Agency Information Collection Activities; MedWatch: The Food and Drug Administration Medical Products Reporting Program
0910-0291
SUPPORTING STATEMENT

Terms of Clearance: none

A. Justification

1. Circumstances Making the Collection of Information Necessary

Abstract: To ensure the marketing of safe and effective products, postmarketing adverse outcomes and product problems must be reported for all FDA-regulated human healthcare products, including drugs, both prescription and over-the-counter (OTC), biologics, medical devices, dietary supplements and other special nutritional products (e.g. infant formula and medical foods) and cosmetics. In addition, FDA has regulatory responsibility for tobacco products and an interest in receiving reports about adverse outcomes and product problems for these products. To implement these provisions for reporting on human medical products during their post-approval and marketed lifetimes, two forms are available from the Agency. Form FDA 3500 is used for voluntary (i.e., not mandated by law or regulation) reporting by healthcare professionals and the public. Form FDA 3500A is used for mandatory reporting (i.e., required by law or regulation). Respondents to this collection of information are healthcare professionals, medical care organizations and other user-facilities (e.g. extended care facilities, ambulatory surgical centers), consumers, manufacturers of biological, dietary supplement and drug products or medical devices, and importers. Mandatory reporting, since 1993, has been supplemented by voluntary reporting by both healthcare professionals, their patients and consumers via the MedWatch reporting process. To carry out its responsibilities, the agency needs to be informed when an adverse event, product problem, error with use of a human medical product or evidence of therapeutic failure [inequivalence] is suspected or identified in clinical use. When FDA receives this information from either healthcare professionals or patients, the report becomes data that will be used to assess and evaluate the risk associated with the product, and then take whatever action is necessary to reduce, mitigate or eliminate the public's exposure to the risk through regulatory and public health interventions.

Authorizing Statutes: Under sections 505, 507, 512, 513, 515, 519 and 903 of the Federal Food, Drug, and Cosmetic Act (the act); (21 U.S.C. 355, 357, 360b, 360c, 360e, 360i and 393); and section 351 of the Public Health Service Act (42 U.S.C. 262), FDA has the responsibility to ensure the safety and effectiveness of drugs, biologics, and devices. Under section 502(a) of the act (21 U.S.C. 352(f)(2)), a drug or device is misbranded if its labeling is false or misleading. Under section 502(f)(1) of the act it is misbranded if it fails to bear adequate warnings, and under section 502(j), it is misbranded if it is dangerous to health when used as directed in its labeling. Under section 502(t)(2) of the act, devices are considered to be misbranded if there has been a failure or refusal to give required notification or to furnish required material or information required under section 519.

Requirements regarding mandatory reporting of adverse events or product problems have been codified in parts 310, 314, 600, and 803 (21 CFR 310, 314, 600, and 803), specifically §§ 310.305, 314.80, 314.98, 600.80, 803.30, 803.50, 803.53, 803.56. and specified in FDCA §§ 760 and 761. Mandatory reporting of adverse reactions for human cells, tissues, and cellular- and tissue-based products [HCT/Ps] have been codified in 21 CFR 1271.350. FDA regulates the safety (i.e., adulteration) of dietary supplements under section 402 of the act (21 U.S.C. 342). Dietary supplements do not require premarket approval by FDA and the agency bears the burden to gather and review evidence that a dietary supplement may be adulterated under section 402 of the act after that product is marketed. Under section 761(b)(1) of the Act (21 U.S.C 379aa-1(b)(1)) a dietary supplement manufacturer, packer, or distributor whose name appears on the label of a dietary supplement marketed in the United States is required to submit to FDA any serious adverse event report it receives regarding use of the dietary supplement in the United States.

To implement these provisions for reporting on human medical products during their post-approval and marketed lifetimes, two forms are available from the Agency. Form FDA 3500 is used for voluntary (i.e., not mandated by law or regulation) reporting by healthcare professionals and the public. Form FDA 3500A is used for mandatory reporting (i.e., required by law or regulation).

Respondents to this collection of information are healthcare professionals, medical care organizations and other user-facilities (e.g. extended care facilities, ambulatory surgical centers), consumers, manufacturers of biological, dietary supplement and drug products or medical devices, and importers.

USE OF FORM FDA 3500 [VOLUNTARY VERSION]

The voluntary version of the form is used to submit all reports not mandated by federal law or regulation. Individual health professionals are not required by law or regulation to submit reports to the Agency or the manufacturer, with the exception of certain adverse reactions following immunization with vaccines as mandated by the National Childhood Vaccine Injury Act (NCVIA) of 1986. Those mandatory reports are not submitted to FDA on the 3500 or 3500A form, but are submitted to the joint FDA/Centers for Disease Control and Prevention (CDC) Vaccines Adverse Event Reporting System (VAERS) on the VAERS-1 form [see http://www.vaers.org/pdf/vaers_for.pdf]

Hospitals are not required by federal law or regulation to submit reports associated with drug products, biological products or special nutritional products. However, hospitals and other user facilities are required by federal law to report medical device-related deaths and serious injuries.

