PDUFA IV Information Technology Assessment

Fiscal Year 2009

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Executive Summary

The Prescription Drug User Fee Act (PDUFA) IV program has enabled the Food and Drug Administration (FDA) to make significant progress toward achieving the long-term FDA Information Technology (IT) goal of a fully electronic submission and review environment for of all regulatory documents and data. The FDA is working diligently, and making progress, to develop a strong environment for successful coordination with the regulated industry and other stakeholders, as we move to more efficient communication and processing through IT systems.

FDA is obligated to conduct an annual assessment of progress against the IT plan and publish a summary of the assessment within two months after the close of each fiscal year. This document provides a current-state IT Assessment against the PDUFA IV IT Plan, published in May 2008.

During this assessment period, FDA continues to demonstrate that relevant programs are on target and in line with PDUFA goals. This past year resulted in the resolution of many near-term planning activities and IT strategic investment decisions, including the design of two new data centers, organizational adjustments to centralize support and structure, and specific regulation and project progress. Most accomplishments contribute directly to the establishment of an IT foundation that continues to enhance the electronic environment.

From an organizational perspective, FDA has made substantial changes in both the Office of Information Management and the Bioinformatics Board. In doing so, FDA has centralized technology and related processes around business. Furthermore, the Data Standards Council continues to make progress on standards development as well as assist with the implementation of data standards, both internally and externally.

From a tactical perspective, progress has advanced in the projects as well. A substantial part of DARRTS as well as the eCTD (electronic common technical document) system, Substance Registration System (SRS), Electronic Labeling, Registration and Listing (eLIST), are operating as designed. These systems incorporate the standards, technology and automation, validation, data sharing, and dissemination capabilities as envisioned. The Gateway has also demonstrated capabilities to sustain a common entryway, and upgrades are planned to support the higher volume anticipated for both pre- and postmarket electronic submissions.

Finally, future legislative and regulatory changes may ultimately require FDA to address project priorities. FDA will continue to coordinate with the regulated industry as electronic processes and projects evolve.

1.0 Purpose

The purpose of this document is to provide a current-state IT assessment against the PDUFA IV IT Plan, published in May 2008. FDA is obligated to conduct an annual assessment of progress against the IT plan and publish a summary of the assessment within two months after the close of each fiscal year. This document is located on the FDA PDUFA Website within the PDUFA IT Plans section at the following link:

http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm183308.htm

The PDUFA IV IT Plan documented CDER and CBER strategic system goals to realize an automated, standards-based environment. The IT assessment provides a specific assessment against those goals, provides current metrics that substantiate those goals, and offers associated insights into the progress and challenges identified in Fiscal Year 2009. This document will also factor into PDUFA IV IT Plan revisions.

Appendix A offers additional descriptions and details of the projects referenced in this document. Each project was highlighted in the original PDUFA IT plan. As expected, some projects may have completed significant work and may no longer require project level tracking. In addition, other ideas may have evolved into projects and will be added to the PDUFA IV IT Plan.

2.0 PDUFA IV IT Vision

FDA's vision is to drive the current IT environment to a target environment that will provide improved program performance, interoperability, improved use of resources, accelerated system implementation, simplified investment decisions, and reduced IT diversity and complexity. Through these initiatives, FDA is working toward specific progress for major supporting components including:

- Business modernization and transformation
- A target architecture
- Guidance, policy and regulation
- Data standards

2.1 Business Modernization and Transformation

FDA's ability to support the development of secure, automated, and consistent systems has improved with recent organizational changes. These changes include the organization and implementation of the Bioinformatics Board (BiB) as

well as the consolidation of IT organizations. With the centralization of activities, supporting governance programs have progressed to streamline decision making, coordinate implementation of systems, and establish processes to leverage different parts of the organization on new development efforts.

The consistency of development, implementation, and maintenance of new information systems supports program efficiency and effectiveness and will enable emphasis on the consistency of interactions with regulated parties and other external stakeholders.

2.1.1 Specific Progress

The BiB continues to oversee the activities related to business automation planning, acquisition, and implementation decisions throughout FDA under a strategic framework for IT modernization established by the Commissioner and implemented by the FDA Management Council. The eleven (11) enterprise projects the BiB has approved are following consistent system development methodologies, leveraging standards where appropriate, and being implemented and maintained in a standard environment.

The BiB continues to mature the governance structure. In the past year, significant attention has been focused on increased staffing to sufficiently support Agency-wide programs. Also, considerable progress was made on establishing common operational processes – both to prioritize new projects and operate efficiently around the current portfolio. The Agency continues to evaluate opportunities for improving the governance model.

Concurrently, on October 1, 2008, the Office of Information Management (OIM) officially began operating as a centralize entity, centralizing information technology resources for the Agency. In its first year, this consolidation has been challenging and several measures have been taken to assess the appropriate workforce skills, identify duplicative and newly needed positions, and assess appropriate staffing levels to enable functioning in an enterprise environment. Additionally, new processes and policies were implemented to formulate a common IT organization that should result in effective and consistent communication and processes across the divisions.

2.2 Target Architecture

In FY09, significant groundwork was laid to address the needs for target architecture to serve as a goal, both physically and logically. The newly centralized OIM enables a more coordinated approach in support of a target architecture and systems development through several divisions within the organization.

2.2.1 Enterprise Architecture

The purpose of OIM's Enterprise Architecture (EA) team is to effectively plan a course for achieving the FDA's IT target architecture to support BiB and other Agency projects. EA implements a business-driven plan that aligns the associated IT drivers including FDA's business architecture, data architecture, applications architecture, technical architecture, security architecture, and standards profile.

2.2.1.1 Specific Progress

Since the creation of the FDA's Strategic Action Plan (SAP) the EA team has worked to define an approach to realize the IT target architecture. This architecture is based on the Federal Segment Architecture Methodology.

The activities consist of the following work:

- Development of the initial EA segment for FDA's post market surveillance work
- Development of an initial target state architecture
- Development of standardized tools to evaluate IT investments based on their alignment to the FDA's SAP and organizational performance outcome measures
- Identification of an initial set of common components to be used to reduce redundancy in development and spend across projects with common needs
- Development of an integrated roadmap for visualizing and planning functional capabilities

The EA team also initiated the IT Investment Management (ITIM) process to evaluate all of FDA's IT investments so that they advance towards the target architecture. This framework defines standardized evaluation and prioritization processes for IT investments, products and services. The ITIM process aligns to related Federal and HHS defined processes such as the Capital Planning and Investment Control (CPIC), the Federal Enterprise Architecture (FEA), and the HHS Enterprise Architecture Repository (HEAR).

New IT requests are also reviewed for EIM alignment, prioritized, and reviewed through a standardized assessment. Major initiatives are added to the end-state solution architecture and the EIM roadmap to document and monitor the project as it is defined and implemented. As the scope and needs of the Agency change, these projects will influence the EIM vision through its Strategic Capabilities and Building Blocks so that the vision is continually updated as well, to reflect changes within FDA.

