PRESCRIPTION DRUG USER FEE ACT (PDUFA II) INFORMATION MANAGEMENT FIVE YEAR PLAN

FY 2000 Revision

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1.0 BACKGROUND

The Prescription Drug User Fee Act of 1992 (PDUFA) provided FDA with increasing levels of resources for the review of human drug applications. That Act expired on September 30, 1997, but the FDA Modernization Act (FDAMA) of 1997 amended PDUFA and extended it through September 30, 2002 (PDUFA II). This extension will enable FDA to accomplish increasingly challenging goals over the next five years. PDUFA, as amended and extended by FDAMA, and with its new goals, is referred to as PDUFA II and its predecessor is now referred to as PDUFA I.

PDUFA II commits FDA to:

- substantially faster review of some applications;
- new goals for responding to industry requests for meetings, documenting outcomes of those meetings and for handling dispute resolutions; and
- the transition to electronic receipt and review of applications by 2002.

The new goals of PDUFA II are challenging, diverse, and resource intensive. Major components of the review process will be accelerated further. Many of the goals will require the development of technology standards and issuance of guidance documents. In addition, the development of infrastructure to provide the tools necessary to move to electronic application receipt and review will be essential.

The Center for Biologics Evaluation and Research (CBER), the Center for Drug Evaluation and Research (CDER), and the Office of Regulatory Affairs (ORA) have collaborated with the Chief Information Officer and the Office of Information Resources Management (OIRM) to develop an Agency-wide Information Management plan for investing PDUFA II information technology (IT) dollars in an Electronic Regulatory Submission and Review (ERSR) Program. This program and its component projects will support the transition from a largely paper-based regulatory submission and review environment to an electronic environment.

In 1998, the Agency published a PDUFA II Information Management Five-Year Plan that described the strategy for budgeting, managing and expending PDUFA II IT funds during the period FY 1998 to FY 2002. That initial document provided a conceptual view of the components within the ERSR Program. It described the purpose and activities within the PDUFA II ERSR Program, provided a milestone schedule for executing that program, and explained the procedures and policies for monitoring the progress of the program.

1.1 Purpose of this Document

This document provides an update to the planned activities within the ERSR Program. It reflects a project-oriented view of the ERSR program and presents 1) how projects support accomplishing the overall ERSR goal; 2) insight to near-term and ultimate project milestones; and 3) budgets for the ERSR projects. The document is revisited annually to refine scheduling and budgeting forecasts, factor in actual expenses of previous years, and incorporate additional projects as they are identified.

1.2 Document Organization

The PDUFA II Information Management Five-Year Plan (FY 2000 Revision) is organized as follows:

- Section 2.0 describes the PDUFA II goals supported by the establishment and implementation of the ERSR Program;
- Section 3.0 provides an overview of the PDUFA II ERSR Program and describes the strategy for meeting the program goals;
- Section 4.0 presents the projects within the ERSR Program, maps those projects to their respective ERSR subgoals, and presents milestones for project activities;
- Section 5.0 summarizes the overall program oversight processes for the ERSR program; and
- Section 6.0 provides a summary of the ERSR Program.
- Appendix A: ERSR Program
- Appendix B: Glossary of Acronyms

2.0 PDUFA II GOALS

The Agency's PDUFA II program provides funding to implement information technology initiatives that support the expedited approval of human drugs and biological products. PDUFA II goals require the Agency's transition from a largely paper-based regulatory submission and review environment to a new electronic paperless submission and review environment.

New performance goals require faster review times than the goals established and achieved with the original PDUFA legislation. These goals involve further accelerating over five years (FY 1998 through FY 2002) the review of submissions such as New Drug Applications (NDAs), Product License Applications (PLAs), Biologic License Applications (BLAs), efficacy supplements, and manufacturing supplements. Additionally, PDUFA II identified other performance goals in new areas such as responding to industry requests for meetings, providing industry with meeting minutes, and resolving disputes.

From an Information Technology perspective, however, the primary PDUFA performance goal states:

> "*The Agency shall develop and update its information management infrastructure to allow, by fiscal year 2002, the paperless receipt and processing of INDs and human drug applications, as defined in PDUFA, and related submissions.*"

FDA defines "paperless" as an environment with the requisite systems that will provide the capability and capacity for the receipt, review, archival, and tracking of electronic submissions. While PDUFA II specifies INDs and human drug applications, CBER and CDER are planning to accommodate additional application types.

The ERSR Program, therefore, represents the Agency's activities to transition to an environment that will accommodate paperless receipt and processing of submissions. This transition requires the Agency to fulfill four high-level objectives or subgoals:

- Establish standards for the format, content, and technical specifications for electronic submissions;
- Provide guidance for industry to follow in preparing electronic submissions;
- Design and implement systems to provide the capability and capacity for the receipt, review, and tracking of electronic submissions; and
- Update the technical and non-technical infrastructure to support an electronic review environment.

The following section presents the overall strategy for transitioning to a computing environment that will accommodate paperless receipt and processing of submissions.

3.0 ELECTRONIC REGULATORY SUBMISSION AND REVIEW (ERSR) PROGRAM STRATEGY

As mentioned in the previous section, the ERSR Program supports the transition from a largely paper-based regulatory submission and review environment to an electronic environment. The ERSR Program is comprised of a variety of projects, each of which is designed to satisfy a different part of the primary PDUFA IT goal. Additionally, various organizations are responsible for the successful implementation of the ERSR Program.

Roles and Responsibilities
The principal organizations benefiting from user fees are the Center for Biologics Evaluation and Research (CBER) and the Center for Drug Evaluation and Research (CDER). These organizations ultimately are responsible for establishing the capability and capacity to receive, process, and archive submissions electronically within their organizations. These Centers are responsible for addressing the needs of the Agency's Office of Regulatory Affairs (ORA) in accessing information necessary to conduct field inspection activities. ORA, in turn, is responsible for ensuring their field offices have the infrastructure needed to interface with CDER and CBER electronically where necessary. Finally, the Chief Information Officer (CIO) and the Office of Information Resources Management (OIRM) are responsible for ensuring that all PDUFA II IT investments support the Agency's common IT goals, fit into a common computing environment, and follow good IT management practices.

Approach
CDER and CBER's responsibilities in performing product safety and efficacy review activities are similar. However, the products for which CBER and CDER are responsible are very different. The differences in review requirements for handling these products are founded on both legislative and scientific bases. Both organizations are governed by different regulatory statutes and mandates that require different approaches to their respective review processes. Consequently, over time, CBER and CDER's organizational structures have evolved to the business rules and supporting processes specific to their mission and product requirements. For example, CDER's Office of Review Management is organized according to scientific discipline (e.g., Neuropharmacological, Cardio-Renal, Oncologic) and each NDA is addressed by each of the scientific discipline offices during the product review. CBER, however, is organized by product (e.g., Blood, Vaccines, Therapeutics) and the majority of the review is handled within the respective product office.

While internal business processes have evolved based on organizational culture and Center-specific re-engineering efforts, these rules and processes have been harmonized where there were similarities in functions and where there were cost efficiencies to be gained. An overarching goal of ERSR is to create a transparent interface between industry and the Agency. To this end, CBER and CDER are collaborating to develop common technology standards and information formats for electronic submissions. These standards are intended to enable industry to prepare "modular" submissions that can be sent to either Agency organization without significant reformatting.

The ERSR Program has been shared widely with industry since the mid-1990s via conferences and workshops sponsored by the Drug Information Association (DIA), collaboration with PhRMA's Regulatory Affairs Committee (RAC) and RAC's Electronic Regulatory Submissions (ERS) Working Group, participation in the International Conference on Harmonization (ICH) expert working groups, and presentations at industry trade meetings. Through this extensive collaboration within the Agency and with external parties, and as a result of subsequent voluntary pilots with regulated firms, the electronic submission of Case Report Tabulations (CRTs) and Case Report Forms (CRFs) in Portable Data Format

(PDF) was implemented without major problems[1]. This early accomplishment under the ERSR Program demonstrates a successful partnership between the Agency and the industry it regulates. This partnership represents the type of mutual cooperation between FDA and industry that will be key to achieving a paperless review by FY 2002.

Figure 1 provides a conceptual view of the ERSR Program. The explanation following Figure 1 presents the dependencies of the various portions of the Program and shows how they support the ERSR subgoals.

