SUPPORTING STATEMENT

A. Justification

1. Circumstances of Information Collection

In the FEDERAL REGISTER of October 7, 2008 (73 FR 58604) FDA announced the availability of a concept paper entitled "PDUFA Pilot Project Proprietary Name Review." The concept paper describes how pharmaceutical firms may evaluate proposed proprietary names and submit the data generated from those evaluations to FDA for review under a pilot program to begin by the end of FY 2009.

On September 27, 2007, the President signed into law the Food and Drug Administration Amendments Act of 2007 (Pub. L. 110-85, 121 Stat. 823), which includes the reauthorization and expansion of the Prescription Drug User Fee Act (PDUFA IV). As part of the reauthorization of PDUFA IV, FDA committed to certain performance goals, including the goal of using user fees to implement various measures to reduce, among other things, medication errors related to look-alike and sound-alike product proprietary names. FDA also agreed to develop and implement a voluntary pilot program to enable pharmaceutical firms participating in the pilot to evaluate proposed proprietary names and to submit the data generated from those evaluations to the FDA for review. The concept paper is intended to help pharmaceutical firms choose appropriate proprietary names for their drug and biological products before submitting marketing applications to FDA and describes how pharmaceutical firms may use "best practices" to carry out their own proprietary name reviews and provide FDA with the data that result from those reviews. The goals of the concept paper and the voluntary pilot program are to minimize the use of names that are misleading or that are likely to lead to medication errors, to make

FDA's marketing application review more efficient, and to make regulatory decisions more transparent. The concept paper explains how an applicant who chooses to participate in the pilot program could assess a proposed proprietary name for safety (i.e., potential for medication errors) and, at the applicant's option, for promotional implications, before marketing application approval and subsequent marketing of a drug or biological product in the United States, and how to submit the results of the assessment for review under the pilot program.

As explained in the concept paper, FDA has for decades considered the role of names and naming processes in medication errors as part of the Agency's focus on the safe use of medical products. FDA has developed internal procedures and processes that are part of its marketing application review process for evaluating the potential for a proposed product name (submitted as part of a new drug application (NDA), biologics license application (BLA), or abbreviated new drug application (ANDA)) to cause or contribute to medication errors. The goal of the pilot program is to test a process that could enable pharmaceutical manufacturers to carry out proprietary name reviews of their products prior to submitting marketing applications to FDA, so that the FDA review of proprietary names would be more efficient.

A medication error is “any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient, or consumer.” Such events may be related to professional practice, healthcare products, procedures, and systems, including prescribing; order communication; product labeling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use Medication use errors may occur due to sound-alike or look-alike names, unclear labels, or poorly designed packaging. In the U.S. healthcare

system, healthcare practitioners rely on a product's name as the critical identifier of the appropriate therapy in a market of thousands of products. Therefore, accurate interpretation of a product's name is essential to ensure that the correct product is procured, prescribed, prepared, dispensed, and administered to the patient. Product names that look or sound alike can lead to medication errors and, potentially, to patient harm by increasing the risk of a healthcare practitioner's misprescribing or misinterpreting the correct product name, dispensing and/or administering the wrong product, or dispensing it incorrectly. Because of the many potential interactions among the system elements, multiple opportunities for medical care-related confusion and medication errors exist. The concept paper explains how an applicant who chooses to participate in the pilot program could assess a proposed proprietary name for safety (i.e., potential for medication errors), and, at the applicant's option, for promotional implications, before application approval and subsequent marketing of a product in the United States and submit the results of the assessment for review under the planned program, as outlined in the goals letter.

The information collection that will result from the voluntary pilot program, as described in the concept paper, consists of the following:

(1) Applicants should contact FDA to register and indicate the approximate date of their proprietary name submission, as described in the concept paper and as will be described in more detail when FDA announces OMB's approval and the specific information on participating in the pilot program.

