The Future of the FDA: Operating in an "Electronic World"

A White Paper by:

AXENDIA

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Introduction

Historically, interactions between the FDA and the companies it regulates have involved the creation, printing and delivery of volumes of paper documents. These documents may have been delivered as part of an application, or reviewed onsite, in the course of an inspection.

Over the past few years, the FDA and the industries it regulates have recognized the need for a modern, well-integrated, reliable, efficient and affordable electronic information infrastructure to support FDA administrative, regulatory and business operations.

To achieve this transformational goal, the agency has embarked on a series of organizational and information technology activities. These activities are aimed at advancing ongoing electronic communications inside the agency, with the public and between the FDA the companies it regulates.

This whitepaper discusses FDA transformational activities that promise to usher in a new era of electronic interactions between the agency and its constituents, and is based on primary research conducted by Axendia, Inc. and commissioned by MasterControl.

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>
> Dr. Armando Oliva
> FDA Deputy Director for Bioinformatics, FDA

Research Approach

The research by Axendia Inc. identified key organizational and technology initiatives the FDA is undertaking to advance ongoing electronic communication and interactions.

The research was based on one-on-one interviews with FDA officials and other FDA sources, as well as on publicly available information.

Bioinformatics Board

According to Dr. Armando Oliva, FDA Deputy Director for Bioinformatics, "It's fair to say that the [FDA] is actively moving toward an electronic world where all regulated product information comes in electronically. I couldn't tell you when that is going to happen, but certainly there are active discussions underway to move to an 'all electronic submission environment' for all FDA regulated product information, whether it be product quality, manufacturing, pre-market, or post market data."

The Bioinformatics Board (BiB) is at the center of the agency's e-transformation.
In February 2006, the FDA's senior management approved the formation of the Bioinformatics Board (See Figure 1: FDA Bioinformatics Board organizational chart), and charged it with overseeing the planning and control of bioinformatics activities, as well as ensuring that these activities are communicated throughout all levels of the agency.

The BIB's goal is to manage the implementation of a modern, well-integrated, reliable, efficient and affordable information infrastructure to support the agency's administrative and regulatory business operations.

The BiB reports directly to the FDA Management Council. The Bioinformatics Board, in coordination with the Office of Information Management, is responsible for determining the FDA's information management strategy across the FDA's various organizations, particularly with respect to business process planning and regulatory policies.