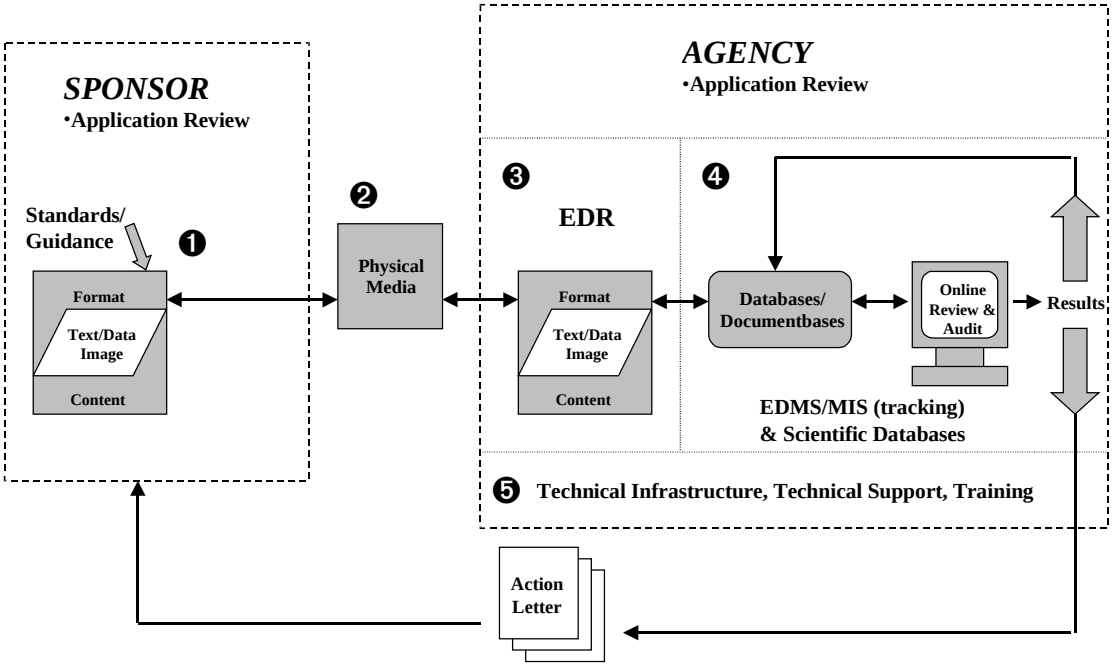


Figure 1

Establish standards (❶)
FDA participates in several standards-related projects to define the format and content of regulatory submissions. The Agency actively participates in activities of the International Conference on Harmonization (ICH), which is a science-driven initiative to curtail regulatory duplication by working towards a common worldwide drug and biologic registration package. These standards activities are essential for ensuring a consistent basis upon which to provide guidance to industry for electronic submissions. Additionally, the Agency must establish and implement standards for secure messaging and secure communications among its Centers, other regulatory authorities, and the regulated industry.

Provide submission guidance (❶)
Upon establishment of the standards, FDA provides written guidance for industry to follow in preparing electronic submissions. Guidance documents are posted in FDA's public docket. Industry training is provided at technical workshops and IT conferences hosted by organizations such as DIA. The development and completion of guidance documents serve

[1] CRTs and CRFs are paper-intensive portions of a new drug application. These parts often make up approximately two-thirds of the paper submitted with NDAs.

as the foundation for enabling regulated industry to exchange electronic submissions with the Agency.

Physical Media (❷)
Electronic submissions that conform to the established standards and industry guidance are submitted via a defined storage format.[2]

Design and implement systems (❸,❹)
There are various systems required to provide the capability and capacity for receiving, reviewing, archiving, and tracking submissions electronically. An electronic document room accommodates the receipt, archive, and storage of these submissions. Management information systems enable reviewers to operate in an electronic review environment with appropriate access to IND/BLA/NDA tracking data, electronic submissions, and related historical review documents and access to scientific databases). Electronic document management systems provide capability to store, route, and retrieve at a later date.

Update the technical and non-technical infrastructure (❺)
All aspects of the ERSR Program are supported by an infrastructure including standard hardware/software (e.g., desktops, network, office automation tools, servers, Internet/Intranet) and additional capabilities as needed, such as a secure e-mail package for communicating with regulated industry, capability for field component access, and access to analytical tools needed by reviewers for use with structured databases. In addition, there are foundational support aspects to ERSR such as training and technical support.

The next section presents a mapping of each project within the ERSR Program to its respective ERSR subgoal and presents near-term and long-term activities associated with those projects.

[2] The development of an electronic Gateway for the transmission of electronic submissions was evaluated but not selected for implementation. Electronic submissions will be received in a defined format and saved to CD ROMs.

4.0 IMPLEMENTATION OF THE ERSR PROGRAM

The scope of the ERSR Program is very large and encompasses a broad range of activities. To accommodate the paperless receipt and processing of submissions, the Agency must plan, coordinate, and execute activities across the ERSR Program in such a way that these actions are integrated successfully and ultimately enable the Agency to meet the overall "paperless by 2002" goal as described in Section 2.0.

The various activities within the ERSR Program have been subdivided into the four subgoals of the ERSR Program presented in Section 2.0. This section provides a description of the activities being conducted toward meeting each subgoal and a summary of milestones for those activities.

4.1 Establish Standards

> *ERSR Subgoal: Establish standards for the format, content, and technical specifications for electronic submissions.*

The success of ERSR is dependent upon accurate and thorough definition of data and reporting standards for the format and content of regulatory submissions and the dissemination of guidance for industry to prepare submissions. Additionally, the key to success of the ERSR Program is the consistent and standard application of IT across the various systems developed and infrastructure established within the PDUFA funded organizations.

Standards for Electronic Submissions

FDA is involved in several standards-related projects that impact the format and content of regulatory submissions. FDA plays an active role in the development of standards and guidelines as issued by organizations such as the National Institute of Standards and Technology (NIST), the International Organization for Standardization (ISO), and the US Pharmacopeia.

A major standards development activity in which the Agency actively participates is the International Conference on Harmonization (ICH), a collaborative effort involving the regulatory authorities of Europe, Japan and the United States and experts from the pharmaceutical industry in those three regions. The purpose of ICH is to recommend ways to achieve greater harmonization in the interpretation and application of technical guidelines and requirements to curtail regulatory duplication by working towards a common worldwide drug and biologic registration package.

The activities within the ERSR program are influenced most by the ICH M2 Expert Working Group (EWG) which focuses on Electronic Standards for Transmission of Regulatory Information. The goal of M2 is to identify, evaluate, and recommend appropriate and relevant standards to facilitate the electronic transfer of regulatory information between industry authorities and among regulatory agencies. The FDA representative from CDER serves as the Rapporteur for the M2 EWG and the FDA's representative from CBER is a participant. The M2 EWG maintains a series of recommendations for facilitating electronic communications, including recommendations for physical media, networking, secure EDI transmission over the Internet, and electronic document format. FDA is also active in the ICH M4 EWG, which focuses on the Common Technical Document (CTD) for the technical content of sections of the NDA. The electronic CTD work is planned for completion by the end of FY2001.

Throughout the remainder of the PDUFA II period, both CBER and CDER will continue to play active roles in the standards development activities of the ICH and other standards organizations and these standards will be implemented, where appropriate, within the ERSR Program.

Standard Computing Environment

Over the last few years, the Agency has been proceeding aggressively with its Information Systems Architecture (ISA) initiative. FDA has established a common computing environment through the implementation of ISA by standardizing desktops and networks across the Agency. Patchwork initiatives over time left an FDA IT environment that consisted of numerous layered and often incompatible product suites. Operating within that environment, significant time and energy were expended in moving information throughout the Agency, to the industry it regulates, and to the general population that it serves.

The IT infrastructure that the Agency is migrating toward through the ISA initiative:

- Improves communication;
- Enables collaboration;
- Increases productivity; and
- Creates a more manageable and cost effective environment.

The ISA initiative standardizes the information systems architecture of the entire Agency beginning with the e-mail system, the network operating system, and the desktop operating system. The ISA decreases operations and maintenance costs and decreases training time and costs by providing users with a common environment for basic computing needs.

4.2 Provide Guidance

ERSR Subgoal: Provide guidance for industry to follow in preparing electronic submissions.

Upon establishment of a common set of standards for basic document formatting, electronic integration, and electronic filings, FDA provides written guidance for industry to follow in preparing electronic submissions. Guidance documents are posted in FDA's public docket. Industry training is provided at technical workshops and IT conferences hosted by organizations such as DIA.

