 U.S.C. 355(i)).

All drug products exported under section 802 of the act are, however, subject to certain general requirements. Section 802(f) of the act prohibits export if the unapproved new drug: (1) Is not manufactured, processed, packaged, and held in substantial conformity with current good manufacturing practice requirements; (2) is adulterated under certain provisions of section 501 of the act (21 U.S.C. 351); (3) does not comply with section 801(e)(1) of the act (21 U.S.C. 381(e)(1)), which requires that the exported product be intended for export, meet the foreign purchaser's specifications, not be in conflict with the laws in the importing country, be labeled on the outside of the shipping package that the products are intended for export, and not be sold or offered for sale in the United States; (4) is the subject of a determination by FDA that the probability of reimportation of the exported drug would present an imminent hazard to the public health and safety of the United States; (5) presents an imminent hazard to the public health of the foreign country; (6) fails to comply with labeling requirements in the country receiving the exported drug; or (7) is not promoted in accordance with labeling requirements in the importing country and, where applicable, in the listed country in which the drug has valid marketing authorization. Section 802(g) of the act also imposes certain recordkeeping and notification obligations on drugs exported under section 802 of the act; these recordkeeping and notification obligations were the subject of a final rule that appeared in the **Federal Register** of December 19, 2001 (66 FR 65429).

The new export provisions in section 802 of the act have significantly reduced the number of requests under the 312 program from an annual average of 570 requests to 100 requests. This proposed rule would conform the present regulation to the provisions of, and would be consistent with, the FDA Export Reform and Enhancement Act of 1996.

II. Description of the Proposed Rule

The proposed rule would amend § 312.110 to provide four mechanisms for exporting investigational new drugs, eliminate unnecessary language in the current regulation, and streamline the export requirements for the ''312 program.'' The proposed rule would not contain any new recordkeeping requirements because such records would already be required under § 312.57 or the final export notification and recordkeeping rule that appeared in the **Federal Register** of December 19, 2001 (66 FR 65429).

Proposed § 312.110(b)(1) would represent the first mechanism for exporting an investigational new drug and would apply if the foreign clinical investigation is to be done under an IND. Exports under proposed § 312.110(b)(1) could be made to any foreign country. Proposed § 312.110(b)(1) would provide that an investigational new drug may be exported from the United States if an IND is in effect for the drug under § 312.40, the drug complies with the laws of the country to which it is being exported, and each person who receives the drug is an investigator in a study submitted to and allowed to proceed under the IND. This is similar to current § 312.110(b) although it would expressly, rather than implicitly, require the exported drug to comply with the laws of the foreign country.

Drugs that are the subject of an IND may be exported to any country in the world if the export is for the purpose of conducting an investigation in the importing foreign country. The agency reiterates that the requirements in proposed § 312.110(b)(1) would apply only if the foreign clinical investigation is to be done under an IND.

Proposed § 312.110(b)(2) would represent the second mechanism for investigational new drug exports and would implement section 802(b)(1) of the act with respect to exports of unapproved new drugs for investigational use. Under the proposal, if a drug product that is not approved for use in the United States has valid marketing authorization in Australia, Canada, Israel, Japan, New Zealand, Switzerland, South Africa, or in any country in the EU or the EEA, the drug may be exported for any use, including investigational use, to any country, provided that the export complies with all applicable requirements pertaining to exports. Prior FDA approval to export the drug would not be required. The proposal also would not require the drug to be the subject of an IND, but would not preclude the exporter from obtaining an IND if it chose to submit an IND to the agency. The exporter and the exported products, however, would have to comply with the foreign country's laws and with requirements in section 802(f) and (g) of the act. Recordkeeping requirements are the subject of § 1.101, which was published in the **Federal Register** of December 19, 2001.