(2) Applicants should contact the appropriate FDA center 120 days prior to the intended date of the proposed proprietary name submission to discuss the specific details of the planned

submission. Applicants should communicate with the Director in the Division of Medication Error Prevention and Analysis in the Office of Surveillance and Epidemiology in the Center for Drug Evaluation and Research, or the Branch Chief at the Advertising and Promotion Labeling Branch of the Division of Case Management in the Office of Compliance and Biologics Quality in the Center for Biologics Evaluation and Research, concerning any questions about their proposed submissions. For prescription products, applicants should inform the appropriate center at the 120-day pre-submission discussion if they plan to use alternative or additional methods to evaluate the safety of their proposed proprietary name. For nonprescription products, sponsors should discuss with FDA different protocols that could be used for their specific drug products prior to the submission of the proprietary name.

(3) Applicants should submit two separate sets of product name-related information to enable parallel reviews by FDA: (a) A comprehensive evaluation of the proposed proprietary name including the information and data listed in Appendix B ("Proposed Template For A Pilot Program Submission") of the concept paper; and (b) the proprietary name information that they would ordinarily submit under FDA's current practice.

(4) After review of the proprietary name submissions, and if FDA informs the applicant that the proposed first-choice proprietary name is unacceptable, the applicant should confirm in writing that it would like its originally submitted second-choice name reviewed, or the applicant should submit an alternative second-choice name along with the information described in the concept paper. At that time, FDA will begin review of the second-choice name. If an applicant has submitted a complete proprietary name analysis for the second-choice name, the responsible center will use discretion to determine whether to review the applicant's analysis in addition to

conducting its own analysis using the traditional approach. Although FDA would ideally review the applicant's completed proprietary name analysis for the second-choice name, factors such as staffing and timelines will be used in making this determination.

2. Purpose and Use of Information

As part of the reauthorization of PDUFA IV, FDA committed to certain performance goals, including the goal of using user fees to implement various measures to reduce, among other things, medication errors related to look-alike and sound-alike product proprietary names. FDA also agreed to develop and implement a voluntary pilot program to enable pharmaceutical firms participating in the pilot to evaluate proposed proprietary names and to submit the data generated from those evaluations to the FDA for review. The concept paper is intended to help pharmaceutical firms choose appropriate proprietary names for their drug and biological products before submitting marketing applications to FDA and describes how pharmaceutical firms may use "best practices" to carry out their own proprietary name reviews and provide FDA with the data that result from those reviews. The goals of the concept paper and the voluntary pilot program are to minimize the use of names that are misleading or that are likely to lead to medication errors, to make FDA's marketing application review more efficient, and to make regulatory decisions more transparent. The concept paper explains how an applicant who chooses to participate in the pilot program could assess a proposed proprietary name for safety (i.e., potential for medication errors) and, at the applicant's option, for promotional implications, before marketing application approval and subsequent marketing of a drug or biological product in the United States, and how to submit the results of the assessment for review under the pilot

program.

3. Use of Improved Information Technology

Applicants should submit the information described in the concept paper in the same manner that other application-related submissions are submitted. FDA has made available several guidances on how to submit marketing applications. These guidance documents and others are available at FDA's web site http://www.fda.gov/cder/guidance/index.htm.

4. Efforts to Identify Duplication

This information does not duplicate any other collection.

5. Involvement of Small Entities

Although new drug development is typically an activity completed by large multinational drug firms, the information collection required under 21 CFR 314 applies to small as well as large companies submitting marketing applications. However, under the Regulatory Flexibility Act, FDA regularly analyzes regulatory options that would minimize any significant impact on small entities. FDA also assists small businesses in complying with regulatory requirements.

6. Consequences If Information Collected Less Frequently

As part of the reauthorization of PDUFA IV, FDA committed to certain performance goals, including the goal of using user fees to implement various measures to reduce, among other things, medication errors related to look-alike and sound-alike product proprietary names.

7. Consistency with the Guidelines in 5 CFR 1320.5(d)(2)

There is no inconsistency.

