FDA RAPID RESPONSE SURVEYS
OMB No. 0910-0500
SUPPORTING STATEMENT

A. Justification

1. Circumstances Making the Collection of Information Necessary

The Food and Drug Administration (FDA) is requesting approval from the Office of Management and Budget (OMB) for the generic clearance, FDA Rapid Response Surveys. The purpose of the information collection is to provide a tool to obtain quickly vital information from appropriate sources so FDA may take suitable public health or regulatory action.

This program support quick-turnaround decision-making about potential safety problems or risk management solutions. FDA will collect this information to determine whether a problem impacts the public health from health professionals, hospitals, and other user facilities (for example, nursing homes, ambulatory surgical and outpatient diagnostic and treatment facilities, etc.), consumers, importers, as well as sponsors, manufacturers and distributors of medical products, food additives, cosmetics and dietary supplements.

While the form for data collection will be standardized (please see Attachment A – Standardized Form), the actual information to be collected will vary from survey to survey. The specific information FDA needs for risk/management or hazard analysis will depend on the product in question and the particular adverse event under investigation. Responses to the information collection questions are strictly voluntary and anonymous.

FDA is the regulatory agency responsible for the safety and effectiveness of medical products including biologics, drugs, foods, cosmetics, medical products, radiological products, and animal drugs. Important questions about FDA-regulated products, such as those concerning user experience, durability, and rare effects may not be answered until after the product has been marketed. To protect the public health, FDA must be able to collect rapidly information pertaining to adverse events associated with FDA-regulated products after they have been marketed.

Section 505 of the Federal Food, Drug and Cosmetic Act (the Act)(21 U.S.C. 355), codified under 21 CFR part 314) requires 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 (21 U.S.C. 372) authorizes investigational powers of the FDA for the enforcement of the Act.

Under section 519 of the Act (21 U.S.C. 360(i)), FDA is authorized to require manufacturers to report medical device related deaths, serious injuries, and malfunctions and to require user facilities (hospitals, nursing homes, ambulatory surgical facilities and outpatient diagnostic and treatment facilities) to report medical device-related deaths directly to FDA and to manufacturers, and to report serious injuries to the manufacturer.

Section 522 of the Act (21 U.S.C. 360(l)) authorizes FDA to require manufacturers to conduct postmarket surveillance of medical devices.

Section 705(b) of the Act (21 U.S.C. 375(b)) authorizes FDA to collect and disseminate information regarding medical products or cosmetics in situations involving imminent danger to health, or gross deception of the consumer.

Section 903(d)(2) (C) of the Act (21 U.S.C. 393(d)(2)(C)) authorizes the Commissioner of the FDA to implement general powers (including conducting research) to carry out effectively the mission of the FDA.

Section 409 of the Act (21 U.S.C.348) defines what is considered to be an unsafe food additive and specifies the information that must be submitted by a petitioner to establish the conditions under which a food additive may be safely used.

Section 201(s) of the act (21 U.S.C. § 321(s)) defines a generally recognized as safe (GRAS) substance as an exception from the legal definition of a food additive. This section defines a substance as GRAS if it is generally recognized among experts qualified by scientific training and experience to evaluate its safety, to be safe through either scientific procedures or common use in food under the conditions of its intended use. To implement the GRAS provisions of § 201(s), FDA has issued procedural regulations in 21 CFR part 170. The procedural regulations at 21 CFR 170.30 are designed to delineate and specify, with particularity, eligibility for classification as GRAS, and to set forth the information that must be submitted to FDA to gain agency concurrence that a substance is GRAS. The regulations add no substantive requirements to the law, but attempt to explain the requirements for classification as GRAS. More specifically, the procedural regulations in 21 CFR 170.35(c)(1) provide a standard format for submission of GRAS affirmation petitions.

Under Section 404 the Act (21 U.S.C. 344), FDA promulgated regulations (21 CFR 108.25(a) and 108.35(a)) that require low-acid and acidified food processing establishments to register their firms, file scheduled process information, maintain records of processing and production records, and fulfill the mandatory provisions of the Good Manufacturing Practices (21 CFR 113 and 114). The requirements are intended to ensure risk to public health does not increase from improper or inadequate manufacture, processing and packing of such foods, and to permit FDA to verify that appropriate procedures are being followed.

