USE OF FORM FDA 3500/3500A FOR REPORTING TO FDA

JUSTIFICATION

Docket No. 2004N-0535

1. Circumstances That Make Information Collection Necessary

Under sections 505, 507, 512, 513, 515, and 903 of the Federal Food, Drug, and Cosmetic Act (the act); (21 U.S.C. 355, 357, 360b, 360c, 360e, and 393); and sections 351 and 361[Biologics] of the Public Health Service Act (42 U.S.C. 262), the U.S Food and Drug Administration (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. Therefore, manufacturers are required to allow FDA to review the safety and efficacy of these products both prior to marketing and once the product is marketed and used in clinical care.

The Dietary Supplement Health and Education Act of 1994 (21 U.S.C. 301), while allowing manufacturers to market dietary supplements without FDA prior approval, puts the burden of proving that a particular supplement is unsafe on the Federal government. On December 22, 2006, the President signed into law the Dietary Supplement and Nonprescription Drug Consumer Protection Act. (Pub. L. 109-462, 120 Stat. 3469). This law amends the Federal Food, Drug, and Cosmetic Act (FD&C Act) with respect to adverse event reporting and recordkeeping for dietary supplements and non-prescription drugs marketed without an approved application. The law provides for the mandatory reporting to the Food and Drug Administration (FDA) of serious adverse events for dietary supplements and for nonprescription drugs marketed without an approved application (also know as over-the-counter, or OTC, drug products). The authority is 21 U.S.C. 379aa-1(a) (3), (b) (1) and/or section 761(a) (3) and (b) (1) of the FD&C Act. This law was self-implementing, so there are no new regulations to cite below.

For cosmetics, the FD&C Act does not give FDA the authority to require manufacturers to register their cosmetic establishments, file data on ingredients, conduct safety testing, or report cosmetic-related injuries. Only post-market surveillance allows FDA to assess cosmetic problems in the marketplace. If a problem is detected, it is up to the Agency to demonstrate that the product is harmful when used according to label directions or under customary conditions of use.

To ensure the safety, and identify any risks, harms, or other dangers to health, for all FDA-regulated human healthcare products, the Agency needs to be informed whenever an adverse event, product quality problem or product use error occurs. This risk identification process is the first necessary step that allows the agency to gather the information necessary to be able to evaluate the risk associated with the product, and take whatever action is necessary to mitigate or eliminate the public's exposure to the risk. , Certain adverse events must be reported to FDA as mandated in law and regulation. Requirements regarding mandatory reporting of adverse events or product problems have been codified in 21 CFR parts 310, 314, 600, 803 and 1271, specifically §§ 310.305, 314.80, 314.98, 314.540, 600.80, 803.30, 803.40,803.50, 803.53, 803.56 and 1271.350(a).

To facilitate the reporting of adverse events, product problems and medication/device use errors for FDA regulated products such as medications, devices, biologics, special nutritional products and cosmetics, as well as any other products that are regulated by FDA, two forms are available from the Agency. Form FDA 3500, is used for voluntary reporting (i.e., that not mandated by law or regulation) of adverse events, product problems and product use errors by health professionals and consumers. Form FDA 3500A is used for mandatory reporting required of manufacturers, packers and distributors of medications and biologics; and of all manufacturers, importers and user-facilities for medical devices. Reporting regulations for human cellular tissues and recent regulations for dietary supplements mandate the use of the FDA 3500A form for reporting by manufacturers. For nonprescription drugs, FDA (see the draft guidance at http://www.fda.gov/cder/guidance/7950dft.pdf) allows e- reporting in addition to the use of Form FDA 3500A.

Respondents to this collection of information are healthcare professionals, hospitals and other user-facilities (e.g., nursing homes, etc.), consumers, manufacturers of biological and drug products or medical devices, and importers.