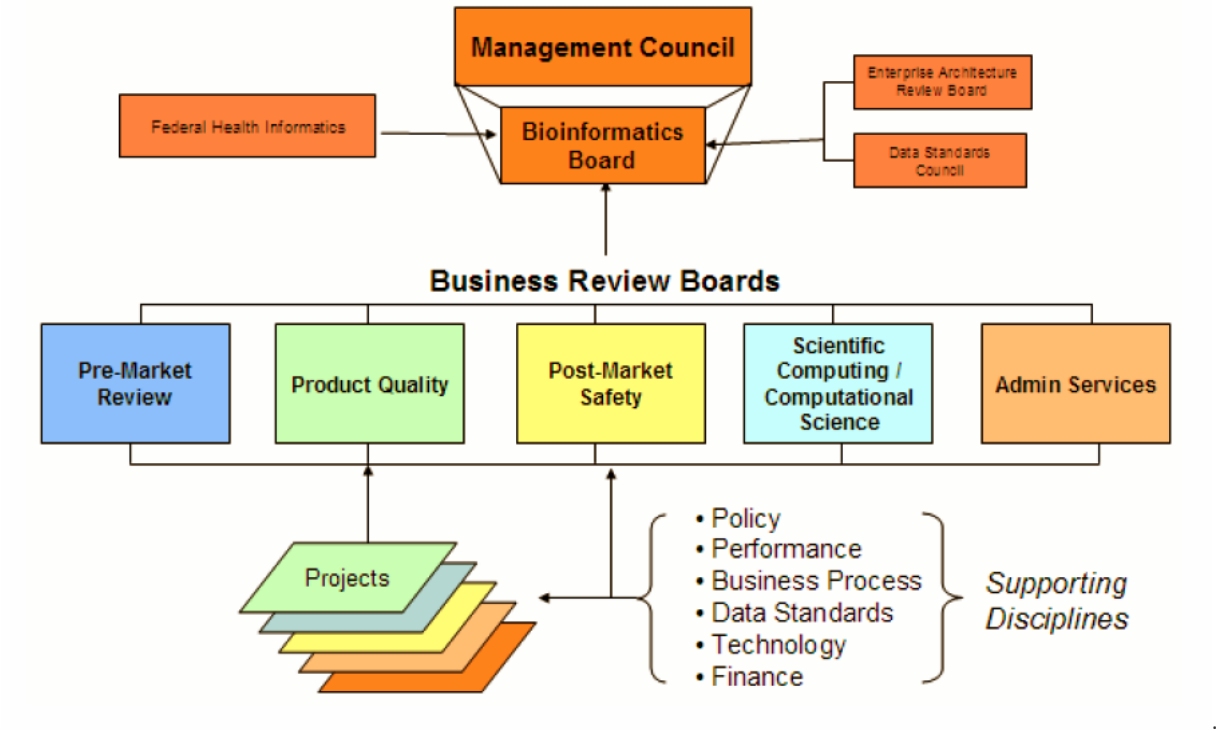

Figure 1: FDA Bioinformatics Board organizational chart.

The BiB consists of five Business Review Boards (BRBs), each responsible for agency-wide projects in each functional area. These include pre-market review, product quality, post-market safety, scientific computing and computational science, and administrative services.

The responsibilities of each BRB are summarized below:

- Pre-Market Review is responsible for the electronic submission, tracking and review of pre-market data. Key initiatives for this BRB are the Regulatory Product Submissions (RPS) initiative, the Information Computer Technology for the 21st Century (ICT21) initiative, and the common Electronic Document Room (EDR) initiative.
- Product Quality and Compliance is responsible for the electronic regulation of manufacturing processes and the tracking of inspections/ product movement. A key initiative for this BRB is the Harmonized Inventory of FDA-Related Entities initiative.
- Post-Market Safety is responsible for electronic adverse event reporting and database management. Key initiatives include the MedWatch Plus (FDA-wide Adverse Event Reporting System or "FAERS") initiative and the Sentinel initiative.
- Scientific Computing / Computational Science is responsible for determining the needs of laboratories and quantitative scientists. A key initiative is the Janus initiative.
- Administrative Services is the BRB responsible for providing the administrative services that are necessary for the other business review boards to perform their responsibilities for the FDA successfully.

Shifting to an Agency-Wide IT

Due to a variety of external pressures, the FDA is conducting studies to determine a strategy for modernizing its IT infrastructure and services. The agency is working to shift its IT decision-making and governance structure to an agency-wide, less decentralized model.

To determine the best strategies for modernizing its IT infrastructure and services, the FDA is conducting a series of studies. The study objectives are to determine how to shift the FDA's IT decision-making and governance structure from its current decentralized configuration to an agency-wide, centralized model. The structure will institute an enterprise approach for automating common or "special purpose" IT solutions by defining roadmaps for each business process area. These process areas will then be further refined into discrete IT solutions.

Service Oriented Architecture (SOA)

Historically, FDA IT initiatives have been driven by rigid, "center"-based organizational structures. As a result, the agency currently has numerous information systems executing overlapping business and information processes, and relies on a number of technologies that are expensive to maintain. This is not unlike the situation that industry faces.

Historically, these systems also were specked, funded and implemented by of many functional areas. Their primary objective was to meet their particular portion of the business requirement with little regard for integration to other functions in the organization.

Along came Global IT organizations with a new way to reduce costs and streamline operations: Service Oriented Architecture (SOA). Also known as a Web-services or component-based approach, this approach separates the functionality and capabilities of a business process or application into discrete components that can be shared and reused across the enterprise.

As a result, SOA provides a more cost effective way to breakdown silos, reduce implementation costs, time, and effort, as well as to reduce the total cost of ownership.

The FDA is also migrating toward a more service-oriented and component-based approach in its IT architecture. This approach, consistent with government and industry best practice, will enable the FDA to "build once, use often."

Real Promise of Electronic Review

According to Donna-Bea Tillman, Ph.D., Director of the Office of Device Evaluation CDRH, "The real promise of electronic review lies beyond simply receiving submissions in electronic format."