Additional information on the SAP is available at the following link:

http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/StrategicActionPlan/default.htm

2.2.2 Systems Development

OIM's Division of Systems (DoS) has both benefited greatly and encountered the most challenges from the IT restructuring process. As noted, several system development teams were consolidated, requiring considerable change and consensus to operate effectively and in coordination, all while continuing the support of critical systems and operations. Several refinements have occurred to ensure this part of the organization succeeds so that system development does in fact result in coordinated and efficient systems to support increasingly complicated business requirements.

In FY2009, foundational activities were explored and implemented to achieve a more harmonious system development team that could leverage best practices, Commercial-Off-The-Shelf (COTS), and reusable components rather than the traditional development of custom applications. This has proven extremely challenging, yet has enabled the teams to improve development coordination and standards, maintain needed legacy system knowledge, and leverage technologies.

2.2.2.1 Specific Progress

Through these organizational restructuring efforts, OIM has worked through challenges, bringing the different IT offices together to support not only enterprise initiatives, but also maintain support for the current Center and Office systems. Initial work is underway to evaluate the various standards, technologies, and platforms with the goal of defining a target system framework.

DoS also created standard operating processes to prioritize the development of common functional IT components. As part of the common components framework initiatives, a repository was developed to house and make available common components code, documents, and associated implementation guidance for systems to develop in a consistent way.

Additionally, as part of the migration process to the new data centers, work is focused on documenting commonly processed components and testing target architecture assumptions. Among many aspects, common services include centralized documentation, policy, standard operating procedures, technology, components, configuration management, security, governance, and issue tracking.

2.2.3 e-Platform

FDA committed to exploring issues related to the concept and feasibility of a public/private partnership in collaborating with the creation and management of an electronic platform to facilitate the exchange of clinical research information

and other regulatory product information (i.e., the data normally collected during the course of a clinical trial, as well as the submission, receipt, and management of regulatory product information).

2.2.3.1 Specific Progress

During 2009, FDA completed an examination of the available information through literature review and stakeholder interviews to identify and characterize the needs of an e-Platform from both the perspectives of FDA, as well as industry and other stakeholders. The results of the review were summarized in a report entitled *Business Model for Partnerships to Develop and Implement an Electronic Data Exchange Project*. The FDA is currently reviewing the report's recommendations.

During 2009, FDA was working in collaboration with CRIX International on a version of the FIREBIRD application to test the e-platform concept. As of September 2009, CRIX is seeking a new development partner. The FIREBIRD project is on hold.

2.3 Guidance, Policy and Regulation

As part of the PDUFA IV strategy to move to a fully electronic submission and review environment, FDA is developing regulations and guidance to improve the consistency of submission processing, access to documents and data, and evaluation of submission information. FDA also continues to update technical specifications and IT-related guidance documents in support of an electronic environment.

2.3.1 Specific Progress

During this assessment period, the following IT guidance was published in final form:

- Providing Regulatory Submissions in Electronic Format–Drug Establishment Registration and Drug Listing (5/28/09)

This guidance was published to assist regulated parties in submitting registration and listing information in electronic format.

As of June 1, 2009, FDA no longer accepts drug registration and listing information in paper format without a waiver. This rule, in and of itself, decreases paper reviews and supplements the electronic requirements associated with Structured Product Labeling (SPL). FDA has worked diligently to ensure information, assistance, training, and vendor education is available and offers best practices to regulated parties to increase the success rate of electronic submissions.

2.4 Data Standards: Clinical/Nonclinical Data Standards Initiative

In the PDUFA IV IT Plan, FDA committed to a long-term goal of an automated standards-based information technology environment for the exchange, review, and management of information supporting the process for the review of human drug applications throughout the product lifecycle. Development and implementation of data standards are integral to the efficient and effective drug products review, ultimately improving public health and safety.

FDA currently receives massive amounts of study data submitted using disparate structures, content formats, and terminologies. FDA is in the process of standardizing using HL7v3 exchange standards for submission data. These HL7 exchange standards provide a consistent way to exchange information between computer systems in various organizations and help ensure that the sending and the receiving systems both understand unambiguously what information is being exchanged (semantic interoperability). It is expected that implementation of HL7v3 exchange standards will provide a more robust data exchange model for research observations and provide better integration with clinical observations exchanged among electronic health record (EHR) systems that are relevant for clinical research.

2.4.1 Specific Progress

Data exchange standards include Study Data, SPL, Product Stability Data, Annotated ECG Waveform data, and Regulated Product Submission standards.

- FDA continues to work with stakeholders to coordinate the implementation of standards through public meetings, pilot testing, external training and tutorial sessions. FDA, other HHS agencies and groups continue to be involved in the development and early adoption of standards based on the HL7 v3 Reference Information Model (RIM) for many purposes including the EHR.

- FDA developed the HL7 Data Exchange Service for receiving, validating, and storing submitted information using the HL7 v3 based data exchange standards. The HL7 Data Exchange Service is an automated system that processes data files based on the HL7 v3 standard. After undergoing an automated validation, the data is loaded into a data repository based on the HL7 v3 Reference Information Model. The data then can be loaded from the HL7 Data Exchange Service into data management systems such as the Janus database where it can be used to create the various datasets required for review. The HL7 Data Exchange Service is already being used for processing HL7 v3 SPL files. The information stored in the HL7 Data Exchange Service could include data from any process that uses the HL7 v3 standards such as study data and post market surveillance.

- FDA has developed a series of exchange standards for study data. The Subject Data standard is for the exchange of the data collected during a study. It is based on the HL7 v3 Continuity of Care Document (HL7 CCD), which is designated as an electronic health record (EHR) format for exchanging healthcare information for patients. To ensure that the same standard is used for research studies, FDA added the concept of a study subject such as healthy volunteers, laboratory animals, parts of the body (e.g., a blood vessel) and even groups of animals (e.g., a heard of cows).

- FDA has also added two additional HL7 v3 data exchange formats for study data describing the design of a research study (Study Design) and subjects participating in a study (Study Participation), respectively. This is in addition to the standard for exchanging adverse effects occurring during the course of a study (Individual Case Safety Reports).

- FDA successfully completed initial testing of the Study Data standards using the HL7 Data Exchange Service. Example files were generated and validated against the HL7 schema. These files were then loaded using the HL7 Model Interchange Format (MIF) files into a RIM derived database. Sample reports taking data from the study data, ICSR and/or SPL files were generated. Additional testing is ongoing.
- FDA continues to work toward being capable of receiving and processing data structured in accordance with the HL7 v3 Study Data standards (Study Design, Study Participation and Subject Data) by 2013. FDA is working on a transition plan for moving from current process of receiving study data using SAS XPORT files to using HL7 v3 Study Data XML files including a period where both HL7 v3 Study Data XML files and SAS XPORT files will be accepted.
- FDA is also working on development of data analysis standards. CDER is actively working with CDISC to refine and expand the Study Data Tabulation Model (SDTM) and ADaM to provide datasets that facilitate the analysis of clinical safety and efficacy data. CBER is conducting a pilot to determine the suitability of SDTM for use in their review process.
    - SPL is implemented for receiving drug labeling, drug establishment registration, and drug product listing information. The product model in this standard is being harmonized with product models in other standards as part of the Common Product Model project in HL7.
    - Work toward implementing Product Stability Data continues. The Agency is working on tools and documentation for creating the files for submission as well as tools for using the files for review.
    - Work on the next release of Regulated Product Submission which includes two-way communications, continues.