Reporting by health professionals and consumers of adverse events, product problems and product use errors, either directly to FDA or indirectly to FDA by the manufacturer from these same initial reporting categories, is an essential element in an effective national postmarketing surveillance system. The MedWatch Program is the FDA's national outreach initiative to educate health professionals and consumers about the importance of the voluntary reporting of serious adverse events, product quality problems and product use errors, to facilitate reporting to the Agency if they choose to do so, and to provide alerts to the health professional community and their patients as new safety information becomes available, often as the result of information generated from these reports.

In 1993, a single form replaced all forms previously used by the Agency for reporting on medications and devices. The use of a single form ensures the collection of a standard set of data elements from reporters regardless of product type. The two versions of the reporting form, Form FDA 3500 and 3500A are often referred to, by both voluntary and mandatory users, as the 'MedWatch' form. The first page of both versions has similar, but not identical, data fields and the formatting is different. The second page of the voluntary reporting version (Form FDA 3500) contains advice for reporting, a description of the public reporting burden information, and a self-mailer so that the form can be submitted to FDA at no expense to the reporter. The second page of the mandatory reporting version (Form FDA 3500A) contains additional required data elements and the manufacturer/user-facility/importer public reporting burden information. The 3500A also has a space for the report number.

The FDA is requesting OMB approval for continued use of Form FDA 3500 and Form FDA 3500A, without revision or modification, for the reporting of adverse events, product quality problems and product use errors with human medications, medical devices, and other products (such as human cell, tissue and cellular and tissue-based products, special nutritional products and cosmetics) that are regulated by the Agency.

USE OF THE VOLUNTARY VERSION (Form FDA 3500)

Individual health professionals are not required by law or regulation to submit adverse event, product problem or product use reports to the Agency or to the manufacturer. There is one exception. The National Childhood Injury Act of 1986 mandates that certain adverse events following immunization be reported by health care providers to the joint FDA/Centers for Disease Control and Prevention (CDC) Vaccine Adverse Event Reporting System (VAERS). The vaccine adverse event reporting process uses Form VAERS-1 (http://www.vaers.org/pdf/vaers_for.pdf), not Form FDA 3500.

Hospitals are not required by law or regulation to submit adverse event reports on drug or biological products. Hospitals and other medical facilities are required by federal law to report medical device related deaths and serious injuries, biological product deviation reports and fatality reports as a complication of blood collection or transfusion.

There are no mandatory requirements for individual healthcare professionals to report adverse events or product problems with other products such as dietary supplements and cosmetics. Therefore, voluntary reporting directly to FDA by health professionals and consumers on Form FDA 3500 is critical in detecting potential problems with these products.

USE OF THE MANDATORY VERSION (Form FDA 3500A)

Drug and biologic products

In sections 505(k) and 704 (21 U.S.C. 374) of the FD&C 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 Federal Food, Drug, and Cosmetic 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 sections 310 & 314 (drugs) and 600 (biologics) of the Code of Federal Regulations. Agency draft guidance also

permits drug manufacturers to submit mandatory reports using electronic methods as an alternative to the Form FDA 3500A. (http://www.fda.gov/cder/guidance/5161dft.pdf)

Biologic regulations 21 CFR 600.14 and 606.171 require that biologic product deviation reports, which are similar to drug product problem reports, be submitted to FDA on a form other than the 3500A. The FDA proposed rule on Safety Reporting Requirements for Human Drug and Biological Products [Federal Register: March 14, 2003 (Volume 68, Number 50), Page 12405-12497] has recommended amending 21 CFR 606.170 to require suspected adverse reactions and fatalities related to the collection or transfusion of blood and blood components be reported to the Agency using form 3500A.

Public Law 109-462 amends the Federal Food, Drug, and Cosmetic Act (the Act) to add safety reporting requirements for OTC drug products that are marketed without an approved application under section 505 of the Act (21 U.S.C. 355). A Manufacturer, packer, or distributor whose name (under section 502(b)(1) of the Act (21 U.S.C. 352(b)(1))) appears on the label of an OTC drug marketed in the United States without an approved application (referred to as the *responsible person*) must submit to FDA any report received of a serious adverse event associated with such drug when used in the United States, accompanied by a copy of the label on or within the retail package of such drug (section 760(b)(1) of the Act). In addition, the responsible person must submit follow-up reports of new medical information related to a submitted serious adverse event report that is received within 1 year of the initial report (section 760(c)(2) of the Act). Serious adverse event reports received through the address or telephone number described on the product label, as well as all follow-up reports of new medical information, must be submitted to FDA no later than 15 business days after a report of a serious adverse event or the new medical information is received by the responsible person (section 760(c)(1) and 760(c)(2) of the Act). Agency guidance specifies the submission of these serious adverse event reports using FDA Form 3500A or via electronic submission.