CBER and CDER are working collaboratively to develop a series of guidance documents to assist applicants in making regulatory submissions in electronic format. In some cases, guidance differs from CBER to CDER because of differences in the business processes and regulatory mandates between the Centers. The Centers are working to minimize differences wherever possible. In January 1999, the FDA published *Guidance for Industry: Providing Regulatory Submissions in Electronic Format - General Considerations* and *Guidance for Industry: Providing Regulatory Submissions in Electronic Format – NDAs.* These guidance documents provide for the receipt and archive of full electronic NDAs without an accompanying paper archival copy.

An important challenge affecting guidance for and the receipt and archive of submissions is the electronic records/electronic signature issue. The final rule in the Code of Federal Regulations for electronic records/electronic signature (21 CFR Part 11) was posted in the Federal Register in March 1997. That rule explains the regulations that provide criteria for acceptance by FDA of electronic records, electronic signatures, and handwritten signatures executed to electronic records as equivalent to paper records and handwritten signatures executed on paper.[3]

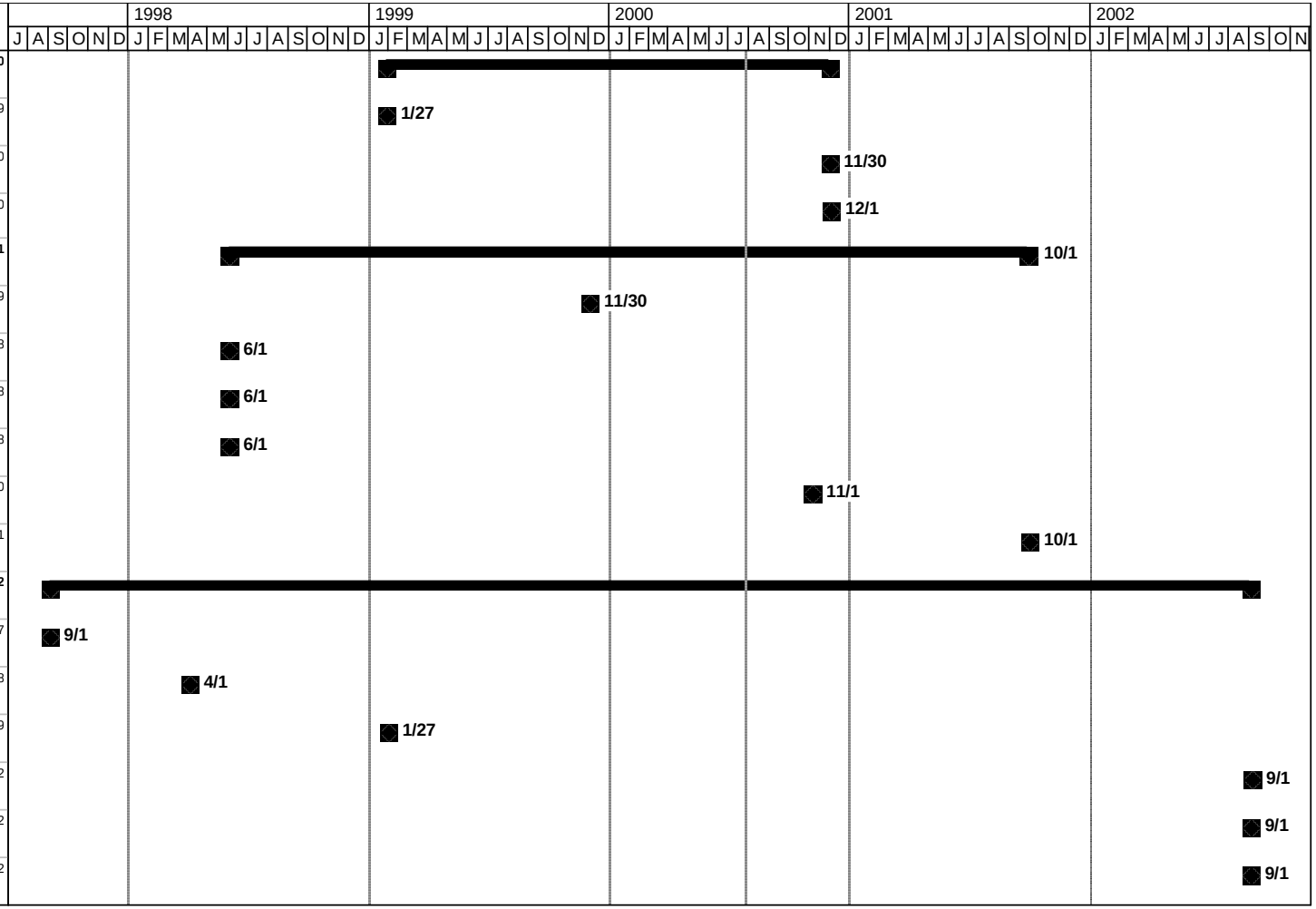
Guidance documents and target dates for publishing those documents are provided below[4]:

November 1999	(CBER) Publish guidance for electronic submission of a Biologics License Application (BLA), Product License Application (PLA)/Establishment License Application (ELA) and New Drug Applications (NDAs) to CBER.
November 2000	(CDER & CBER) Publish joint guidance document for advertising and promotional labeling.
November 2000	(CBER) Develop and publish guidance to define general considerations for secure electronic mail.
December 2000	(CDER & CBER) Publish joint guidance document for the electronic submission of Investigational New Drug (IND) Applications.
October 2001	(CBER) Develop and issue guidance to industry that defines electronic submission guidelines for Pre-market approval (PMAs) and premarket notification (510Ks).
September 2002	(CDER) Develop and publish guidance documents for the electronic submission of Drug Master Files (DMFs) and Annual Reports.

The chart on the following page shows the schedule for these guidance activities.

[3] Policy regarding Part 11 will be coordinated through the Office of Regulatory Affairs. The role of the IT and the ERSR project will be to execute that policy.
[4] Note: Accomplishments from prior periods are reflected in the Project Plan Gantt Charts.

ID	Task Name	Finish
1	**CDER/CBER Joint Guidance**	**Fri 12/1/00**
2	Joint Guidance (CDER) on General Considerations for Submitting Applications	Wed 1/27/99
3	Advertising and Prom. Labeling	Thu 11/30/00
4	Investtigational New Drug (IND) Guidance	Fri 12/1/00
5	**CBER Guidance Activities**	**Mon 10/1/01**
6	Guidance for electronic submissions of a BLA, PLA/ELA and NDA	Tue 11/30/99
7	Guidance for Electronic Submissioins of CRFs, CRTs and Data	Mon 6/1/98
8	Pilot Program for Electronic Investigational New Drug (eIND) Applications for Biological Products	Mon 6/1/98
9	Instructions for Submitting Electronic Lot Release Protocols	Mon 6/1/98
10	Guidance for secure electronic mail general considerations for submissions	Wed 11/1/00
11	Guidance for submitting PMAs/510Ks electronically	Mon 10/1/01
12	**CDER Guidance Activities**	**Sun 9/1/02**
13	Guidance for Archiving Submissions in Electronic Format - NDAs (CRTs/CRFs only)	Mon 9/1/97
14	Draft Guidance for Providing Regulatory Submissions in Electronic Format - NDAs" (Complete archive copy)	Wed 4/1/98
15	Final guidance for Providing Regulatory Submissions in Electronic Format (Full NDA)	Wed 1/27/99
16	Guidance for electronic submission for INDs	Sun 9/1/02
17	Guidance for electronic submission of Drug Master Files (DMFs)	Sun 9/1/02
18	Guidance for electronic submission of Annual Reports	Sun 9/1/02



4.3 Design and Implement Systems

ERSR Subgoal: Design and implement systems to provide the capability and capacity for the receipt, review, archive and tracking of electronic submissions.

The largest component of the PDUFA II ERSR Program involves the design, development, and implementation of systems that will enable the Agency to receive, review, archive, and track submissions electronically. Electronic submissions that conform to the established standards and industry guidance are transmitted via acceptable physical media to an Electronic Document Room. Systems have been developed to provide an automated means for creating, managing, and archiving internally generated review documents. Other systems track the status and progress of submissions submitted to the Agency for action, generate mandatory user fee reports, and enable tracking of milestones and workload statistics for improved management accountability. In addition, there are many design and implementation activities being conducted regarding scientific databases (also known as structured databases) needed by reviewers to perform standard analytical processes on electronic submissions directly from the desktop.

