Drafting Information

The principal author of this document was Bill Conrad, Regulations Branch, Office of Regulations and Rulings, U.S. Customs Service.

List of Subjects in 19 CFR Part 12

Customs duties and inspections, Imports, Cultural property.

Amendment to the Regulations

Accordingly, Part 12 of the Customs Regulations (19 CFR part 12) is amended as set forth below:

PART 12—[AMENDED]

1. The general authority and specific authority citations for Part 12, in part, continue to read as follows:

Authority: 5 U.S.C. 301, 19 U.S.C. 66, 1202 (General Note 23, Harmonized Tariff Schedule of the United States (HTSUS)), 1624;

* * * * *

Sections 12.104 through 12.104i also issued under 19 U.S.C. 2612;

* * * * *

§ 12.104g [Amended]

2. In § 12.104g(a), the list of agreements imposing import restrictions on described articles of cultural property of State Parties is amended in the entry for Peru by adding ''extended by T.D. 02–30'' immediately after ''T.D. 97–50'' in the column headed ''T.D. No.''.

Approved: June 3, 2002

Robert C. Bonner,

Commissioner of Customs.

Timothy E. Skud,

Deputy Assistant Secretary of the Treasury.

[FR Doc. 02–14219 Filed 6–5–02; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 822

[Docket No. 00N–1367]

Postmarket Surveillance

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is implementing the postmarket surveillance (PS) provisions of the Federal Food, Drug, and Cosmetic Act (the act), as amended by the Food and Drug Administration Modernization Act of 1997 (FDAMA). The purpose of this rule is to provide for the collection of useful data about devices that can reveal unforeseen adverse events or other information necessary to protect the public health.

DATES: This rule is effective July 8, 2002.

FOR FURTHER INFORMATION CONTACT: David L. Daly, Center for Devices and Radiological Health (HFZ–510), Food and Drug Administration, 1350 Piccard Dr., Rockville, MD 20850, 301–594–3060.

SUPPLEMENTARY INFORMATION:

Table of Contents

I. What Is the Background of This Rulemaking?

In the **Federal Register** of August 29, 2000 (65 FR 52376), we (FDA) published a proposed rule implementing the PS provisions in section 522 (21 U.S.C. 360l) of the act, as amended by FDAMA. We provided a period of 90 days for comments from interested parties. We received comments from four entities. We summarize and discuss these comments below, and we have revised the final rule appropriately.

II. What Comments Did FDA Receive on the Proposed Rule? How Did These Comments Affect the Final Rule?

A. Organization and Format

(Comment 1) We received several comments commending the use of plain English, logical formatting, and the question and answer style.

We appreciate the positive comments and will continue to use the plain English concepts.

B. General Comments

(Comment 2) One comment suggested that § 822.1 be revised to include the statutory criteria for imposing PS. This would make the scope of the regulation clearer.

We agree, and have modified § 822.1 accordingly.

(Comment 3) Several comments expressed concern that the proposed rule would impose substantial, unnecessary burdens on device manufacturers, and proposed a number of changes that would reduce the burden. Individual changes are addressed in the appropriate regulation sections. One comment stated that existing systems, such as medical device reports (MDRs), are adequate to provide safety and effectiveness information.

We do not agree. If Congress thought that existing mechanisms were sufficient, it would not have provided for PS. We recognize the potential for PS to be burdensome, but do not agree that any burden imposed by PS would be unnecessary. We intend to impose PS only when necessary to address a postmarket public health question. We also intend to work with the affected manufacturer(s) to identify the least burdensome approach that will adequately address the surveillance question.

(Comment 4) Two comments stated that FDA does not have the authority to require clinical studies, citing the legislative history of FDAMA and the changes in language in the act from ''protocol'' to ''plan'' and ''investigator'' to ''designated person.''

We disagree. As originally enacted in the Safe Medical Devices Act of 1990 (SMDA), PS under section 522 of the act was automatically required for certain devices, and the statutory language allowed little flexibility in designing a PS study. In FDAMA, Congress eliminated this automatic PS, giving FDA discretion to require PS when appropriate, and also gave FDA greater discretion in crafting the form of the surveillance. This broader discretion means that we can accept PS plans that are less rigorous (and less burdensome) than clinical studies, such as literature reviews and analyses of complaint information. The agency expects that it would rarely if ever demand an adequate and well-controlled double-blind clinical trial as the only means of collecting clinical data to satisfy a PS requirement. On the other hand,

collection of clinical data may take many forms, and the agency continues to believe that prospective clinical data will be necessary in about 10 percent of all instances of PS. Congress addressed its concern that FDA not require burdensome longitudinal studies not by prohibiting clinical studies altogether but by limiting the duration of any PS study to 3 years unless manufacturers agree to a longer period. If no agreement can be reached, the dispute resolution process described in section 562 of the act (21 U.S.C. 360 bbb–1) will be used to resolve issues related to duration. This time limit on PS is incorporated into our regulations. Thus while FDAMA gave FDA power to eliminate unnecessary burden from PS, it does not prohibit us from requiring clinical studies where necessary to protect the public health and where conducted within applicable time limits.

(Comment 5) Two comments expressed concern that we intend to increase the amount of data required to support a new indication for use by imposing PS.

We do not intend to impose PS for every new indication for use, nor do we expect imposition of PS to increase the data requirements for a new indication for use. Instead, we expect PS to be used in some instances to shift some data collection from pre- to postmarket, allowing a device to reach the market sooner. For example, this mechanism could be used for a device that is going from clinical use to home use.

C. Notification

(Comment 6) Two comments stated that PS orders should contain the justification for selecting PS over other, less burdensome alternatives.

We agree that PS should not be imposed without considering less burdensome alternatives. Our guidance document entitled ''Criteria and Approaches for Postmarket Surveillance'' (*www.fda.gov/cdrh/modact/critappr.pdf*) discusses our present thinking on this and other criteria that we will use to determine whether to impose PS. We consider this justification part of the ''reason that we are requiring postmarket surveillance'' that will be contained in a PS order, so there is no need to modify § 822.5.

(Comment 7) One comment objected to the application of PS to in vitro diagnostic (IVD) biologics, stating that these devices are already under PS, including lot release, reporting changes, and reporting errors.

We acknowledge that there are other PS requirements for IVD biologics, and it is not intended that PS duplicate or supersede any existing requirements. We would take these existing requirements into consideration when evaluating whether and what form of PS is the appropriate mechanism for addressing the PS question.

(Comment 8) Several comments stated that FDA should be required to meet with manufacturers prior to issuing a PS order, to discuss whether PS is necessary or whether our concerns could be addressed by other, less burdensome mechanisms.

As noted in the preamble to the proposed rule, we anticipate meeting with the affected manufacturer(s) prior to issuing a surveillance order for a particular device for the first time. A requirement that we meet with affected manufacturers prior to issuing subsequent orders for the same device would be burdensome for manufacturers as well as for FDA. We are, therefore, retaining the flexibility to issue PS orders without first meeting with the affected manufacturer(s).

(Comment 9) Several comments urged FDA to modify the rule or issue guidance to advise manufacturers as to what sort of devices may be subject to PS. Knowledge of PS requirements would be an important consideration for a manufacturer contemplating entering a specific market. It was also suggested that we maintain an Internet Web page that lists devices for which PS has been ordered.

We acknowledge that the possibility that PS may be required for a particular device may influence a manufacturer's decision to enter a particular market. There are, currently, few devices subject to PS. We cannot predict which specific devices may be subject to PS in the future. A PS order is issued to address a specific PS question, which may surface at any time in the device's life cycle. The guidance document entitled ''Criteria and Approaches for Postmarket Surveillance'' discusses the criteria we will use to determine whether to impose PS. We will publish a list of devices subject to PS and make it available through the Internet and Facts-on-Demand.

D. Postmarket Surveillance Plan

(Comment 10) We received several comments that questioned whether domestic manufacturers of devices for export only should be subject to PS. These devices cannot be marketed in the United States and it is illogical to impose PS on these products.

We agree. Devices manufactured for export only, in compliance with section 801(e) of the act (21 U.S.C. 381(e)), are subject to the requirements of the importing country and will not be subject to PS under this rule.

(Comment 11) We received two comments that we should modify the rule to utilize a ''two-tier'' system for PS. The first tier would involve the manufacturer collecting information regarding significant complications, using selected centers and clinical report forms. If the first tier resulted in identification of a specific question, i.e., unexpected serious illness, the second tier would involve a more in-depth information collection. If no specific question were identified, PS would be considered complete.

We do not agree that a ''two-tier'' approach is more likely to generate useful information. The ''two-tier'' approach assumes no information is available regarding significant complications. We do not intend to impose PS unless we have identified a need for information or data. This need may be identified during the review of a marketing application or after the device has been marketed. For devices already on the market, PS may be ordered to collect information about an unanticipated adverse event. We believe that the ''two-tiered'' approach suggested by the comments would actually be more burdensome for manufacturers, since it would require data collection in the absence of a clearly defined need. We do agree that the results of a PS plan may, in some cases, raise new questions that may need to be addressed by a second PS plan. The rule, as written, allows for, but does not require, a two-tiered approach.