Under federal law and regulation [section 761(b)(1) of the Act (21 U.S.C 379aa-1(b)(1))], a dietary supplement manufacturer, packer, or distributor whose name appears on the label of a dietary supplement marketed in the United States is required to submit to FDA any serious adverse event report it receives regarding use of the dietary supplement in the United States. However, FDA bears the burden to gather and review evidence that a dietary supplement may be adulterated under section 402 of the act after that product is marketed. Therefore, the Agency depends on the voluntary reporting by health professionals and especially by consumers of

suspected serious adverse events and product quality problems associated with the use of dietary supplements.

USE OF FORM FDA 3500A [MANDATORY VERSION]

A. Drug and biologic products

In sections 505(j) and 704 (21 U.S.C. 374) of the act, Congress has required that important safety information relating to all human prescription drug products be made available to the FDA so that it can take appropriate action to protect the public health when necessary. Section 702 of the act authorizes investigational powers to the FDA for enforcement of the FD&C Act. These statutory requirements regarding mandatory reporting have been codified by FDA under 21 parts 310 and 314 (drugs) and 600 (biologics) of the Code of Federal Regulations. Parts 310, 314, and 600 mandate the use of the FDA Form 3500A form for reporting to FDA on adverse events that occur with drugs and biologics. Mandatory reporting of adverse reactions for HCT/Ps has been codified in 21 CFR 1271.350.

B. Medical device products

Section 519 of the act (21 U.S.C. 360i) requires manufacturers and importers, of devices intended for human use to establish and maintain records, make reports, and provide information as the Secretary of Health and Human Services may by regulation reasonably require to assure that such devices are not adulterated or misbranded and to otherwise assure its safety and effectiveness. The Safe Medical Device Act (SMDA) of 1990, signed into law on November 28, 1990, amends Section 519 of the act. The amendment requires that user facilities such as hospitals, nursing homes, ambulatory surgical facilities and outpatient treatment facilities report deaths related to medical devices to FDA and to the manufacturer, if known. Serious illnesses and injuries are to be reported to the manufacturer or to FDA if the manufacturer is not known. These statutory requirements regarding mandatory reporting have been codified by FDA under 21 CFR part 803 (part 803). Part 803 mandates the use of the FDA Form 3500A for reporting to FDA on medical devices. The Medical Device User Fee and Modernization Act of 2002 (MDUFMA), P.L. 107-250, signed into law October 26, 2002, amended section 519 of the act. The amendment [Section 303] required FDA to revise the MedWatch forms "to facilitate the reporting of information . . . relating to reprocessed single-use devices, including the name of the reprocessor and whether the device has been reused."

C. Non-prescription drug products and Dietary supplements

Section 502(x) in the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 352(x)) implements the requirements of The Dietary Supplement and Nonprescription Drug Consumer Protection Act, which became law (P.L.109- 462) on December 22, 2006. These requirements apply to manufacturers, packers, and distributors of nonprescription (over-the-counter (OTC)) human drug products marketed without an approved application. The law requires reports of serious adverse events to be submitted to the Food and Drug Administration by manufacturers of dietary supplements and nonprescription drugs.

2. Purpose and Use of the Information Collection

To implement these provisions for reporting on human medical products during their post-approval and marketed lifetimes, two forms are available from the Agency. Form FDA 3500 is used for voluntary (i.e., not mandated by law or regulation) reporting by healthcare professionals and the public. Form FDA 3500A is used for mandatory reporting (i.e., required by law or regulation).

Respondents to this collection of information are both individuals and the private sector. Individual (voluntary) respondents include healthcare professionals, medical care organizations and other user-facilities (e.g. extended care facilities, ambulatory surgical centers), and consumers. Private sector respondents include manufacturers of biological, dietary supplement and drug products or medical devices, and importers.

All information received by FDA from either Form FDA 3500 or 3500A is entered into one of several databases for direct review by the postmarket safety surveillance staff within the individual FDA Centers that regulate human medical products [Drugs, Medical Devices, Special Nutritional Products, Biologics and Tobacco]. The information in these reports may be identified as a previously unknown signal, suggesting an adverse outcome, unexpected harm or risk associated with a specific human medical product or class of products.

