# Prescription Drug User Fee Act (PDUFA) IV Drug Safety Five-Year Plan

## 2008-2012

2009 Update of Activities

**June 2010**

# PDUFA IV FIVE-YEAR PLAN — 2009 UPDATE ON ACTIVITIES IN SUPPORT OF COMMITMENTS FOR ENHANCEMENT AND MODERNIZATION OF THE DRUG SAFETY SYSTEM

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## INTRODUCTION

The Prescription Drug User Fee Act (PDUFA), first enacted in 1992, provides authority for FDA to collect fees from industry that support the FDA drug evaluation process while maintaining excellence and innovation in drug product review. Reauthorized for the fourth time under The Food and Drug Administration Amendments Act in 2008 (PDUFA IV), PDUFA has seen a progression of performance commitments designed to speed drug development while optimizing FDA's high standards for safety, effectiveness, and product quality.

Title I of PDUFA IV called for a Drug Safety Five-Year Plan that would establish FDA strategies for meeting designated commitments for enhancing and modernizing the agency's drug safety system. That plan, completed in December 2008, detailed strategies for improving the agency's scientific, technical, and administrative expertise in monitoring medical product safety.[1]

During negotiations with regulated industry, FDA established a number of post-marketing drug safety performance goals, described in the PDUFA Reauthorization Performance Goals and Procedures, Fiscal Years 2008 through 2012 ("Goals Letter") in Section VIII (Enhancement and Modernization of the FDA Drug Safety System) and Section IX (Review of Proprietary Names to Reduce Medication Errors).[2]

The complete text of Section VIII and Section IX is included below. Each commitment is referenced (hyperlinked) to the location in the Update that describes accomplishments and progress made against that commitment.

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[1] Prescription Drug User Fee Act (PDUFA) IV Drug Safety Five-Year Plan, 2008-2012, available at: http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM119244.pdf

[2] Complete text of PDUFA Reauthorization Performance Goals and Procedures, Fiscal Years 2008 through 2012, available at: http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm119243.htm

**Section VIII (Enhancement and Modernization of the FDA Drug Safety System)**

**A.1 The FDA will develop and periodically update (not less than annually) the Five-Year Plan describing activities that will lead to enhancing and modernizing FDA's drug safety activities/system. Activities described in the plan will include:**

***a) Assessment of current and new methodologies to maximize the public health benefit associated with collecting adverse event information at various points during the product lifecycle***

***b) With input from academia, industry, and others from the general public, identification of epidemiology best practices and developing guidance(s) describing these practices***

***c) Expanding CBER/CDER's database acquisition and use for the purposes of targeted post-marketing surveillance and epidemiology***

***d) Developing and validating risk management and risk communication tools, including assessing the effectiveness of risk management plan agreements and developing, implementing, and evaluating mechanisms for public communications about the benefits and risks of drugs and biological products***

***e) Improving post-market IT systems (e.g., FAERS, safety tracking systems, and opportunities for linked data management)***

***f) Enhancing and improving communication and coordination between the Office of Surveillance and Epidemiology (OSE) and the Office of New Drugs (OND) in CDER and the Office of Biostatistics and Epidemiology (OBE) and the pre-market product review Offices in CBER, including activities to assess the impact and value of routinely including post-market review staff on pre-market review teams***

**Section IX (Review of Proprietary Names to Reduce Medication Errors)**

***To enhance patient safety, FDA will utilize user fees to implement various measures to reduce medication errors related to look-alike and sound-alike proprietary names and such factors as unclear label abbreviations, acronyms, dose designations, and error prone label and packaging design.***

# PDUFA IV FIVE-YEAR PLAN — 2009 UPDATE

## Section VIII (Enhancement and Modernization of the FDA Drug Safety System)

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*Commitment (Section VIII, A.1)*
Develop and periodically update (not less than annually) a Five-Year Plan describing activities that will lead to enhancing and modernizing FDA's drug safety activities and systems

*Background*
FDA published a draft of the Five-Year Plan in March 2008, solicited public comments, made revisions and, in December 2008, published the final version, "Prescription Drug User Fee Act (PDUFA) IV Drug Safety Five-Year Plan 2008-2012."[1]

*2009 Accomplishment*
This document is the first annual assessment, describing progress on PDUFA IV drug safety commitments through the end of FY 2009.