Figure 2 uses the conceptual diagram provided in Figure 1 to identify (in **SHADED BOXES**) the systems being developed within the ERSR Program. Figure 2 below is a description of each of the systems and future activities planned for each system.

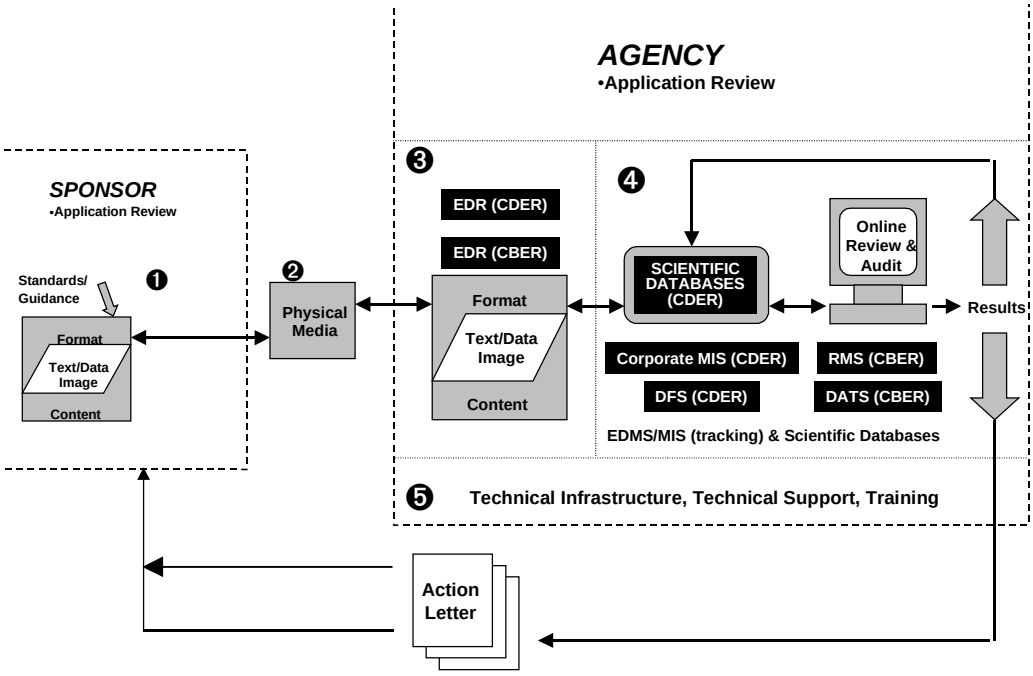


Figure 2

CDER Electronic Document Room (EDR)
CDER currently provides the capability to receive, archive, and store full electronic New Drug Applications (NDAs). Ultimately, CDER's EDR will also accommodate Investigational New Drugs (INDs), Drug Master Files (DMFs), and Annual Reports. Submissions to the EDR come in on one of several physical media types as defined in the industry guidance posted in the public docket.

CDER began developing its Electronic Document Room during FY 1997. The EDR was established initially to accommodate electronic Case Report Forms (CRFs) and Case Report Tabulations (CRTs) for NDAs without an accompanying paper copy. In FY 1999, the EDR was expanded to accommodate full electronic NDAs. Approximately 40% of original NDAs received in CDER now include sections that conform to the electronic submission guidance. From January 1999 to September 1999, CDER received 36 original NDAs that included electronic components and nine NDAs that were fully electronic.

CDER's targeted activities are the following:

3rd quarter FY 2001	CDER plans to have expanded the capability and capacity of the EDR to accommodate INDs.
4th quarter FY 2002	CDER expects to accommodate DMFs, and Annual Reports by the end of September 2002.

CDER Scientific Databases
Scientific Databases (also known as structured databases) are needed by reviewers to perform standard analytical processes on electronic submissions directly from the desktop. CDER is developing carcinogenicity and reproductive/developmental toxicity databases to allow rapid access to summary toxicology information on pharmaceuticals in CDER files, with links to associated references and reviews. These databases will facilitate and improve the review process by functioning as a source of institutional memory for regulatory decision support and a resource for regulatory guidance development and scientific research.

Another CDER activity involving scientific databases is the assembly of drug-drug interaction data in a unified database. This activity will make it possible to rapidly identify known and potential drug-drug interactions based on either drug substance or chemical structure.

Targeted activities for CDER's Scientific Databases are:

4th quarter FY 2000	CDER expects to complete the assembly of the drug-drug interaction data in a unified database to facilitate retrieval and analysis by September 2000.
4th quarter FY 2002	CDER anticipates completing databases for all major toxicology studies submitted for drug approval, carcinogenicity, reproductive and developmental toxicity, genotoxicity, and acute/chronic toxicity studies by September 2002.

CDER Division Files System (DFS)
DFS is CDER's Electronic Document Management System (EDMS). The goal of this system is to provide an easy-to-use, automated means for creating, managing, electronic signature, and archiving of internally generated documents pertaining to the IND/NDA review process. DFS makes it possible for CDER reviewers to file reviews electronically and access historical data and consult reviews on-line from their desktops rather than relying on paper copies.

During FY 1999, CDER completed deployment of DFS to all new drug review divisions throughout the Center. As of October 1999, approximately 47,000 review documents had been checked into DFS.

Targeted activities for CDER's DFS are:

3rd quarter FY 2000	CDER plans to complete Phase II of DFS and field version 2.0. DFS v2.0 is driven by the Center Director's mandate to cut document room costs by eliminating the document room's acceptance of paper review materials generated in the process of an IND or NDA review and data entry pertaining to those materials. DFS will also reduce costs by eliminating the need for document room personnel to reproduce and distribute final form copies. The scope of DFS v2.0 has been defined as providing the capability to 1) update assignment information when reviewers check in their reviews, 2) update the corporate database when an approval, not approvable, or withdrawal letter is checked into DFS for a major amendment on an NDA, 3) append electronic signatures to documents, and 4) distribute copies of final form documents.
4th quarter FY 2000	Concurrent to fielding DFS, CDER is working on an electronic document query project. CDER currently employs three document management solutions. Several CDER components have been using Excalibur's Electronic Filing System (EFS) to search and display documents that have been scanned and stored electronically. DFS uses Documentum's tools to track and store internally generated review documents. The EDR employs a web interface to locate documents submitted electronically. The objectives of the electronic document query project are to replace the EFS and to pilot an electronic document query and retrieval system that encompasses CDER's electronic documents and data.

Corporate Database Redesign

The Centerwide ORACLE Management Information System (COMIS) is CDER's legacy enterprise-wide MIS supporting both the pre-market and post-market regulatory activities. Information is stored in a single ORACLE database and is accessible from any personal computer or terminal in the Center. The Corporate MIS is an umbrella name for multiple applications that store and retrieve data in a single integrated Corporate Database. The Corporate Database is used to track the status and progress of each submission (NDAs, INDs) submitted to the Agency for action. It is also used to generate mandatory user fee reports and to enable tracking of milestones and workload statistics for improved management accountability. The Corporate Database is used by DFS and the EDR to prevent data redundancies and ensure data integrity.