In most cases, Agency regulatory actions to reduce or eliminate the public's exposure to these medical product risks are not taken on a single case report but are dependent on aggregate analysis of trends in reports to signal potential problems that require further epidemiological investigation. Reports that may at first appear relatively insignificant may be forerunners of the development of more serious conditions (e.g., reports of pancytopenia early in the marketing of a drug may herald later reports of life-threatening aplastic anemia.) Therefore, reports received early in the marketed life of a product may play a role in determining the need for later regulatory action.

After identifying a suspected new risk, the Agency can take the next steps in the Risk Management process including: 1) risk evaluation, using this same information supplemented by additional data sources, 2) when indicated, will develop a risk intervention or mitigation plan to modify and use of the product to reduce the potential for harm , and 3) a risk communication strategy to share the new management steps with both the general public and those healthcare professionals and their organizations who serve the public.

The FDA's MedWatch program issues over 150 safety alerts annually and from 30-60 drug safety labeling changes each month to inform the health care community and the U.S. public of newly discovered safety information for all human medical products. See http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm279222.htm for a recent example of safety-related drug labeling changes. Many of these actions start with an initial report from a health professional or patient, whether directly to FDA or indirectly to the manufacturer and then to FDA. All new safety information is posted on the Internet, as it becomes available (see , for example, http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm251443.htm. Notifications of new postings are also sent out via e-mail notification to over

200,000 individual recipients, by text messaging and RSS feeds to both individual providers and patients and to over 100 MedWatch Partner organizations.

3. Use of Improved Information Technology and Burden Reduction

Burden Reduction: FDA supports and encourages direct reporting to the Agency by consumers [patients and their caregivers] of suspected serious adverse outcomes and other product problems associated with human medical products, [http://www.fda.gov/Safety/ReportaProblem/default.htm]. Since the inception of the MedWatch program, launched in July 1993 by then FDA Commissioner David Kessler [*Introducing MEDWatch: A New Approach to Reporting Medication and Device Adverse Effects and Product Problems*, Kessler DA, JAMA, 269(21), 2 Jun 1993, pp 2765-2768] the program has been promoting and facilitating voluntary reporting by both the general public and healthcare professionals. FDA has further encouraged voluntary reporting by the U.S. public by mandating inclusion of the MedWatch toll-free phone number or the MedWatch Internet address on all outpatient drug prescriptions dispensed, per section 17 of the Best Pharmaceuticals for Children's Act [BPCA; Public Law 107-109] , see: http://frwebgate2.access.gpo.gov/cgi-bin/PDFgate.cgi?WAISdocID=TzPeGU/4/2/0&WAISaction=retrieve.

On March 25, 2008, Section 906 of the FDA Amendments Act [FDAAA], amended Section 502(n) of the Federal Food, Drug, and Cosmetic Act (FDCA), and mandated that published direct- to-consumer (DTC) advertisements for prescription drugs include the following statement printed in conspicuous text (this includes vaccine products):

> "You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088."

Most private vendors of consumer medication information [CMI], the drug product-specific instructions dispensed to consumers at outpatient pharmacies, remind patients to report 'side effects' to FDA and provide contact information to permit reporting via the MedWatch process and Form FDA 3500.

Currently, the non-healthcare professional public may submit voluntary reports using Form FDA 3500, [http://www.fda.gov/Safety/MedWatch/HowToReport/ucm053074.htm]. This reporting form was created twenty years ago, and modeled after an earlier version of the Agency's reporting form for healthcare professionals. Form FDA 3500, is provided in both paper and electronic formats [HTML version at www.fda.gov/medwatch/report.htm and fillable pdf version at http://www.fda.gov/downloads/Safety/MedWatch/HowToReport/DownloadForms/ucm082725.pdf], and is used to report to the Agency about serious adverse events, product problems, product use errors and therapeutic failure [therapeutic inequivalence]. Reporting is supported for all FDA-regulated human medical care products, including drugs, biologicals, medical devices, special nutritional products, dietary supplements, cosmetics and non-prescription (over the counter (OTC)) human drug products marketed without an approved application.

Qualitative assessment by social scientists and comments and feedback from the public has recognized that Form FDA 3500 is written and formatted at a literacy/comprehensibility level that far exceeds the level recommended for the general public by health literacy experts and does not conform to recommendations in the Plain Writing Act of 2010 [http://www.gpo.gov/fdsys/pkg/PLAW-111publ274/pdf/PLAW-111publ274.pdf] .