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*Commitment (Section VIII, A.1.a)*
Assessment of current and new methodologies to maximize the public health benefit associated with collecting adverse event information at various points during the product lifecycle

*Background*
The Five-Year Plan committed to publication, by the end of FY 2008, of a Request for Proposals (RFP) for research on how to maximize the benefit of collecting spontaneous adverse event reports information. This research would assist the agency in better understanding and optimizing public health benefits associated with collecting and reporting adverse events occurring throughout the life cycle of a drug product.

To initiate this process, FDA held a public workshop on January 29, 2008, "Maximizing the Public Health Benefit of Adverse Event Collection Throughout a Product's Marketed Life Cycle." The Workshop solicited perspectives from stakeholders and other interested parties toward development of key questions that would inform a RFP.

Based on workshop and internal input, FDA issued a Request for Information (RFI) to determine which contract research organizations would be both interested in and have demonstrated capabilities to conduct research on the Agency's adverse event

surveillance. The RFI was issued on April 29, 2008. Responses were received by May 18, 2008.

*2009 Accomplishments*
After receiving and reviewing RFIs, an RFP was issued on July 17, 2009. Following review of proposals, a contract was awarded on September 18, 2009 to Pharmaceutical Product Development, Inc. (PPD). PPD's formal evaluation of the value and contribution of FDA's adverse event surveillance system to safety-related regulatory actions is now underway. PPD's analysis will inform FDA's development of new surveillance system applications as the agency optimizes its larger pharmacovigilance efforts.

Completion of this work is anticipated in FY 2011.

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*Commitment (Section VIII, A.1.b)*
With input from academia, industry, and the general public, identification of epidemiology best practices and developing guidance(s) describing these practices

*Background*
FDA uses epidemiologic data in interpreting adverse event "signals"—incoming information suggesting potential risk related to use of a drug product. These signals, relayed through the Adverse Event Reporting System (AERS), are assessed in the context of epidemiologic evaluation tools to determine validity (strength) and severity, and to quantify and characterize related drug safety risks.

The Epidemiology Best Practices and Guidance Document Work Group is a collaboration of the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER). A public workshop, "Developing Guidance on Conducting Scientifically Sound Pharmacoepidemiologic Safety Studies Using Large Electronic Healthcare Data Sets," was held on May 7, 2008, to provide input for the Work Group's recommendations.

*2009 Accomplishments*
The CDER/CBER Work Group reviewed input from the workshop and subsequent comments received from academia, industry, and the public. These comments were considered in draft guidance development, underway throughout 2009. Publication of this draft guidance in the Federal Register is anticipated before the end of 2010. CDER/CBER will then review and consider all public comments and hold internal meetings before revising and submitting a Final Guidance for clearance. An approved Guidance is expected on or before Sept. 30, 2011.

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*Commitment (Section VIII, A.1.c)*
Expanding CBER/CDER's database acquisition and use for the purposes of targeted post-marketing surveillance and epidemiology

*Background*
Expanded access to additional healthcare databases is central to improving FDA's epidemiological assets and implementation of best practices. Ongoing initiatives to expand database access are facilitated through partnerships within the federal government as well as collaborations with non-governmental organizations, industry, academia, and the United Kingdom's drug regulatory agency, the Medicines and Healthcare products Regulatory Agency (MHRA).

These initiatives actively assist FDA in acquiring and expanding data sources, building capacities for assessment of large datasets, instituting near-real time surveillance of adverse events, and refining agency abilities to target specific areas of drug product safety signaling and potential regulatory concerns.

FDA is also supporting these initiatives with an increased investment in human capital, including more training for existing staff and hiring of additional staff qualified to use newly acquired data resources.

Accomplishments in 2009 as detailed below include specific projects and initiatives that involve new database acquisition, development of existing database opportunities, as well as utilization of data resources researching specific questions or hypotheses.