In addition to data exchange standards, FDA continues work on terminology and code set standards. Initiatives include the National Drug Code system and the

Substance Registration System. Terminology and code sets are also identified for individual data exchange standards. The FDA completed the development of code sets for the established pharmacological class, mechanism of action, pharmacological effect, and structural class for all approved drugs.

FDA also collaborates with other organizations on terminology standards. FDA has been working with Dun and Bradstreet on using the D-U-N-S Number as an identifier for business entities. FDA collaborates with the National Cancer Institute Enterprise Vocabulary Service to maintain many terminology and code sets. FDA also collaborates with the National Library of Medicine in maintaining RxNorm medication terminology by supplying SPL files provided by the companies through the automated drug listing process.

3.0 PDUFA Projects

This section is divided into two sub-sections; premarket activities and postmarket activities. This section describes the current IT environment at a high level and shows FDA's progress through projects that directly relate to these lines of business.

3.1 Premarket Activities

The PDUFA IV IT objective is to apply technology to the FDA regulatory review process in the most efficient and effective way possible to make sure reviewers have the information and tools they need to make more informed and timely decisions. This strategy supports FDA's vision of a fully electronic submission and review environment for all regulatory documents and data and the ultimate elimination of paper-based submissions.

An automated review environment comprises many components. Although many projects contribute to the success of an automated review environment, PDUFA focuses on projects that offer high impact for automated tracking, validation, document management, and data sharing. Projects include:

- Information and Computing Technologies for the 21st Century (ICT21)
- The Document Archiving, Reporting and Regulatory Tracking System (DARRTS)
- Regulated Product Submission (RPS)
- The FDA Gateway
- The common Electronic Document Room (cEDR)
- The electronic Common Technical Document (eCTD) Review System
- Modular Data Exchange for Labeling Submissions

- Janus

3.1.1 ICT21

Information and Computing Technologies for the 21st Century (ICT21) project provides an Agency-wide computing environment for the 21st century that is efficient, effective, scalable, flexible, reliable, and meets FDA's business requirements. The successful delivery of these objectives will enable FDA to create a secure infrastructure, with improved service, response times, and overall performance.

FDA has successfully designed and prepared for two new data centers, one for development and test and another for production data. In conjunction with the development of the new data centers, OIM has also defined and implemented a centralized security program, allowing for better oversight of both the networks and environments.

Currently, FDA is in the process of moving systems to the new data centers. This process started in October 2009 and will take several months to complete.

3.1.2 DARRTS – Document Archiving, Reporting & Regulatory Tracking System

The DARRTS Version 3.0 release on July 27, 2009, added the ability to manage, track and report on new drug applications, abbreviated new drug applications, pediatrics, meetings, post-marketing requirements and commitments, and FDA Amendments Act (FDAAA) provisions. Integrating this new capability with the current tracking and reporting of investigational new drugs, safety issues, emergency use authorizations, and master files will ensure that the program objectives remain on track.

Overall, this program has successfully implemented automated tracking and management capabilities to:

- Reduce the number of systems used to manage, track, receive and report
- Increase automation
- Implement workflow management
- Improve accuracy and timeliness of data
- Build and easily change the business rules to support increased regulatory changes and complexity

The most recent release retired 17 legacy systems. The next DARRTS release incorporates Division of Drug Marketing, Advertising, and Communications (DDMAC) submissions and is anticipated to be implemented by June 2010. This implementation will retire an additional two legacy systems. Also, FDA is

initiating the planning phase for DARRTS release 4.0, which includes CDER and CBER biologics license applications (BLAs).

3.1.3 Regulated Product Submission (RPS)

The RPS is a Health Level Seven (HL7) standard to facilitate the processing and review of regulated product information. RPS was selected to be used for the next major version of the eCTD. The FDA plans on using the RPS standard to meet the PDUFA goals of cross-referencing previously submitted electronic materials through standardized automated links and to enable two-way communication between sponsors and FDA by incorporating these requirements into release 2.0 of the RPS message.

During this assessment period, the RPS release 2.0 project has completed the Health Level 7 (HL7) message development phase. The next step is a HL7 Draft Standard for Trial Use (DSTU) ballot in January 2010. The DSTU phase of the project will enable FDA and regulated industry to test the RPS functionality to ensure that its meets eCTD submission requirements and the PDUFA IV requirements. FDA plans to use the first half of 2010 to prepare for DSTU testing and to use the second half of 2010 to conduct internal and industry testing. The DSTU objective is to test the functionality of the RPS message. The DSTU testing will not include all the necessary processing modifications required to fully implement two-way communication. This will be done during the next phase of the project.

3.1.4 FDA Gateway

The FDA Gateway currently provides the technical capability for two-way exchange of information between FDA and the public; however, it is not content driven and is currently only sending acknowledgements for SPL submissions. The vision for the ultimate level of service would extend to include additional content validation related to the application submission structure.

3.1.5 cEDR - Common Electronic Document Room

FDA's cEDR will establish an Agency-wide, standards-based EDR, as a single repository for all FDA-regulated product documents. A common EDR will give FDA the capability to streamline the submission process, provide reviewers additional collaboration capabilities, and provide reviewers secure access to and the ability to search for information across traditional organizational boundaries.

During the current assessment period, the cEDR project completed requirements gathering, including draft use cases, taxonomy, alternatives analysis and research on content management tools and an overall concept of operation. Requirements are under final review.

3.1.6 eCTD – Electronic Common Technical Document Review System

FDA's eCTD Review System allows reviewers to review submissions submitted in the International Conference on Harmonisation (ICH) eCTD format. In addition, the system provides submission validation and review capabilities to users throughout the Agency.

FDA is working with its vendor to resolve validator issues encountered during the implementation of the upgraded validation program, including the ability to track eCTD submission errors. A revised implementation date has not yet been finalized.

3.1.7 Modular Data Exchange for Labeling Submissions

In FY2008, progress was made to understand the modular data exchange requirements as they relate to labeling submissions. In FY2009, ELIPS was retired as SPL submissions were incorporated into the eLIST system. In light of the implementation and operations of SPL and eLIST, the modular data exchange functionality is under evaluation.

3.1.8 Janus

The Janus initiative has entered the planning phases and will provide insights into the feasibility and impact of implementing data standards related to clinical and nonclinical data. This is appropriate timing due to the activities associated with establishing a suitable infrastructure that will enable the proper management and analyses of these data sets.