All milk and cream imported into the fifty States and the District of Columbia is subject to the requirements of the Federal Import Milk Act of 1927 (FIMA) (21 U.S.C. 141-149) (Attachment A). Under the regulations implementing FIMA (21 CFR Part 1210) (Attachment B), milk or cream may be imported into the United States only by the holder of a valid import milk permit. Before such permit is issued: (1) cows must be physically examined and found healthy; (2) if the milk or cream is imported raw, all cows must pass a tuberculin test; (3) the dairy farm and each plant in which the milk or cream is processed or handled must be inspected and found to meet certain sanitary requirements; (4) bacterial counts of the milk at the time of importation must not exceed specified limits; and, (5) the temperature of the milk or cream at time of importation must not exceed 50° F.

Section 721(a) of the Act provides that a color additive shall be deemed to be unsafe unless it meets the requirements of a listing regulation, including any requirement for batch certification, and is used in accordance with the regulation. FDA lists color additives that have been shown to be safe for their intended uses in Title 21 of the Code of Federal Regulations (CFR). FDA requires batch certification for all color additives listed in 21 CFR part 74 and for all color additives provisionally listed in 21 CFR part 82.

These sections of the Act enable FDA to enhance consumer protection from risks associated with medical product usage that are not foreseen or apparent during the application, premarket notification and review process.

Regulations governing medical devices are codified under 21 CFR Part 803.

Currently, FDA monitors medical products related postmarket adverse events via both the mandatory and voluntary MedWatch Reporting System. Using FDA forms 3500A (mandatory form) and 3500 (voluntary form) approved under OMB Control Number: 0910-0291 (expires 10/31/2008), and Form VAERS-1 for the Vaccine Adverse Event Reporting System (VAERS), all reports are submitted to FDA.

Over the years, medical science and technology have become increasingly complex. Due to economic pressures and organizational changes within health care organizations, this science and technology is not only used by highly trained health care professionals, but has also moved into facilities where the users may not be as sophisticated. Additionally, many of these increasingly complex drugs and medical products are now found in the home. These changes have increased the need to obtain timely information from postmarket surveillance systems and to disseminate quickly information to the health care and consumer communities on public health safety issues.

Analysis of a potential health or medical problem often cannot be made based on the information contained in a few adverse event reports submitted through the MedWatch program. Section 522 of the Act gives FDA the authority to instruct manufacturers to conduct surveillance of medical devices and sections 702 and 903 to investigate and to conduct research to allow FDA to enforce the Act and to carry out the mission of the Agency. For instance, for devices, it can take up to 90 days before the surveillance plan is begun (i.e., the manufacturer has 30 days after receiving notification that FDA is requesting surveillance of a particular product to submit a surveillance plan, and FDA then has 60 days to accept the plan), and much longer until the plan has been completed. This link to the manufacturing community does not fulfill the need for rapid information when FDA must decide quickly if particular adverse event reports signal a widespread public health problem. FDA requires a timely link to the clinical community in order to obtain information for more emergent situations.

The reports of adverse events that FDA receives from the clinical community typically are not complete and hence there is considerable underreporting. When necessary, FDA contacts the individual reporter of a particular adverse event to obtain more information than what was provided in the MedWatch report. However, there is often insufficient information from the reporter to determine whether an adverse event signals a potential public health hazard. Lack of sufficient information often hampers FDA's ability to understand quickly and thoroughly evaluate the problem; determine the factors that contributed to the adverse event; determine the scope of a possible

public health problem; and determine what steps must be recommended to the health-care community to prevent further injury.

In order to perform risk analyses and determine the appropriate action plan, FDA must have the tools to investigate fully medical product problems. Therefore, FDA implemented this information collection program, FDA Rapid Response Surveys, which provides the necessary timely link to the clinical community**.**

No more than 30 rapid response survey questionnaires will be sent to the appropriate medical professionals, health care institutions, consumers, sponsors, manufacturers and/or importers of other FDA-regulated products each year. The data collected will provide FDA with information to allow a more complete analysis of the problem; determine the existence and extent of a public health problem; and then, if necessary, to disseminate the information to the health care community. All of these processes must be accomplished in a timeframe that limits, to the extent possible, further incidents causing injury to the public.