*2009 Accomplishments*

***CDER Programs with Federal Partners***

<u>Centers for Medicare & Medicaid Services (CMS)</u>

- An in-depth study (The Fluoroquinolones and Acute Achilles Tendon Rupture Risk Study) is evaluating links between fluoroquinolone antibiotic use, Achilles tendon rupture, and long-term sequelae in the elderly.
- Three of four feasibility studies have led to initiation of in-depth studies:
    - Fracture risk, all-cause mortality, and cardiac arrhythmias with the use of propoxyphene and other analgesics
    - Potential interactions between concurrent use of two anti-diabetic drugs (rosiglitazone and pioglitazone) and fibrates (cholesterol-reducing drugs) and the risk of heart attack, stroke, and death in elderly patients with type 2 diabetes. Completion of data analysis is expected by the third quarter of FY 2010.
    - A study of exenatide compared to sitagliptin (different types of drugs that are both indicated for the treatment of type 2 diabetes) and the risk of

severe acute pancreatitis in the elderly. Completion of data analysis is expected by the fourth quarter of FY 2010.

Agency for Healthcare Research and Quality (AHRQ)

- Four collaborative studies are underway:
  - A comparative assessment of the safety of antipsychotic agents.
  - Tissue necrosis factor (TNF) blockers (agents used to treat inflammatory conditions) and multiple safety outcomes.
  - Patterns of acetaminophen use and knowledge of safety issues.
  - Pediatric inpatient drug use data and feasibility of making national projections.

Veterans Health Administration (VHA)

- Four studies (one of which includes the Department of Defense (DoD) as a third collaborator):
  - A study of HMG-CoA reductase inhibitor (statins) use and risk of amyotrophic lateral sclerosis (ALS) has received institutional review board (IRB) approval and is now launched.
  - Antipsychotic use and risk of mortality.
  - Antipsychotic use and differential risks of tardive dyskinesia (abnormal movements).
  - Varenicline (a drug used as a smoking cessation aid) and the risk of serious psychiatric disorders (done in partnership with FDA, VHA and DoD). VHA IRB approval for this study has been obtained. DoD IRB review is underway, as are DoD approval processes for medical record verification.

Department of Defense (DoD)

- Software enhancement for drug safety signal identification and confirmation via epidemiologic studies. Work continued throughout 2009 on the development of software to conduct automated epidemiologic analyses and studies, including integration of laboratory and radiological procedures and vital sign data. It is anticipated that two more FDA/DoD studies will be implemented during FY 2010, as needed.

Centers for Disease Control and Prevention (CDC)

- Under an interagency agreement, FDA provided funds to CDC to develop a user-friendly query tool for National Electronic Injury Surveillance System Cooperative Adverse Drug Event Surveillance (NEISS-CADES), an emergency medicine database, for more efficient use by CDER's Office of Surveillance and Epidemiology (OSE) safety evaluators and epidemiologists.
- Selected review and data collection projects using NEISS or NEISS-CADES in 2009 include intravenous iron and allergic reactions, accidental ingestion of opioids by children, and acetaminophen-related emergency department visits. Data from

the last study were presented at a Joint Meeting of the Drug Safety and Risk Management and Anesthetic and Life Support Drugs Advisory Committees on June 29, 2009.[3]

### *CDER Programs with Private Collaborators*[4]

These collaborations support ongoing studies that bring FDA greater access to large pharmacoepidemiologic databases, including data on drug use, patient outcomes, special populations, and comparative data on in-hospital drug use:

- A multi-site study of drugs used to treat attention deficit/hyperactivity disorder (ADHD) and possible associated risks for serious cardiovascular outcomes (sudden cardiac death, heart attack, or stroke) in children. This study was initiated by FDA in collaboration with AHRQ; private collaborators were engaged as additional funding was allocated to include outcomes in adult populations. Study completion is expected in the fall of 2010. (FDA collaboration with Vanderbilt University, Ingenix Inc., Kaiser Foundation Research Institute, and the HMO Research Network.)
- Two studies on oral bisphosphonate use: (1) bisphosphonates and associated risk of atrial fibrillation (AF), and (2) investigation into the prevalence of and risk factors for osteonecrosis of the jaw among users of bisphosphonates. Estimated completion of AF study is spring or summer of 2010, followed by development of a manuscript and subsequent publication in the peer-reviewed medical literature. The bisphosphonate/osteonecrosis study report was in press as of September 2009. (FDA collaboration with Kaiser.)
- Data collection completed for a multi-site study of newer combined hormonal contraceptive products to examine their risk for blood clot-related events such as sudden death, heart attack, pulmonary embolism and deep vein thrombosis. (FDA collaboration with Kaiser and Vanderbilt.)
- Three feasibility studies in a multi-site program entitled the Medication Exposure in Pregnancy Risk Evaluation Program (MEPREP) were underway in FY 2009 to initiate data linkages for studies of drugs used during pregnancy and potential adverse outcomes in the newborn. These data linkages can facilitate the rapid launch of multiple studies as potential safety signals emerge. Feasibility work will continue through September 2010. (FDA collaboration with HMORN, Vanderbilt, and Kaiser.)

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[3] Presentation slides available at: http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/UCM171579.pdf

[4] Ingenix, Inc., Kaiser Foundation Research Institute, Vanderbilt University, HMO Research Network (HMORN)

*General Practice Research Database (GPRD)*
The GPRD is the world's largest computerized medical records database, with data on more than 3 million patients actively participating in the U.K. national healthcare system. The GPRD provides population-based data on drug use, safety signals, and health outcomes that supports evidence-based regulatory decision-making. GPRD is in active use by both CDER and CBER researchers in both Center-specific and collaborative epidemiology and surveillance studies, including:

- maternal exposure to antidepressant drugs and Persistent Pulmonary Hypertension in the Newborn (PPHN)
- anti-diabetic agents and the risk of cancer
- novel approaches for validation of PPHN cases in the GPRD

Further CBER surveillance studies of adverse events after use of biologics will be developed and executed in the next year using the GPRD.

The GPRD also speaks to another PDUFA commitment (to improve post-market IT systems and opportunities for linked data management); see further discussion of FDA initiatives under that topic below.

***CBER Ongoing Initiatives***

*The Flu Vaccine Safety Project*. A collaboration with CMS to use Medicare data for active surveillance of influenza vaccine safety, CBER developed methods to perform rapid rate-based monitoring of adverse events among millions of vaccinees. This work focuses specifically on surveillance for serious events such as Guillain-Barre-Syndrome. The methods have been successfully implemented during the 2009-2010 influenza season to monitor H1N1 and seasonal influenza vaccines.

*CBER/CDC Vaccine Safety Datalink Inter-Agency Agreement*. CBER's Office of Biostatistics and Epidemiology (OBE) drafted an inter-agency agreement with CDC for collaboration on the Vaccine Safety Datalink (VSD) for near-real time surveillance of vaccine adverse events.

The VSD monitors immunization safety and serves as an informational and research resource for rare and serious post-immunization events. FDA joins the VSD's existing collaboration between CDC's Immunization Safety Office and eight managed care organizations (MCOs) throughout the United States. The VSD includes a linked database that uses data sources at each MCO.

Throughout 2009:

- FDA assigned a VSD liaison and alternates who participated in regular conference calls providing updates and preliminary findings on VSD rapid-cycle analyses (RCA) projects, including post-marketing surveillance of the human papillomavirus (HPV) vaccine, active surveillance for pandemic H1N1 influenza

vaccine (and seasonal influenza vaccine), as well as other projects involving VSD RCA analyses. FDA has also provided timely updates from its other collaborative projects (e.g., with CMS, DoD, and the VA) on vaccine safety surveillance for the pandemic H1N1 influenza vaccine.