In order to reduce both the barriers to voluntary reporting by the public and reduce the burden of those consumers who chose to voluntarily report this information to FDA, the Agency has proposed a consumer version of the existing voluntary Form FDA 3500 to serve as a 'consumer-friendly' alternative to the existing form. The proposed consumer version will request no new data from the voluntary reporter not already included in the existing Form FDA 3500 that is currently used for reporting from both healthcare professionals and consumers [patients]. Certain existing fields, not considered essential data for the consumer report but present on the standard [i.e. healthcare professional] version of Form FDA 3500, have been eliminated to facilitate and expedite consumer submissions and reduce reporting burden. The formatting and the plain language used is compatible with the intent of the Plain Writing Act and is expected to provide non-healthcare professionals with a second option to the existing Form FDA 3500 that will reduce the burden of reporting by facilitating their understanding of the requested data and further clarifying the voluntary reporting process.

The Agency recognizes that many consumer reporters have a preference for accessing a copy of the voluntary reporting form on the Internet or submitting to the FDA using an electronic version of the form. The Agency currently supports voluntary reporting with the forms submitted by mail, by fax, by phone via the toll free 800 number and online at www.fda.gov/medwatch/report.htm. It is the Agency's expectation that an approved consumer version of the voluntary form will be provided for consumer use by these same channels.
Use of Improved Information Technology: There are no technical or legal obstacles to the use of improved information technology to reduce the burden of reporting the information.
Reporting by consumers and health professionals directly to the FDA is voluntary. To facilitate such reporting, the Agency has two toll-free numbers available. The number 1-800-FDA-1088 may be used to report by phone, to request forms and information on reporting, or to have a blank form faxed or mailed to the potential reporter. The number 1-800-FDA-0178 is used for faxing completed forms to the Agency.

Since 1997, both consumers and healthcare professionals have been offered an opportunity to use one of several web-based versions of Form FDA 3500 for submission of this adverse event and product quality information. The online HTML version of the form at, http://www.fda.gov/medwatch/report.htm, has been revised and updated in the past three years to clarify the instructions for reporting and to facilitate movement between the reporting screens. These fillable electronic reports are triaged by a Central Triage Unit to the appropriate Center and database for review and evaluation. In addition, FDA has provided fillable versions of both Form FDA 3500 and 3500A, with instruction and help buttons imbedded, in order to facilitate completion of the forms. At present, these fillable pdf versions must be submitted electronically by fax. However, FDA is actively exploring the initiation in 2012 of several pilot projects with medical care organizations and other voluntary reporting sources whereby this type of adverse event reporting information can by transmitted directly through a secure electronic gateway using standardized HL-7 compliant messaging.

In 2010, FDA estimates that between 65 and 70% of voluntary reporters submitted Form FDA 3500 using the electronic, fillable form to file their adverse event reports with FDA. While mandatory reporters from industry and user facilities continue to have the opportunity to use non-electronic means to comply with mandatory requirements, in 2010 over 80% of mandatory reports submitted to the AERS database for drugs and biologicals were submitted via an electronic gateway with standardized medical terminology, standardized data elements and electronic transmission standards as recommended by International Conference on Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use in the M1 (International Medical Terminology), M2 (Electronic Standards for the Transfer of Regulatory Information), and E2B (Data Elements For Transmission of Individual Case Safety Reports) initiatives.

4. Efforts to Identify Duplication and Use of Similar Information

The necessary information on serious, unexpected and unknown adverse events and product quality problems for all regulated medical products that is used on a daily basis by FDA to conduct its postmarket human medical product safety surveillance is not available from any other source.

Use of Form FDA 3500A and Form FDA 3500 as well as the electronic submission of the individual case reports as described above are means by which FDA obtains the information needed to monitor the safety of marketed medications, medical devices and other FDA-related products. The information collected using the MedWatch reporting forms FDA 3500 and 3500 are individual reports of single, unique events experienced by a patient and/or observed by a healthcare professional. These unique events are then submitted either directly to the FDA or indirectly to the manufacturer or other mandatory reporter and then to FDA. There is no duplication of these individual reports and similar information is not collected by other organizations. Adverse events attributed to vaccines that are regulated by FDA are reported through a separate process, the Vaccine Adverse Event Reporting System [VAERS] which is maintained through shared responsibility between FDA and CDC. These vaccine reports are unique and not duplicated elsewhere.

Similar existing formation on suspected adverse events and product quality problems are collected by regulatory agencies of other western nations, and while summary data may be shared or published and while the Agency communicates regularly with these foreign regulatory bodies to discuss safety signals of concern, there is not direct access to these foreign data sources, nor is this foreign data sufficiently ‘similar’ to data on U.S. products to serve as a substitute source.