Proposed § 312.110(b)(3), the third mechanism for investigational new drug exports, would implement section 802(c) of the act with respect to exports of unapproved new drugs for investigational use. In brief, if an unapproved drug is to be exported for investigational use to any listed country in accordance with the laws of that country, then no prior FDA authorization would be required. Export of a drug for investigational use under proposed § 312.110(b)(3) would have to comply with the foreign country's laws and the applicable provisions in section 802(c), (f), and (g) of the act. Recordkeeping requirements, as stated earlier, were the subject of § 1.101 which was published in the **Federal Register** of December 19, 2001.

FDA anticipates that most investigational new drugs would be exported under proposed § 312.110(b)(3), because the agency's experience indicates that most investigational new drugs are exported to the listed countries.

FDA interprets section 802(c) of the act, and proposed § 312.110(b)(3), to permit exportation of investigational new drugs to the listed countries, but not to permit the transshipment of investigational new drugs to nonlisted countries. (''Transshipment'' refers to the practice of shipping a product to a country from which it will later be shipped to another country.) The agency is aware that some firms have interpreted section 802(c) of the act as permitting transshipment to unlisted countries; section 802(c) of the act is silent with respect to transshipment, however, and a more reasonable interpretation is that the provision does not allow transshipments. Interpreting section 802(c) of the act to allow transshipment would be inconsistent with FDA's traditional practice under § 312.110; would presume, in the absence of any supporting language in the statute or its legislative history, that the listed countries may serve as mere transfer points or conduits for investigational new drugs and devices destined for unlisted countries; and would make the limitation to the listed countries in section 802(c) of the act virtually meaningless.

FDA, however, interprets section 802(c) of the act as permitting investigational new drugs to be sent to principal investigators in a listed country who use the investigational new drug in an unlisted country if the principal investigator conducts the clinical investigations in accordance with the requirements of both the listed country and the unlisted country where the investigation is conducted. For example, if firm A exported an investigational new drug to principal investigator X in Norway (a listed country), section 802(c) of the act would

permit exportation to proceed without prior FDA authorization so long as firm A and the exported drug met all other statutory conditions pertaining to the exportation. Principal investigator X could then administer the investigational new drug in an unlisted country so long as principal investigator X conducts the clinical investigation in accordance with Norwegian requirements and any requirements in the unlisted country where the investigational new drug is administered.

If the drug presents an imminent hazard to the public health or safety of the foreign country, fails to comply with labeling requirements, or is not promoted in accordance with labeling requirements, section 802(f) of the act requires the agency to consult with the appropriate public health official in the foreign country. Section 802(g) of the act requires exporters to maintain records of all drugs exported under section 802 of the act. This provision of the act allows enforcement of section 802 of the act because it provides FDA with a means to determine what drugs have been exported under section 802 of the act and where the drugs were sent. Consequently, although proposed § 312.110(b)(3) would not require firms to submit reports to the agency concerning exported drugs, it would, consistent with section 802 of the act, require firms to maintain records documenting their compliance with section 802(c) and (f) of the act. In the **Federal Register** of December 19, 2001 (66 FR 65429), FDA published a final rule concerning the recordkeeping and notification requirements for products exported under sections 801(e) and 802 of the act and section 351(h) of the Public Health Service Act; the recordkeeping and notification requirements will be codified in a new § 1.101.

Additionally, proposed § 312.110(b)(3) would provide that exports of drugs that are not under an IND to the listed countries for investigational use under section 802(c) of the act do not have to comply with the labeling requirement in § 312.6(a). Section 312.6(a) requires that the immediate package for an investigational new drug bear the following statement: ''Caution: New Drug–Limited by Federal (or United States) law to investigational use.'' In response to industry concerns, FDA is proposing to exempt unapproved new drugs exported under section 802(c) of the act and that are not under an IND from the label statement requirement in § 312.6(a). The industry expressed concerns in response to a preliminary, informal FDA interpretation shortly after enactment of the FDA Export Reform and Enhancement Act of 1996 indicating that all unapproved new drugs exported for investigational use under section 802(c) of the act should carry the label statement provided in § 312.6(a). After careful consideration, FDA has decided that drugs exported under section 802(c) of the act that are not under an IND should be exempted from the label statement in § 312.6(a). FDA is proposing the exemption because the principal authority for § 312.6 is section 505(i) of the act, but section 802© of the act expressly declares that exports under section 802© of the act are not subject to the requirements in section 505(i) of the act. An investigational new drug exported under an IND, however, would continue to be subject to the label requirement as the investigational new drug remains subject to section 505(i) of the act by virtue of the IND.