The Janus initiative will involve the:

- Development of standards-based scientific data exchange networks needed to ensure the quality, safety, and efficacy of medical and consumer products as defined by FDA's regulatory mandate.
- Establishment of an enterprise-wide data architecture and standards that facilitates the integration of data from a wide variety of internal and external sources to create large-scale data-sharing infrastructures to support clinical trials and postmarket safety, registration activities, and manufacturing life-cycle activities.
- Creation of scientific data repositories that support the acquisition, validation, integration, and extraction of data from the increasingly large and complex datasets received by the Agency.
- Use of enhanced analytical, mathematical, visualization, and other computational tools and techniques that enable reviewers to search, model, and analyze data to conduct better safety and efficacy analyses.

3.2 Postmarket Activities

The modernized postmarket safety related IT systems will ensure the best collection, evaluation, and management of the vast quantity of safety data that is received by FDA. Improvement in the infrastructure will support access to and the analyses of externally linked databases, as well as a system to replace FDA's current Adverse Event Reporting Systems (AERS) and safety signal detection and management tools.

- The MedWatch Plus initiative will create a common FDA portal for electronic receipt of adverse event reports from the public and will provide direct electronic transfer of these reports to an agency-wide repository and data analysis tools.
- The Sentinel System will enable FDA to query multiple, existing data sources, such as electronic health record systems and medical claims databases, for information about medical products.

3.2.1 MedWatchPlus/FAERS

The MedWatchPlus/FAERS initiative will enable FDA to improve the timeliness, accuracy, and usability of its product safety surveillance data by significantly reducing delays and errors associated with manual data entry and coding of paper reports. It will provide:

- A user-friendly internet portal for anyone to report an adverse event resulting from a FDA-regulated product
- An Agency-wide repository of adverse event reports (FAERS) with integrated safety signal management and analytical tools

3.2.1.1 Specific Progress

In this assessment period, many activities related to the definition of adverse event data, which includes data intake, validation, analysis, and dissemination activities. Additionally, the following accomplishments give FDA a solid foundation to begin work on a comprehensive adverse event driven system:

- Established Joint FDA/NIH Internet/Portal Working Group for integration and implementation of the Federal Safety Reporting Portal
- Completed the safety reporting portal to deliver a Rational Questionnaire (RQ) Prototype
- Developed a new service-level agreement with NIH to guide the cooperative effort between NIH and FDA in the development of the Rational Questionnaire.
- Selected Oracle AERS for COTS implementation; initial configuration focused on CDER and CBER.

3.2.2 Sentinel

The Sentinel initiative is drawing on existing electronic healthcare data from multiple sources to actively monitor the safety of medical products continuously and in real-time. The goal of the initiative is to build and implement a new active surveillance system that will ultimately be used to monitor all FDA-regulated products. Sentinel will enable FDA to actively query diverse automated healthcare data holders—like electronic health record systems, administrative and insurance claims databases, and registries—to evaluate possible medical product safety issues quickly and securely.

Establishing a long-term, sustainable system raises many questions of great public interest, including issues about governance, privacy, data standards and public availability of results. Establishment of the Sentinel System and the Sentinel System architecture raises a number of administrative, organizational, procedural, and methodological challenges. For this reason, Sentinel's development will require considerable stakeholder participation.

The FDA continues to make progress by fostering broad public forums to explore the difficulties of developing such a system. Meetings have been conducted with a variety of stakeholders and studies contracts have been granted to examine a range of subjects that will affect Sentinel. In addition, pilot projects are under way that will contribute toward answering some of the many technical and policy issues that must still be addressed.

During this assessment period, FDA awarded several contracts as well as published several reports to explore options, feasibility of data sources and their associated constraints, as well as the development of specific methods of surveillance.

4.0 Performance Metrics

The PDUFA metrics measure progress and achievement of objectives throughout PDUFA IV in alignment with the PDUFA IV performance goals and the PDUFA IT Plan

4.1 PDUFA Spending

To better understand the progress towards a common PDUFA IT environment, FDA is reporting on the percentage of annual spending on maintenance of legacy systems and enterprise IT systems. Enterprise IT systems are categorized as common across organizational divisions participating in the process for the review of human drug and biologic applications. Legacy IT systems are those that are in use in a single center. Enterprise IT systems are categorized as those systems that are common across organizational offices and divisions participating in the process for the review of human drug and biologic

applications. Examples of Enterprise IT systems are software applications, tools, and other products that both CDER and CBER use or plan to use to receive, track, and review PDUFA submissions. Enterprise architecture activities and IT infrastructure consolidation activities are incorporated into this category of spending.

Figure 1: 2008 and 2009 New vs. Legacy Spending, shows that spending on legacy programs has increased since 2008. The increase is a direct result of maintenance activities to ensure successful migration of legacy systems into the new data center and implementing the necessary reporting mandates to support FDAAA legislation. IT spending on legacy systems should decrease significantly in 2010 due to additional consolidation, operations in new data centers, and progress on the enterprise programs.

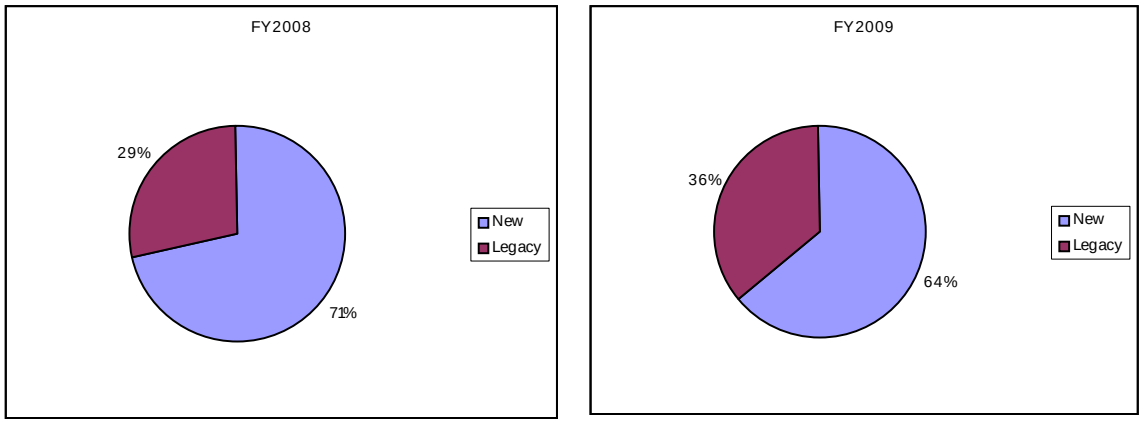

Figure 1: 2008 and 2009 New vs. Legacy Spending

4.2 Electronic Submission Adoption

Increasing the number and percentage of IND, NDA, and BLA submissions received in valid electronic format is a goal that is supported by the FDA and industry stakeholders. To support the assessment of this goal, the following information will be tracked and reported at least annually:

Figure 2: Electronic Submissions Categorized by Application provides the total number of eCTD electronic submissions categorized by type of submission.