A standard survey form will be used, with the addition of questions that specifically address the medical product problem under investigation. Prior to sending out each survey, FDA will send a memorandum with the survey attached to OMB for its sign-off. FDA requests that OMB sign-off be obtained within 3 to 10 days.

2. How, by Whom and For What Purpose the Information is to be Used?

FDA monitors the reports of adverse events associated with the use of medical products that enter the MedWatch mandatory and voluntary reporting programs. Reports are triaged based on perceived risk to the patient. Some reports signal an immediate hazard, but more commonly it is the experienced FDA clinical analysts that detect product problems, particularly those related to product use, through careful investigation of reported incidents and searching for additional sources of information.

The degree of perceived risk to the public is the most important consideration for any FDA public health action (product recall, Safety Alert, Public Health Notification, Ad Hoc Committee, workshop, publication, etc.) It is imperative that these risk determinations are completed as quickly as possible to avoid further deaths or injuries from occurring. Currently, FDA analysts make these determinations based on information contained in adverse event reports; obtained from contacting the individuals who made the reports; gathered from expertise of scientists within, and sometimes outside, the agency; and from any other data sources available.

When these data sources fail to provide enough information to perform a risk/hazard analysis, FDA proposes to use the FDA Rapid Response Surveys to answer these important questions. The problems encountered with a variety of FDA-regulated products dictates that each survey effort will be unique in that each will involve a different type of product used by different health care professionals.

For example: an adverse event report may be received describing an anaphalatic-type reaction during the use of a certain catheter. Evaluation of this problem includes questions such as: was this reaction related to the patient's illness or the stress of the procedure; and is therefore not medical product related or, is there a biomaterial in this medical product that could cause this reaction? Because the health care community often does not recognize that a product may have

contributed to an adverse event and because there is significant underreporting, it is critically important to know whether other health care professionals may have seen this problem. These other professionals may have not reported a similar event because they did not recognize that the reaction might have been related to the product. If FDA has the ability to survey quickly the appropriate user population (in the example cited, this would be the IV Nurses Association), FDA could immediately determine if the report was an isolated incident or had occurred more often and was a signal of a potentially serious problem with the product.

FDA works with other government agencies and private sector organizations to help reduce the risk of tampering or other malicious, criminal, or terrorist actions on the food (including dietary supplements) and cosmetic supply. There are a variety of ways the FDA is alerted to potential problems with products, including consumer complaints, inspection data, test results, adverse event reports and reports of illness. We might also learn of a problem from industry, one of our state or federal partners or from governments of other countries. When FDA receives such information, the agency may have an immediate need for additional data to better understand potential vulnerabilities or to perform a risk/hazard analysis. Information that FDA might need would vary depending upon the situation but might include, for example, the likelihood that a certain food caused the illness; the severity of the illness; and any steps taken during production to reduce the likelihood of contamination. FDA proposes to use the FDA Rapid Response Surveys to further develop tools and science necessary to better understand where vulnerabilities are and the most effective ways to minimize them, as well as to intervene and respond once a problem occurs.

The targeted population to respond to the particular survey questions, and the specific survey questions, will change depending on the particular product in question.

The data will be collected and analyzed by the Agency's postmarketing surveillance offices conducting the Rapid Response Survey. Public health analysts and epidemiologists, and when necessary, statisticians and other Agency scientists, will analyze the data to determine whether a public health risk exists, and how it must be addressed.

As directed by OMB's terms of clearance of approval of this information collection a summary follows at the end of this justification provided by the Centers on rapid response surveys they have conducted over the past 18 months.

3. To What Extent the Collection of Information involves the use of Automated, Electronic, Mechanical, or Other Technological Collection Techniques

The methodology for contacting the reporting sample will vary depending on the product and the health professionals and others targeted as respondents. Some of the data collections will involve mailings from FDA, some will be accomplished with the help of professional associations (either direct mailouts from the associations to its members, or the associations may provide contact lists to FDA), and some will be conducted electronically.

Whenever possible, and on a small scale, and to avoid the burden of responding by mail, electronic collections will be conducted. For example, as directed by the Food and Drug Modernization Act of 1997, FDA is developing a

"sentinel" system to represent the various types of user facilities in the United States. In order to comply with the Government Paperwork Elimination Act of 1998, these facilities will report to FDA via the Internet, and FDA will have the ability to contact the sites via e-mail. This system is currently in place, will eventually represent a group of hospitals, nursing homes, home health care agencies, and other medical product user facilities. The risk managers at different groups (hospitals, nursing homes, etc.) of these sentinel sites would function as the sample when the product in question is used at their type of facility.