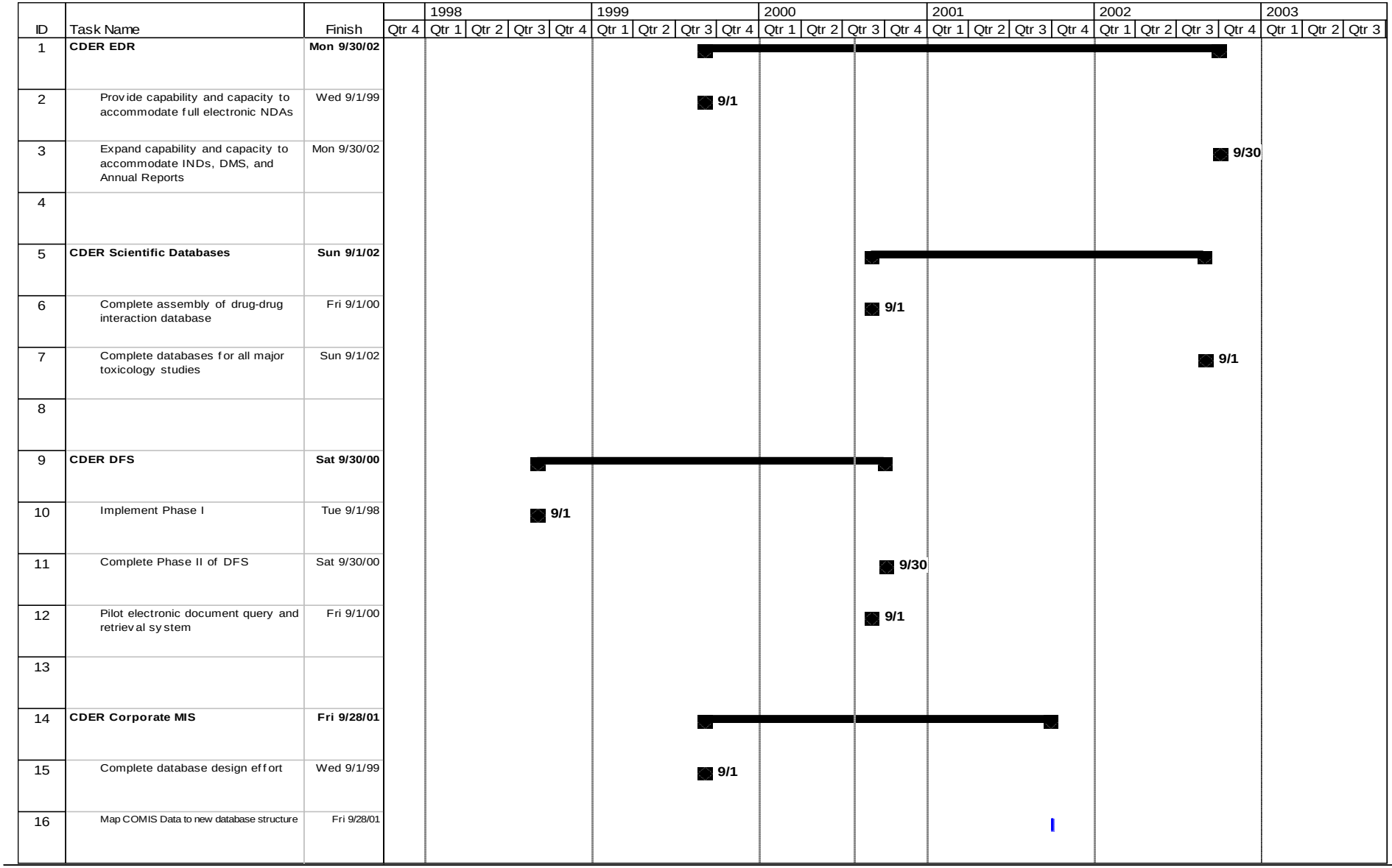
The foundation for application development in CDER is the Corporate Database. The integrity and quality of this database directly impacts the usefulness of data entry and query screens and reports used by CDER personnel. To provide high quality applications and maintain and enhance them in an effective and timely manner, CDER is in the process of redesigning its Corporate Database to develop a modern, flexible, and comprehensive database structure on which to base future applications development.

During FY 1999, CDER completed the definition of data and functional requirements to meet the needs of FDAMA, PDUFA II, ERSR and other critical tracking and review activities. CDER also developed a logical data model for the redesigned Corporate Database and initiated and issued a contract for migration of legacy data.

Targeted activities for CDER's Corporate MIS are:

2nd quarter FY2000	CDER plans to have gathered and documented the data requirements and associated functional requirements for the Corporate Database Redesign project.
4th quarter FY 2001	CDER plans to have completed all software development required for this project.
3rd quarter FY2001	CDER expects to have completed the mapping of existing COMIS data to the new database structure. Additionally, CDER plans to have developed a strategy for migrating data to the new structure and to have completed actual data migration.

The chart on the following page shows the schedule of CDER's system development activities.


ID
Task Name
Finish
1998
1999
2000
2001
2002
2003
Qtr 4
Qtr 1
Qtr 2
Qtr 3
Qtr 4
1 CDER EDR Mon 9/30/02
2 Provide capability and capacity to accommodate full electronic NDAs Wed 9/1/99
3 Expand capability and capacity to accommodate INDs, DMS, and Annual Reports Mon 9/30/02
4
5 CDER Scientific Databases Sun 9/1/02
6 Complete assembly of drug-drug interaction database Fri 9/1/00
7 Complete databases for all major toxicology studies Sun 9/1/02
8
9 CDER DFS Sat 9/30/00
10 Implement Phase I Tue 9/1/98
11 Complete Phase II of DFS Sat 9/30/00
12 Pilot electronic document query and retrieval system Fri 9/1/00
13
14 CDER Corporate MIS Fri 9/28/01
15 Complete database design effort Wed 9/1/99
16 Map COMIS Data to new database structure Fri 9/28/01
9/1
9/30
9/1
9/1
9/1
9/30
9/1
9/1

CBER Electronic Document Room (EDR)

CBER must provide a capability and the capacity to accommodate receipt and archive of electronic biologics submissions. The purpose of the EDR is to provide a facility to house the hardware and software that will store, track, and retrieve electronic documents such as the Investigational New Drug (IND) applications, Biologics Licensing Applications (BLAs), New Drug Applications (NDAs), lot release protocols, and other types of submissions. Submissions to the EDR will come in on one of several physical media types as defined in the industry guidance posted in the public docket.

Targeted activities for CBER's EDR are:

3rd quarter FY 2000	By June 2000, CBER expects to have implemented Phase I of the EDR. In this Phase, CBER will have established the basic infrastructure for the EDR to include hardware and software architecture and security controls and some functionality such as support the receipt and reviewing of electronic BLAs, INDs and process CBER Internal Documents for electronic BLAs.
1st quarter FY 2001	By October 2000, CBER anticipates completion of Phase II of their EDR. At completion of Phase II, CBER will have provided capability to receive additional Internal Draft and Final Documents integrated the EDR with RMS-BLA, DATS, and BIMS, and accept electronic signature and secure e-mail.
4th quarter FY 2001	By September 2001, CBER plans to have completed Phase III of the EDR. With completion of Phase III, CBER will have finalized eFOIA requirements.
4th quarter FY 2002	By September 2002, CBER plans to have completed Phase IV of the EDR. This final phase will provide enhancements and capacity upgrades and will provide the capability to receive and archive all paperless applications.

CBER Regulatory Management System (RMS)

In CBER, RMS will perform the activities of an electronic document management system as well as a management information system. RMS will be an integrated system for creating, managing and archiving internal review documents concerning a submission, as well as tracking the status of the submission. RMS incorporates the new business rules that CBER is applying to track and review BLA submissions, and hence is also known as RMS-BLA. This module will replace the legacy Biologics Regulatory Management System (BRMS). RMS-BLA will interface to CBER's legacy Biologics IND Management System (BIMS) system.

Targeted activities for CBER's RMS are:

3rd quarter FY 2000	By July 2000, CBER expects to have Phase I of the RMS-BLA module completed. This phase will provide CBER the functionality to process therapeutics, vaccine, and blood product submissions. Also in this phase, CBER will have completed all data migration required for the functionality from the BRMS system.
4th quarter FY 2001	By September 2001, CBER will have completed the enhancement of the RMS-BLA module, and most of the remaining data migration.
1st quarter FY 2002	In October 2001, CBER expects to have integrated with the BIMS system.
4th quarter FY 2002	By September 2002, CBER will have completed Phase II of the RMS-BLA module. With completion of this phase, CBER will be able to track all applications.