The real promise lies in the agency's being poised to provide a new Target Enterprise Architecture (EA). This Target EA will provide a business-driven plan that describes the desired end-state for the FDA's business architecture, data architecture, applications architecture, technical architecture, security architecture, and standards profile.

Target Enterprise Architecture (EA)

The primary purpose of the target EA is to effectively plan a course for achieving the FDA's strategic vision and goals. It is one element in a broader set of interrelated activities that collectively enable FDA managers and staff to define a vision, develop strategies and plans for achieving the vision, make resource decisions, and implement strategies and evaluate performance.

By defining the end-state from several distinctive perspectives (e.g., business, data, etc.), the target EA will also provide stakeholders with a view into the complex relationships that exist among these different perspectives.

For example, the target EA will provide insight into how a particular need translates into a set of target FDA business processes, and how these business processes can be supported by a common set of technologies.

Specific objectives of the FDA's Enterprise Architecture are to:

- Improve Program Performance
  The overarching benefit of the target EA is that it provides opportunities to improve the efficiency and effectiveness of the FDA's programs. It ensures that data is optimized to support business functionality, and that technology solutions are driven by business needs. It also allows the FDA to more readily share services/data across organizational and functional lines.

- Improve Interoperability
  The target EA establishes enterprise-wide standards that promote platform and vendor independence, enabling greater interoperability across disparate applications, both internal and external.

- Improve Utilization of Resources
  The target EA reduces system development, operation and maintenance costs by eliminating duplicative investments, promoting the sharing of common services, and establishing agency-wide standards.

- Accelerate System Implementation
  The target EA equips the agency's system developers and architects with an inventory of component-based services from which to choose that provide well defined functionality, thus maximizing reuse and portability of previously developed processes, components, code, etc.

- Simplify Investment Decisions
  The target EA provides a view from strategy to business function to technology, allowing decision makers to more quickly assess the relative value of initiatives, and to identify duplicative and misaligned initiatives.

Building on Standards

The FDA recognizes the importance of, and is committed to, using open-consensus based data standards to support this transformation process. To that end, it has created the Data Standards Council as shown in Figure 2.

Moreover, the FDA is actively involved in interactions with standards development and maintenance organizations, and with exchange standards development. Some of these activities involve:

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- Data standards requirements gathering and use case development.
- Modeling requirements and use cases (e.g., modeling to the Health Level Seven1 (HL7) Reference Information Model).
- Testing models against requirements and use cases, to include the development of visualization tools (e.g., stylesheets, XForm), documentation, and coordination assistance.
- Balloting (e.g., ballot preparation, presentation and reconciliation).
- Accreditation.

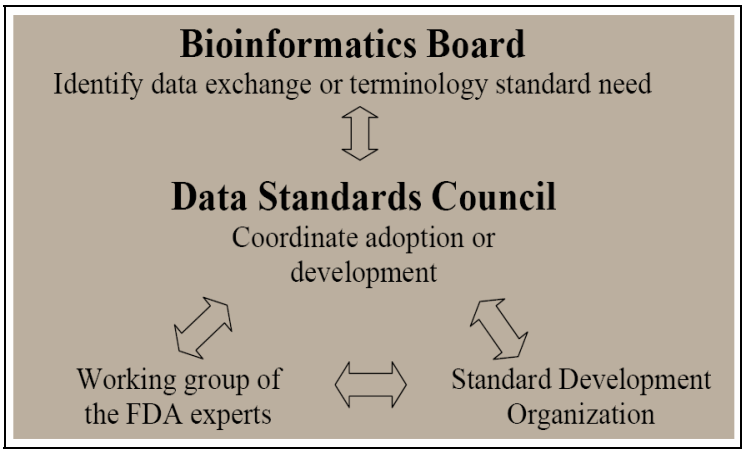

Figure 2: FDA's Data Standards Council.

The FDA divides data standards into two broad categories: terminology standards and exchange standards.

- Terminology standards provide a consistent way to describe concepts. The Unique Ingredient Identifiers (UNII) developed by the FDA, for example, provide a consistent way to describe substances in foods and drugs. Similarly, the vocabulary developed by the National Cancer Institute's Enterprise Vocabulary Services provides a consistent way to describe terminology related to cancer.[2]

- Exchange standards provide a consistent way to exchange information between organizations and computer systems. Exchange standards help ensure that the sending and the receiving system both understand unambiguously what information is being exchanged. Examples of exchange standards adopted by the FDA include:

    - Structured Product Labeling (for the exchange of product labeling information).