Proposed § 312.110(b)(4) would represent the fourth mechanism for exporting an investigational new drug and would pertain to unapproved new drugs exported to any country for investigational use without an IND, although the agency anticipates that the provision would be used by persons who intend to export a drug for investigational use to countries that are not listed in section 802 of the act and proposed § 312.110(b)(2). Proposed § 312.110(b)(4) would streamline the requirements for the 312 program by eliminating the requirement of prior FDA authorization. Instead, the proposal would require a person seeking to export an unapproved new drug for investigational use without an IND to send a written certification to FDA. The certification would be submitted at the time the drug is first exported and would describe the drug being exported (i.e., trade name (if any), generic name, and dosage form), identify the country or countries to which it is being exported, and affirm that:

- The drug is intended for export;[1]
- The drug is intended for investigational use in a foreign country;
- The drug meets the foreign purchaser's or consignee's specifications;
- The drug is not in conflict with the importing country's laws;
- The outer shipping package is labeled to show that the package is intended for export from the United States;
- The drug is not sold or offered for sale in the United States;
- The clinical investigation will be conducted in accordance with § 312.120;
- The drug is manufactured, processed, packaged, and held in substantial conformity with current good manufacturing practices;
- The drug is not adulterated within the meaning of section 501(a)(1), (a)(2)(A), (a)(3), (c), or (d) of the act;[2]
- The drug does not present an imminent hazard to public health, either in the United States if the drug were to be reimported or in the foreign country;
- The drug is labeled in accordance with the foreign country's laws; and
- The drug is promoted in accordance with its labeling.

In short, the certification in proposed § 312.110(b)(4) would combine the statutory requirements at sections 801(e)(1) and 802(f) of the act with the requirements of informed consent and the use of qualified clinical investigators at section 505(i) of the act. This approach is intended to accomplish several goals.

First, because the agency's experience with the 312 program indicates that very few investigational new drug exports under the existing program raise any safety, quality, or other public health concerns, the certification would eliminate the requirement of prior FDA authorization of a request to export a drug for investigational use. Instead, a certification would be sent to FDA's Office of International Programs (formerly the Office of International Affairs) when the drug is exported.

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[1]This requirement would be consistent with a decision by the United States Court of Appeals for the Fourth Circuit in *United States* v.*Kanasco, Ltd.*, 123 F.3d 209 (4th Cir. 1997), in which a firm sought to claim that drugs that were not manufactured in accordance with good manufacturing practices (GMPs) were nevertheless exempt from the GMP requirements because they were intended for export. However, the firm did not have a foreign purchaser for the drug and could not identify a specific foreign country to which the drug would be exported; instead, it argued that it could find a foreign purchaser at a future date and that the drugs met the requirements of unnamed and unspecified foreign countries. The Court of Appeals rejected the arguments that the drug was intended for export, stating that the firm's argument ''would create an unwarranted escape hatch for violators of the Act'' (id. at page 212).

[2]In brief, these sections of the act state that a drug shall be deemed to be adulterated if it consists in whole or in part of any filthy, putrid, or decomposed substance; if it has been prepared, packed, or held under insanitary conditions whereby it may have been contaminated with filth, or whereby it may have been rendered injurious to health; if its container is composed in whole or in part of any poisonous or deleterious substance which may render the contents injurious to health; if the drug's strength differs from or its purity or quality falls below that which it purports or is represented to possess; or if any substance has been mixed or packed with the drug so as to reduce the drug's quality or strength or any substance has been substituted in whole or in part for the drug.