(Comment 12) We received two comments about the applicability of regulations concerning informed consent (part 50 (21 CFR part 50)) and institutional review boards (IRBs) (part 56 (21 CFR part 56)). They noted that PS is not within the scope of part 50 or part 56, and that only a very limited consent involving confidentiality of patient records is appropriate.

These comments agree with our statements in the preamble to the proposed rule. We agree that informed consent under part 50 and IRB review under part 56 are not applicable to many PS plans. However, there are surveillance plan designs, e.g., a prospective, clinically-based data collection, under which some or all of the provisions of parts 50 and 56 would be appropriate. Other designs, e.g., a registry maintained by a manufacturer, may require modification to the patient consent form to indicate that data may be provided to FDA. We do not require, nor do we generally expect, PS to result in the collection of personal identifiers. In any PS plan, we expect the manufacturer to ensure that the

surveillance approach used incorporates whatever measures are necessary to protect patient privacy. We will ensure that the appropriate patient protection measures are in place through the review and approval of each PS plan.

(Comment 13) One comment requested clarification of our requirement (§ 822.9(a)(8)) that the PS plan include the indications for use and claims for the device. The comment asked if we intended for the manufacturer to submit copies of all labeling and promotional materials for the device.

We do not expect copies of all labeling and promotional material to be included in the submission. This information may be incorporated by reference to another submission, including a marketing application. In general, you may submit a statement of any claims that are relevant to the performance of the device, rather than copies of promotional materials.

(Comment 14) One comment stated that the incorporation of guidance as substance in § 822.12 violated notice and comment requirements.

We do not agree that § 822.12 incorporates guidance as substance. This section of the proposed rule referred the reader to two current guidance documents in response to the question, ''Do you have any information that will help me prepare my submission or design my postmarket surveillance plan?'' Guidance documents represent the agency's current interpretation of, or policy on, a regulatory issue. They do not establish legally enforceable rights or responsibilities and do not legally bind the public or FDA. You may choose to use an approach other than the one set forth in a guidance document, as long as your alternative approach complies with the relevant statutes and regulations.

Nonetheless, to avoid confusion and to ensure that the regulations do not become outdated should the agency revise its guidance documents, we have revised § 822.12 and other references to guidance documents in the regulations to alert the reader to the availability of guidance generally, and have clarified the role of guidance documents in relation to specific regulatory and statutory requirements.

E. FDA Review and Action

(Comment 15) Two comments asked that we identify the criteria we will use for evaluating PS plans and define the term ''scientific soundness.''

The regulation states that, among other things, we will evaluate whether the PS plan is likely to provide useful information that will address the PS question. Specific criteria will depend on the surveillance question and the approach used. We intend to provide the affected manufacturer(s) with as much guidance as possible and we expect the review of a PS plan to be interactive. ''Scientific soundness'' indicates that a plan was developed using scientific principles. We expect a clearly defined hypothesis and a plan that can reasonably be expected to develop data that will address the hypothesis.

(Comment 16) Two comments objected to the requirement that any changes to an approved PS plan be submitted to and approved by us prior to making the change. The comments suggested that we should only require prior submission and approval of ''significant'' changes, i.e., those that would affect the nature of data collected in accordance with the plan.

We agree. We have modified § 822.21 to indicate that only changes that will affect the nature or validity of data collected in accordance with the plan require prior approval. Such changes are those for which a revised surveillance plan will be needed, and we have modified the section to clarify this, as well as to emphasize that in preparing the revised plan, you may reference information submitted in your approved surveillance plan or other submissions, in accordance with § 822.14. Changes that will not affect the nature or validity of data collected in accordance with the plan must be reported in the next interim report required by your approval order. No revised surveillance plan is needed for such changes.

We have altered § 822.21 to clarify the number of copies of a change request that should be submitted, and the address to which they should be sent.

(Comment 17) One comment suggested that the language concerning confidentiality in § 822.23 was not clear and that it should be revised to indicate that we will not disclose the contents of a submission before the plan is approved and that we will not disclose confidential information.

We agree and have revised § 822.23 accordingly.

(Comment 18) Two comments objected to the disclosure of PS plans, amendments, supplements, and reports under the Freedom of Information Act (FOIA) once the PS plan is approved. Both comments stated that the contents of the submissions should be confidential until the manufacturer's final report is submitted. Early disclosure could provide competitors with commercially sensitive information.

Under FOIA, we have no basis for continuing to hold a PS plan confidential in its entirety once it has been approved. As noted in the rule, the submission will remain confidential until the plan is approved, and we will continue to protect the confidentiality of trade secret or confidential commercial information, or information identifying patients.

F. Records and Reports

(Comment 19) Two comments suggested that PS program inspections be subject to FDA's ''Preannounced Inspection Policy.''

Policies and procedures concerning the planning and conduct of inspections are not within the scope of this regulation. We believe that PS program inspections should be conducted in accordance with policies and procedures in place at the time of the inspection.

(Comment 20) One comment stated that the reporting requirements are not authorized by the PS provisions in the act and that they are unduly burdensome, in contravention of section 519(a)(4) of the act (21 U.S.C. 360i(a)(4)).

We do not agree. We have ample authority to establish these requirements. These PS regulations are authorized under section 701(a) of the act (21 U.S.C. 371(a)) because they establish recordkeeping and reporting requirements that are necessary for FDA to verify that devices comply with PS orders issued under section 522 of the act. As explained in the preamble to our proposed regulation, these regulations are also authorized by section 519 of the act, which permits FDA to establish by regulation reporting requirements necessary to assure that a device is not misbranded, because a device that does not comply with a section 522 of the act PS plan is misbranded under section 502(t) of the act (21 U.S.C. 352(t)). In light of the public health benefits achieved by compliance with PS orders, these recordkeeping and reporting requirements are not unduly burdensome. Our analyses under the Paperwork Reduction Act of 1995 (the PRA) and of the economic impact address the annual recordkeeping and reporting burdens imposed by these regulations in detail and demonstrate that they are not unduly burdensome.

G. Economic Impact

(Comment 21) One comment objected to the idea that manufacturers would conduct PS plans involving 30,000 subjects, stating that our concept of PS is unrealistic.

We agree that a PS plan calling for 30,000 observations is unrealistic. It was not our intent to suggest that PS plans of this size would be required; instead the example demonstrates that PS to detect very rare events would be impractical, if not impossible.

(Comment 22) One comment argued that we do not have the authority to require clinical studies.

We do not agree. As discussed under section II.B of this document, ''General Comments,'' we do not believe that the statutory language precludes us from ordering PS that involves clinical data collection. We do not anticipate that clinical studies will be required for a significant number of PS plans. The estimates used in section II.G of this document, ''Economic Impact'' are intended to yield an over-estimate of the cost of PS.

(Comment 23) One comment stated that, while the guidance document entitled ''Criteria and Approaches for Postmarket Surveillance'' provides some examples, more specificity is needed for determining when different types of data collection might be used.

We agree that a clear understanding of the type of data collection appropriate for PS would be useful to a prospective manufacturer of a device. While this information may be available for a device already subject to PS, we cannot predict what surveillance questions may arise in the future and therefore cannot identify what type of data collection would be most appropriate to address the surveillance question. As we gain more experience with PS under section 522 of the act, we may be able to provide additional guidance.

(Comment 24) One comment objected to an estimated cost of $324,000 for a plan requiring primary data collection, believing that the cost would be significantly higher. The comment asks that we clarify how we arrived at the various cost estimates.

We acknowledge that precise costs may vary by specific PS order, but believe the costs are reasonable representations of typical clinical data collection efforts. As detailed for the proposed rule, we have attempted to provide reasonable descriptions of cost elements for a 36-month investigation. We have not received any data that refute the cost estimates.

(Comment 25) One comment questioned the identification of the categories of devices that are likely to be affected by the rule.

The categories[1] used in the Small Business and Regulatory Flexibility analyses are those used by the Census Bureau. While these categories do not coincide with either the class or medical specialty designations that we use to classify devices, they do include the majority of medical device manufacturers. These categories were used to estimate the proportion of medical device manufacturers that would be designated ''small businesses.'' Although the percentages varied slightly, the business size for all of the categories cited was overwhelmingly ''small.'' Therefore, the economic analysis assumed that the majority of manufacturers affected by this regulation would be considered ''small businesses.''

H. Paperwork Reduction Act

(Comment 26) Two comments noted that the collection of information is unnecessary for devices manufactured for export only and for minor changes to an approved PS plan.

We agree, and have modified the regulation accordingly, as noted under ''Postmarket Surveillance Plan'' (devices for export only) and ''FDA Review and Action'' (changes to approved PS plan).

(Comment 27) Two comments contained suggestions to enhance the quality, utility, and clarity of information collected under the PS rule.

The first suggestion, that we be required to meet with the affected manufacturer(s) prior to issuing a PS order, is discussed in section II.C of this document, ''Notification.'' The second suggestion, that we provide more guidance as to what we expect in a PS plan and the criteria that will be used in evaluating the plan, has been addressed in section II.E of this document, ''FDA Review and Action.''

III. What is the Economic Impact of This Regulation?

A. Introduction

We have examined the impact of the regulations under Executive Order 12866, 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 (UMRA) (Public Law 104–4). Executive Order 12866 directs us 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). We believe that this final rule is consistent with the regulatory philosophy and principles identified in the Executive order. This final rule, however, is not a significant regulatory action as defined by the Executive order.