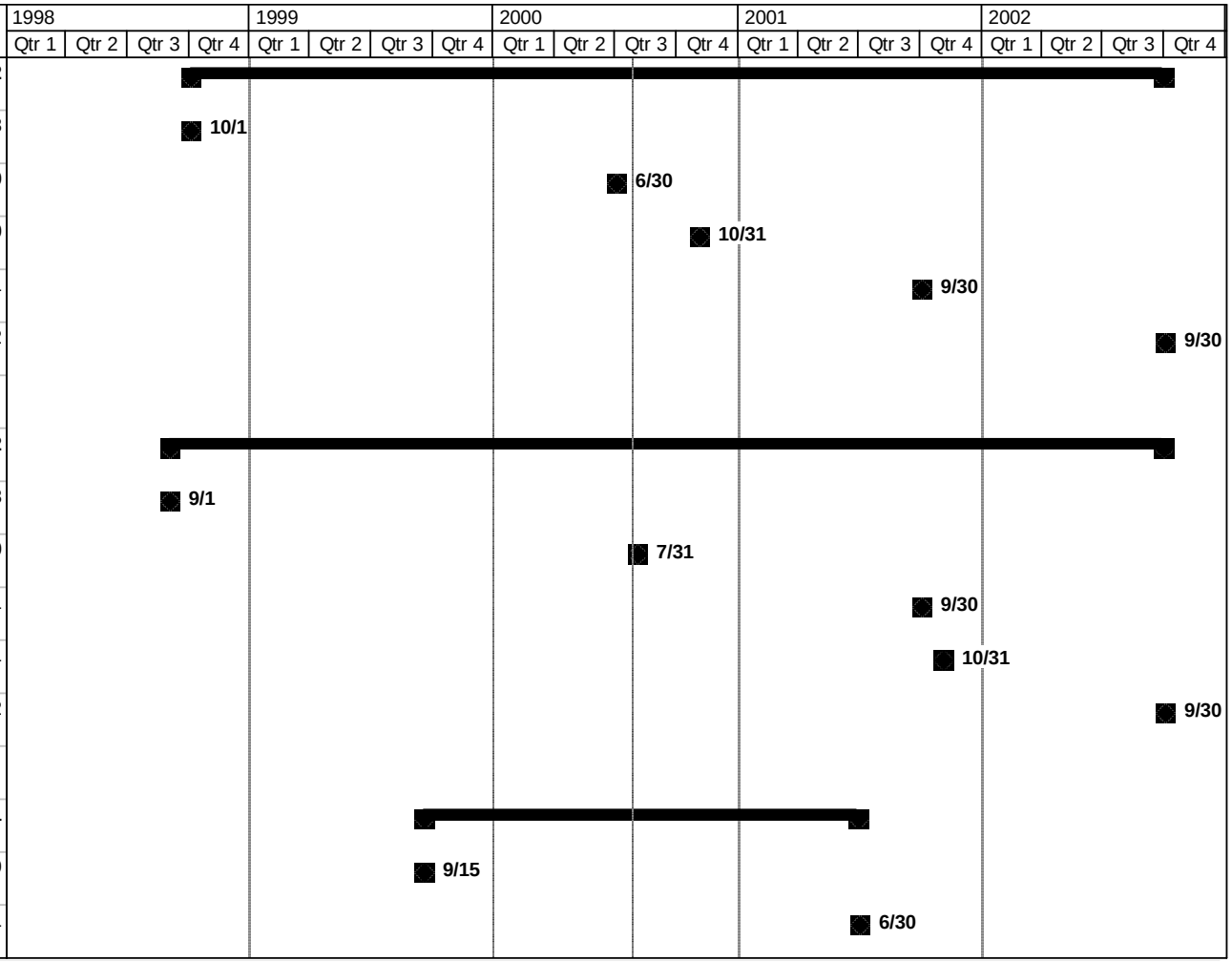
CBER Document Accountability and Tracking System (DATS)

CBER is developing DATS to consolidate administrative document logging and circulation control activities by replacing two legacy systems. While DATS will be available for use by most Center employees, the primary user will be Document Control Center (DCC) personnel who will use DATS to capture receipt and document data, enter and update routing and circulation data, and maintain location and inventory information for physical files. DATS will also provide the capability to enter key information from FDA Form 1571 that is submitted by sponsors to FDA as part of an IND Original Submission or as part of an Amendment to an existing IND.

3rd quarter FY 2001	CBER will complete Phase II of DATS. Phase II will provide the capability to track routing and circulation information.

The chart on the following page shows the schedule of CBER's system development activities.

ID	Task Name	Finish
1	**CBER EDR**	**Mon 9/30/02**
2	Conduct Requirements Analysis	Thu 10/1/98
3	Implement Phase I of EDR	Fri 6/30/00
4	Complete Phase II of EDR	Tue 10/31/00
5	Complete Phase III of EDR	Sun 9/30/01
6	Complete Phase IV of EDR	Mon 9/30/02
7		
8	**CBER RMS**	**Mon 9/30/02**
9	Complete Development of Clinical Trials Communications	Tue 9/1/98
10	Complete Phase I of the RMS-BLA module	Mon 7/31/00
11	Complete enhancement of RMS-BLA module	Sun 9/30/01
12	Integrate BIMS system	Wed 10/31/01
13	Complete Phase II of RMS-BLA module	Mon 9/30/02
14		
15	**CBER DATS**	**Sat 6/30/01**
16	Implement and field Phase I of DATS	Wed 9/15/99
17	Complete Phase II of DATS	Sat 6/30/01



4.4 Update Technical/Non-Technical Infrastructure

ERSR Subgoal: Update the technical and non-technical infrastructure to support an electronic review environment.

Activities supporting this subgoal are associated with the technical infrastructure of the ERSR Program (e.g., acquiring, configuring, and implementing hardware and software). These activities support multiple projects and are coordinated with projects' functionality, as appropriate. Infrastructure includes standard hardware/software (e.g., desktops, network, office automation tools, servers, Internet/Intranet) needed to support system development. Activities also include additional capabilities as needed, such as a secure e-mail package for communicating with regulated industry and analytical tools needed by reviewers. Other tools include library references such as the scientific Library Electronic Reference Network (LERN). Another significant activity toward meeting this subgoal involves addressing the needs for Center communication with ORA Field Offices. ORA's requirements will be integrated as appropriate with the ERSR-related functional capabilities developed in CBER and CDER.

Infrastructure also includes the foundational support aspects of the ERSR Program common to CBER, CDER, and ORA's PDUFA II IT solution:

Technical Support – Provides support to end users for hardware/software installation, software development, maintenance, and trouble shooting.

Training – Covers provision of training for development staffs and end users sufficient to ensure qualified technical support to the ERSR Program and to allow reviewers to function in an electronic review environment.

The ERSR project members had considered utilizing an Electronic Gateway to receive submissions directly but this framework was not selected due to concerns of security, reliability and overall efficiency—from both an industry and Center perspective. As technology advances, an electronic Gateway may be reconsidered but for the foreseeable future, the approach for submission, as indicated in the guidance documentation, is the use storage of data to CD ROM diskettes.

The following paragraphs provide, by PDUFA organization, planned activities for updating the technical and non-technical infrastructure to support an electronic review environment.

Center for Biologics Evaluation and Research (CBER)
Enhancing and upgrading CBER's network architecture is key to achieving the PDUFA II ERSR performance goals. CBER's current capabilities must be improved to support the proposed processes and architecture. CBER plans to upgrade network communications between all CBER locations, the network systems hardware, and desktop workstations.

The targeted activities for updating CBER's technical infrastructure are:

4th quarter FY 1999	Upgrade desktops within the Center to the ISA-standard desktop configuration (Windows 95, Office 97, Outlook 97). Migrate network infrastructure to ISA standards (BackOffice 4.5, CAT 5 cabling).
4th quarter FY 2000	Upgrade networking capability by completing the installation of dark fiber

	between the Center's component offices.
1st quarter 2001	CBER will implement a secure messaging capability between Agency Center/Offices and the regulated industry by October 2000.

Center for Drug Evaluation and Research (CDER)

CDER is conducting several activities related to updating its technical infrastructure. A significant effort involves CDER's Enterprise Computing Architecture (ECA) which reflects the current business processes, information flows, applications, data, and technical infrastructure of CDER. The ECA provides CDER with an enterprise-wide conceptual framework for planning the migration to a paperless review environment.

During FY 1999, CDER completed its secure e-mail pilot, installed over 400 flat-screen and dual-screen monitors for reviewers to use with electronic NDAs, and replaced desktops and laptops that were not Year 2000 compliant.

The targeted activities for updating CDER's technical infrastructure are:

1st quarter FY 2000	Procure and configure the hardware and software for secure e-mail for the initial production environment.
On-going activities	Maintain the ECA Description document, incorporating changes to the computing architecture. Additionally, CDER will be developing, documenting, and maintaining policies and procedures for use when developing and modifying systems within the Center's architecture. In addition to providing the necessary resources for the operations and maintenance of the hardware and software that support the systems within the ERSR program, CDER continues to upgrade the desktops and network operations to ISA-standard configurations. Continue providing operations and maintenance support for the technical infrastructure.