    - Study Data Tabulation Model (for the exchange of study data); this model was developed by the Clinical Data Interchange Standards Consortium (CDISC).

Central to FDA's strategic plan is the use of HL7 exchange standards for all submitted data. HL7 is an international, ANSI accredited, open, consensus-based standards development organization. It integrates with research and healthcare-related exchange standards and mandates, such as the Reference Information Model (RIM), Electronic Healthcare Records, and Consolidated Health informatics, among others.[3]

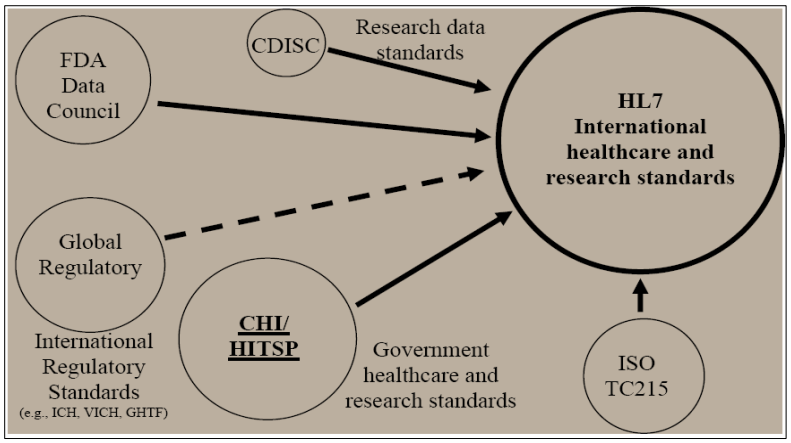

Figure 3: HL7 exchange standards and their interaction with FDA and standard organizations.

Current eFDA Initiatives

A number of IT initiatives are currently underway at the agency to support this transformation. Figure 4 provides a detailed list of the projects and the goals they support.

FDA Initiatives	PDUFA IV Information Technology Goals						Drug Safety Goals		
	Implement new systems consistently across divisions	Update Tech Specifications as needed	Extend single entry to two way transmission	Electronic IND, NDA and BLA with Automated Links	Human drug labeling modular system/exchange	Standards based postmarket systems	Enhanced adverse event reporting system and surveillance tools	IT infrastructure to support access and analyses of externally-linked databases	Workflow tracking system
E-Platform Initiatives									
Firebird	√	√							
Collaboration	√	√			√				
Pre-Market Initiatives									
Regulated Product Submission (RPS)	√	√	√	√					
Electronic Submissions Gateway (ESG)	√	√	√	√					
eCTD Review System	√	√	√	√					
Workflow Tracking and Information Management System (DAARTS)	√			√					√
Information and Computer Technologies for the 21st Century (ICT21)	√		√	√	√	√	√		√
Common Electronic Document Room (EDR)						√			√
Electronic Labeling Review System	√	√		√	√				√
Electronic Listing	√	√		√					√
Substance Registration System	√			√	√				√
Clinical/Preclinical Data Standards and Initiatives									
CDISC - HL7 Project	√	√				√		√	
BRIDG Model	√	√				√		√	
Janus Data Warehouse	√	√	√			√	√	√	
Standard for Exchange of Nonclinical Data (SEND) Pilot	√	√							
Electronic Case Report Form (eCRF) Pilot	√	√				√		√	
Clinical Data Acquisition Standards Harmonization (CDISC CDASH)	√	√				√		√	
Product Stability Data Standard	√	√		√	√				
CDISC ADaM Analysis Data Model	√	√				√		√	
Post-Market Initiatives									
MedWatch Plus	√	√				√	√		√
Sentinel System						√	√	√	√

Figure 4: FDA initiatives to modernize agency infrastructure and services.

Some of these initiatives, as well as related initiatives, are discussed in more detail on the following page.