The Regulatory Flexibility Act requires us to analyze regulatory options that would minimize any significant impact of a rule on small entities. This rule is likely to have potential significant impacts on substantial numbers of small entities. We have included a Final Regulatory Flexibility Analysis at the end of this section. Finally, this regulation will not impose costs of $100 million or more in any one year on either the private sector or State, local, and tribal governments in the aggregate, and therefore we are not required to prepare a summary statement of analysis under section 202(a) of UMRA.

B. Objective of the Regulation

The objective of the regulation is to enhance the public health by reducing the incidence of medical device adverse experiences. The primary problem is that we currently lack data that may reveal unforeseen adverse events relevant to the safety and effectiveness of specific devices. The regulation will address this concern by implementing section 522 of the act, as amended by FDAMA to require manufacturers of specific medical devices to conduct PS. We expect PS to identify uncommon, but potentially serious, device-related adverse outcomes that were not noted during premarket development, or were noted as a continuing concern but did not warrant withholding the device from the market.

C. Risk Assessment/Baseline Conditions

In the absence of the regulation, neither FDA nor device manufacturers will have complete confidence that uncommon and unforeseen events have been adequately identified for marketed devices. Currently, hundreds of medical devices are marketed each year that either: (1) Are intended to be implanted in the human body for more than 1 year; (2) are life-sustaining or life-supporting and used outside a device user facility; or (3) for which failure could be reasonably likely to have serious adverse health consequences. Devices with these characteristics range from implantable pacemaker pulse generators and vascular graft prostheses to dental and orthopedic implants.

[1]The categories and percentages have been updated in this final rule to indicate more recent data for the current classification system used by the Census Bureau, the North American Industries Codes (NAIC). The slight changes in the categories and numbers do not affect our conclusion that the majority of device manufacturers likely to be affected by this rule are small entities.

Our decision to approve or clear a particular device for marketing is based on a comparison of the expected health benefits of the device to the expected risk of adverse outcomes due to device failure. Premarket clinical studies, however, are typically designed to detect only relatively frequent adverse events. As a result, we often base premarket approval decisions on risk/benefit relationships that include only relatively frequent risks. Given this lack of complete data, neither FDA nor device manufacturers can be confident about the likelihood of serious, but infrequent, adverse events. Such events can have drastic consequences for dozens, if not hundreds, of patients when a device is marketed to thousands of patients. Postmarket surveillance provides a mechanism for gaining an early awareness and better understanding of such relatively rare events, thus preventing further unnecessary risk to patients. Surveillance may identify actions that minimize risks, such as training, labeling, design modification, or patient selection criteria. In extreme cases, surveillance may show that the subject device should be removed from the market.

D. Costs of Postmarket Surveillance

A critical cost factor is the size of the expected surveillance. Although SMDA granted us the authority to require surveillance, and FDAMA maintained it, there is currently no specific mechanism for conducting this surveillance. We have approved some surveillance protocols under SMDA, but rescinded most of these upon passage of FDAMA. While we cannot be precise, we estimate, based on a review of currently marketed devices, that an average of six generic device types, each with an average of five manufacturers, may be the subject of PS orders each year. This frequency would result in the initiation of 30 PS orders each year. Assuming that the duration of each PS is limited to 3 years, at any given time, 90 PS studies could be ongoing and subject to FDA review. An additional 30 PS would be in preliminary, design stages.

The surveillance becomes larger and more extensive as the acceptable rate of adverse events becomes smaller. Statisticians explain that if one assumes a cumulative Poisson distribution, a 0.95 probability of noting an adverse event with the incidence rate of (p) implies that the product of p and the number of observations (n) must approximately equal 3 (i.e., pn=3). For example, the surveillance must include about 30,000 observations to be 95 percent confident that a PS will detect events that occur at a frequency of 0.0001 (one event in 10,000 patients). The PS designed to detect more frequent events requires fewer observations. The surveillance must include about 1,800 observations to be 95 percent confident that PS will detect events that occur at a frequency of 0.002 (two events in 1,000 patients). We, along with device manufacturers, will need to take these considerations into account when designing PS plans.

The manufacturer would generally complete the required PS within 36 months, with at least semiannual observations. (PS utilizing literature searches may require monthly searches, although less frequent reviews may be appropriate at times.) These observations would be collected by either primary data collection from controlled clinical studies, secondary data collected from other databases or sources (such as Medicare databases, registries or tracking systems, and other types of studies), or published studies in the medical literature as supplemented by our current reporting systems. For purposes of this analysis, we estimate that 10 percent of the PS will require primary data collection, 50 percent may utilize secondary data sources, and 40 percent may collect adequate data from published reports. Manufacturers will incur varying costs for both design and analysis/reporting/recordkeeping phases of each surveillance in addition to the costs of data collection. In addition, we will incur costs to review the data submitted by manufacturers.

1. Design Costs

We would expect the manufacturer of each device that is subject to a PS order to develop an analysis plan for implementing the data collection. We would review and approve this plan prior to initiation. The design of a PS utilizing primary data collection would require more resources than either secondary collection or literature searches. Senior industry regulatory staff would review and approve each type of PS, however, before submission to us. For this estimate, we have assumed that the design of PS utilizing primary data collection would require 3 weeks of industry staff time, PS utilizing secondary data sources would require 2 weeks of time, and PS utilizing published literature would require only 1 staff-week. According to the BLS, in 1997 the median weekly rate of compensation for managerial and professional personnel in this industry group (NAIC339112) was approximately $1,300. We have assumed an additional cost of $700 per week to account for administrative and clerical resources for a total estimate of industry resources at $2,000 per week. Therefore, the design of PS utilizing primary data collection would equal $6,000, PS utilizing secondary data collection would equal $4,000, and PS utilizing only a literature search would equal $2,000. These costs would occur prior to the first year of surveillance for each study.

2. Costs of Data Collection

a. *Costs for primary data collection.* Primary data collection utilizing clinical trials will generally be impractical because of difficulties obtaining patient and clinician participation. In addition, this type of data collection would have significant resource requirements. Primary data could, however, be used to survey smaller populations, or populations that could experience relatively high rates of adverse events. For this analysis, we have assumed that a rigorous PS plan might call for observing 300 subjects semiannually over a 3-year period. This plan would generate 1,800 total observations and might be confidently expected to identify adverse events that occur with a frequency of 0.002, or 2 per 1,000. Moreover, patient dropouts would occur and some observations would not result in usable data, raising the number of required subjects to perhaps 350. Physicians would examine patients and provide the results of these required observations directly to manufacturers.

The costs of this data collection would be significant. While in most cases, we would not require additional procedures or tests for a patient, it is possible that some extra examinations would be required to ensure that the patient's device was still functional. In addition, normal physiologic data would likely be consistently recorded, submitted to the device manufacturers, and archived for further review. Based on the experience of the National Cancer Institute in administering grants for similar research the typical cost per clinical observation to collect patient data is approximately $150. Therefore, the cost of collecting these data would equal $300 per patient per year, or $105,000 per year. The present value of the costs of collecting these primary data over a 3-year period (using a 7 percent discount rate) is $276,000 per PS.

In addition, the patient/subject is likely to incur opportunity costs associated with being part of PS clinical studies. Because the ultimate purpose of the PS is to continue marketing the device, the patient is likely to incur such opportunity costs for procedures and tests that provide him or her no direct benefit. We have estimated that PS clinical studies may require

approximately 1 hour of patient time (including travel). Assuming that the opportunity cost of patients is approximately $26 per hour, the annual cost to patients of lost opportunity for PS utilizing primary data is $18,200 per year. The present value of the costs of 3 years of data collection (at 7 percent discount rate) is $48,000.

We therefore estimate the total present value of the costs for primary data collection to be $324,000 per PS study.

b. *Costs for secondary data collection.* The use of secondary data for PS would not be as costly as the use of primary data. Manufacturers may obtain secondary data sets from both public and private sources, depending on the nature of the surveillance. Based on typical costs we have experienced for acquisition of similar databases, we estimate that these data would cost approximately $50,000 per year to obtain and maintain for each surveillance. These data would include sufficient observations to assure that infrequent events would be identified, but the expected frequency level may vary by device and patient characteristics. The present value of the costs of using secondary data sources for PS (at a 7 percent discount rate for 3 years) is $131,000.

c. *Costs of conducting literature searches.* We believe that PS utilizing reviews of published literature and analyses of our current reporting system may require monthly collections, although less frequent reviews may be acceptable for some surveillances. As a rule, we assume that a professional employee would take approximately 3 days per month to assess published accounts and ensure that any useful data are considered. As stated earlier, the median compensation rate for professional employees in this industry was approximately $1,300 in 1997. This implies that the cost of reviewing published literature would equal $780 per month for professional staff resources. Administrative and clerical support would likely add an additional $420 per month for a total cost of $1,200. Annual costs for conducting this type of PS would equal $14,400, and at a 7 percent discount rate for 3 years, the present value of the costs of this data collection equals $38,000.

3. Costs of Data Analysis, Reporting and Recordkeeping

PS is likely to entail the preparation and submission of four reports during the course of all types of surveillance: An initial report at the outset, two annual interim reports, and a final report including data analysis. In addition, manufacturers will be required to keep data available for 2 years. We assume that this category of costs is likely to be equivalent for each type of PS.