Second, by requiring exports under the 312 program to comply with requirements that are similar to those under sections 801(e)(1) and 802(f) of the act, exports under the 312 program would be subject to the same minimum export requirements as other exports of unapproved new drugs for investigational use.

Third, by conditioning exports to unlisted countries under the 312 program on the conduct of clinical investigations in accordance with § 312.120, the use of investigational new drugs under the 312 program would be clearly subject to internationally recognized requirments for clinical investigations. This aspect of the proposed rule also reflects the fact that section 505(i) of the act, which authorizes FDA to issue regulations pertaining to investigational new drugs, is the authority for the 312 program. (In contrast, unapproved new drugs exported for investigational use to listed countries under section 802(c) of the act are not subject to the requirements in section 505(i) of the act.)

Thus, the proposed rule would streamline the 312 program by eliminating, in all cases, the requirement of prior FDA authorization of exports. At the same time, the proposal would increase the safeguards for exports under the 312 program through the responsibilities placed on the sponsor as a result of the required certification.

Persons exporting investigational new drugs under an IND or under the 312 program should note that section 402(j) of the Public Health Service Act (42 U.S.C. 282(j)) directs the Secretary of Health and Human Services to establish, maintain, and operate a data bank of information on clinical trials for drugs for serious or life-threatening diseases and conditions. FDA invites comment on whether the agency should make available information on clinical trials involving investigational new drugs exported under the 312 program.

Proposed § 312.110(b)(4) would also require the person exporting the investigational new drug to retain records showing its compliance with the provision's requirements.

Proposed § 312.110© would prohibit exports under certain conditions. For example, for drugs under an IND that are exported under proposed § 312.110(b)(1), exportation would not be allowed if the IND were terminated. For drugs exported under proposed § 312.110(b)(2), (b)(3), or (b)(4), exportation would not be allowed if the requisite conditions underlying or authorizing the exportation are no longer met. For all investigational new drugs exported under § 312.110, exportation would not be allowed if the drug no longer complied with the laws of the importing country.

Currently, § 312.110(b)(4) states that the requirements in § 312.110(b) do not apply to the export of new drugs (including biological products, antibiotic drugs, and insulin) approved or authorized for export under section 802 of the act or section 351(h)(1)(A) of the Public Health Service Act. The proposal would redesignate § 312.110(b)(4) as new § 312.110(d) and revise the text to state that the export requirements in § 312.110 do not apply to insulin or to antibiotic drug products exported for investigational use. This provision would reflect section 802(i) of the act which provides that insulin and antibiotics may be exported in accordance with the export requirements in section 801(e)(1) of the act without complying with section 802 of the act. The proposed change would also eliminate a potentially confusing and incorrect reference to new drugs ''approved or authorized for export under section 802 of the act * * * or section 351(h)(1)(A) of the Public Health Service Act'' because the proposal does, indeed, address exports of unapproved new drugs for investigational use under section 802(b)(1) and (c) of the act. Also, § 312.110, and the regulations in part 312 generally, apply only to exports of investigational new drugs, so there is no need for § 312.110 to expressly exclude exports of unapproved new drugs for other, noninvestigational uses. For example, exports of unapproved new drugs for marketing purposes or exports in anticipation of market authorization occur under the authority in section 802 of the act, and obviously are not investigational uses. As for section 351(h) of the Public Health Service Act, it pertains to exports of partially processed biological products that are: (1) Not in a form applicable to the prevention, treatment, or cure of diseases or injuries of man; (2) not intended for sale in the United States; and (3) intended for further manufacture into final dosage form outside the United States. Thus, partially processed biological products exported under section 351(h) of the Public Health Service Act are not exported for investigational use, so they do not have to be mentioned in § 312.110. (FDA also notes that the FDA Export Reform and Enhancement Act of 1996 revised and renumbered section 351(h) of the Public Health Service Act, and so the revised section no longer contains a paragraph (h)(1)(A).)