8. Consultation Outside the Agency

In the Federal Register of December 23, 2008 (73 FR 78813), FDA published a 60-day notice requesting comments on the information collection. We received one comment, which raised the following issues:

(1) The comment stated that the focus of the Pilot Program should be on safety evaluations for drug products that will be marketed in the United States. The comment said that trademark clearance from both the legal and regulatory perspectives is often conducted by sponsors to support the geographic markets for the product and therefore often extends beyond the United States. The comment said it is not uncommon for pharmaceutical companies to develop trademarks that will be granted registrations from trademark offices in connection with approvals from health authorities in multiple countries with the goal of becoming global trademarks. Except for product names in foreign markets that are identical to the trademark under review, the comment recommended that FDA limit its requests for search data to clearance activities relating to trademarks that are in use or appear likely from public sources to be in use in the near future in the United States. The comment said that data from outside the United States can be voluminous and are not necessary for the proper performance of FDA's functions or for determining the appropriateness of the name in the United States.

The comment also expressed concern with "FDA's proposed broad request for trademark search-related information insofar as they apply to all search queries." (The comment referenced bullet points on pages 14 and 36 of the concept paper). The comment said that FDA under-estimates the burden of collecting such information. At the early stages of trademark clearance, the comment noted that a sponsor generally begins with a list that could include hundreds of candidates, and that this list is typically narrowed in successive waves of more in-depth searches of candidates based on legal and regulatory concerns. The comment said that because a sponsor cannot determine in advance which of the candidates on the initial list will survive the clearance process, sponsors would have to maintain the records of the early-stage, en masse searches relating to possibly hundreds of names on the list to comply with a request for all search queries. The comment said that sponsors should not be expected to maintain search query information for en masse search investigations on name candidates, especially those which had been eliminated previously and well before submission to FDA as proposed trademarks. It also asserted companies' entitlement to maintain applicable legal privileges for information and communications developed in the course of trademark availability assessment.

(2) The comment also said that medication errors can be caused by any number of system failures or other causes at any one or more stages in the process of prescribing, dispensing, and administering medications, and that medication errors are the result of multiple causes. The comment said that there is no scientifically valid and reliable method for measuring the extent to which pharmaceutical proprietary names might contribute to

the risk of such errors or whether such methods could ever adequately take into account the subjectivity and complexity of human perception. It also stated that the agency's proprietary name review process must be guided by the First Amendment.

(3) The comment noted that the burden of the collection of information should be minimized by using various automated collection techniques and other forms of information technology, and referred to the computerized databases listed in Attachment A of the concept paper. The comment said that some of the databases listed have limited value because they are substantially redundant with the collective content of the remaining databases, are not amenable to automated searching, or have more limited automated searching capabilities than others. The comment also noted that some sponsors may not have the resources to subscribe to many databases and will have to rely on the search capabilities of vendors, and questioned whether vendors that offer search services include all of the sources listed on Attachment A.

FDA response:

To evaluate the proposed information collection, FDA believes it is important to recall that the information collection not only supports the Agency's statutory mandates to ensure that drugs are safe and effective and are not misbranded, but also that it is part of a voluntary pilot program intended to make FDA's regulatory decisions more transparent and to explore ways to make FDA's application review more efficient. As indicated in

the Concept Paper, FDA committed to this program in conjunction with the reauthorization of the Prescription Drug User Fee Act (PDUFA IV), after extensive discussion with industry, to support the goals of reducing medication errors related to look-alike and sound-alike proprietary names, unclear label abbreviations, acronyms, dose designations, and error-prone label and packaging designs. The pilot program is intended not only to minimize the use of names that are misleading or that are likely to lead to medication errors, but also to provide a basis for FDA to determine whether in the future, it would be feasible and preferable for FDA to achieve these goals through review of analyses of proprietary names conducted and submitted by applicants, as many applicants have suggested, rather than conducting its own analyses, as is the current practice. To this end, the proposed information collection recommended in the pilot program is largely modeled on the information that FDA itself currently generates and analyzes in evaluating proposed proprietary names, in accordance with its statutory authorities and the First Amendment. FDA requests that these elements be submitted by pilot program participants because of its own direct experience supporting the utility of such information, but as the pilot program Concept Paper makes clear, applicants can still participate in the pilot program if they plan to deviate from the proposed proprietary name safety evaluation methods recommended in the concept paper and instead use alternative or additional methods. Also, to the extent that the comment also suggests that the information collection for the pilot program should also be limited to information related to safety concerns, we note that applicants can participate in the pilot program without submitting any information to evaluate the promotional implications of their

proposed proprietary names.