The initial and interim progress reports are expected to be relatively brief. We expect that each report would require only 1 resource-week of supported professional time to be completed for a cost of $2,000 per report. The final data analysis and report would be much more extensive, and could require up to 3 months of resources to complete (statistical, medical research, legal, and senior regulatory affairs staff would likely all have input to final reports). The estimated cost of preparing and submitting a final PS report is $26,000.

We estimate that the total cost of maintaining records for 2 years after completion of the surveillance will equal $500 per year. The present value of these reporting/recordkeeping costs (at a 7 percent discount rate) equals $28,000 per surveillance.

4. Total Private Costs of Postmarket Surveillance

The annual cost for the conduct of PS is the sum of the present value of the costs of the expected studies. Each PS requiring primary data collection has a present value cost of $358,000 ($6,000 for design, $324,000 for data collection (including $48,000 of patient opportunity cost), and $28,000 for reports and recordkeeping). Each PS requiring secondary data collection has a present value cost of $163,000 ($4,000 for design, $131,000 for data collection, and $28,000 for reports and recordkeeping). Each PS requiring literature searches has a present value cost of $68,000 ($2,000 for design, $38,000 for data collection, and $28,000 for reports and recordkeeping).

We expect to issue 30 PS orders each year. We expect that 10 percent (3 PS') of these will require primary data collection. The present value of the costs for these surveillances is $1.1 million. We expect that 50 percent (15 PS') of the 30 PS orders will use secondary data collection. The present value of the costs for these surveillances is $2.4 million. The remaining 40 percent of annual PS orders (12 PS') will use literature searches. The present value of the costs for these surveillances is $0.8 million. Since we expect to issue only 30 surveillance orders each year, the annual cost to industry of this regulation is the sum of the present value costs, or $4.3 million.

5. Costs to FDA for Oversight and Review

We expect that 120 reports will be submitted each year as a result of this regulation (30 initial reports, 60 interim progress reports, and 30 final data analyses). If each report, on average, required 2 weeks of review time, we will need five additional review full-time employee (FTE) resources to oversee the program. In addition, we would require an additional 2.5 FTE's in support and management resources. We have estimated that the loaded cost of each FTE is approximately $117,300. Therefore, the annual cost to FDA of maintaining PS is estimated to equal $0.9 million per year.

6. Total Annual Costs of Postmarket Surveillance

We estimate that the total annual cost for operating and maintaining a PS program is $5.2 million. Most of these costs ($4.3 million) are direct costs to manufacturers while $0.9 million are our costs of operating the program.

E. Benefits of the Regulation

The expected benefit of the regulation is the reduction in avoidable adverse events attributable to the early detection of potential problems. Possible outcomes of PS include withdrawal of the device from the market, changes in labeling, changes in user training, modification of the device design, or (most likely) assurance that the device does not pose an unreasonable risk to the public health. These benefits are not easily quantified because they would vary by device; but the greatest benefit would be realized when other regulatory safeguards, such as early warning through the MDR system or preproduction design controls, fail to detect and resolve serious problems. To illustrate the potential benefits of PS, we reviewed our historical records to identify and quantify the benefits of a major adverse event that could reasonably have been mitigated if this regulation had been in place.

1. Chronology of Historical Event

A particular type of implanted heart valve was approved and quickly accepted for patient use in 1979, because of its ability to reduce the risk of blood clots in patients. The premarket decision to approve the device considered clinical data that included an observation of one failure. The device was marketed for 8 years and implanted a total of 82,000 times. By 1999, there were 462 device failures and 300 resultant fatalities.

During the first marketing year, 5,000 patients received the device and 2 devices failed. During the second year, an additional 11,000 devices were implanted and 3 devices failed. During the third year, 14,000 devices were implanted and 7 devices failed. At this point of marketing, a total of 30,000 devices had been implanted and 12 had

failed. No failures were reported in other similar devices marketed during this period.

We believe that had PS been in effect at that time, we would have likely made this device subject to a PS order because of the noted premarket strut failure. In general, any failure to any heart valve would be deemed serious and potentially catastrophic. We would have been concerned about the occurrence of a strut failure during premarket testing. While this concern would not have delayed marketing approval, subsequent strut failures would have been sufficient to start the PS mechanism, if it had been available. A likely surveillance plan would have required the manufacturer to determine the frequency of strut failures and identify contributing causes. Such a plan would have likely detected problems with the device by the end of the third year; potentially avoiding a total of 52,000 implants (82,000 - 30,000). Given the substantial number of patients implanted and the relatively low failure rate for the number of semi-annual patient observations after three years (12 ÷ 102,000 = .0001), it is unlikely that the required PS would have involved the collection of primary data through prospective trials. Nevertheless, by analyzing their respective failure rates by using patient registries that would include all implanted devices, the manufacturer would have noted all complications and failures. Close attention would have been paid to all adverse events (both expected and unexpected), with special attention being paid to strut fractures, early valve replacement, and deaths. Because all patients and all implants would have been entered into this registry, each occurrence of valve fracture would have been noted, and this information would have been used to determine the best course of action to protect the public health. In this case, it is likely that no valves would have been implanted in patients after the third year of marketing.

2. PS and Risk Reduction

If PS prevented 63 percent of the actual implants (52,000/82,000), then it is likely that about 63 percent of the device failures could also have been avoided. As of 1999, the device has failed 462 times. Consequently, if the device had been removed from the market after its third year, about 293 failures would have been avoided over an 18-year period (1981 to 1999). Moreover, the 65 percent fatality rate for failures implies that the 190 fatalities associated with these 293 failures would have been avoided.

3. Value of Avoided Mortality

There are no precise methodologies for estimating the value of preventing human fatalities. Economists, however, have attempted to place a dollar value on the avoidance of fatal risks based on society's implicit willingness to pay to avoid such risks. Currently, the literature shows that $5 million may represent an approximate value of society's willingness to pay to avoid a statistical fatality. This value is reduced by an appropriate discount factor, however, to the extent that the averted fatalities would occur in future time periods.

4. Frequency of Adverse Events

To develop a possible scenario of future benefits we have assumed that, once within the next 25 years, the rule would prevent an event with characteristics identical to the heart valve incident discussed above. We cannot predict the precise year of the expected future event, but based on the past pattern of device failures, if the regulation identified a device with the described failure characteristics in the first year after completion of the first surveillance group (actually the fourth year of implementation), the current present value dollar benefit (assuming a 7 percent interest rate) of the avoided fatalities would be $405.5 million. If PS identified a potential device failure during the 10^{th} project year, the present value of the dollar benefits for that event would be $270.2 million. If the device failure were not identified until the 25th year, the present value of the monetized benefits would be $97.9 million. Because we assume that, in the absence of this rule, the device failure would occur only once during the next 25 years, the likelihood of an initial failure in any one future year is only .04. Thus, we estimate the overall expected present value of avoiding such a future device failure at $192.0 million.

However, PS is not expected to be infallible. We have estimated that typical PS design will provide a 95 percent confidence that infrequent adverse events will be identified. Therefore, we would expect to identify potential device failures such as described 95 percent of the time. To account for this, the present value of avoiding future device failures attributable to this regulation is expected to equal 95 percent of the total amount, or $182.4 million.

5. Annual Benefits of the Regulation

In the illustrative case described above, we have amortized society's willingness to pay to avoid these fatalities over the evaluation period. This is because the costs of PS are on-going and would be expended each year whether a device failure occurred or not. The current net value of avoiding these fatalities ($182.4 million), when amortized over 25 years, using a 7 percent discount rate, will result in average annualized benefits of $15.7 million.

Of course, we believe the regulations will result in other benefits, such as reductions in psychological stress and worry associated with device failures and the avoidance of morbidities or medical procedures required by non-fatal results of device failure. These benefits may be somewhat offset by the loss of the original therapeutic benefit provided by the device for patients who do not experience an adverse event.

F. Annual Costs and Benefits of the Regulation

We have estimated the annual costs of PS to equal $5.2 million. We estimated benefits based on the avoidance over the next 25 years of just one serious event to equal $15.7 million per year.

G. Small Business Analysis/Regulatory Flexibility Analysis

We believe that it is possible that the regulation will have a significant impact on a substantial number of small entities and have conducted a regulatory flexibility analysis. This analysis is intended to assess the impact of the rule on small entities and to alert any potentially impacted entities of the expected impact. We requested that such entities review the rule and submit comments to us, and we have responded to these comments in section II.G of this document.

1. Description of Impact

The objective of the regulation is to reduce the number of adverse events associated with failure of medical devices by implementing section 522 of the act, as amended by FDAMA, to require PS of specific devices. This surveillance will be designed to identify, as early as possible, potentially dangerous but rare events that could endanger public health. Our statutory authority for the rulemaking is discussed earlier in this preamble.