5. Impact on Small Businesses or Other Small Entities

All mandatory reporting from respondents using the 3500A form is from businesses. In 2010, the percentage of voluntary reporters using the 3500 form who self-reported as doctors or dentists was approximately 15%, or accounting for 6,000 reports.
The information being requested from voluntary reporters on Form FDA 3500 or required of mandatory reporters on Form FDA3500A has been held to the absolute minimum required for the intended use of the data. The data collected in each form is essentially the content requested in 1992 when the two forms were created, modified or supplemented only based on requirements

secondary to new federal law and the final published rules and regulations that were implemented to carry out those mandates.
FDA believes that its duty requires the equal application of the regulations to all enterprises. While FDA does not believe it can apply different standards with respect to statutory requirements, the Agency does provide special help to small businesses. A small business coordinator is available within each FDA Center. This coordinator is available to provide small businesses with help in dealing with FDA regulatory requirements, to ensure that they have an adequate opportunity to express their concerns and to keep FDA management apprised of how regulatory decisions might impact the small business community. The availability of Form FDA 3500A in a fillable pdf format, offered on the MedWatch website at www.fda.gov/medwatch/getforms.htm, facilitates the mandatory reporting efforts to FDA from small businesses.

6. Consequences of Collecting the Information Less Frequently

Voluntary reporting is done by consumers/patients and their healthcare professionals on an ad hoc basis not at any suggested or required frequency. FDA encourages voluntary reporters to identify and report suspected serious adverse events in a timely fashion after experiencing or observing the event. Less frequent data collection would delay identification of products responsible for adverse reactions, including fatalities and permanent injuries. Appropriate FDA action, such as changes in labeling, implementation of a Risk Evaluation and Mitigation Strategy (REMS) or withdrawal from the market, would be delayed by less frequent reporting.

Mandatory reporting by manufacturers has a stratified reporting frequency based on the seriousness and unexpectedness of the event as specified in regulations. Reports of death, serious injury or illness are collected only at the frequency that they occur but must be reported within 15 days. However, in order to reduce reporting burden, other categories of less serious or more well characterized events are reported at either quarterly or annual intervals.

7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

Mandatory reporters using Form FDA 3500A are required by regulation to report certain serious and unexpected adverse events associated with drugs and medical devices on an ad hoc basis and within a specified time interval after the reporting entity learns about the report from either the patient or healthcare professional. Except for that circumstance necessary to avoid delay in FDA's learning of and evaluating the safety of a drug or device and implementing mitigating actions. There are no other special circumstances for this collection of information."

8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

8a. Publication in the FEDERAL REGISTER

In accordance with 5 CFR 1320.8(d), FDA published a 60 day notice for public comment in the FEDERAL REGISTER of 09/09/2011 (76 FR 55919). Seven comments were received.

MedWatch 60-day Federal Register Notice – Response to Comments

1. 3500 form

Comment – One commenter observed that it may be difficult for FDA to identify the pregnancy status of the person experiencing the reported adverse event, and suggested that the Agency add a separate field for documenting pregnancy status.

> FDA response – FDA agrees that documenting pregnancy status is important; however, FDA does not plan to add an additional checkbox for pregnancy to the forms at this time. In 2005, FDA proposed adding checkboxes for both ‘‘Product Used During Pregnancy’’ and ‘‘Product Used During Breast Feeding’’ to section B.5 of both forms. FDA received comments expressing concern that these new data fields introduced divergence from International Council on Harmonisation (ICH) standards and appeared to duplicate information that is usually provided in the narrative section and in coded adverse event terms. The pregnancy status data can also be captured in field B7 as “other relevant history”. FDA agreed with the commenters and did not include these checkboxes with the 2005 revisions; FDA believes these reasons are still valid.

Comment – One commenter encouraged the FDA to use the voluntary consumer version of the form to allow for electronic filing of reports and to continue to promote the reporting process to the public, whether by the traditional paper-based route or electronically.

> FDA response – FDA agrees with the comment and expects to support both the promotion of the use of the new consumer version of the voluntary form and to explore methods of facilitating reporting and reducing reporter burden by using online and other electronic means of report submission.

Comment – One commenter supported the plan to deploy a consumer version of the voluntary form and suggested that its use also be promoted to health care providers for their use. The commenter also encouraged the Agency to expedite a process for converting the paper-based reporting process to allow for electronic submission of voluntary reports using the consumer version of the form.

> FDA response – FDA agrees that support of electronic submissions of voluntary reports should be supported and facilitated. The new form was designed as a consumer-friendly option for use by non-health care professionals. The standard Form FDA 3500 will continue to be the primary form offered to health care professionals. FDA encourages the continued use of Form FDA 3500 by healthcare professionals; however, if a healthcare professional chooses to submit a report using the consumer form, it will be accepted by FDA.

Comment – One commenter stated that implementing a consumer friendly version of Form FDA 3500 would not ‘serve any value’ and suggested that instead a more comprehensible form created that would be used by health care professionals and consumers.