With regard to the specific elements of the comment;

(1) FDA does not seek to expand the burden of collecting trademark search-related information, and is not requesting that sponsors submit broad trademark search queries or other search-related screening information about any preliminary or early-stage proprietary name candidates which the sponsor eliminated from consideration and therefore did not submit to FDA for review as part of the proprietary name pilot program. FDA is interested in collecting all search queries that are specific to the proposed proprietary name a sponsor submits to the pilot program for review, including all existing, publicly available drug names initially identified as a potential source of confusion with respect to the proposed name. Specifically, FDA requests that a sponsor submit all of the search queries that were generated only for the specific proposed proprietary name submitted to FDA. For each query, the results are dependent upon how each data source was searched. Thus, in order for FDA to evaluate the strength of the results, information pertaining to each query, such as -- the system parameters that were used for each search; the precise databases that were searched; any thresholds imposed on the output; the date the search was conducted or the last update of the database searched; the pooled results with source citation and full product characteristics of each name identified as a possible source of confusion with the proposed name -- should be provided on the proposed name submitted to FDA for evaluation. Providing FDA with

all of the search queries relevant to the proposed name and associated tests, including the Failure Mode and Effects Analysis, will permit FDA to understand and evaluate the basis for the sponsor's conclusions that existing drug names that are identical or potentially similar to the proposed proprietary name would not be likely to cause confusion and medication errors. By submitting this information, the sponsor would be supporting the goals of the concept paper and the voluntary pilot program. Such goals include not only minimizing the use of names that are misleading or that are likely to lead to medication errors in the clinical setting (due to look-alike and sound-alike proprietary names), but also include allowing FDA to evaluate whether to have applicants perform their own name analysis and submit resulting data to FDA for review. At the conclusion of the pilot program, FDA will be evaluating what information would be most useful as the basis of those industry-conducted proprietary name reviews. These evaluations will be largely qualitative. The results of the pilot program and recommended additions and changes to methods based on the reported results will be discussed in a future public meeting. With regard to the comment addressing legal privilege related to trademark evaluations, as noted previously, applicants can participate in the voluntary pilot program even if they deviate from the proposed proprietary name safety evaluation methods recommended in the concept paper, and therefore may determine for themselves how to submit useful information without compromising legal privileges related to trademark.

FDA also acknowledges that "search data" for trademark clearance activities collected from outside the United States can be voluminous, particularly if sponsors are seeking to register a

single global trademark for their drug in multiple countries. As already indicated FDA is not seeking broad trademark clearance search data but is interested in information specifically relevant to assessing the potential for medication error related to the specific proprietary name proposed for the U.S. For this purpose, FDA agrees that the most relevant information includes information identifying product names in foreign markets that are identical to the name proposed for the U.S. market, regardless of active ingredient or other product characteristic. In addition, FDA agrees that it is important to collect information regarding phonological or orthographic similarities between the proposed name and foreign drug names that are in use or appear likely from public sources to be in use in the near future in the United States; such names should be considered in the same way as the names of any other drug products also in use in the United States. FDA believes that in certain circumstances, however, it is in the interest of public health for sponsors to provide the agency with other data that they may possess that indicates close similarities in spelling and pronunciation between the proprietary name proposed for the U.S. and foreign drug names. For example, patients in the United States may experience medication errors related to confusion of the names of a drug marketed in the United States and one obtained from a foreign country, either while the patient was abroad or through other means, whether or not the foreign drug is intended for the U.S. market by the manufacturer. This potential situation presents a particular public health risk where a drug product is currently marketed in a foreign country under a proprietary name which is identical or very similar to the proposed proprietary drug name under FDA review, but the drugs contain a different active ingredient. FDA therefore believes it is useful and supportive of the agency's drug safety mandates to encourage the submission of such data in the pilot program.