Medical device products

Section 519 of the FD&C Act requires manufacturers and importers of devices intended for human use to establish and maintain records, make reports, and provide information as the Secretary may by regulation reasonably require to assure that such devices are not adulterated or misbranded and to otherwise assure its safety and effectiveness. Furthermore, the Safe Medical Device Act (SMDA) of 1990, signed into law on November 28, 1990, amends Section 519 of the FD&C 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 section 803 of the Code of Federal Regulations. These regulations require the use of Form FDA 3500A.

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."

Dietary Supplements

On December 22, 2006 the Dietary Supplement and Nonprescription Drug Consumer Protection Act was published. (Pub. L. 109-462, 120 Stat. 3469). This law amends the Federal Food, Drug, and Cosmetic Act (FD&C Act) with respect to adverse event reporting and recordkeeping for dietary supplements and non-prescription drugs marketed without an approved application. The law requires mandatory reporting to the Food and Drug Administration (FDA) of serious adverse events for dietary supplements using FDA Form 3500A. The authority is 21 U.S.C. 379aa-1(a) (3), (b) (1) and/or section 761(a) (3) and (b) (1) of the FD&C Act. Draft guidance on how to fill out a dietary supplement 3500A form has been published. This law was self-implementing, so there were no new regulations required.

2. Purpose of Information Collection

FDA is the federal agency charged with the responsibility for ensuring that marketed products used in medical therapy are safe and effective. To carry out its responsibilities, the Agency needs to be informed whenever an adverse event, product problem or product use error occurs. Only if FDA is provided with

such information in a timely fashion will it be able to evaluate the risk, if any, associated with the product and take whatever action is necessary to reduce or eliminate the public's exposure to this risk.

A strong post-marketing surveillance program is vital to ensure the safety of products approved by FDA. Through the identification of potential problems the Agency is able to take appropriate regulatory action ranging from labeling changes to the rare product withdrawal from the market. This system depends in large measure on timely reporting by health professionals and consumers of adverse events and other problems to the Agency either directly or via the manufacturer. Therefore, it is critical that the Agency provide health professionals with the knowledge, means, and motivation to report.

FDA received over 628,000 reports of adverse events, product quality problems and product use errors for CY2007. Through the MedWatch Safety Information and Adverse Event Reporting Program, the Agency encourages health professionals and consumers to report serious adverse events, actual or potential medication or device use errors and product quality problems in order to allow Agency safety evaluators to focus on those events with the greatest public health impact.

In most cases, Agency regulatory actions to reduce or eliminate the public's exposure to medical product risk 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.

The Agency issues or approves numerous safety alerts, public health advisories, “Dear Healthcare Professional” letters and countless safety labeling changes each year to inform the health care community of newly discovered safety information. See http://www.fda.gov/medwatch/SAFETY/2008/jul08_quickview.htm for a recent example of safety-related 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 http://www.fda.gov/medwatch/SAFETY/2008/safety08.htm). Notifications of new postings are also sent out via e-mail and RSS feeds to both individual providers and patients and to over 130 MedWatch Partner organizations.

3. 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 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.

Both versions of the forms and instructions are available on the FDA’s MedWatch website, as is a fillable pdf file (see http://www.fda.gov/medwatch/safety/FDA-3500_fillable.pdf) that can be downloaded and installed locally so that computers can be used on-site to fill out and print the report, which then can be mailed or faxed to the Agency.

An online version of Form FDA 3500 [voluntary version] is available at www.fda.gov/medwatch/report.htm to allow health professionals and consumers to complete the form and transmit it electronically to the agency.