This regulation affects manufacturers of: (1) Devices for which failure would be reasonably likely to have severe health consequences; (2) devices to be implanted in a human body for more than 1 year; and (3) devices that are life sustaining or supporting and are used outside a device user facility regardless of size, because PS will likely be required for some of their currently marketed and new devices. There are four industries[2] affected by the

[2]The categories that we use in the Small Business and Regulatory Flexibility analyses are those used

regulations: Surgical and Medical Instrument Manufacturing (NAIC 339112), Dental Equipment and Supplies Manufacturing (NAIC 339114), Ophthalmic Goods Manufacturing (NAIC 339115), and Surgical Appliances and Supplies Manufacturing (NAIC 339113). Manufacturers in these industries are highly specialized, with between 93 and 98 percent of establishment sales within the affected industries. In addition, between 93 and 98 percent of medical, dental, and ophthalmic products are supplied by establishments within these industries.

For each of these four industries, the Small Business Administration classifies as small any entity with 500 or fewer employees. Under this definition, 95 percent of the manufacturers within these industry groups are small businesses, and account for approximately 65 percent of the value of the shipments for the affected industries. Over 68 percent of the establishments in these four industries have 20 or fewer employees and the companies have an average of 1.08 establishments per company. The average company in these industries has about $7.5 million in annual revenues and about 60 employees. Consequently, there is a high likelihood that manufacturers of some of the devices that would be subject to this regulation will be small entities.

Based on the cost assumptions described above, any company conducting PS with primary data collection would expend 4.3 percent of annual revenues. Secondary data collection would cost an average company 2.2 percent of annual revenues. (Literature searches are not expected to impose significant costs.) Since 60 percent of the expected PS orders would require significant outlays, we believe that a substantial number of small entities would be significantly affected.

Any PS effort would require professional resources. Primary data collection would require clinical researchers, data analysts, and legal staff. Other PS would require data analysts and support. Manufacturers of devices likely to be subject to PS orders would be familiar with data analysis and the clinical community because of their pre- and postmarket experience. They would therefore have access to the professional skills needed to conduct PS.

2. Analysis of Alternatives

We examined and rejected the following alternatives to the rule: (1) No action; (2) reliance on premarket approval application (PMA) annual reports; (3) increased use of PMA postapproval studies; (4) reliance on MDR reports; (5) increased educational effort to improve all reporting mechanisms; and (6) exempting small manufacturers from PS requirements. We have rejected these alternatives at this time for the following reasons:

Alternative 1

Other sources of postmarket data or information exist, including PMA annual reports and other mechanisms. However, these sources are not always adequate to address specific postmarket issues that arise for specific devices. The regulation is intended to identify sources of information available to the agency and determine their ability to address the postmarket issue prior to issuing a PS order. We would be able to meet with the affected industry sector to determine what information is currently available and whether that information may be modified to answer specific public health questions. Reliance on the current sources of postmarket data would not efficiently meet the objective of reducing avoidable adverse events.

Alternative 2

We considered increasing the requirements for data submission in PMA annual reports. This alternative was rejected because not all devices that meet the PS criteria are subject to PMA annual reports, and annual reports would not be specific enough to address issues for each type of device. In addition, the costs of requiring detailed data submissions for all affected devices would be extremely high. We rejected this alternative.

Alternative 3

If we increased postapproval studies, the expected compliance costs would be much greater, since postapproval studies generally consist of primary data collection. If a postmarket issue is identifiable at the time of approval, postapproval studies could be designed to collect meaningful data. However, if an issue would arise after FDA approval, this mechanism would not be helpful in meeting the objectives of the regulation. In addition, since all class II devices are marketed through premarket notification procedures, postapproval studies are not an option for those devices. We rejected this alternative.

Alternative 4

We rejected the alternative of relying on an enhanced MDR system. While MDRs are extremely important in assessing public health, it is a passive system of data collection in that it relies on reports from concerned professionals who become aware of device problems to manufacturers or their representatives. While manufacturers must report these adverse events, they are not required to actively go out and look for problems with their devices under the MDR provisions. Often MDR reports are not specific enough to address discrete issues. We believe that the public health objectives are clearly met by requiring more active data collection and analysis by the responsible manufacturers of devices.

Alternative 5

FDA did not select the alternative of increased education in lieu of PS because any educational effort would require that FDA have sufficient information. Surveillance would be ordered to collect information that might lead to educational efforts to correct any noted problem. Thus, FDA did not believe that education alone would reduce adverse events.

Alternative 6

We rejected the alternative of exempting small device manufacturers from the requirements. We recognize that an order to conduct surveillance would likely cause a significant impact on a small entity. However, unless and until a PS order affecting a device that it manufactures is issued, this regulation creates no impact on a manufacturer regardless of size. Section 522 of the act, which this regulation implements, is intended to protect the health by authorizing PS orders to be issued for devices meeting statutory criteria when there is a question indicating a potential public health risk, regardless of who manufactures the device. Because devices manufactured by small entities could pose a public health risk meeting the statutory criteria for imposing PS as easily as could devices manufactured by large entities, and because FDA cannot predict who will manufacture devices meriting PS in the future, exempting all small manufacturers from this rule is not consistent with the objectives of the underlying statute. This is particularly clear because, as stated earlier, 95 percent of the manufacturers in the affected industries are considered small business entities, and these small entities account for approximately 65 percent of the aggregate value of shipments in their industries. Consequently, exempting small entities from the rule could reduce the effectiveness of the rule by 65 percent or more.

3. Ensuring Small Entity Participation in Rulemaking

by the Census Bureau. Since the publication of the proposed rule, the Census Bureau has modified their categorization and coding scheme. These changes did not affect the types of manufacturers that we anticipate may be subject to PS, nor did they affect our conclusion that the majority of medical device manufacturers would be considered small entities.

We believe it is possible that this rulemaking could have a significant impact on a substantial number of small entities. The impact would include the costs of conducting PS for specific devices. The proposed regulation was available on our Web site (www.fda.gov), and we announced the availability of the proposed regulation, requesting comments, at several meetings at which members of the affected industries were present. We solicited comments from affected entities to ensure this impact was analyzed. We received one comment questioning the identification of the affected entities impacted by the rule (comment 25 of this document). As noted in response to that comment, these categories were used to estimate the proportion of medical device manufacturers that would be designated ''small businesses.'' Although the percentages varied slightly, the business size for all of the categories cited was overwhelmingly ''small.'' Therefore, the economic analysis assumed that the majority of manufacturers affected by this regulation would be considered ''small businesses.''

H. Conclusions

We have examined the impacts of the regulation implementing PS for specific medical devices. Based on these estimates, the average annual quantified benefits ($15.7) million exceed the average annualized costs of conducting surveillance ($5.2 million). In addition, we expect that between 3 and 4 statistical fatalities will be avoided each year because of this regulation.

We have examined the impacts of the regulation and have concluded that it is likely that a substantial number of small entities will be significantly impacted.

IV. How Does This Regulation Comply With the Paperwork Reduction Act of 1995?

This final rule contains information collection requirements that are subject to review by the Office of Management and Budget (OMB) under the PRA of 1995 (44 U.S.C. chapter 3501–3520). The title, description, and respondent description of the information collection requirements 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: Postmarket Surveillance Recordkeeping and Reporting Requirements for Manufacturers of Class II and Class III Devices[3]

Description: This final rule implements the PS provisions of section 522(a) of the act, as added to the act by SMDA and amended by the FDAMA (Public Law 105–115). The reporting and recordkeeping provisions of the rule implement the collection of useful data or other information necessary to protect the public health and to provide safety and effectiveness information about the device. The final rule applies to manufacturers of class II and class III devices who have received an order to conduct PS of a particular device. These device manufacturers must develop and submit for FDA approval a plan for PS designed to answer the question(s) posed in FDA's order. As they conduct this surveillance, manufacturers must maintain records of the surveillance and submit interim and final reports to FDA.

Description of Respondents: Manufacturers of class II or class III devices that have received an order to conduct PS from FDA.

FDA received several comments on the collection of information described in the proposed rule. Two comments noted that the collection of information is unnecessary for devices manufactured for export only and for minor changes to an approved PS plan. We agree, and have modified the regulation accordingly, as noted under ''Postmarket Surveillance Plan'' (devices for export only) and ''FDA Review and Action'' (changes to approved PS plan).

Two comments contained suggestions to enhance the quality, utility, and clarity of information collected under the PS rule. The first suggestion, that we be required to meet with the affected manufacturer(s) prior to issuing a PS order, is discussed in section II.C of this document, ''Notification.'' The second suggestion, that we provide more guidance as to what we expect in a PS plan and the criteria that will be used in evaluating the plan, has been addressed in section II.E of this document, ''FDA Review and Action.''

The FDA has had limited experience with PS under SMDA, and FDAMA significantly modified the provisions of section 522 of the act. Based on current staffing and resources, we anticipate that we will issue PS orders for six generic devices each year, each manufactured by an average of five manufacturers. Therefore, 3 years after implementation, we would expect that the recordkeeping requirements would apply to a maximum of 90 manufacturers (30 added each year) and 270 investigators (3 per surveillance plan). After 3 years, we would expect these numbers to remain level as the surveillance plans conducted under the earliest orders reach completion and new orders are issued. Each manufacturer will be required to submit a PS plan (§§ 822.9 and 822.10) and interim and final reports on the progress of the surveillance (§ 822.38). We anticipate that a small number of respondents will propose changes to their PS plans (§ 822.21), request a waiver of a specific requirement of this regulation (§ 822.29), or request exemption from the requirement to conduct PS of their device (§ 822.30). Our experience has shown that a few respondents will go out of business (§ 822.27) or cease marketing the device subject to PS (§ 822.28) each year. In addition, manufacturers must certify transfer of records when a sponsor or investigator changes (§ 822.34). We anticipate that this will apply to a small number of respondents. We expect that at least some of the manufacturers will be able to satisfy the PS requirement using information or data they already have. For purposes of calculating burden, however, we have assumed that each PS order can only be satisfied by a 3-year clinically-based surveillance plan, using three investigators. These estimates are based on our knowledge and experience with limited implementation of section 522 under SMDA.