(2) Concerning the comment that there is no scientifically valid and reliable method for measuring the extent to which pharmaceutical proprietary names might contribute to the risk of medication errors, FDA agrees that medication errors can be caused by any number of system failures or other contributing factors at any one or more stages in the medication use system, and that medication errors may be the result of multiple causes, many of which are not easily controllable. However, proprietary product names have been widely recognized as one important contributing source of medication errors, and one that is amenable to control. In the U.S. healthcare system, healthcare practitioners rely on a product's name as the critical identifier of the appropriate therapy in a market of thousands of products. Although review of proprietary names will not eliminate all medication errors, it can help reduce the risk of such errors by identifying and eliminating a contributing factor prior to drug approval. The Institute of Medicine (IOM) has repeatedly recognized that medication use errors may occur due to sound-alike or look-alike names, unclear labels, or poorly designed packaging and are pivotal causes of these system-wide problems (*To Err is Human—Building a Safer Health System* (2000) and *Preventing Medication Errors* (2006)). (See section II.A. of the concept paper for a brief summary of pertinent IOM conclusions). In 2007 Congress responded to these IOM findings, and as part of the reauthorization of PDUFA IV, mandated FDA's collection and use of user fees for, among other things, the review of drug applications and drug safety activities, in support of which FDA committed to meet performance goals, several of which highlighted the importance of considering proprietary names as a potential source of medication errors. These PDUFA IV goals, communicated to Congress, include FDA's commitment to implement this pilot program as one measure to help reduce medication errors related to look-alike and sound-alike

proprietary names.

FDA has acknowledged in three public meetings on proprietary drug review (held in June 2003, December 2003, and June 2008) that there is no gold standard for testing proprietary drug product names to assess the risk of medication error. At the public technical meeting held in June 2008, topics included subsequent review of developments in the science and practice of proprietary name analysis since the 2003 meetings, the strength of evidence for the current approaches to name review for prescription and nonprescription products, and in the absence of a gold standard, the elements of best practices in testing. At the June 2008 public meeting, all of the proposed evaluation methods were judged by individual experts participating in the public meeting to be complementary and were considered to offer value in the name testing process. As discussed in section IV of the concept paper, in the absence of a gold standard, FDA emphasizes that the best approach has proved to be the use of a combination of tests to evaluate name appropriateness. The concept paper contains FDA's current thinking on the logistics and name testing and evaluation under the pilot program. However, docket number FDA 2008-N-0281 remains open for comment during the pendency of the pilot program and FDA invites comments on human factors testing. In addition, after accruing two years of experience with pilot program submissions, including reviewing applicants' name analyses that use alternative methodologies, FDA is committed to publish draft guidance on best test practices for proprietary name review following public consultation with industry, academia, and others from the general public. Thus, the pilot program, in which participants are free to propose and provide results of alternate methodologies for name assessment, is in part intended to help inform potential future program

modifications and changes in information collected to help prevent medication error.

(3) Concerning the comment that some of the databases listed in the concept paper have limited value because of redundancy with the collective content of the remaining databases, and because they are not amenable to automated searching or have more limited automated searching capabilities than others, FDA understands that there may be some overlap across some of the databases and/or some limitation to automated search capabilities. However, as discussed in section IV.A.3. of the concept paper, the majority of names with similarity to the proposed proprietary name can be identified through database searches, and a variety of publicly available databases and resources containing product names can be used to identify similar names. FDA itself uses databases, the Internet, and other printed and electronic drug product resources to search for orthographic and phonological name similarities. The concept paper recommends that applicants search a variety of sources and, at a minimum, search the publicly available databases listed in Appendix A of the concept paper "Computerized Resources" because these databases are ones that FDA itself uses and considers the information in these references useful screening tools if properly searched. If a name appears in more than one database, it is acceptable to list the name once and list the sources along with the identified name. In addition, in most cases, the computerized resources listed in Appendix A are publicly available, including the POCA software (see FDA's notice of availability, 74 FR 7450 (Feb. 17, 2009). As part of the pilot program, FDA encourages sponsors to identify any new databases or those databases which are more amenable to automated searching.