FDA is also proposing to amend the authority citation for part 312 to reflect additional statutory provisions, such as sections 801, 802, 803, and 903 of the act (21 U.S.C. 381, 382, 383, and 393), that affect investigational new drug exports, FDA's international activities, and rulemaking. In addition, the proposal would remove the existing text at § 312.110(b)(3); the existing text states that the export requirements in § 312.110(b) apply only where the drug is to be used for the purpose of a clinical investigation. FDA is proposing to delete this language because the proposed rule expressly refers to exports of investigational new drugs for use in clinical investigations.

Firms evaluating whether to export a drug under these provisions should carefully consider the consequences of any decision. FDA notes that exports under section 802(b)(1)(A) and (c) of the act do not require the exporter to be a sponsor of an IND. However, the existing patent term restoration provision in 35 U.S.C. 156 defines the ''regulatory review period'' for drugs and biologics as starting on the date on which an IND becomes effective.[3] Thus, if the drug product is ultimately approved or licensed for marketing and the patent is otherwise eligible for patent term extension under 35 U.S.C. 156, firms that conducted clinical investigations without an IND may have relinquished the opportunity to extend a patent term to compensate for any patent life lost during the ''testing phase'' for their drugs (although they may still be able to receive an extended patent term based on the ''approval phase'' for their products). Therefore, as a general matter, firms may find it in their interests to obtain an IND regardless of where the clinical investigations will occur.

III. Legal Authority

Section 505(i) of the act authorizes the agency to issue regulations pertaining to drugs intended solely for investigational use by experts qualified by scientific training and experience to investigate the safety and effectiveness of drugs. Under this authority, FDA has, for many years, approved the export of certain unapproved new drugs for investigational use in one or more foreign countries. Additionally, FDA can, under its general authority over

[3]For drugs, the ''regulatory review period'' consists of two parts, a ''testing phase''—the time between the effective date of an IND and the submission of a marketing application (a new drug application or a product license application) to FDA—and an ''approval phase''—the time between submission and approval of the marketing application. The regulatory review period calculation forms the basis for the extended patent term.

investigational new drugs, terminate an IND under certain conditions.

The proposed rule is consistent with section 505(i) of the act insofar as proposed § 312.110(b)(1) would pertain to drugs that are the subject of an IND and proposed § 312.110(b)(4) would require clinical investigations involving an investigational new drug without an IND that is exported to a foreign country to be conducted in accordance with § 312.120. Section 505(i) of the act also gives FDA express authority to issue regulations pertaining to investigational new drugs.

The proposed rule is also authorized by sections 801(e) and 802 of the act. Sections 801(e) and 802 of the act both address the export of drug products that may not be marketed or sold in the United States, but in different ways. Under section 801(e)(1) of the act, a drug product intended for export will not be considered to be adulterated or misbranded if it: (1) Accords to the specifications of the foreign purchaser, (2) is not in conflict with the laws of the country to which it is intended for export, (3) is labeled on the outside of the shipping package that it is intended for export, and (4) is not sold or offered for sale in domestic commerce. Section 801(e)(1) of the act reflects a general view that a U.S. producer should be able to make products intended for export that do not meet U.S. requirements provided that the products meet the requirements of both the purchaser and receiving country. Although section 801(e)(1) of the act does not expressly apply to unapproved new drugs, the requirements in section 801(e)(1) of the act do apply to all drug products exported under section 802 of the act (see section 802(f)(3) of the act).

Section 802 of the act applies to unapproved drug products intended for export. Section 802© of the act applies to exports of unapproved drug products intended for investigational use. As stated earlier, section 802© of the act permits the export of a drug or device intended for investigational use to Australia, Canada, Israel, Japan, New Zealand, Switzerland, South Africa, or any country in the EU or EEA in accordance with the laws of the importing country. No prior FDA authorization is required, and exports under section 802© of the act are also exempt from regulation under section 505(i) of the act. However, section 802(f) of the act prohibits export of a drug if certain conditions are not met (such as conformity with current good manufacturing practices, compliance with section 801(e)(1) of the act, and certain practices that would cause the drug to be adulterated under certain provisions of section 501 of the act).