FDA response – The agency disagrees. The current Form FDA 3500 is widely known, well accepted and used by the range of health care professionals. Assessment of, and feedback from, consumers has demonstrated the demand and need for a modified form that would serve those non-health care professional reporters, using both literacy-appropriate language and formatting that will serve consumers but not be optimal for health care professional reporting.

Comment – A commenter suggested that for the proposed change to field E4 from "other" to "unique identifier" that the term used be "UDI#".

FDA response – FDA agrees with this comment.

Comment – One commenter supported the development of a consumer-friendly version of the voluntary form but observed that with the anticipated increase in the number of consumer-initiated reports that the agency consider a process for 'broader sharing with industry sponsors of AE reports made directly to FDA".

FDA response – FDA agrees that adverse event report data should be more readily available to the public (which includes industry). The current mechanisms that FDA has to share reports with industry are the MedWatch to Manufacturer Program, and through requests to Freedom of Information. In addition, as part of Phase II of the FDA Transparency Initiative, FDA is planning to provide the public with online access (in a searchable format) to public information from adverse event reports submitted to FDA.

2. 3500A form

Comment – One commenter asked that no changes be made to the Form FDA 3500A at the present time due to consideration of the costs and expenditure of resources incurred by mandatory reporters who are often using electronic systems to do their required reporting to FDA. In addition, the commenter noted that there are several proposed or not yet finalized rules that might further impact the content of the mandatory Form FDA 3500. A commenter stated that they would ask for a 12 month implementation time to allow for design, testing and validation of any software changes necessary.

FDA response – The Agency has considered the impact of implementing changes to Form FDA 3500A and the need for mandatory reporters to change their electronic systems to comply with the proposed changes. FDA will allow for sufficient time for design, testing, and validation of any software changes as a result of any new data requirements that may follow from new requirements based on final rules and regulations.

Comment - One commenter stated that for mandatory reporters the estimate of burden has been underestimated and fails to take into consideration the effort by firms to collect facts, prepare investigations and evaluate the data.

FDA response – The Agency disagrees that the estimate for the average time to complete a given report is low. This estimate is intended not to represent the totality of the effort for completing the postmarket drug and device safety surveillance process mandated by law, rule and regulation for application holders, but a fair estimate of data collection, organization, entry and submission time for a given 'average' report.

Comment – A commenter suggested that for the proposed change to field D4 from "other" to "unique identifier" that the term used be "UDI#".

FDA response – FDA agrees with this comment. We recommend changing this to UDI#.

Comment – A commenter disagreed with requesting an email address from the reporter in field E1, and a second commenter expressed similar reservations but suggested that, if used, the initial reporter understand that this information is optional.

FDA response – FDA recognizes that an email address is one of several elements in the contact information that may assist FDA and others in effective post-market safety surveillance and follow-up inquiries. The reporter is not compelled to complete the information in this field in order for the report to be considered complete and registered in the appropriate database. A statement that this information is optional will be made clear in the instructions for completing the form.

Comment – A commenter disagreed with the proposed change in the Section H heading from "Device Manufacturers Only" to "Manufacturers Only"
FDA response – This change is necessary since this field is currently required for use by other types of mandatory reporters than only device manufacturers.

FDA response: FDA agrees that this title should not be changed. Section H should be titled "Device Manufacturers Only" as it currently appears.

Comment – Two commenters recommended the addition of a new checkbox field in Section/field H2 names "final report" that would be used to "reflect the best efforts of the manufacturer to retrieve and analyze information pertaining to the reported event".

FDA response- FDA disagrees that "Final report" should be added to Section H2. This information can be added as part of the text narrative in Section H10.

Comment – Two commenters disagreed with the removal of filed H1's "other" checkbox and stated that there are rare examples of events that do not meet the regulatory definition of death, serious injury or malfunction but are considered by the mandatory reporting entity to be necessary and required reports. One commenter suggested that if the

checkbox is removed that specific instruction be provided for handling reports that would have been compatible with an "other" designation.

FDA response – FDA disagrees. FDA recommends removal of the "Other" checkbox. In lieu of the checkbox, FDA proposes that rare events that fit the definition of "other significant adverse device experiences" as specified in FDCA Section 519(a)(3) can be submitted to the FDA using the mailing address identified in 21 CFR Part 803.12(a).

Comment – One commenter suggested changing the title of field B4 from "Date of This Report" to "Date of First Contact with Initial Reporter".

FDA response - FDA disagrees. On August 21, 2009, FDA published a proposed rule (74 FR 42203) to amend part 21 CFR Part 803 to require manufacturers, importers, and user facilities to submit MDRs to the Agency in an electronic format (i.e. the 2009 proposed rule). The Section II(4)(d)(2) specified that in the final rule, FDA specifically proposed to change §§803.32(b)(4), 803.42(b)(4), and 803.52(b)(4) from "date of report by the initial reporter" to "date of this report". Further it states "This change would make part 803 consistent with the way that other FDA Centers interpret FDA Form 3500A, Block B4 and how Block B4 appears on FDA Form 3500A.