FDA does have a goal of switching the submission of mandatory reports to electronic format. The Centers with mandatory reporting requirements are at varying stages toward achieving that goal. In the *Federal Register* of November 5, 1998 (63 FR 59746), the Agency published an advanced notice of proposed rulemaking to notify drug and biologic manufacturers that it is considering preparing a proposed rule that would require them to submit individual case reports electronically. The electronic submissions would use 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. Many pharmaceutical companies are currently participating in an Adverse Event Reporting System (AERS) electronic submission program on a voluntary basis using a draft guidance- (http://www.fda.gov/cder/guidance/5161dft.pdf).

The Center for Biologics Evaluation and Research (CBER) recently revised biological product deviation report regulation to provide the option for submission of reports in an electronic format to save time and resources for both the reporting firms and FDA.

The Center for Devices and Radiological Health (CDRH) is currently receiving voluntary electronic submissions of MDR events under its eMDR program. CDRH worked with the Health Level 7 (HL7) standards organization to establish a standardized message format for the FDA 3500A MedWatch Form approved by OMB in October, 2003. CDRH developed two electronic reporting options; one for low volume reporters (CeSub)and the other for high volume reporters (HL7ICSR). The CeSub option is available as a free download from CDRH. However, both options require the purchase and use of a digital certificate to submit the reports via FDA's electronic submission gateway (ESG). Using one of these two options, electronic reporting of MDR events is currently available to all manufacturers, user facilities and importers. At present, approximately a dozen firms are using one method or the other to regularly submit their MDR events; other firms are in various stages of testing and expect to move to full production in the near future. Electronic submissions will save time, resources and expense for both the firms and FDA. A proposed regulation to mandate the electronic submission of MDRs required by 21CFR803 is currently under review.

4. Efforts to Identify Duplication and Availability of Similar Information

Reporting on adverse events with vaccines is covered by separate regulations that require the use of a form different than the MedWatch form. The National Childhood Vaccine Injury Act of 1986, at Section 2125 of the Public Health Service Act as codified at 42 U.S.C. 300aa-25 (Suppl 1987), requires health professionals and vaccine manufacturers to report to the Department of Health and Human Services (DHHS) specified adverse events following the administration of specific vaccines. In 1990, DHHS established the Vaccine Event Reporting System (VAERS) co-administered by FDA and the CDC to accept all reports of suspected adverse events after administration of a vaccine (21 CFR 600.80).

Biologic regulations CFR 600.14 and 606.170 require that biologic product deviation reports, which are similar to drug product problem reports, be submitted to FDA in another format. Fatalities as a complication of blood collection or transfusion are reported as per 606.170.

The required information on all other medical products 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 under section 3 above are means by which FDA obtains the information needed to monitor the safety of marketed medications, medical devices and other FDA-related products.

5. Small Business Considerations

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 Less Frequent Information Collection

Reports of death, serious injury or illness are collected only at the frequency that they occur. 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.

CDRH established a program that permits firms to report limited information on certain well known, well documented events less frequently. Manufacturers must submit a written request to join the program and may not use the program without CDRH approval.

7. Special Circumstances That Require Departures from 5 CFR 1320.5

The specific reporting and recordkeeping timeframes are justified in the respective regulatory approvals.

8. Efforts to Consult with Non-Agency Personnel

In the FEDERAL REGISTER of February 15, 2008, (73 FR 8879), FDA published a 60-day notice requesting public comment on the information collection provisions. FDA received three comments. There were no comments submitted concerning the Form FDA 3500, voluntary reporting form. All comments addressed Form FDA 3500A, the mandatory reporting form. There were no comments submitted concerning the mandatory 3500A form that addressed questions of whether the information obtained is necessary for the proper performance of FDA's functions or comments about the practical utility of this information. There was one comment about the accuracy of the burden estimate for a subset of reports (dietary supplements). The remainder of the comments were specific suggestions for modifications of either the content or format of various fields to enhance clarity of information. There was also one comment about the use of information technology to support collection.