Office of Regulatory Affairs (ORA)

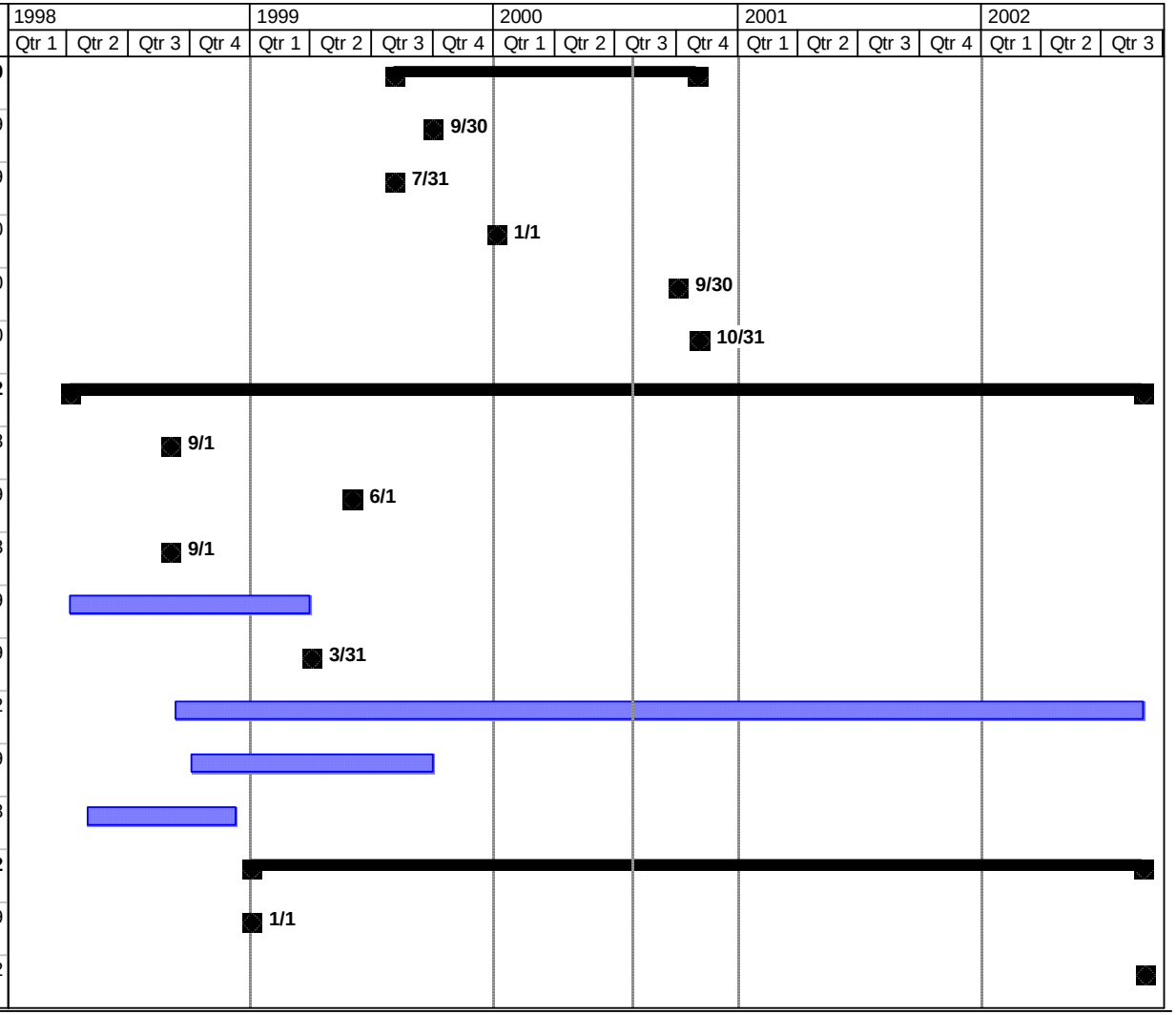
To fully achieve the goals of the ERSR program, ORA investigators and compliance officers in the field offices will need to access documents electronically. ORA envisions that they will need the capability to 1) provide each district office, each laboratory, some large resident posts on the network, and each regional office access to the electronic documents maintained by CDER and 2) provide the ability to browse and search for the documents pre-authorized for viewing by ORA investigators and compliance officers. ORA does not require detailed access to CBER's BLA applications. One solution being considered is to provide a seamless dial-up capability to access the information needed by ORA and to have added electronic storage capability.

The targeted activities for updating ORA's technical infrastructure are:

4th quarter FY 2002	ORA expects to design, procure, and install the necessary infrastructure to enable ORA field users to access the requisite material for conducting field inspections.

The chart on the following page shows the targeted activities for all PDUFA organizations in updating the technical/non-technical infrastructure within the ERSR program.

ID	Task Name	Finish
1	**CBER**	**Tue 10/31/00**
2	Uprade desktops to ISA-standard desktop configuration	Thu 9/30/99
3	Migrate network infrastructure to ISA standards	Sat 7/31/99
4	Certify mission critical systems are Y2K compliant	Sat 1/1/00
5	Complete installation of dark fiber between CBER component offices	Sat 9/30/00
6	Implement a secure e-mail solution	Tue 10/31/00
7	**CDER**	**Sun 9/1/02**
8	Define and document requirements for secure electronic mail	Tue 9/1/98
9	Conduct a secure e-mail pilot	Tue 6/1/99
10	Publish draft Enterprise Computing Architecture Description document	Tue 9/1/98
11	Conduct Y2k testing and IV&V of mission critical systems	Wed 3/31/99
12	Certify mission critical systems are Y2K compliant	Wed 3/31/99
13	Continue developing ECA description document	Sun 9/1/02
14	Continue upgrading desktops and network operations to ISA standard configurations	Thu 9/30/99
15	Replace obsolete disk drives, upgrade network, upgrade desktop SW/HW, replace LAN printers	Thu 12/10/98
16	**ORA**	**Sun 9/1/02**
17	Complete ORA's functional requirements analysis	Fri 1/1/99
18	Complete design, procurement, and installation of necessary infrastructure	Sun 9/1/02



5.0 OVERALL PROGRAM OVERSIGHT

The CIO is responsible for ensuring that PDUFA II IT investments fit into a common computing environment and follow current IT management practices. ERSR projects are reviewed for business and technical soundness through the IT Business Planning process established by the Agency in accordance with the Clinger-Cohen Act of 1996.

Consistent with Department of Health and Human Services (DHHS) policies and recent legislation, including the Clinger-Cohen Act, the Agency has developed a process to become more accountable for the economic and efficient management of IT and to implement a sound and integrated IT architecture.

An integral part of the FDA business planning process is the review of the major IT investments to ensure that they are achieving defined performance goals which support the Agency mission, in terms of the project plan (i.e., milestones and resources) and expected outcomes (e.g., programmatic improvements), and are compliant with standards defined by the Agency's information systems architecture (ISA).

The IT Business Planning (ITBP) process has been utilized to review existing ERSR IT projects.

One major component of the ITBP process is a review of investments by a Technical Review Board (TRB) composed of Information Resource Management (IRM) Directors from each of the Centers/Offices. The goal of the TRB is to assess Agency IT investments with regard to the technical soundness of the investment, the consistency of the IT solution with the Agency's ISA, compliance with Agency IT security standards and the potential redundancy of the investment with other Agency efforts. Once the TRB has completed its assessment and determined that there are no significant technical risks that could prevent successful implementation of the IT solution, the members "credential" the investment. Though projects may be "credentialed" by the TRB, members may raise technical issues that must be addressed by project managers but do not preclude a project from proceeding.

Annually, the PDUFA II Information Management Five-Year Plan is revised to update the plans, budgets, and milestone schedules for each of the ERSR projects. This plan is a means of communicating the progress and status of the ERSR Program to both internal and external parties. Additionally, information about ERSR issues and activities is shared with industry through the Information Management Advisory Board (IMAB). This Board is comprised of both Agency management and industry representatives. The Board functions as a steering committee that ensures the PDUFA II Information Management Plan reflects the interest of all stakeholders and utilizes information management/technology best practices, and that the PDUFA II information management program implementation is consistent with that plan. The IMAB provides a forum for any issues or questions not addressed by this plan. Specific issues raised at the IMAB can then be channeled to the appropriate Agency organization.