8b. Outside Consultation

The proposed consumer version of Form FDA 3500 evolved from several iterations of draft versions, with input from human factors experts, from other regulatory agencies and with extensive input from consumer advocacy groups and the general public. Prior to development of the consumer version two 90 minute sessions were held for face-to-face consultation with both representatives of consumers groups, for example, the National Consumers League, and with public librarians who have direct interactions with the public at the community level. During the process of refining the draft versions of the consumer-friendly form, two more sessions were held with both consumer organization representatives and with unaffiliated consumers to assess both usability and comprehension. In addition, internal consultation within the Agency was obtained from the safety surveillance staff.

9. Explanation of Any Payment or Gift to Respondents

There is no remuneration, payment or gifts to any respondents to the Form FDA 3500 [voluntary] or 3500A [mandatory]. Respondents to Form FDA 3500 receive a follow-up message by either email or standard mail to confirm their submission, acknowledge the processing of their information and thank them for their report.

10. Assurance of Confidentiality Provided to Respondents

The HIPAA Privacy Rule recognizes the legitimate need for public health authorities and others responsible for ensuring public health and safety to have access to protected health information to carry out their public health mission. [DISCLOSURES FOR PUBLIC HEALTH

ACTIVITIES, *45 CFR 164.512(b)*] The Rule also recognizes that public health reports made by covered entities are an important means of identifying threats to the health and safety of the public at large, as well as individuals. Accordingly, the Rule permits covered entities to disclose protected health information without authorization for specified public health purposes. Covered entities may disclose protected health information to a person subject to FDA jurisdiction, for public health purposes related to the quality, safety or effectiveness of an FDA-regulated product or activity for which that person has responsibility. Examples of purposes or activities for which such disclosures may be made include, but are not limited to:

- Collecting or reporting adverse events (including similar reports regarding food and dietary supplements), product defects or problems (including problems regarding use or labeling), or biological product deviations;
- Tracking FDA-regulated products;
- Enabling product recalls, repairs, replacement or look back (which includes locating and notifying individuals who received recalled or withdrawn products or products that are the subject of look back); and
- Conducting post-marketing surveillance.

The "person" subject to the jurisdiction of the FDA does not have to be a specific individual. Rather, it can be an individual or an entity, such as a partnership, corporation, or association.

Release of information submitted to FDA in voluntary adverse experience reports is governed by 21 CFR 20.63(f), which prohibits FDA and a manufacturer in possession of such reports from releasing to the public the names of patients, individual reporters, health care practitioners, hospitals, and any geographic identifiers.

The voluntary version of the form used by health professionals and consumers to report directly to the FDA (Form FDA 3500) informs the reporter that their identity, including self-reporters, will be shared with the manufacturer of the product unless they indicate otherwise by checking box G5 on the form [see attached Form FDA 3500]. This limited disclosure will not trigger release of such information under FOI.

11. Justification for Sensitive Questions

No questions of a private or sensitive nature are asked.

12. Estimates of Annualized Burden Hours and Costs

12 a. Annualized Hour Burden Estimate

The estimated annual reporting burden hours for this information is 860,007 hours.
(Form FDA 3500 = 20,577 hours plus Form FDA 3500A = 839,430 hours)

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

Table 1.--Estimated Annual Reporting Burden

FDA Center	No. of	No. of Responses	Total Annual	Average	Total Hours

21 CFR Section	Respondents	per Respondent	Responses	Burden per Response	
CBER/CDER					
Form 3500	28,952	1	28,952	0.6	17,371
Form 3500A (§§ 310.305, 314.80, 314.98, 600.80)	600	683	*409,608	1.1	450,568
CDRH					
Form 3500	4,585	1	4,585	0.6	2,751
Form 3500A (§803)	2,000	167	334,805	1.1	368,285
CFSAN					
Form 3500	759	1	759	0.6	455
Form 3500A	0	0	0	1.0	0
Total Form 3500					20,577
Total Form 3500A					839,430
Total					860,007

NOTE: CBER, Center for Biologic Evaluation and Research; CDER, Center for Drugs Evaluation and Research; CDRH, Center for Devices and Radiological Health; and CFSAN, Center for Food Safety and Applied Nutrition. FDA Form 3500 is for voluntary reporting; FDA Form 3500A is for mandatory reporting. * The majority of the indirect, mandatory reports were not received by Agency on a paper version of form 3500A [by mail or fax] but via an electronic submission route.