Application	No. of Applications	No. of Sequences
IND	2,081	47,688
NDA	1,443	21,791
ANDA	2,514	11,359
BLA	138	6,396
MF	394	1,020
FDA Internal	386	698
Total	6,967	88,952

Figure 2: Electronic Submissions Categorized by Application

Figure 3: FDA eCTD Submissions in Electronic Format, shows the total number of submissions in valid electronic format in compliance with FDA standards

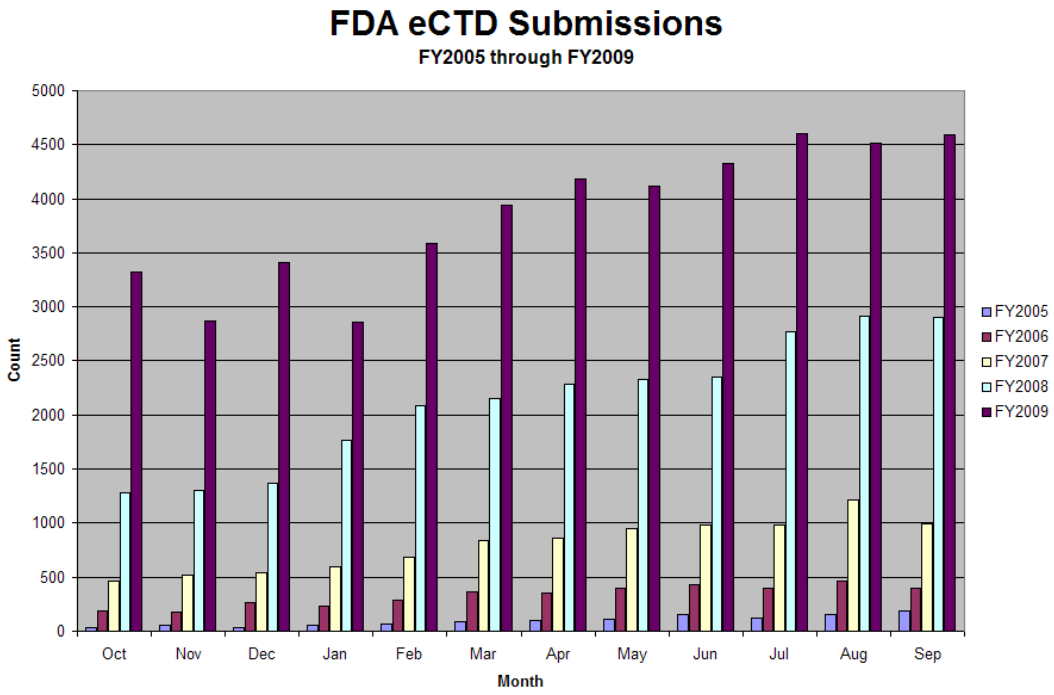

Figure 3: FDA eCTD Submissions in Electronic Format

Figure 4: Submissions Through Secure Electronic Single Point of Entry presents the total number of submissions received through the secure electronic single point of entry (i.e. Gateway) versus other methods.

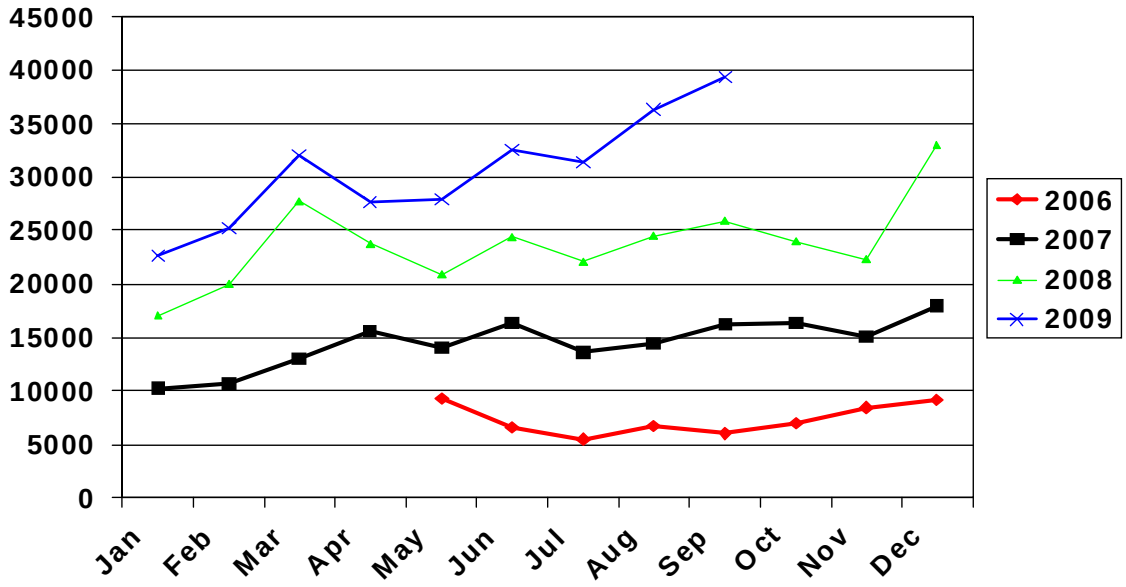

Figure 4: Submissions Through Secure Electronic Single Point of Entry

Figure 5: Gateway Accounts, provides counts for the current number of Gateway trading partners at FDA.

Production and Pre-Production Stats			
	Production		Pre-Production
	on July 09	Today	Today
# of accounts			
AS2	**55**	**59**	**107**
WT	**799**	**1252**	**2167**
Total	854	1311	2274
# of companies			
AS2	**42**	**43**	**69**
WT	**282**	**517**	**1082**
Total	242	560	1151
AS1	**0**	**0**	**0**

Figure 5: Gateway Accounts

Figure 6: Percentage of Submissions Received provides data to determine the total number of submissions received substantially on paper. Analysis suggests the following:

- The percentage of IND Originals in electronic and standardized format remained relatively stable, the number of amendments in electronic and standardized formats have nearly doubled.
- The percentage of new NDAs/supplements submitted electronically has remained relatively stable, the number submitted in eCTD format rose between 28% to 51%

	FY2008						FY2009				
	Total	Electronic	%	eCTD	%		Total	Electronic	%	eCTD	%
CDER IND	85617	13319	15.56%	12555	14.66%		86989	25387	29.18%	24770	28.47%
CBER IND	7026	1357	19.31%	771	10.97%		6502	2135	32.84%	1552	23.87%
TOTAL	**178260**	**27995**	**15.70%**	**25881**	**14.52%**		**180480**	**52909**	**29.32%**	**51092**	**28.31%**
CDER NDA	22290	11266	**50.54%**	7412	**33.25%**		22086	11535	**52.23%**	11129	**50.39%**
CBER NDA	34	0	0.00%	0	0.00%		150	4	2.67%	4	2.67%
TOTAL	**22324**	**11266**	**50.47%**	**7412**	**33.20%**		**22236**	**11539**	**51.89%**	**11133**	**50.07%**
CDER BLA	2171	902	41.55%	544	25.06%		2571	1887	73.40%	1721	66.94%
CBER BLA	11522	1473	12.78%	842	7.31%		11228	1818	16.19%	1104	9.83%
TOTAL	**13693**	**2375**	**17.34%**	**1386**	**10.12%**		**13799**	**3705**	**26.85%**	**2825**	**20.47%**
TOTAL	**214277**	**41636**	**19.43%**	**34679**	**16.18%**		**216515**	**68153**	**31.48%**	**65050**	**30.04%**