FDA estimates the burden for this collection of information as follows:

[3]FDA has changed the title from the PRA section of the proposed rule to more accurately describe the nature of the information collection provisions of the rule.

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
822.9 and 822.10	30	1	30	120	3,600
822.21	4	1	4	40	160
822.27	1	1	1	8	8
822.28	3	1	3	40	120
822.29	5	1	5	40	200
822.30	1	1	1	120	120
822.34	5	1	5	20	100
822.38	90	2	180	80	14,400
Total					18,708

[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	No. of Recordkeepers	Annual Frequency of Recordkeeping	Total Annual Records	Hours per Record	Total Hours
822.31	90	1	90	20	1,800
822.32	270	1	270	10	2,700
Total					4,500

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

As explained in section II.B, General Comments, under comment 16 of this preamble, the final version of § 822.21 differs from the proposed version of the rule. These changes do not materially alter the average burden of that rule and thus do not substantially modify the collection of information from the proposed version of that section (5 CFR 1320.5(g) and 1320.11(h)(2)). Requirements for manufacturers proposing major changes to approved plans remain substantially unchanged from those posed under the proposed rule, requiring an estimated 40 hours per response, but FDA has revised the burden chart to reflect the prediction that four manufacturers will annually propose such major changes, rather than the seven respondents predicted under the proposed rule. Under the final rule, manufacturers making minor changes must report their changes in the interim report required under § 822.38, and the burden of this requirement is reported and approved under that section.

Section 822.26 does not constitute information collection subject to review under the PRA because ''it entails no burden other than that necessary to identify the respondent, the date, the respondent's address, and the nature of the instrument.'' (21 CFR 1320.3(h)(1).)

Individuals and organizations may submit comments on these burden estimates or on any other aspect of these information collection provisions, including suggestions for reducing the burden, and should direct them to the Office of Surveillance and Biometrics (HFZ–510), Attn: David L. Daly, 1350 Piccard Dr., Rockville, MD 20850.

The information collection requirements in this final rule have been approved under OMB control number 0910–0449. This approval expires November 30, 2003. 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.

List of Subjects in 21 CFR Part 822

Postmarket surveillance, Medical devices, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 822 is added to read as follows:

PART 822—POSTMARKET SURVEILLANCE

Subpart A—General Provisions

Sec.
822.1 What does this part cover?
822.2 What is the purpose of this part?
822.3 How do you define the terms used in this part?
822.4 Does this part apply to me?

Subpart B—Notification

822.5 How will I know if I must conduct postmarket surveillance?
822.6 When will you notify me that I am required to conduct postmarket surveillance?
822.7 What should I do if I do not agree that postmarket surveillance is appropriate?

Subpart C—Postmarket Surveillance Plan

822.8 When, where, and how must I submit my postmarket surveillance plan?
822.9 What must I include in my submission?
822.10 What must I include in my surveillance plan?
822.11 What should I consider when designing my plan to conduct postmarket surveillance?
822.12 Do you have any information that will help me prepare my submission or design my postmarket surveillance plan?
822.13 [Reserved]
822.14 May I reference information previously submitted instead of submitting it again?
822.15 How long must I conduct postmarket surveillance of my device?

Subpart D—FDA Review and Action

822.16 What will you consider in the review of my submission?
822.17 How long will your review of my submission take?
822.18 How will I be notified of your decision?
822.19 What kinds of decisions may you make?
822.20 What are the consequences if I fail to submit a postmarket surveillance plan, my plan is disapproved and I fail to submit a new plan, or I fail to conduct surveillance in accordance with my approved plan?
822.21 What must I do if I want to make changes to my postmarket

Authority: 21 U.S.C. 331, 352, 360i, 360l, 371, 374.

Subpart A—General Provisions

§ 822.1 What does this part cover?

This part implements section 522 of the Federal Food, Drug, and Cosmetic Act (the act) by providing procedures and requirements for postmarket surveillance of class II and class III devices that meet any of the following criteria:

(a) Failure of the device would be reasonably likely to have serious adverse health consequences;

(b) The device is intended to be implanted in the human body for more than 1 year; or

(c) The device is intended to be used outside a user facility to support or sustain life. If you fail to comply with requirements that we order under section 522 of the act and this part, your device is considered misbranded under section 502(t)(3) of the act and you are in violation of section 301(q)(1)(C) of the act.

§ 822.2 What is the purpose of this part?

The purpose of this part is to implement our postmarket surveillance authority to maximize the likelihood that postmarket surveillance plans will result in the collection of useful data. These data can reveal unforeseen adverse events, the actual rate of anticipated adverse events, or other information necessary to protect the public health.

§ 822.3 How do you define the terms used in this part?

Some of the terms we use in this part are specific to postmarket surveillance and reflect the language used in the statute (law). Other terms are more general and reflect our interpretation of the law. This section of the part defines the following terms:

(a) *Act* means the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 301 *et seq.*, as amended.

(b) *Designated person* means the individual who conducts or supervises the conduct of your postmarket surveillance. If your postmarket surveillance plan includes a team of investigators, as defined below, the designated person is the responsible leader of that team.

(c) *Device failure* means a device does not perform or function as intended, and includes any deviation from the device's performance specifications or intended use.

(d) *General plan guidance* means agency guidance that provides information about the requirement to conduct postmarket surveillance, the submission of a plan to us for approval, the content of the submission, and the conduct and reporting requirements of the surveillance.

(e) *Investigator* means an individual who collects data or information in support of a postmarket surveillance plan.

(f) *Life-supporting or life-sustaining device used outside a device user facility* means that a device is essential to, or yields information essential to, the restoration or continuation of a bodily function important to the continuation of human life and is used outside a hospital, nursing home, ambulatory surgical facility, or diagnostic or outpatient treatment facility. A physician's office is not a device user facility.

(g) *Manufacturer* means any person, including any importer, repacker, and/or relabeler, who manufactures, prepares, propagates, compounds, assembles, processes a device, or engages in any of the activities described in § 807.3(d) of this chapter.

(h) *Postmarket surveillance* means the active, systematic, scientifically valid collection, analysis, and interpretation of data or other information about a marketed device.

(i) *Prospective surveillance* means that the subjects are identified at the beginning of the surveillance and data or other information will be collected from that time forward (as opposed to retrospective surveillance).

(j) *Serious adverse health consequences* means any significant adverse experience related to a device, including device-related events that are life-threatening or that involve permanent or long-term injuries or illnesses.

(k) *Specific guidance* means guidance that provides information regarding postmarket surveillance for specific types or categories of devices or specific postmarket surveillance issues. This type of guidance may be used to supplement general guidance and may address such topics as the type of surveillance approach that is appropriate for the device and the postmarket surveillance question, sample size, or specific reporting requirements.

(l) *Surveillance question* means the issue or issues to be addressed by the postmarket surveillance.

(m) *Unforeseen adverse event* means any serious adverse health consequence that either is not addressed in the labeling of the device or occurs at a rate higher than anticipated.

§ 822.4 Does this part apply to me?

If we have ordered you to conduct postmarket surveillance of a medical device under section 522 of the act, this part applies to you. We have the authority to order postmarket surveillance of any class II or class III medical device, including a device reviewed under the licensing provisions of section 351 of the Public Health Service Act, that meets any of the following criteria:

(a) Failure of the device would be reasonably likely to have serious adverse health consequences;

(b) The device is intended to be implanted in the human body for more than 1 year; or

(c) The device is intended to be used to support or sustain life and to be used outside a user facility.

Subpart B—Notification

§ 822.5 How will I know if I must conduct postmarket surveillance?

We will send you a letter (the postmarket surveillance order) notifying you of the requirement to conduct postmarket surveillance. Before we send the order, or as part of the order, we may require that you submit information about your device that will allow us better to define the scope of a surveillance order. We will specify the device(s) subject to the surveillance order and the reason that we are requiring postmarket surveillance of the device under section 522 of the act. We will also provide you with any general or specific guidance that is available to help you develop your plan for conducting postmarket surveillance.

§ 822.6 When will you notify me that I am required to conduct postmarket surveillance?

We will notify you as soon as we have determined that postmarket surveillance of your device is necessary, based on the identification of a surveillance question. This may occur during the review of a marketing application for your device, as your device goes to market, or after your device has been marketed for a period of time.

§ 822.7 What should I do if I do not agree that postmarket surveillance is appropriate?

(a) If you do not agree with our decision to order postmarket surveillance for a particular device, you may request review of our decision by:

(1) Requesting a meeting with the Director, Office of Surveillance and Biometrics, who generally issues the order for postmarket surveillance;

(2) Seeking internal review of the order under § 10.75 of this chapter;

(3) Requesting an informal hearing under part 16 of this chapter; or

(4) Requesting review by the Medical Devices Dispute Resolution Panel of the Medical Devices Advisory Committee.