- FDA staff collaborated with CDC and VSD investigators in decisions regarding outcomes for pandemic H1N1 vaccine during the 2009-2010 influenza season, and incorporated these outcomes into analyses being performed by CDC and VSD investigators in the military population.
- Clinical reviewers from the FDA's Office of Vaccine Research and Review (OVRR) serve as experts on specific vaccines and are consulted when needed.
- CBER assigned OBE medical officers to specific vaccine products where they serve as consultants in developing RCA projects. Additionally, staff within the OBE's Analytic Epidemiology Branch was involved in the initial development of national and international RCA projects examining adverse outcomes associated with the pandemic H1N1 influenza vaccine.
- CBER staff worked with CDC in determining priorities for specific RCA projects, including evaluation of the safety of the pandemic H1N1 influenza vaccine, the HPV vaccine, the measles-mumps-rubella-varicella (MMRV) vaccine, pneumococcal conjugate vaccine (PCV13), and Zostavax (varicella zoster vaccine).
- In the course of clinical trials and post-marketing surveillance throughout 2009, CBER clinical reviewers and medical officers provided guidance on regulatory issues surrounding particular vaccines.

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*Commitment (Section VIII, A.1. d)*
Developing and validating risk management and risk communication tools, including assessing the effectiveness of risk management plan agreements and developing, implementing, and evaluating mechanisms for public communications about the benefits and risks of drugs and biological products

*Commitment (Section VIII, A.1.f)*
Enhancing and improving communication and coordination between the Office of Surveillance and Epidemiology (OSE) and the Office of New Drugs (OND) in CDER and the Office of Biostatistics and Epidemiology (OBE) and the pre-market product review Offices in CBER, including activities to assess the impact and value of routinely including post-market review staff on pre-market review teams

*Background*
During FY 2008, FDA committed to the development of a plan to identify, with input from academia, industry, and the public, risk management tools and programs for evaluation purposes, and to conduct assessments of Risk Minimization Action Plans (RiskMAPS) and current risk management and risk communication tools.

*2009 Accomplishments*

- The ***Risk Communication Advisory Committee*** (RCAC) reviewed and evaluated public communication programs and strategies concerning risks and benefits of FDA-regulated products, and advised the agency on matters related to public awareness of drug safety issues. The RCAC conducted three drug safety-related meetings in 2009. Online links to summaries of results and RCAC recommendations follow each meeting description.

    - Discussion of different types of prescription drug information currently available to patients, February 26-27: http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/RiskCommunicationAdvisoryCommittee/UCM152593.pdf

    - Discussion of the FDA Draft Strategic Plan for Risk Communication and risk communication research needs, April 30-May 1: http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/RiskCommunicationAdvisoryCommittee/UCM190625.pdf

    - Discussion of strategies and programs designed to communicate with the public regarding risks and benefits of FDA-regulated products so as to facilitate optimal use of these products, November 12-13: http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/RiskCommunicationAdvisoryCommittee/UCM199226.pdf

- A two-day public meeting to obtain input from a wide range of stakeholders on issues and challenges associated with the development and implementation of risk evaluation and mitigation strategies (REMS) for drugs and biological products was planned during 2009. This meeting is scheduled for July 27-28, 2010. In addition to obtaining input about the REMS program and its impact, this meeting will gather additional input on a draft guidance issued on September 30, 2009 entitled, "Format and Content of Proposed Risk Evaluation and Mitigation Strategies (REMS), REMS Assessments, and Proposed REMS Modifications." FDA will carefully consider the information it obtains from this meeting in its implementation of the REMS program and in the development of the final guidance and future guidance documents.

- OSE, OND, and OBE in CBER will continue their collaboration with regularly scheduled safety reviews. This collaboration also serves to meet the Plan commitment (Section VIII, A.1.f) to enhance communication and coordination between these offices, including activities that assess the impact and value of including post-market review staff on pre-market review teams.

*Commitment (Section VIII, A.1.e)*
Improving post-market IT systems (e.g., FAERS, safety tracking systems, and opportunities for linked data management)

*Background*
Per commitments outlined in the Five-Year Plan, FDA will establish or enhance standards-based information technology (IT) systems to support the agency's capacity to obtain and analyze post-market drug safety data, manage emerging drug safety information, enhance adverse event reporting system and surveillance tools, and generally improve IT infrastructure to support access and analyses of externally-linked databases and workflow tracking systems.