4. Describe Efforts to Identify Duplication

FDA scientists routinely utilize literature searches and other secondary data sources to aid in answering some questions about the use of medical products. However, many of the product issues relate to emerging technologies and sciences where little has been written about these problems. FDA's surveillance system is a large national system that is designed to pick up not only common problems, which may appear in the literature, but more importantly, to pick up signals for seemingly rare events that may have far reaching public health implications. These rare events usually have not been identified previously, or when they do appear in a journal, they are reported as "case studies" which do not provide FDA with the broader scope needed to define the public health impact.

Manufacturers are contacted routinely to learn of their experience in investigating and evaluating particular issues. Additionally, FDA scientists contact other public and private health organizations and associations, such as the Center for Disease Control, Product Quality Research Institute, American Association of Pharmaceutical Scientists, Generic Pharmaceutical Industry Association, National Association of Pharmaceutical Manufacturers, Nonprescription Drug Manufacturers Association, National Pharmaceutical Alliance, Parenteral Drug Association, Pharmaceutical Research and Manufacturers of America, American College of Radiology, Senior Citizen Groups, or ECRI (formerly the Emergency Care Research Institute), to determine if the databases maintained at those organizations contain any useable information. In addition, FDA will contact other experts in science, medicine and public health as well as consumers, product sponsors and manufacturers, importers, and retailers.

While these outreach efforts can be useful, they may not be complete enough to aid FDA in determining rapidly the exact nature and public health impact of a problem. Therefore, FDA needs the additional tool of the information collection proposed in the FDA Rapid Response Surveys requested in this document.

5. Small Business

It is possible, but unlikely; that respondents contacted will be small businesses. Most product adverse events that will be under investigation are rare events, and larger institutions are more likely to have experience with these products. In the event that smaller entities are included in a survey, their participation will be voluntary and the burden estimated as no more than .5 hours per respondent.

6. Describe consequences to Federal program or policy if the collection is not conducted

The FDA postmarket surveillance program will be less effective in providing timely, necessary information to the health care community on avoiding serious injuries and

deaths with medical products for those products whose problem mechanisms are not well understood and for which FDA has no tool to obtain needed information.

To demonstrate the importance of establishing a Rapid Response Survey information collection program**,** two sample surveys are provided (Attachment B). This sample demonstrates when an immediate means of information collection would have resulted in more effective, timely feedback to the public.

7. Special Circumstances

Requiring respondents to prepare a written response to a collection of information in fewer than 30 days after receipt of the questionnaire.

Given the need for FDA to obtain information about possible risks to the public health in a rapid timeframe, 30 days will be the outside limit of the requested length of time to respond. If there is the possibility of a public health emergency, respondents may be asked to respond within 15 days. For any necessary shorter turnaround timeframes, electronic contact will be made to encourage faster responses.

8. Describe efforts to consult with person outside the agency to obtain their views on the availability of data, etc.

In accordance with 5 CFR 1320.8(d), on January 7, 2004, (69 FR 923), a 60-day notice for public comment (Attachment C) was published in the Federal Register. FDA received no comments.

9. Explanation of Any Payment or Gift to Respondents

Respondents will receive no gift or payment for their participation in the questionnaires.

10. Assurance of Confidentiality (Anonymity) Provided to Respondents

The identity of the respondent providing information to the FDA Rapid Response Surveys will be anonymous.

Written or electronic questionnaire forms sent from FDA will not ask for identifying information and they will not be coded in any way that will identify the respondent. Therefore, FDA will not know the identity of the respondent to any returned form. E-mail surveys will give clear directions that the responses are not to be returned via e-mail. To avoid creating a link between the respondents' responses and the respondents, the surveys must be copied from the e-mail, and faxed or mailed to FDA. Identifiers on faxed data will be removed and return envelopes will be destroyed before the information is given to the analysis team.

Whenever possible, we will work through a third party (i.e. health care association) so that the third party may contact a particular respondent for follow-up when necessary, while still keeping the identification of the respondent unknown to FDA.