(b) You may obtain guidance documents that discuss these mechanisms from the Center for Devices and Radiological Health's (CDRH's) Web site (www.fda.gov/cdrh/resolvingdisputes), and from the CDRH Facts-on-Demand system (800–899–0381 or 301–827–0111).

Subpart C—Postmarket Surveillance Plan

§ 822.8 When, where, and how must I submit my postmarket surveillance plan?

You must submit your plan to conduct postmarket surveillance within 30 days of the date you receive the postmarket surveillance order. For devices regulated by the Center for Devices and Radiological Health, you should send three copies of your submission to the Center for Devices and Radiological Health, Postmarket Surveillance Document Center (HFZ–510), 1350 Piccard Dr., Rockville, MD, 20850. For devices regulated by the Center for Biologics Evaluation and Research, send three copies of your submission to the Center for Biologics Evaluation and Research, Document Control Center, 1401 Rockville Pike, suite 200N, Rockville, MD 20852–1448. When we receive your original submission, we will send you an acknowledgment letter identifying the unique document number assigned to your submission. You must use this number in any correspondence related to this submission.

§ 822.9 What must I include in my submission?

Your submission must include the following:

(a) Organizational/administrative information:

(1) Your name and address;

(2) Generic and trade names of your device;

(3) Name and address of the contact person for the submission;

(4) Premarket application/submission numbers for your device;

(5) Table of contents identifying the page numbers for each section of the submission;

(6) Description of the device (this may be incorporated by reference to the appropriate premarket application/submission);

(7) Product codes and a list of all relevant model numbers; and

(8) Indications for use and claims for the device;

(b) Postmarket surveillance plan;

(c) Designated person information;

(1) Name, address, and telephone number; and

(2) Experience and qualifications.

§ 822.10 What must I include in my surveillance plan?

Your surveillance plan must include a discussion of:

(a) The plan objective(s) addressing the surveillance question(s) identified in our order;

(b) The subject of the study, e.g., patients, the device, animals;

(c) The variables and endpoints that will be used to answer the surveillance question, e.g., clinical parameters or outcomes;

(d) The surveillance approach or methodology to be used;

(e) Sample size and units of observation;

(f) The investigator agreement, if applicable;

(g) Sources of data, e.g., hospital records;

(h) The data collection plan and forms;

(i) The consent document, if applicable;

(j) Institutional Review Board information, if applicable;

(k) The patient followup plan, if applicable;

(l) The procedures for monitoring conduct and progress of the surveillance;

(m) An estimate of the duration of surveillance;

(n) All data analyses and statistical tests planned;

(o) The content and timing of reports.

§ 822.11 What should I consider when designing my plan to conduct postmarket surveillance?

You must design your surveillance to address the postmarket surveillance question identified in the order you received. You should consider what, if any, patient protection measures should be incorporated into your plan. You should also consider the function, operating characteristics, and intended use of your device when designing a surveillance approach.

§ 822.12 Do you have any information that will help me prepare my submission or design my postmarket surveillance plan?

Guidance documents that discuss our current thinking on preparing a postmarket surveillance submission and designing a postmarket surveillance plan are available on the Center for Devices and Radiological Health's Web site and from the Center for Devices and Radiological Health, Office of Surveillance and Biometrics (HFZ-510), 1350 Piccard Dr., Rockville, MD 20850. Guidance documents represent our current interpretation of, or policy on, a regulatory issue. They do not establish legally enforceable rights or responsibilities and do not legally bind you or FDA. You may choose to use an approach other than the one set forth in a guidance document, as long as your alternative approach complies with the relevant statutes (laws) and regulations. If you wish, we will meet with you to discuss whether an alternative approach you are considering will satisfy the requirements of the act and regulations.

§ 822.13 [Reserved]

§ 822.14 May I reference information previously submitted instead of submitting it again?

Yes, you may reference information that you have submitted in premarket submissions as well as other postmarket surveillance submissions. You must specify the information to be incorporated and the document number and pages where the information is located.

§ 822.15 How long must I conduct postmarket surveillance of my device?

The length of postmarket surveillance will depend on the postmarket surveillance question identified in our order. We may order prospective surveillance for a period up to 36 months; longer periods require your agreement. If we believe that a prospective period of greater than 36 months is necessary to address the surveillance question, and you do not agree, we will use the Medical Devices Dispute Resolution Panel to resolve the matter. You may obtain guidance regarding dispute resolution procedures from the Center for Devices and Radiological Health's (CDRH) Web site (www.fda.gov/cdrh/resolvingdisputes/ombudsman.html) and from the CDRH Facts-on-Demand system (800–899–0381 or 301–827–0111, document number 1121). The 36-month period refers to the surveillance period, not the length of time from the issuance of the order.

Subpart D—FDA Review and Action

§ 822.16 What will you consider in the review of my submission?

First, we will determine that the submission is administratively complete. Then, in accordance with the law, we must determine whether the designated person has appropriate qualifications and experience to conduct the surveillance and whether the surveillance plan will result in the collection of useful data that will answer the surveillance question.

§ 822.17 How long will your review of my submission take?

We will review your submission within 60 days of receipt.

§ 822.18 How will I be notified of your decision?

We will send you a letter notifying you of our decision and identifying any action you must take.

§ 822.19 What kinds of decisions may you make?

If your plan:	Then we will send you:	And you must:
(a) Should result in the collection of useful data that will address the postmarket surveillance question	An approval order, identifying any specific requirements related to your postmarket surveillance	Conduct postmarket surveillance of your device in accordance with the approved plan
(b) Should result in the collection of useful data that will address the postmarket surveillance question after specific revisions are made or specific information is provided	An approvable letter identifying the specific revisions or information that must be submitted before your plan can be approved	Revise your postmarket surveillance submission to address the concerns in the approvable letter and submit it to us within the specified timeframe. We will determine the timeframe case-by-case, based on the types of revisions or information that you must submit
(c) Does not meet the requirements specified in this part	A letter disapproving your plan and identifying the reasons for disapproval	Revise your postmarket surveillance submission and submit it to us within the specified timeframe. We will determine the timeframe case-by-case, based on the types of revisions or information that you must submit
(d) Is not likely to result in the collection of useful data that will address the postmarket surveillance question	A letter disapproving your plan and identifying the reasons for disapproval	Revise your postmarket surveillance submission and submit it to us within the specified timeframe. We will determine the timeframe case-by-case, based on the types of revisions or information that you must submit

§ 822.20 What are the consequences if I fail to submit a postmarket surveillance plan, my plan is disapproved and I fail to submit a new plan, or I fail to conduct surveillance in accordance with my approved plan?

The failure to have an approved postmarket surveillance plan or failure to conduct postmarket surveillance in accordance with the approved plan constitutes failure to comply with section 522 of the act. Your failure would be a prohibited act under section 301(q)(1)(C) of the act, and your device would be misbranded under section 502(t)(3) of the act. We have the authority to initiate actions against products that are adulterated or misbranded, and against persons who commit prohibited acts. Adulterated or misbranded devices can be seized. Persons who commit prohibited acts can be enjoined from committing such acts, required to pay civil money penalties, or prosecuted.

§ 822.21 What must I do if I want to make changes to my postmarket surveillance plan after you have approved it?

You must receive our approval in writing before making changes in your plan that will affect the nature or validity of the data collected in accordance with the plan. To obtain our approval, you must submit three copies of the request to make the proposed change and revised postmarket surveillance plan to the applicable address listed in § 822.8. You may reference information already submitted in accordance with § 822.14. In your cover letter, you must identify your submission as a supplement and cite the unique document number that we assigned in our acknowledgment letter for your original submission, specifically identify the changes to the plan, and identify the reasons and justification for making the changes. You must report changes in your plan that will not affect the nature or validity of the data collected in accordance with the plan in the next interim report required by your approval order.

§ 822.22 What recourse do I have if I do not agree with your decision?

(a) If you disagree with us about the content of your plan or if we disapprove your plan, or if you believe there is a less burdensome approach that will answer the surveillance question, you may request review of our decision by:

(1) Requesting a meeting with the Director, Office of Surveillance and Biometrics, Center for Devices and Radiological Health (CDRH), who generally issues the order for postmarket surveillance;

(2) Seeking internal review of the order under § 10.75 of this chapter;

(3) Requesting an informal hearing under part 16 of this chapter; or

(4) Requesting review by the Medical Devices Dispute Resolution Panel of the Medical Devices Advisory Committee.

(b) You may obtain guidance documents that discuss these mechanisms from the CDRH Web site and from the CDRH Facts-on-Demand System (800–899–0381 or 301–827–0111).

§ 822.23 Is the information in my submission considered confidential?

We consider the content of your submission confidential until we have approved your postmarket surveillance plan. After we have approved your plan, the contents of the original submission and any amendments, supplements, or reports may be disclosed in accordance with the Freedom of Information Act. We will continue to protect trade secret and confidential commercial information after your plan is approved. We will not disclose information identifying individual patients. You may wish to indicate in your submission which information you consider trade secret or confidential commercial.

Subpart E—Responsibilities of Manufacturers

§ 822.24 What are my responsibilities once I am notified that I am required to conduct postmarket surveillance?