12b. Annualized Cost Burden Estimate

The information collection costs imposed on the user-facilities, and pharmaceutical, biological and device industry are as follows:

Approximately 409,608 reports from pharmaceutical [drugs and biologics] manufacturers, and 334,805 device reports from user-facilities, importers or manufacturers, including follow-up reports, were submitted to FDA in CY2010 using the mandatory Form FDA 3500A. Each report requires 1.1 hour for data entry and review. This includes 36 minutes for a data entry keyer at a pay rate of $15.17 per hour and 30 minutes for a health practitioner at a pay rate of $32.74 per hour for review. [Bureau of Labor Statistics May 2010; Occupational Employment Statistics, National Industry-Specific Occupational Employment and Wage Estimates - NAICS 325400 Pharmaceutical and Medicine Manufacturing]

Cost per response is estimated at 1.1 hours @ 36 minutes ($9.10) and 30 minutes ($16.37) or $25.47 per report submitted]. Based on a total information collection burden of 744,413 responses for mandatory form 3500A, the annual labor cost to user-facilities, and pharmaceutical, biological and device industries would be $18,960,200.00.

13. Estimates of Other Total Annual Costs to Respondents and/or Recordkeepers/Capital Costs

There are no capital, start-up, operating or maintenance costs associated with this information collection. Those industry and other business respondents who are submitting mandatory reports to the Agency using Form FDA 3500A, expend capital for goods and services that support the ongoing internal functions of their business only as part of usual and customary business practices. The supplemental process for handling information transmitted to FDA has costs that are documented in section 12b, but there are no additional costs identified.

14. Annualized Cost to the Federal Government

The estimated cost to the Federal Government for forms FDA 3500 and FDA 3500A is $8,831,000.

CENTER	Number of Reponses	Hours per Response	Total Cost
CBER/CDER	409,608	.6	Total contract reflected below
CDRH	334,805	.6	Total contract reflected below
CFSAN	759	.6	Total contract reflected below
Total	**745,172**		$8,831,000

(NOTE: CBER - Center for Biologic Evaluation and Research; CDER - Center for Drugs Evaluation and Research; CDRH - Center for Devices and Radiological Health; CFSAN – Center for Food Safety and Applied Nutrition)

409,608 pharmaceutical [drug and biologics] reports and 334,805 medical device reports can be expected to be submitted to FDA annually, either directly (voluntary reports) or via the manufacturer (mandatory reports). An additional 759 reports are submitted voluntarily on CFSAN products [special nutritionals and cosmetics].

CDER/CBER Contracts: Adverse event reporting data entry, MedDRA coding, and quality control ($4.111 million/year)
CDRH Contract: processing of medical device reports, including receipt of device reports by phone, coding, and data entry ($3.769 million/year)
CFSAN Contract: data entry and processing + maintenance of IT system ($951.561.00)

Reports processed by FDA staff require about 36 minutes for data entry and review. This includes 18 minutes for a GS-7/step 1 at a pay rate of $20.22 per hour for the data entry and 18 minutes for a GS-13/step 1 at a pay rate of $ 42.66 per hour for review. [From http://www.opm.gov/oca/11tables/pdf/dcb_h.pdf, 2011 Table]

15. Explanation for Program Changes or Adjustments

FDA is requesting a renewal with both a program change and minor adjustments in the existing Forms FDA 3500 and 3500A.

The program change is a result of an Agency intention and goal of improving the number and quality of voluntary reports from consumers of serious adverse events and product quality problems **by introducing a new consumer-friendly version of the existing From FDA 3500**. The Agency estimates that the hour burden with use of a consumer version of the existing voluntary reporting form can be reduced based on informal testing of the final, proposed version of the form, from the current 36 minutes per report to 25 minutes, a reduction of 30%. It is estimated that in CY2011, 35% of the 40,000 direct, voluntary reports submitted using the Form FDA 3500 will be from consumers/patients. The reduction in reporting burden hours for that population of voluntary consumer-reporters would be 14,000 reporters x 0.183 hours, or a total annual burden-hour reduction of 2,562 hours.

The existing Forms FDA 3500 and 3500A have proposed minor changes to each form, with no additional questions added and several questions omitted as redundant information that is able to be addressed in other questions. Several fields have had the label or title modified in response to a change in law, rule or regulation or to clarify the type of information to be entered in a given field. The agency estimates that these changes will have no substantial impact on either reporting burden-hours or costs.

16. Plans for Tabulation and Publication and Project Time Schedule

The Agency has no plans for either tabulation or publication of this information collection.

17. Reason(s) Display of OMB Expiration Date is Inappropriate

The Agency is not seeking approval to not display the expiration date of OMB approval.

18. **Exceptions to Certification for Paperwork Reduction Act Submissions**

There are no exceptions to the certification.