One comment noted that there was no burden estimate offered for the mandatory reports that would be expected for serious adverse events associated with dietary supplement products. In addition, the commenter offered an estimate of 30 minutes to one hour for the time to complete, route for approval and submit a mandatory report for a dietary supplement product. FDA agrees with this estimate and, for mandatory reports, has used a 1.1 hour estimate for time to complete a report. FDA has chosen to not attempt to estimate a reporting burden for mandatory dietary supplement report volume, since the burden estimate used in this request for extension of both reporting forms is based on actual reports for the calendar year 2007 and there was no requirement for submission of mandatory dietary supplement reports until December 22, 2007. To address PRA burden estimates for mandatory reporting required for both dietary supplements and over-the-counter products under the Dietary Supplement and Nonprescription Drug Consumer Protection Act. (Pub. L. 109-462, 120 Stat. 3469) of 2006, FDA will submit this burden estimate information under a separate federal register notice process.

There were several comments suggesting a variety of changes in both the formatting of certain fields in the mandatory form, changes to existing text or addition of extra text. These changes were suggested to ‘reduce confusion and capture additional clarifying information’. For example, it was suggested that more space be allotted to certain fields to accept more text or that certain text fields be modified to ask supplemental questions of the reporter.

FDA has carefully considered each of these changes but does not concur with making these elective changes, which are not based on any changes in law, rule, or regulation. Since FDA encourages electronic submission of post-marketing adverse event reports by mandatory reporters, and the majority of mandatory reporters use the paper-based Form FDA 3500A only for backup purposes, FDA believes that it would be an unfair burden to manufacturers who submit electronically to expend resources to change their electronic versions of the paper document which would be used only in times of rare network or server outages. FDA believes that each of these suggested elective text changes and additions can be addressed satisfactorily with specific clarifying information provided in the instructions section that supplements Form FDA 3500A.

One comment suggests that FDA modify the forms to include wording as a ‘disclaimer by consumer authorizing the treating physician to speak with a manufacturer’s representative’. FDA disagrees with the inclusion of this type of information within the standard reporting form and believes that this type of information is best treated as part of other documentation maintained by the mandatory reporter.

One comment suggests that provisions be made to allow for the inclusion of attachments with the serious adverse event report. FDA agrees and attachments are currently permitted both as supplements to mailed and faxed submissions.

One comment acknowledged and supported the recently announced development of a unified federal approach to adverse event reporting, and suggested that this approach will ease the reporting burden for both industry and FDA and indirectly benefit consumers.

The newly revised Forms 3500 and 3500A with updated instructions, which will address several commenter's concerns about clarity, will be made available, upon OMB approval, on the FDA's MedWatch website at http://www.fda.gov/medwatch/getforms.htm.

9. Payment or Gifts

FDA did not provide any payment or gift to respondents.

10. Assurances of Confidentiality

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. Additional Assurances of Privacy

No questions of a private or sensitive nature are asked.

12. Estimates of the Burden Collection

The estimated annual reporting burden for this information is 682,482 hours.
(Form FDA 3500 = 16,732 hours plus Form FDA 3500A = 665,751 hours)

Table 1 - ESTIMATED ANNUAL REPORTING BURDEN

FDA Center(s) (21 CFR Section)	No. of Respondents	Annual Frequency Per Response	Total Annual Responses	Hours per Response	Total Hours
CBER/CDER					
Form 3500	23,033	1	23,033	0.6	13,820
Form 3500A (310.305,314.80, 314.98, and 600.80) See note below	600	765	459,102	1.1	505,012
CDRH					
Form 3500	4,375	1	4,375	0.6	2,625
Form 3500A (part 803)					
User Facilities	1,084	3	3,252	1.1	3,577
Importers	80	18	1,470	1.1	1,617
Manufacturers	2,946	48	141,405	1.1	155,545
Total 3500A					160,739
Total CDRH					**163,364**
CFSAN					
Form 3500	479	1	479	0.6	287
Form 3500A (No mandatory requirements – see note below)	0	0	0	1.1	0
Total Hours					**682,483**
Form 3500					16,732
Form 3500A					665,751

(NOTE. – The figures shown in the above table are based on actual calendar year 2007 reports and respondents. There is no burden calculation for the mandatory reporting requirements which went into effect on December 22, 2007 for dietary supplements [CFSAN] or over-the-counter drugs [CDER]. These estimates and opportunities for public comment will be addressed separately by FDA and will also be incorporated in subsequent requests for extension of Forms FDA 3500 and 3500A.)