Figure 6: Percentage of Submissions Received

Figure 7: Invalid CDER Submissions in 2009, represents the number of invalid CDER submissions received in the calendar year 2009. Analysis suggests the following:

- Rejections represent an extremely small percentage of submissions
- Predominant reasons for rejection are duplicate submissions
- Standardization of submission format does not appear to be contributing to an increase in rejected submissions

Reason	IND	NDA	BLA
Broken or corrupted media received	6	5	0
Duplicate content received	2	3	0
Duplicate Core ID received	0	0	0
Duplicate sequence received	58	39	4
GS Validate high error	12	5	0
Invalid application or sequence	6	3	1
Mismatched application, sequence or type	13	12	7
No data received	20	11	12
Not in standard eCTD format	33	24	3
Sent to wrong center	20	6	7
Total	170	108	34

Figure 7: Invalid CDER Submissions in 2009

5.0 Appendix A: Project Level Status

The following table reflects the current status of the projects associated with the PDUFA IV IT Plan, published in May 2008.

This table was developed to assist in providing accurate tracking of the projects referenced in the PDUFA IIV IT Plan. The projects listed in this table were described in the IT Plan by category (i.e. Premarket, Postmarket, and Data Standards).

The table contains three columns. The first column lists the name of each project and a short description. The second column describes the projects' milestones noted in the PDUFA IT Plan. The last column reflects the status of each project, as of September 2009.

PDUFA IV IT Assessment
Project Status

Project Name and Description	*IT Plan Milestones*	*FY2009 Status*
e-Platform A common electronic platform for the exchange of clinical research data.	Finalize the MOU between FDA/NCI and CRIX International. Begin the FIREBIRD demonstration project.	• Finalizing the report of the business needs of the Agency and outside stakeholders for an e-Platform. A public version will be released CY Q1.
FIREBIRD A common electronic platform for the exchange of clinical research data.	Complete harmonized FDA requirements for CDER, CBER and CDRH. Functionality includes 1572 data extraction, inspection data entry, query and reporting capabilities, integration with Center application tracking systems, and data migration from existing clinical investigator and bioresearch monitoring systems. 3rd Quarter, 2008 Finalize the MOU Create a project team, define roles, and develop and project plan 4th Quarter, 2008 Design the pilot platform Review and finalize FDA requirements	• CRIX International, the company adapting NCI's FIREBIRD application to meet the needs of the pharmaceutical industry, is seeking a new development partner in order to continue work. As of September 2009, there has been no delivery of a fully functional application. We are discussing our options within the Agency and with NCI. D9This project is currently on hold.
Regulated Product Submission (RPS) RPS is a Health Level Seven (HL7) data exchange standard that will support improvements to the processing and review of regulated product information.	Implement/accept RPS submissions in the 2nd Quarter of 2008 for: SPL submissions to a paper NDA/BLA Electronic datasets to a paper IND/NDA/BLA Single investigator IND Target for addressing PDUFA requirments RPS DSTU Release 2 - HL7 ballot 2nd Quarter, 2009 Test RPS Release 2 submissions with completion of the testing targeted for 2nd Quarter, 2010 Develop PDUFA RPS Implementation Guide and modify standard (based on test results) with completion targeted for the 4th Quarter, 2010 Target for accepting RPS Release 2 submissions in the 2nd Quarter, 2011	• Completed RPS Release 2 message requirements and development. • The HL7 RPS Work Group is currently planning for the next release of the RPS message. RPS Release 3 will include ICH requirements not covered in the DSTU Release 2 ballot and will also include additional regional requirements. The HL7 RPS Release 3 project will start in early 2010. • The updated FDA schedule for implementation of the RPS Release 2 message is; January 2010 - RPS Release 2 Draft Standard for Trial Use (DSTU) ballot 2010 4th Quarter – Conduct industry testing 2011 3rd Quarter - Develop PDUFA RPS Implementation Guide 2012 1st Quarter - Conduct RPS2 production pilot 2012 3rd Quarter - RPS2 production **UPDATE:** In the PDUFA IV IT Plan (May 2008), FDA stated that CDER and CBER would start to accept RPS for the limited set of submissions in the RPS format. • SPL submissions to a paper NDA/BLA • Electronic datasets to a paper IND/NDA/BLA • Single investigation IND FDA has revised this strategy and is not planning to accept these submissions using the RPS exchange message,
Electronic Submissions Gateway (ESG) An FDA-wide solution that enables the secure submission of electronic regulatory submissions and has been in production since May 2006. ESGprovides the single point of entry for the receipt and processing of all PDUFA submissions.	As stated in the PDUFA IT Goals, the FDA will extend the capability of the secure single point of entry to include two-way transmission of regulatory correspondecnce. The FDA has had preliminary planning discussions on expanding the ESG functionality to meet this goal. The FDA does not plan on expanding the ESG functionality in this area in 2008. Depending on the progress garnered as well as the uptake by interested parties, the FDA could expand the ESG in several areas during 2008. Begin planning for testing of VAERS infrastructure capability. Begin limited testing in support of the use of the SPL standard version 4 for registration and listing.	• The ESG has currently received and processed over 235 submissions through the end of August 2009. We are receiving an average of 24,000 post-marketing safety reports monthly in CY 2009. • The number of new Industry ESG production WebTrader accounts in June and August equaled the total number of new Industry accounts in all of 2008. The driver for this increase is the Agency's electronic Registration and Listing program. The contract modification to support this effort was let on September 18, 2009. • As part of the Extranet Database Separation Project, the ESG recently received four new database servers-two production and two pre-production. This infrastructure configuration change will lead to greater system uptime for the ESG as a result of removing dependencies on shared hardware. the ESG and the FDA industry systems (FIS) Extranet has just completed the standing of a test and development area complete with network head. The new network head will be shared with the present pre-production environment. The production environment now utilizes a separate network head. • FDA/CDC ESG VAERS build is coming to completion. The FDA's portion of this project will be completed by October 16, 2009. The FDA has worked in concert with Industry and SRA staff on behalf of the CDC to develop and deliver the capability to receive and process fully electronic VAERS reports in ICSR format from our industry partners in a store and forward paradigm. We fully anticipate that this functionality will be officially released into production before the end of the CY 2009 in the form of a pilot with the big six vaccine manufacturers. • The FDA has been working with Axway staff in order to resolve the issues with their WebTrader software. Axway has put in place a dedicated team to address and resolve the FDA's software issues. We anticipate receiving version 5.5.2 – sp14 on October 23, 2009. If all goes well, the software will be in production by Thanksgiving.
eCTD Review System The FDA eCTD Review System was implemented in 2005, and allows reviewers to review submissions submitted I the ICH eCTDformat.	The FDA is currently testing the updated validation component and anticipates its implementation by the end of the 3rd Quarter, 2008. FDA is reviewing potential changes to the Module 1 specifications.	• FDA is working with its vendor to resolve validator issues encountered during the implementation of the upgraded validator. • A revised implementation date has not yet been finalized. • FDA is identifying changes to Module 1 to streamline the submission of information and provide greater support for the submission of advertising and promotional materials.
Workflow Tracking and Information Management System (DARRTS) A flexible, integrated, fully electronic workflow tracking and information management system to receive, log, track, assign, process, and manage official submissions with internal and external stakeholders.	Release 3.0 requirements completed application development, reports development and data migration underway. Release 3.0-1st Quarter, 2009 for all CDER NDAs and ANDAs. Release 3.x for CBER and CDER BLAs.	• Release 3 implemented successfully in July 2009 • Next Release incorporates DDMAC submissions into DARRTS (planned in Q2 CY2010) • Retired 17 legacy systems • Initiating the planning phase for DARRTS Release 4 • Retiring 6 legacy systems Includes CDER and CBER BLAs