9. <u>Remuneration of Respondents</u>

FDA has not provided and has no intention to provide any payment or gift to respondents under these requirements.

10. Assurance of Confidentiality

Confidentiality of the information submitted under this information collection is protected under 21 CFR 314.430 and under 21 CFR part 20. The unauthorized use or disclosure of trade secrets required in applications is specifically prohibited under Section 310(j) of the Act.

11. Questions of a Sensitive Nature

There are no questions of a sensitive nature.

12. Estimates of Annualized Hour Burden

The information collection that will result from the voluntary pilot program, as described in the concept paper, consists of the following:

(1) Applicants should contact FDA to register and indicate the approximate date of their proprietary name submission, as described in the concept paper and as will be described in more detail when FDA announces OMB's approval and the specific information on participating in the pilot program.

(2) Applicants should contact the appropriate FDA center 120 days prior to the intended date of the proposed proprietary name submission to discuss the specific details of the planned submission. Applicants should communicate with the Director in the Division of Medication Error Prevention and Analysis in the Office of Surveillance and Epidemiology in the Center for

Drug Evaluation and Research, or the Branch Chief at the Advertising and Promotion Labeling Branch of the Division of Case Management in the Office of Compliance and Biologics Quality in the Center for Biologics Evaluation and Research, concerning any questions about their proposed submissions. For prescription products, applicants should inform the appropriate center at the 120-day pre-submission discussion if they plan to use alternative or additional methods to evaluate the safety of their proposed proprietary name. For nonprescription products, sponsors should discuss with FDA different protocols that could be used for their specific drug products prior to the submission of the proprietary name.

(3) Applicants should submit two separate sets of product name-related information to enable parallel reviews by FDA: (a) A comprehensive evaluation of the proposed proprietary name including the information and data listed in Appendix B ("Proposed Template For A Pilot Program Submission") of the concept paper; and (b) the proprietary name information that they would ordinarily submit under FDA's current practice. (Note: The proprietary name information ordinarily submitted under FDA's current practice is not included in the estimates in Table 1 of this document because this information collection is already approved under OMB Control Numbers 0910-0001 and 0910-0338).

(4) After review of the proprietary name submissions, and if FDA informs the applicant that the proposed first-choice proprietary name is unacceptable, the applicant should confirm in writing that it would like its originally submitted second-choice name reviewed, or the applicant should submit an alternative second-choice name along with the information described in the concept paper. At that time, FDA will begin review of the second-choice name. If an applicant has submitted a complete proprietary name analysis for the second-choice name, the responsible

center will use discretion to determine whether to review the applicant's analysis in addition to conducting its own analysis using the traditional approach. Although FDA would ideally review the applicant's completed proprietary name analysis for the second-choice name, factors such as staffing and timelines will be used in making this determination.

FDA estimates the burden of this collection of information in Table 1. The "hours per response" is for all of the submissions and notifications to FDA described under paragraphs numbered 1 through 4 above, and is based on information provided by industry as well as FDA's familiarity with the time required for this information collection.

Table 1 -- Estimated Annual Reporting Burden

	Number of Respondents	Number of Responses per Respondent	Total Annual Responses	Hours Per Response	Total Hours
Pilot Project Proprietary Name Review	20	1	20	480	9,600
Registration	25	1	25	.5	12.5
				Total	9612.5

13. <u>Estimates of Annualized Cost Burden to Respondents</u>

FDA estimates an average pharmaceutical industry loaded wage rate of $74.00 per hour for preparing and submitting the information collection under 21 CFR 314. Multiplied times the total hour burden estimated above, the total cost burden to respondents is $ 710,400.

14. Estimates of Annualized Cost Burden to the Government

FDA estimates the cost to the Federal Government is $3,332.

15. Changes in Burden

This is a new collection.

16. Time Schedule, Publication and Analysis Plans

FDA does not intend to publish tabulated results of these information collection requirements.

17. Exemption for Display of Expiration Date

All forms associated with this collection will bear the OMB approval date.

18. Certifications

There are no certifications required.