You must submit your plan to conduct postmarket surveillance to us within 30 days from receipt of the order (letter) notifying you that you are required to conduct postmarket surveillance of a device.

§ 822.25 What are my responsibilities after my postmarket surveillance plan has been approved?

After we have approved your plan, you must conduct the postmarket surveillance of your device in accordance with your approved plan. This means that you must ensure that:

(a) Postmarket surveillance is initiated in a timely manner;

(b) The surveillance is conducted with due diligence;

(c) The data identified in the plan is collected;

(d) Any reports required as part of your approved plan are submitted to us in a timely manner; and

(e) Any information that we request prior to your submission of a report or in response to our review of a report is provided in a timely manner.

§ 822.26 If my company changes ownership, what must I do?

You must notify us within 30 days of any change in ownership of your company. Your notification should identify any changes to the name or address of the company, the contact person, or the designated person (as defined in § 822.3(b)). Your obligation to conduct postmarket surveillance will generally transfer to the new owner, unless you and the new owner have both agreed that you will continue to conduct the surveillance. If you will continue to conduct the postmarket surveillance, you still must notify us of the change in ownership.

§ 822.27 If I go out of business, what must I do?

You must notify us within 30 days of the date of your decision to close your business. You should provide the expected date of closure and discuss your plans to complete or terminate postmarket surveillance of your device. You must also identify who will retain the records related to the surveillance (described in subpart G of this part) and where the records will be kept.

§ 822.28 If I stop marketing the device subject to postmarket surveillance, what must I do?

You must continue to conduct postmarket surveillance in accordance with your approved plan even if you no longer market the device. You may request that we allow you to terminate postmarket surveillance or modify your postmarket surveillance because you no longer market the device. We will make these decisions on a case-by-case basis, and you must continue to conduct the postmarket surveillance unless we notify you that you may stop your surveillance study.

Subpart F—Waivers and Exemptions

§ 822.29 May I request a waiver of a specific requirement of this part?

You may request that we waive any specific requirement of this part. You may submit your request, with supporting documentation, separately or as a part of your postmarket surveillance submission to the address in § 822.8.

§ 822.30 May I request exemption from the requirement to conduct postmarket surveillance?

You may request exemption from the requirement to conduct postmarket surveillance for your device or any specific model of that device at any time. You must comply with the requirements of this part unless and until we grant an exemption for your device. Your request for exemption must explain why you believe we should exempt the device or model from postmarket surveillance. You should demonstrate why the surveillance question does not apply to your device or does not need to be answered for the device for which you are requesting exemption. Alternatively, you may provide information that answers the surveillance question for your device, with supporting documentation, to the address in § 822.8.

Subpart G—Records and Reports

§ 822.31 What records am I required to keep?

You must keep copies of:

(a) All correspondence with your investigators or FDA, including required reports;

(b) Signed agreements from each of your investigators, if your surveillance plan uses investigators, stating the commitment to conduct the surveillance in accordance with the approved plan, any applicable FDA regulations, and any conditions of approval for your plan, such as reporting requirements;

(c) Your approved postmarket surveillance plan, with documentation of the date and reason for any deviation from the plan;

(d) All data collected and analyses conducted in support of your postmarket surveillance plan; and

(e) Any other records that we require to be maintained by regulation or by order, such as copies of signed consent documents, evidence of Institutional Review Board review and approval, etc.

§ 822.32 What records are the investigators in my surveillance plan required to keep?

Your investigator must keep copies of:

(a) All correspondence between investigators, FDA, the manufacturer, and the designated person, including required reports.

(b) The approved postmarket surveillance plan, with documentation of the date and reason for any deviation from the plan.

(c) All data collected and analyses conducted at that site for postmarket surveillance.

(d) Any other records that we require to be maintained by regulation or by order.

§ 822.33 How long must we keep the records?

You, the designated person, and your investigators must keep all records for a period of 2 years after we have accepted

your final report, unless we specify otherwise.

§ 822.34 What must I do with the records if the sponsor of the plan or an investigator in the plan changes?

If the sponsor of the plan or an investigator in the plan changes, you must ensure that all records related to the postmarket surveillance have been transferred to the new sponsor or investigator and notify us within 10 working days of the effective date of the change. You must provide the name, address, and telephone number of the new sponsor or investigator, certify that all records have been transferred, and provide the date of transfer.

§ 822.35 Can you inspect my manufacturing site or other sites involved in my postmarket surveillance plan?

We can review your postmarket surveillance programs during regularly scheduled inspections, inspections initiated to investigate recalls or other similar actions, and inspections initiated specifically to review your postmarket surveillance plan. We may also inspect any other person or site involved in your postmarket surveillance, such as investigators or contractors. Any person authorized to grant access to a facility must permit authorized FDA employees to enter and inspect any facility where the device is held or where records regarding postmarket surveillance are held.

§ 822.36 Can you inspect and copy the records related to my postmarket surveillance plan?

We may, at a reasonable time and in a reasonable manner, inspect and copy any records pertaining to the conduct of postmarket surveillance that are required to be kept by this regulation. You must be able to produce records and information required by this regulation that are in the possession of others under contract with you to conduct the postmarket surveillance. Those who have signed agreements or are under contract with you must also produce the records and information upon our request. This information must be produced within 72 hours of the initiation of the inspection. We generally will redact information pertaining to individual subjects prior to copying those records, unless there are extenuating circumstances.

§ 822.37 Under what circumstances would you inspect records identifying subjects?

We can inspect and copy records identifying subjects under the same circumstances that we can inspect any records relating to postmarket surveillance. We are likely to be interested in such records if we have reason to believe that required reports have not been submitted, or are incomplete, inaccurate, false, or misleading.

§ 822.38 What reports must I submit to you?

You must submit interim and final reports as specified in your approved postmarket surveillance plan. In addition, we may ask you to submit additional information when we believe that the information is necessary for the protection of the public health and implementation of the act. We will also state the reason or purpose for the request and how we will use the information.

Dated: December 26, 2001.

Margaret M. Dotzel,

Associate Commissioner for Policy.

[FR Doc. 02–14100 Filed 6–5–02; 8:45 am]

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DEPARTMENT OF STATE

22 CFR Parts 41 and 42

[Public Notice 4028]

Documentation of Immigrants and Nonimmigrants Under the Immigration and Nationality Act, as Amended—Visa Fees: Interim Rule With Request for Comments

AGENCY: Department of State.

ACTION: Interim rule with request for comments.

SUMMARY: This rule reflects and conforms visa regulations to the changes made in a final rule amending the Schedule of Consular Services Fees published on Thursday, May 16, 2002. The latter rule waives all nonimmigrant visa fees for U. S. Government foreign national employees who are travelling to the United States on official business. It also provides for merging the processing and issuance fees associated with immigrant visas. Each of those changes necessitates the revision of related visa regulations. Finally, this rule eliminates a subsection relating to the validity of visas issued to certain residents of Hong Kong, because the law underlying that provision expired on January 1, 2002.

DATES: Written comments may be submitted on or before July 8, 2002.

ADDRESSES: Written comments may be submitted, in duplicate, to the Legislation and Regulations Division, Visa Services, Department of State, Washington, DC 20520–0106 or by e-mail to *visaregs@state.gov.*

FOR FURTHER INFORMATION CONTACT: Elizabeth J. Harper, Legislation and Regulations Division, Visa Services, Department of State, Washington, D.C. 20520–0106, (202) 663–1221, e-mail *harperb@state.gov,* or fax at (202) 663–3898 with respect to the legal sufficiency of this rule or similar matters. For enquiries about the effect of this rule on individual cases, contact the Visa Office by e-mail at *www.usvisa.state.gov.* See reference to Susan Abeyta below, regarding comments on the changes in the Schedule of Fees.

SUPPLEMENTARY INFORMATION: A current regulation, at 22 CFR 41.107(c), lists the two classes of aliens who are exempt from the payment of nonimmigrant visa fees. This rule adds foreign employees of the U.S. Government who will travel to the United States on official business to that list.

With respect to immigrant visas, 22 CFR 42.71(b) currently identifies two levels of activity for which fees are assessed. The first is for the processing of an application for an immigrant visa and the second is for the issuance of such a visa. It also sets forth different time frames for the collection of such individual fees. As the Department is combining these fees into a single fee covering all processing functions, editorial changes to 42.71 have become necessary. The timing of the payment of these fees and the basis for the refund of the single fee have been appropriately modified to accord with having one fee rather than separate fees for separate services.

Why Are These Changes Being Made?

The changes in this interim rule are necessary, as stated above, because the Schedule of Consular Services Fees was recently amended in a final rule published May 16, 2002 (Public Notice 4016; 67 FR 34831).

Why Was the Fee Schedule Changed?

A cost study underlies the changes in the proposed new Schedule of Consular Fees, which includes some modest increases in some visa fees. The considerations taken into account are set forth fully in the rule pertaining to the new Schedule. Any questions regarding the changes in the fee schedule should be directed to Susan Abeyta, Office of the Executive Director, Bureau of Consular Affairs, telefax: (202) 663–2499; e-mail: fees@state.gov as noted in that proposed rule.

Why Is There a Waiver of Fees for Some Nonimmigrants and Not Others?

The Congress in a public law enacted one of the current waivers of fees and