The proposed rule is, therefore, authorized by sections 801(e)(1) and 802 of the act because proposed § 312.110(b)(2) would pertain to drugs exported under section 802(b) of the act and would require that such exports comply with section 802(f) of the act (which includes compliance with section 801(e) of the act). Proposed § 312.110(b)(3) would pertain to exports of investigational new drugs to listed countries, under section 802© of the act, and would also require compliance with section 802(f) of the act. Authority to issue regulations to implement sections 801(e) and 802 of the act, and for the efficient enforcement of the act generally, is authorized under section 701(a) and (b) of the act (21 U.S.C. 371(a) and (b)). Section 903 of the act also provides general powers for implementing policies respecting FDA programs and activities.

Thus, the proposed rule implements sections 505(i), 801(e)(1), and 802 of the act. Furthermore, it is also authorized under FDA's rulemaking authorities at sections 505(i) and 701(a) of the act, and FDA's general authority at section 903 of the act.

IV. Environmental Impact

FDA has determined under 21 CFR 25.30(h) and (i), and 25.31(e) 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.

V. Paperwork Reduction Act of 1995

This proposed rule contains information collection provisions requirements that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). A description of these provisions is given 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.

FDA invites comments on: (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 of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Title: Investigational New Drug Applications: Export Requirements for Unapproved New Drug Products.

Description: The proposed rule would provide four different mechanisms for exporting an investigational new drug. First, an investigational new drug could be exported under an IND to any country. Second, an investigational new drug that has received valid marketing authorization from a listed country may be exported for investigational use in any country subject to certain conditions (such as being in substantial conformity with current good manufacturing practice). Third, an investigational new drug could be exported to any listed country without prior FDA authorization for use in a clinical investigation, but would be subject to certain conditions (such as being in substantial conformity with current good manufacturing practices). Fourth, an investigational new drug could be exported provided that the sponsor submits a certification that the drug meets certain export criteria at the time the drug is exported. The proposal would also require persons exporting an investigational new drug under either the second, third, or fourth mechanisms to maintain records documenting their compliance with statutory and regulatory requirements.

Description of Respondents: Businesses.

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN[1]

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
312.110(b)(4)	100	1	100	12	1,200

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN[1]—Continued

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
Total					1,200

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

TABLE 2.—ESTIMATED ANNUAL RECORDKEEPING BURDEN[1]

21 CFR Section	Statute	No. of Recordkeepers	Annual Frequency per Recordkeeping	Total Annual Records	Hours per Recordkeeper	Total Hours
312.100(b)(2) and (b)(3)	Sec. 382	470	1	470	3	1,410
312.110(b)(4)		100	1	100	1	100
Total						1,510

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

The estimates are based on average export submissions in previous years and on information supplied by industry sources. For the recordkeeping requirement in proposed § 312.110(b)(2) and (b)(3), FDA used the average annual number of export requests in previous years before enactment of the FDA Export Reform and Enhancement Act (approximately 570) and subtracted the number of export requests that it currently receives under the 312 program (100) to obtain an estimated 470 recordkeepers. These records, in general, would be subject to § 1.101 (66 FR 65429), and the estimated burden hours for the relevant parts of § 1.101 total 3 hours. Thus, the total record burden hours for § 312.110(b)(2) and (b)(3) would be 1,410 hours (470 records multiplied by 3 hours per record).

For proposed § 312.110(b)(4), industry sources indicated that most firms already maintain records to demonstrate their compliance with export requirements, so the agency assigned a value of 1 hour for each response. The total recordkeeping burden for proposed § 312.110(b)(4), therefore, is 100 hours (100 records multiplied by 1 hour per record).

Thus, the total recordkeeping burden would be 1,510 hours (1,410 + 100 = 1,510). Of this recordkeeping burden, 1,410 hours would be a statutory burden (because section 802(g) of the act requires persons exporting drugs under section 802 of the act to maintain records of all drugs exported and the countries to which they were exported).