CBER = Center for Biologics Evaluation and Research; CDER = Center for Drug Evaluation and Research; CDRH = Center for Devices and Radiological Health; and CFSAN = Center for Food Safety and Applied Nutrition.

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13. Cost to Respondents

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

Approximately 459,102 reports from pharmaceutical [drugs and biologics] manufacturers, and 146,127 device reports from user-facilities, importers or manufacturers, including follow-up reports, were submitted to FDA in CY2007 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 $14.91 per hour and 30 minutes for a health practitioner at a pay rate of $26.37 per hour for review. [Bureau of Labor Statistics 2007

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 ($8.95) and 30 minutes ($13.19) or $22.14 per report submitted].

Based on a total information collection burden of 605,229 responses for mandatory form 3500A the annual labor cost to user-facilities, and pharmaceutical, biological and device industries would be $13,399,770.00.

14.Cost to the Federal Government

The estimated cost to the Federal Government for forms FDA 3500 and FDA 3500A is $8,307,000.

CENTER	Number of Reponses	Hours per Response	Cost per Hour	Total Cost
CBER/CDER	482,135	.6		By contract
CDRH	145,780	.6		By contract
CFSAN	479	.6		By contract
Total	**628,394**			$8,307,000

(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)

482,135 pharmaceutical [drug and biologics] reports and 145,780 medical device reports can be expected to be submitted to FDA annually, either directly (voluntary reports) or via the manufacturer (mandatory reports). An additional 479 reports are submitted voluntarily on CFSAN products [special nutritionals and cosmetics].

CDER/CBER Contracts: Adverse event reporting data entry, MedDRA coding, and quality control ($3.857 million/year)

CDRH Contract: processing of medical device reports, including receipt of device reports by phone, coding, and data entry ($3.5 million)

CFSAN Contract: $350,000 (data entry and processing) + 600,000 (maintenance of IT system)

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 $18.85 per hour for the data entry and 18 minutes for a GS-13/step 1 at a pay rate of $ 39.75 per hour for review. [From http://www.opm.gov/oca/08tables/pdf/salhr.pdf]

15. Reason for Changes in Burden

The increase in reporting burden reflects a natural increase in the number of reports coming into the Agency. As more medical products are approved by the FDA and marketed, and as knowledge increases of the importance of notifying FDA when adverse events, product problems and product use errors are observed, it can be expected that more reports will be submitted to the Agency. Increase in burden, as measured in hours, will also increase as both voluntary and mandatory reporters expend increased time in order to provide a more complete and accurate report. Additionally, although not reflected in the data for CY 2007, the new mandatory reporting responsibilities for OTC and dietary supplement manufacturers under Public Law 109-462 [see above] will be expected to change the burden further during the period of the extension of this collection.

PROGRAM	**PREVIOUS BURDEN***	**CURRENT BURDEN****	**CHANGE IN BURDEN**
CBER/CDER	455,849	518,832	+ 62,983

CDRH	66,870	163,364	+ 96,494
CFSAN	399	287	- 112
TOTALS	**523,118**	**682,483**	**+ 159,365**

* previous burden (CY 2004; from previous OMB approval) in hours
** current burden in hours from #12 above

16. Plans for Statistical Use

The information collected will not be used for statistical purposes.

17. Approval for Not Displaying Expiration Date

FDA is not requesting approval for not displaying expiration date.

18. Exception to the Certification Statement; Item 19, OMB Form 83-1

FDA is not requesting an exception to the certification statement identified in Item 19 "Certification for Paperwork Reduction Act Submissions" of OMB Form 83-1.