FDA continued work throughout 2009 on development of an integrated electronic system for receiving, processing, disseminating, and evaluating adverse event reports and other safety information for all FDA-regulated products.

*2009 Accomplishments*

***FDA Adverse Event Reporting System (FAERS)***
The goal of FAERS is to improve quality, usability and efficiency of the passive (voluntary) reporting of a drug's adverse events (AEs). Standard data entry screens for paper and telephone reports, and the use of a more robust and expanded product dictionary and standard terminologies will improve both the quality and completeness of reported AEs. FAERS will perform initial evaluation of AEs based on multi-Center business rules, including CDER, CBER, and CDRH. This will facilitate the process of bringing events to the appropriate analysts' attention sooner, as well as allowing search and association of events using any combination of search criteria. This new repository will enable more efficient and systematic analysis of tens of thousands of safety reports to identify important safety risks.

The first FAERs prototype has been delivered, including support for CDER and CBER, and limited support for CDRH. Frequent incremental releases, culminating in a full production release for CDER and CBER, will occur over the next 12-18 months.

***Document Archiving Reporting and Regulatory Tracking System (DARRTS)***
The goal of DARRTS is to provide users with a fully integrated system combining tracking of incoming submissions, outgoing communications and document generation for all Investigational New Drug Applications, New Drug Applications, Abbreviated New Drug Applications, and Biologics License Applications. DARRTS is a web-based system providing flexible capabilities that meet CDER's current business processes as determined by legal and regulatory requirements.

Trackable issues include significant safety issues that have the potential to lead to:

- Withdrawal of an approved drug from the market
- Withdrawal of an approved indication
- Limitations on use of a drug or drug product in a specific population or subpopulation in the post-market setting
- Changes to the warnings, precautions, or contraindication sections of the labeling (including the addition of a boxed warning to the label)
- The establishment or modification of a risk evaluation and mitigation strategy (REMS)
- The establishment of or changes to the proprietary name, container label, labeling or packaging, to reduce the likelihood of medication errors
- Addition or modification of a Medication Guide or other required Patient Package Insert that addresses a safety issue
- Requiring a manufacturer or product sponsor to conduct a post-market clinical trial or an observational epidemiological study

Issues that are tracked in a DARRTS Safety Issue application:

- Are identified by OSE from their internal work of monitoring AERS and other sources of post-marketing adverse event data
- Are identified by OND (or submitted to them by a sponsor) and require the input of an organization outside of the OND division and its co-locators (i.e., OSE, another OND division, another FDA Center, the participants of a regulatory briefing) for its evaluation
- Have been identified and evaluated during a development program and the approval letter requires a REMS to manage this safety issue in the post-market period
- Have been identified and evaluated during a development program and the approval letter establishes a post-market requirement (PMR) of an observational epidemiological study or clinical trial to evaluate the safety issue further that is conducted by the sponsor

The DARRTS Safety Community of Interest (COI) was established in June 2009 to Implement functional changes and improved processes for managing and tracking safety issues in DARRTS.

DARRTS release 3.0 rollout in July 2009 allowed users to create connections between safety issues and related NDAs and ANDAs. Additional categories of different communications were included to enhance tracking of public notification of safety issues.

The role of Safety Regulatory Project Manager was added to DARRTS in 2009, and enhancements were made to properties for the Safety Application.

Activities and actions planned for 2010 include:

- Launch of the DARRTS COI Newsletter in June 2010, which will communicate DARRTS enhancements in support of CDER safety initiatives
- Enhancements to streamline creation of Tracked Safety Issues
- New safety reports delivered to users on a weekly basis

***General Practice Research Database (GPRD)***

The GPRD is also discussed in relation to meeting Commitment A.1.c above (expansion of database acquisition). The GPRD is a longitudinal electronic medical record database that, among other uses, can be employed for epidemiological analysis of drug safety questions. New IT infrastructure has been established to support studies underway by facilitating access to GPRD data and enhancing system performance, which permits use of the data by more FDA analysts.