For the reporting requirement in proposed § 312.110(b)(4), FDA's experience under the 312 program suggests that extremely few reports would be submitted. Assuming that 100 requests are received (the current number of requests under the 312 program) and that the reporting burden remains constant at approximately 12 hours per response, the total burden under proposed § 312.110(b)(4) would be 1,200 hours. The reporting burden would be a regulatory (rather than statutory) burden.

There are no capital or startup costs or service costs projected for this rule due to the minimal nature of the recordkeeping and reporting requirements. Consultations with industry sources estimate that the average costs of maintaining records would be $100 per record (for a total annual cost of $151,000 (1,510 total records per year x $100 per record)).

The annual reporting cost is estimated to be $36,000. This estimate is based on the estimated total burden hours for the certification (1,200) multiplied by a wage of $30 per hour (1,200 hours x $30 per hour =$36,000).

Thus, the total industry cost would be $187,000 ($151,000 + $36,000 = $187,000).

In compliance with the Paperwork Reduction Act of 1995 (44 U.S.C. 3507(d)), the agency has submitted the information collection provisions of this proposed rule to OMB for review. Interested persons are requested to send comments regarding information collection to the Office of Information and Regulatory Affairs, OMB (address above) by July 19, 2002.

VI. Analysis of Impacts

FDA has examined the impacts of the proposed rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601–612 (as amended by subtitle D of the Small Business Regulatory Fairness Act of 1996 (Public Law 104–121))), 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). Under the Regulatory Flexibility Act, unless an agency certifies that a rule will not have a significant impact on small entities, the agency must analyze regulatory options that would minimize the impact of the rule on small entities.

The Unfunded Mandates Reform Act of 1995 requires that agencies prepare an assessment of anticipated costs and benefits before proposing any rule that may result in an expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100 million or more (adjusted annually for inflation) in any one year.

The agency has reviewed this proposed rule and determined that it is consistent with the regulatory philosophy and the principles identified in the Executive Order 12866 and these two statutes, as it will not result in an expenditure of $100 million or more in any one year. Because the rule raises novel policy issues, OMB has determined that this proposed rule is a significant regulatory action as defined under paragraph 4 of section 3(f) of Executive Order 12866.

The proposed rule would facilitate exports of unapproved new drug products for use in clinical investigations in foreign countries by eliminating the need to submit requests for permission to export the drugs and to receive FDA authorization. This change would reduce the cost to the affected small firms. Thus, the agency certifies that this proposed rule will not have a significant economic impact on

a substantial number of small entities. Therefore, under the Regulatory Flexibility Act, no further analysis is required.

Because the proposed rule does not impose any mandates on State, local, or tribal governments, or the private sector that will result in an expenditure of $100 million or more in any one year, FDA is not required to perform a cost-benefit analysis under the Unfunded Mandates Reform Act of 1995.

Interested persons may submit to the Dockets Management Branch (address above) written or electronic comments regarding this proposal by September 17, 2002. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

List of Subjects in 21 CFR Part 312

Drugs, Exports, Imports, Investigations, Labeling, Medical research, Reporting and recordkeeping requirements, Safety.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR part 312 be amended as follows:

PART 312—INVESTIGATIONAL NEW DRUG APPLICATION

1. The authority citation for 21 CFR part 312 is revised to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 356, 357, 371, 381, 382, 383, 393; 42 U.S.C. 241, 243, 262.

2. Section 312.110 is amended by revising paragraph (b) and by adding paragraphs (c) and (d) to read as follows:

§ 312.110 Import and export requirements.