Lists of all responder samples used for each inquiry will only be held long enough to determine the response rate and to re-contact each respondent if we have not achieved a response rate that permits FDA scientists to judge whether a public health hazard exists. Lists will be destroyed following the data collection and any necessary follow-up so no possible link may be made between the obtained information and the

respondent. For more detail concerning follow-up of non-responders, please see Part B, Section 3.

11. Justification for Sensitive Questions

None of the questions will be sensitive in nature.

12. Estimates of Hour Burden Including Annualized Hourly Costs

This is based on the maximum number of surveys (highly likely that this maximum will not be reached--most respondents will probably never be contacted more than 5 times per year due to the variable nature of the medical product issues and the need to access different respondent groups).

Estimated Annual Reporting Burden

Number of Respondents	Annual Frequency of Responses	Total Annual Responses	Hours per Response	Total Hours
200	30 (maximum)	6,000	.5	3,000

Annualized Hourly Costs

Risk managers working in hospitals will complete the majority of the surveys. Therefore, we based the estimated annual cost on the salary of this professional group to be $34.00 per hour. The estimated annualized annual cost for 3,000 hours of reporting time is $102,000.00.

The number of respondents was determined by the maximum sample size of 200 facilities (or individuals) per questionnaire. This number will vary depending on the product under evaluation. Data from more than 200 sources could not be evaluated in a rapid timeframe.

The annual frequency of responses is determined by the maximum number of questionnaires that will be sent to any individual respondent. As noted earlier, some respondents may be contacted only once per year, while another respondent may be contacted several times depending on the medical product under evaluation.

The total annual responses is estimated to be 200 facilities/sample x 30 questionnaires = 6,000 (unlikely this maximum will be reached). At a maximum, it will take .5 hours for a respondent to gather the requested information and fill in the answers. The total annual burden, therefore, is estimated to be 3,000 hours (6,000 total annual responses x .5 hours/response = 3,000 hours.)

13. Estimate of Other Total Annual Cost Burden to Respondents

There will be no costs incurred by respondents.

14. Annual Cost to the Federal Government

It is anticipated that half of the total number of surveys per year will be issued via e-mail, and the remaining half will be conducted via mailings. Using the maximum number of 30 surveys per year, costs listed below are for 15 surveys conducted by e-mail and 15 by mail.

The cost of administrative help to develop the respondent lists and obtain e-mail addresses is $2,400.00. This represents .06 FTE for 120 hours at a cost of $20.00 per hour (includes administrative costs).

For the 15 surveys conducted by mailings, the cost to the government for administrative help to create respondent lists, photocopy, and stuff envelopes is $1,620.00. This represents .03 FTE for 81 hours at a cost of $20.00 per hour (includes administrative costs).

The cost of postage will be $2,220.00 (to send out 3000 envelopes and for the return postage); the cost of envelopes will be $150.00 (3000 mailed from FDA, and FDA will provide return envelope); and the cost of paper will be $81.00. **Total Cost**: **$6,471.00**

15. Explanation for Program Changes or Adjustments

There are no changes or adjustments.

16. Plans of Tabulation and Publication and Project Time Schedule

Rapid Response Surveys can provide information on potential risk to patients, but they do not yield quantitative data about safety that can be generalized. Policy makers can use Rapid Response Survey findings to test and refine their ideas, but will generally conduct further research before making important decisions such as adopting new policies and allocating or redirecting significant resources to support these policies.

With this in mind, FDA will disseminate Rapid Response Survey findings only when appropriate, strictly following FDA's "Guidelines for Ensuring the Quality of Information Disseminated to the Public", and will include specific discussion of the limitations of survey results with regard to being non-quantitative and not generalizeable. Information quality encompasses (1) utility, the usefulness of the information to its intended users, including the public; (2) objectivity, whether information is being presented in an accurate, clear, complete, and unbiased manner; and (3) integrity, the information is protected from unauthorized access or revision. FDA uses a number of mechanisms to ensure the quality of the information we disseminate. FDA reviews the quality of information before it is disseminated and treats information quality as integral to every step of the development of information, including its creation, collection, maintenance, and dissemination.

17. Reason Display of OMB Expiration Date is Inappropriate

The OMB number and expiration date will be listed on the standard survey form.

18. Exemption to Certification for Paperwork Reduction Act Submissions

No exemptions requested.