The Office of the CIO reviews the major project activities within the ERSR project. The CIO plays the following roles as part of the ERSR project:

- Facilitates coordination of IT project management;
- Reviews progress and integration of major IT projects;
- Ensures compliance with IT security standards; and
- Oversees development and coordination of contingency plans and resources.

In FY2000, the OCIO will focus on developing contingency resources. Additionally, through FY2002, the OICO will coordinate development of the secure messaging processes necessary for ERSR.

In order to provide project management coordination, the OCIO is investing resources in consulting support. Additionally, OCIO is piloting an internal intranet reporting tool to enhance project planning coordination among the Centers and the OCIO.

The targeted activities for the CIO oversight function are:

Through 2002	Develop security and contingency plans.
September 2000	Implement re-engineered IT business processes to support PDUFA oversight.

6.0 SUMMARY

The overall PDUFA goal of developing and updating the information management infrastructure to allow, by fiscal year 2002, the paperless receipt and processing of INDs and human drug applications is composed of four subgoals:

- developing standards;
- issuing guidance for regulated industry for electronic submissions; designing and implementing systems for receiving, reviewing, archiving and tracking electronic submissions; and
- providing the technical and non-technical infrastructure to support an electronic review environment.

FDA organizations have planned the requisite projects and activities to meet the overall PDUFA IT goal. The organizations are participating in a variety of standards development activities and are ensuring that industry guidance for submitting applications electronically is clear, consistent, and standards-based. Efforts toward implementing systems are progressing steadily and are being supported continuously by upgrades to desktop and network infrastructure. To help ensure coordination of all ERSR related activities, the CIO will coordinate an internal forum of key participants to review current project status and forecast the operational impact of the final integrated project.

Throughout the life-cycle of the ERSR Program, FDA organizations will collaborate on system development activities where appropriate. Existing systems and those being developed or re-engineered within the ERSR program are Center-specific due to differing business needs created by statutes and mandates. For example, firms are required to submit a separate application for each therapeutic biological and human drug product. But each application for a blood product, vaccine, or allergenic may contain multiple products; and one product may receive approval while another does not. This situation necessitates unique counting and tracking mechanisms that are not applicable to all applications. Each Center has developed internal business processes to meet their unique regulatory review requirements, and these processes dictate their systems development. However, their corporate database structures are very similar and allow for the data to be shared. Therefore, the technical architecture for both is largely the same and consistent with the Agency's Information Systems Architecture (ISA) program. If submissions enter the Agency based on the published electronic submission guidance, differences in the systems between Centers will not affect regulated industry.

A significant portion of the efforts expended in FY 1999 across the Agency were toward ensuring that systems and infrastructure (both PDUFA and non-PDUFA related) were not vulnerable to the Year 2000 (Y2K) date change. Over the past two years, the FDA has been engaged in an intensive effort that has required a significant expenditure of resources aggressively addressing Y2K issues on multiple fronts: systems, telecommunications, desktop, biomedical and facilities. Of chief importance to the Agency has been the impact of the Y2K issue on its mission-critical functions. Consequently, all efforts were prioritized to ensure neither the Agency nor the public was at risk as a result of the date change. During the latter part of FY 1998 and throughout FY 1999, FDA worked diligently to renovate, validate, and implement Y2K compliant systems and successfully met deadlines established by OMB for completing these activities.

As a result of the pressure imposed by the Y2K focus, several of the systems development projects were put on hold or delayed during FY 1999. PDUFA-related (i.e., pre-market) components within these systems are given the highest priority to meet the overall PDUFA IT goal of having an ability to receive and process submissions electronically by FY 2002.

APPENDIX A

ERSR PROGRAM BUDGET

ERSR Program Budget
(in thousands)

CBER	FY1998 Actual	FY1999 Actual	FY2000 Plan	FY2001 Plan	FY2002 Plan	Total Planned
EDR						
	407	2,106	1,604	1,050	1,050	6,217
Other Information Doc Mgt Systems						
	859	1,148	449	359	339	3,154
Technical Infrastructure						
	1,642	1,863	950	927	927	6,309
RMS						
	3,100	2,261	3,200	2,200	2,000	12,761
Standards						
	50	125	0	0	0	175
CBER Subtotal						
	6,058	7,503	6,203	4,536	4,316	28,616

CDER	FY1998 Actual	FY1999 Actual	FY2000 Plan	FY2001 Plan	FY2002 Plan	Total Planned
Standards						
	130	130	3	160	160	583
EDR						
	401	906	595	611	490	3,003
Scientific Databases						
	90	353	276	510	380	1,609
EDMS/DFS						
	1,763	1,922	2,995	2,671	1,504	10,855
Corporate MIS						
	982	2,915	1,649	1,726	1,135	8,407
Other Initiatives						
	4,152	4,482	5,730	4,765	4,471	23,600
CDER Subtotal						
	7,518	10,708	11,248	10,443	8,140	48,057

ERSR Program Budget, continued
(in thousands)

ORA	FY1998 Actual	FY1999 Actual	FY2000 Plan	FY2001 Plan	FY2002 Plan	Total Planned
Requirements Analysis						
	165	0	0	0	0	165
Design and Implementation						
	347	80	986	773	971	3,170
ORA Subtotal						
	512	80	986	773	971	3,322

CENTER TOTALS	FY1998 Actual	FY1999 Actual	FY2000 Planned	FY2001 Planned	FY2002 Planned	Total Planned
CBER						
	6,058	7,503	6,203	4,536	4,316	28,616
CDER						
	7,520	10,830	11,591	7,064	6,990	43,995
ORA						
	512	80	986	773	971	3,322
Center Total						
	14,090	18,413	18,780	12,193	12,277	75,933

APPENDIX B

ACRONYMS

Acronyms

AERS	Adverse Event Reporting System
AMF	Administrative Management of Files
ANDA	Abbreviated New Drug Applications
BA/BE	Bioavailability/Bioequivalency
BER	Blood Establishment Registration System
BIMO	Biomedical Research Monitoring
BLA	Biologic License Applications
BRMS	Biologics Regulatory Management System
CBER	Center for Biologics Evaluation and Research
CDER	Center for Drug Evaluation and Research
CDR	Central Document Room
CIO	Chief Information Officer
CMC	Chemistry, Manufacturing and Controls
COMIS	Corporate Oracle Management Information System
COTS	Commercial Off-the-Shelf
CRF	Case Report Form
CRT	Case Report Tabulations
CTD	Common Technical Documents
CVM	Center for Veterinary Medicine
DATS	Document Accountability and Tracking System
DCC	Document Control Center
DFS	Division File System
DIA	Drug Information Association
DMF	Drug Master File
DSS	Decision Support System
EDI	Electronic Data Interchange
EDMS	Electronic Document Management System
EDR	Electronic Document Room
EES	Establishment Evaluation System
EFOIA	Electronic Freedom of Information Act
ERS	Electronic Regulatory Submission
ERSR	Electronic Regulatory Submission and Review
EVA	Entry Validation Application
EWG	Expert Working Group
FACTS	Field Accomplishments and Compliance Tracking System
FDA	Food and Drug Administration
FDAMA	FDA Modernization Act
FOI	Freedom of Information
FTE	Full-time Equivalent
GPRA	Government Performance and Results Act
ICH	International Conference on Harmonization

IIS	Internet Information Server
IM	Information Management
IMAB	Information Management Advisory Board
IND	Investigational New Drug
IRM	Information Resources Management
ISA	Information Systems Architecture
IT	Information Technology
ITBP	Information Technology Business Planning
ITCC	IT Coordinating Committee
IV&V	Independent Verification and Validation
LERN	Library Electronic Reference Network
LRS	Lot Release System
M2	ICH M2 Expert Working Group (EWG)
M4	ICH M4 EWG focuses on Common Technical Documents (CTD)
MIS	Management Information System
NDA	New Drug Application
NOS	Network Operating System
NPR	National Performance Review
OC	Office of the Commissioner
OHRMS	Office of Human Resources and Management Services
OIRM	Office of Information Resources Management
OMS	Office of Management and Systems
ORA	Office of Regulatory Affairs
PDF	Portable Data Format
PDUFA	Prescription Drug User Fee Act
PhRMA	Pharmaceutical Research and Manufacturers of America
PLA	Product License Applications
RAC	Regulatory Affairs Committee
RMS	Regulatory Management System
TBD	To Be Determined
TCP/IP	Transmission Control Protocol/Internet Protocol
TRB	Technical Review Board
Y2K	Year 2000