* * * * *

(b) *Exports.* An investigational new drug may be exported from the United States for use in a clinical investigation under any of the following conditions:

(1) An IND is in effect for the drug under § 312.40, the drug complies with the laws of the country to which it is being exported, and each person who receives the drug is an investigator in a study submitted to and allowed to proceed under the IND; or

(2) The drug has valid marketing authorization in Australia, Canada, Israel, Japan, New Zealand, Switzerland, South Africa, or in any country in the European Union or the European Economic Area, and complies with the laws of the country to which it is being exported, section 802(b)(1)(A), (f), and (g) of the act, and § 1.101 of this chapter; or

(3) The drug is being exported to Australia, Canada, Israel, Japan, New Zealand, Switzerland, South Africa, or to any country in the European Union or the European Economic Area, and complies with the laws of the country to which it is being exported, the applicable provisions of section 802(c), (f), and (g) of the act, and § 1.101 of this chapter. Drugs exported under this paragraph that are not the subject of an IND are exempt from the label requirement in § 312.6(a); or

(4) The person exporting the drug sends a written certification to the Office of International Programs, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, at the time the drug is first exported and maintains records documenting compliance with this paragraph. The certification shall describe the drug that is to be exported (i.e., trade name (if any), generic name, and dosage form), identify the country or countries to which the drug is to be exported, and affirm that:

(i) The drug is intended for export;

(ii) The drug is intended for investigational use in a foreign country;

(iii) The drug meets the foreign purchaser's or consignee's specifications;

(iv) The drug is not in conflict with the importing country's laws;

(v) The outer shipping package is labeled to show that the package is intended for export from the United States;

(vi) The drug is not sold or offered for sale in the United States;

(vii) The clinical investigation will be conducted in accordance with § 312.120;

(viii) The drug is manufactured, processed, packaged, and held in substantial conformity with current good manufacturing practices;

(ix) The drug is not adulterated within the meaning of section 501(a)(1), (a)(2)(A), (a)(3), (c), or (d) of the act;

(x) The drug does not present an imminent hazard to public health, either in the United States, if the drug were to be reimported, or in the foreign country;

(xi) The drug is labeled in accordance with the foreign country's laws; and

(xii) The drug is promoted in accordance with its labeling.

(c) *Limitations.* Exportation under paragraph (b) of this section may not occur if:

(1) For drugs exported under paragraph (b)(1) of this section, the IND pertaining to the clinical investigation is no longer in effect;

(2) For drugs exported under paragraph (b)(2) of this section, the requirements in section 802(b)(1), (f), or (g) of the act are no longer met;

(3) For drugs exported under paragraph (b)(3) of this section, the requirements in section 802(c), (f), or (g) of the act are no longer met; or

(4) For drugs exported under paragraph (b)(4) of this section, the conditions underlying the certification are no longer met.

(5) For any investigational new drugs under this section, the drug no longer complies with the laws of the importing country.

(d) *Insulin and antibiotics.* New insulin and antibiotic drug products may be exported for investigational use in accordance with section 801(e)(1) of the act without complying with this section.

Dated: September 18, 2001.

Margaret M. Dotzel,

Associate Commissioner for Policy.

[FR Doc. 02–15358 Filed 6–18–02; 8:45 am]

BILLING CODE 4160–01–S

DEPARTMENT OF TRANSPORTATION

Federal Highway Administration

23 CFR Part 450

[FHWA Docket No. FHWA–99–5933]

FHWA RIN 2125–AE95; FTA RIN 2132–AA75

Statewide Transportation Planning; Metropolitan Transportation Planning

AGENCY: Federal Highway Administration (FHWA).

ACTION: Supplemental notice of proposed rulemaking (SNPRM); request for comments.

SUMMARY: As a result of recent congressional direction regarding consultation with non-metropolitan local officials in transportation planning, and based on the comments the FHWA and the FTA received to the May 25, 2000, Planning NPRM, and the congressional hearings on the NPRM, we are proposing another option on non-metropolitan local official consultation in addition to that proposed in the May 2000 Planning NPRM. This proposal would revise the current statewide planning regulation at 23 CFR 450. Specifically, this SNPRM proposes to closely follow the Transportation Equity Act for the 21st Century (TEA–21), but allows State flexibility to determine who are non-metropolitan local officials and how to consult with them. Consequently, we are soliciting public comment on an additional proposal to incorporate