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Project Status

Project Name and Description	*IT Plan Milestones*	*FY2009 Status*
Information and Computer Technologies for the 21st Century (ICT21) To provide an Agency-wide computing platform for the 21st Century that is scalable, flexible, and reliable and effectively and efficiently meets business	IDIQ contract will supply the data center design and strategy for Application migrations, award 4th Quarter, 2008. Data Center Design Complete 1st Quarter, 2009. Application Migration Wave one 2nd Quarter, 2009. Bioinformatics Pilots Started 2nd Quarter, 2009, Application Migration WAve two 1st Quarter, 2010, Application Migration Wave Three 2nd Quarter, 2011, Complete New Bioinformatics Platform in 2012.	• Production data center is ready and Authority To Operate is expected October 15, 2009 • White Oak data center engineered procured • Completed the placement of the servers and storage
Common Electronic Document Room (cEDR) cEDR will establish an Agency-wide standards based EDR as a single platform repository for all FDA-regulated product documents.	4th Quarter, 2008 Requirements, alternatives analysis, concept of operations Development and Testing of the Common EDR Functionality 3rd Quarter, 2009 Phase I Implementation	• Requirements Document and Requirements Matrix under final review and approval, to be completed in CYQ4/2009. • Completed demonstration Use Cases document. This is a narrative document that presents usage scenarios for the future system based on the defined requirements. • Draft taxonomy and common metadata elements are currently under review and refinement. Final version to be completed CYQ1/2010. • Concept of Operations and Alternatives Analysis to be completed CYQ1/2010.
Electronic Labeling Review System Receives and processes electronic labeling information through the Structured Product Label (SPL) standard format.	Continue with operation and maintenance. Evaluate incorporaton of SPL schema Release 4 into the software.	Functionality has been incorporated into eLIST and ELIPS has been retired.
Electronic Listing Expanded to provide for both registration and listing based on SPL schema release 4 and will provide the ability to automate drug registration and listing information and validation processes.	CRADA partner to deliver electronic registration and listing release 1 supporting SPL schema release 4 during 3rd Quarter, 2008. Electronic submission of registration and listing information required beginning June 1, 2009.	• Averaging over a hundred of submissions a day. • Includes both human and animal drugs and both OTC and prescription. • The automated system processes the submissions as designed. • Updates are sent for distribution daily. • Training sessions are held multiple times per week. • Electronic submission of registration and listing information required as of June 1, 2009.
Substance Registration System Purpose is to support health information technology initiatives by generating Unique Ingredient Identifiers (UNII) for substances in drugs, biologics, foods and devices.	Continue with operation and maintenance. Enhancements to the SRS over the next 6 months will allow release of synonyms in addition to preferred terms and Unique Ingredient Identifiers.	• SRS has been modified to allow 10 digit CAS registry numbers. Mixtures are now explicitly limited to 50 component substances. The UNII has been proposed as the allergen terminology/identity standard for allergens for the Electronic Health Record.
CDISC - HL7 Message Project The FDA plans to transition to HL7 exchange messages for submission of all study data. This initiative is based on the outcomes of the CDISC Content to HL7 Message Exploratory Project.	Message development is underway in HL7. Plan is to go to DSTU (draft standard for trial use) ballot at the end of 3rd Quarter of CY 2008 and to test the messages as part of the Janus phase 3 pilot (see Janus Initiative). Additional milestones: 3rd Quarter of CY2008 - HL7 DSTU Ballot 2008-2009 Testing 3rd Quarter CY2009 -HL7 Normative Ballot 2009-2012-FDA accepts both CDISC-HL7 SML and SAS transport files 2013 and Beyond-FDA accepts only CDISC-HL7 XML	• Study Participation and Study Design Messages passed the second round of draft standard for trial use (DSTU) in September 2009. • The Subject Data Specifications will be updated to reflect the changes (CY04). • Subject Data Message has also passed DSTU in September 2009. • FDA is proceeding with testing the messages. Testing plans will include testing with Industry. • The first phase of testing is completed. Examples for all study data standards including ICSR were created and successfully loaded into the RIM based database using the HL7 Data Exchange Services. These are the same services currently implemented in eLIST for SPL files. Additional testing ongoing prior to use in 2010. As stated in the Assessment, FDA intends to be capable of receiving study data in accordance with HL7v3 study messages by 2013. The FDA has not set a date for only receiving study data using HL7 messaging.
BRIDG Model A domain analysis model representing protocol-driven biomedical/clinical research.	BRIDG Release 2.0 is being released in April 2008. Release 2.0 includes: All semantic content from Release 1.1 plus new semantic content for adverse events and participant registration Full binding of all static attributes to HL7 V3 data types Candidate terminology/value sets for attributes with a Coded Descriptor (CD) data type Mapping from BRIDG to HL7 RIM Supporting BRIDG Model 'sub-domains' (e.g. cancer-specific semantics) using NCIs Clinical Trials Object Model The next release of BRIDG is expected in 4th Quarter, 2008 or 1st Quarter, 2009. It will include complete harmonization of Protocol Representation Version 1, which consists of Trial Design and Clinical Trial Registry. This release will support the CDISC-HL7 messages.	Project deferred
Clinical Data Interchange Standards Consortium (CDISC) SDTM Standard for the submission of human study data for Janus.	Message development is underway in HL7. Plan is to go to DSTU (draft standard for trial use) ballot at the end of 3rd Quarter of CY 2008 and to test the messages as part of the Janus phase 3 pilot (see Janus Initiative). Additional milestones: 3rd Quarter, 2008 2008-2009 Ballot Testing 3rd Quarter 2009 2009-2012 Ballot 2013 and Beyond FDA accepts only CDISC HL7 XML	• CDISC V3.1.2 SDTM Implementation Guide (SDTM-IG) is available. • The Study Data Specifications will be updated to reflect the changes (CY04). • CDER is determining if they need to clarify any ambiguities in the implementation guide. • CDER reviewers have indicated that they need analysis datasets in addition to SDTM datasets. • CBER is pilot testing SDTM. As stated in the Assessment, FDA intends to be capable of receiving study data in accordance with HL7v3 study messages by 2013. The FDA has not set a date for only receiving study data using HL7 messaging.