***FDA Phonetic and Orthographic Computer Analysis (POCA) System: Automated Method of Identifying Potential Look-Alike and Sound-Alike Proprietary and Established Names***

The POCA System is an IT application relevant to post-market safety concerns. Look-alike, sound-alike proprietary names (also known as trade or brand names) of medicines is one of the most common reasons for medication errors and inappropriate dosing of medicine. FDA developed a computerized method to determine orthographic (spelling) or phonetic (sound) similarities between proposed proprietary drug names that might increase risks of confusion and errors. The POCA system is composed of two applications, *POCA Search* and *Rx Studies*. Under PDUFA IV, FDA committed to making the POCA source code available to public parties for further development. POCA disks and documentation are now available on request. The FR notice of availability of the source code and supporting technical documentation was published in the Federal Register on February 17, 2009.[5] The POCA system is described in greater detail below in relation to Section IX, Review of Proposed Proprietary Names of Medicines to Reduce Medication Errors.

[5] 74 FR 7450

**Section IX (Review of Proposed Proprietary names of Medicines to Reduce Medication Errors)**

As part of the Five-Year Plan, the agency made commitments to increase consistent and timely review of proposed new drug proprietary names to prevent name confusion. These included: timely review goals for proposed new proprietary names submitted during the Investigational New Drug (IND), New Drug Application (NDA), and Biologic License Application (BLA) processes; develop new guidance documents for industry as well as internal operating procedures; and conduct a pilot program to evaluate applicants' test methods and data generated for submission to FDA.

*Timely review goals for proposed new trade names submitted during the new drug or biologics application processes*. In FY 2009 the agency committed to review 50% of proprietary name submissions filed during the Investigational New Drug (IND) phase *within 180 days* of receipt of submission, and review 50% of proprietary name submissions filed during the New Drug Application (NDA) or Biologic License Application (BLA) phase *within 90 days*. As of September 30, 2009, the agency was on target to meet these goals.

*Develop new guidance documents for industry as well as internal operating procedures*. Among new guidance documents, the agency committed to developing guidance to industry regarding contents of a complete submission package for the evaluation of proprietary names, as well as Manual of Policy and Procedure (CDER MAPP) / Standard Operating Procedures and Policies (CBER SOPP) guidance documents to ensure the agency's internal processes are consistent with meeting proprietary name goals.

- A CDER/CBER working group completed a draft guidance, *Contents of a Complete Submission for the Evaluation of Proprietary Names*, published on November 24, 2008. Public comment was solicited and received, and the final guidance published in February 2010.[6]
- A working group with representatives from OSE, OND, the Office of Business Process Support, and CBER drafted separate internal procedures for submission of proprietary names submitted with INDs and NDAs/BLAs. The CBER SOPP published in November 2008. The CDER MAPP published in September 2009.

In support of a 2010 goal to publish a draft guidance on best practices for naming, labeling, and packaging drugs and biologics to reduce medication errors, progress was made throughout 2009 toward a public workshop that will initiate dialogue among regulators, researchers, the pharmaceutical industry, health care organizations, health care professionals, and others from the general public about the design of drug and

[6] Guidance for Industry, Contents of a Complete Submission for the Evaluation of Proprietary Names, http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM075068.pdf

therapeutic biologic container labels, carton labeling, product packaging, and practices to develop proprietary names to reduce medication errors. Input from this workshop will be used to develop draft guidance for industry on practices for naming, labeling, and packaging of drugs and biologics to reduce the potential for medication errors. (This workshop will be held on June 24-25, 2010.[7])

*Conduct a pilot program to evaluate new proprietary name review paradigm*. As part of its PDUFA IV negotiated commitments, FDA committed to developing and implementing a pilot program to enable pharmaceutical firms participating in the program to evaluate proposed proprietary names and submit the data generated from those evaluations to the FDA for review. FDA held a public workshop on June 5-6, 2008, to discuss and plan for a pilot program to begin by the end of FY 2009. That workshop supported development of a concept paper that was published in the *Federal Register* on October 7, 2008.[8]

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[7] 75 FR 18514

[8] http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072229.pdf