Project Name and Description	*IT Plan Milestones*	*FY2009 Status*
Standard for Exchange of Nonclinical Data (SEND) Pilot Implementation of the SDTM for animal studies.	Update the SEND implementation guide 2nd Quarter, 2008 Begin receiving SEND pilot submmissions 3rd Quarter, 2008	• SEND pilot (Phase II) continues the evaluation of SEND by CDER. • The SEND Implementation Guide (SENDIG) v3.0 Draft A and the SEND Controlled Terminology for v3.0 Draft A were released on March 14th, 2009 (http://www.cdisc.org/). • SENDIG 3.0 Draft A represents a significant realignment to the SDTM
Electronic Case Report From (eCRF) Pilot Obtain experience with the CDISC Operational Data Model (ODM) based CRFs.	Pilot is underway. Additional test ODM submissions expected in 3rd Quarter, 2008. ODM Style sheet will be modified based on comments from FDA and pilot participants.	• The eCRF/ODM pilot was replaced by the HL7 Study Data initiatives because of the progress in the HL7 standards development
Clinical Data Acquisition Standards Harmonization (CDISC CDASH) Clinical Data Acquisition Standards Harmonization	The CDASH consolidated final draft has been released for public comments. After the public review period of the consolidated final draft ends 14 May 2008, comments will be consolidated and addressed by the CDASH project team. Comments and responses will be posted on www.cdisc.org along with the final CDASH v1.0. The goal is to post the final CDASH version 1.0 by the end of 2nd Quarter, 2008.	• Set of "content standards" for a basic set of global data collection fields to support clinical research studies. • CDISC published Version 1.0 CDASH on Oct 2008 (available on CDISC website). • CDISC continues to collect feedback from early implementers. • Comments, responses and final version will be posted at http://www.cdisc.org.
Product Stability Data Standard Develop a method to provide stability data in a standard lectronic format so that it may be viewed as it appears on paper or electronic paper by regulatory agencies and Industry.	Release 2 HL7 ballot-3rd Quarter CY 2008 Implementation Guide HL7 ballot-3rd Quarter CY 2008 Implement Viewer - 2nd Quarter CY 2009 Accept in place of paper- 4th Quarter CY 2009	• Stability Style sheet procurement announcement made in August 2009. • 4th Quarter CY2009 - implement Style Sheet (not Viewer) • Scope includes development of a style sheet to accompany flat file to view the XML stability data file • 1st Quarter CY2010 - accept in place of paper
CDISC ADaM Analysis Data Model Provides a standard for transferring analysis datasets between sponsors and FDA.	No milestones noted on plan	• ADaM Team is on track to publish ADaM 2.1/ADaM IG 1.0 in December, 2009. • There will be a total of four ADaM trainings this year [at FDA] - three have occurred and the last one is scheduled for November 2009.
Janus Improve FDA management of structured scientific data through the creation of a standards-based infrastructure that supports the exchange and management of structured scientific data about the products that the FDA regulates.	Plan for and implement a Phase 3 pilot that includes extensions of the Janus logical data model and a service-oriented architecture designed to support the submission of HL7 messages and leveraging of NCI's Enterprise Vocabulary Service (EVS) to begin to address controlled vocabulary issues. Plan to publish FR notice announcing Janus Phase 3 Pilot Q3 2008 to engage interested stakeholders in future Janus development. Establish two-way data exchange between FDA and NCI using FDA's ESG. Have the CDISC-HL7 messages completed and tested within the Janus environment 2008-2009	• NCI and FDA are stilling working out the details of the contract • Project initiated at FDA
MedWatch Plus Will enable the FDA to improve the timelienss, accuracy, and usability of its product safety surveillance data by significantly reducing delays and errors associated with manual data entry and coding of paper reports.	Select FAERS COTS toolset Rollout CDER/CBER FAERS release Rollout CDRH/Office of Combination Products release Complete MedWatch Plus Portal and Core Processing components for both electronic and alternative (fax, telephone, paper) AE reports. Complete MedWatch Plus Rational Questionnaire Integrate MedWatch portal with FAERS.	• Established Joint FDA/NIH Internet/Portal Working Group for integration and implementation of the Federal Safety Reporting Portal • Completed the safety reporting portal to deliver an RQ Prototype • Developed new service level agreement with NIH to guide the cooperative effort between NIH and the FDA in the development of the Rational Questionnaire. • Oracle AERS was selected for COTS implementation, initial configuration focus on CDER and CBER. • Developed and implemented the Reportable Food Registry (RFR) to enable reporting of food-related adverse events in compliance with the Congressional FDAAA 1995 Act.
Sentinel System Long-term effort to create a national electronic system for monitoring FDA-regulated product safety.	Strengthen capability to draw data from sources like electronic health records and medical claims. Establish the abililty of the FDA to query other systems quickly and securely for relevant product safety information Establish methodologies to use Sentinel data to support epidemiology and other safety studies	• Report has been completed for Evaluation of Timeliness of Medical Update for Surveillance in Health Care Databases-IMS Government Solutions and is available in docket and website. • Report has been completed for Evaluating Potential Network Data Soruces for Blood and Tissue Product Safety Surveillance and Studies-Pragmatic Data and is available in docket and website. • A Request for Information was posted on February 20, 2009 to collect further information on sources to support development of scientific operations for Sentinel. A pre-solicitation synopsis was posted on May 15, 2009. A Request for Proposals was posted on June 19, 2009. Award is expected in September 2009. • Collaborations with CMS, DoD and VA have been expanded for evaluation of potential safety signals, to include rapid cycle analysis in the various data environments. Interagency Agreements to support this Mini-Sentinel pilot effort have been put in place. • The Agency has awarded a cooperative agreement that will facilitate discussions on topics related to developing and creating active medical product surveillance methods and system. This group will convene a broad range of stakeholders, to include those with relevant expertise, to explore and address methodological, data development, technical, and communication issues related to active medical product surveillance. The findings from these discussions will be communicated to a broad range of organizations and individuals that have the capability to use the information to further develop and create active medical product surveillance methods and systems. • The Agency has awarded a contract to conduct a legal evaluation of state statutes, regulations and practices in each of the 50 states in order to determine whether data sources may participate in the Sentinel Initiative and the conditions on that participation. It is noted that Federal regulations, including the HIPAA Privacy Rule constitutes a minimum for privacy protection, so states can enact more rigorous privacy protection if desired. The Agency is seeking a thorough evaluation of state statutes and regulations to determine whether those state laws impose any additional restrictions on the use or disclosure of health information beyond the federal law requirements discussed in the legal analysis already received by the Agency and if so, to set out what those additional restrictions entail. • The Agency has awarded a contract to identify, describe, and evaluate potential data sources and/or data environments