Pre-market initiatives:

- The Regulated Product Submission (RPS) initiative will define one message structure that can be used for all regulated products. The initiative is necessary because, frequently, files in one submission unit are related to files in earlier submissions. The initiative will facilitate the efficiency and process review of numerous files sent over time.[4]

- The Information Computer Technology for the 21st Century (ICT21) initiative is an extensive IT modernization program encompassing data management, data warehousing, IT infrastructure and IT security.[5]

- The Common Electronic Document Room (EDR) initiative will perform a check on each submission sent to the EDR for file formats used and the integrity of bookmarks and hypertext links.[6]

Product Quality and Compliance initiatives:

- The Harmonized Tracking of FDA Regulated Entities initiative will harmonize and modernize the information management and business processes for tracking regulated establishments and their products. The objective is to improve the regulatory processes that ensure product quality by making them more efficient, reliable, and consistent across the agency. Two components of this initiative are the:
    - Electronic Drug Establishment Registration and Product Listing initiative, which will make the complete list of drug products marketed in the United States readily accessible electronically (this includes human and animal drugs and biologics).[7]
    - Electronic Medical Device Registration and Listing initiative, which will make the complete list of medical device products marketed in the United States readily accessible electronically.

Post-Market initiatives:

- The MedWatchPlus initiative will expand the current MedWatch program and enable the FDA to improve the timeliness, accuracy, and usability of its product safety surveillance data. The MedWatchPlus initiative provides a user-friendly Internet portal for anyone to report an adverse event resulting from an FDA-regulated product. The portal will be supported by an agency-wide repository of adverse event reports (FAERS), which include integrated safety signal management and analytical tools.

- The Sentinel Initiative will involve the creation of a nationwide post-market drug monitoring system. Ultimately the system will support the safety monitoring of all FDA-regulated products by enabling the FDA to query multiple, existing data sources (consistent with strong privacy and security safeguards), such as electronic health record systems and medical claims databases, for information about medical products.

The Janus initiative

- The Janus initiative is designed to improve the FDA's 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. Janus initiative will enable the FDA to:
    - Establish an enterprise-wide data architecture, and standards, for facilitating the integration of structured scientific data (for example, clinical trial data or animal toxicology data) from a wide variety of internal and external sources to create large-scale, data-sharing infrastructures to support clinical trials, post-marketing, registration activities, and manufacturing lifecycle activities;
    - Develop the standards-based scientific data exchange networks that are needed to ensure the quality, safety, and efficacy of medical and consumer products as defined by the FDA's regulatory mandate;
    - Create structured scientific data repositories that support the acquisition, validation, integration, and extraction of data from the increasingly large and complex datasets received by the agency; and
    - Make use of enhanced analytical, mathematical, visualization, and other computational tools and techniques for enabling reviewers to search, model, and analyze data to conduct better safety and efficacy analyses.

Conclusions

The benefits of the FDA's e-transformation could be "game changing". Imagine conducting a label negotiation in real-time with FDA review staff, being able to cooperate and mark up documents in real time, or the possibility of reviewing SOPs and batch records electronically with an investigator.

The agency's move toward an electronic world where all regulated product information comes in electronically is already underway.

In November 2008, the FDA announced the award of up to $2.5 billion in contracts to modernize information technology over the next ten years. This award supports the cornerstone of the FDA's Information Technology and Bioinformatics initiatives, which include extensive IT modernization programs encompassing data management, data warehousing, IT infrastructure and IT security.

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- Don St. Pierre, Associate Director Policy and Operations, CDRH
- Stephen Sykes, Deputy Director, Office of Surveillance and Biometrics, CDRH
- Donna-Bea Tillman, PhD, Director, Office of Device Evaluation, CDRH

References

1. Health Level Seven is one of several American National Standards Institute (ANSI) -accredited Standards Developing Organizations (SDOs) operating in the healthcare arena. Most SDOs produce standards (sometimes called specifications or protocols) for a particular healthcare domain such as pharmacy, medical devices, imaging or insurance (claims processing) transactions. Health Level Seven's domain includes clinical and administrative data.

2. For more information about vocabulary developed by the National Cancer Institute's Enterprise Vocabulary Services, please refer to the following link:
http://ncicb.nci.nih.gov/NCICB/infrastructure/cacore_overview/vocabulary

3. For more information, please refer to the following link:
http://www.fda.gov/oc/datacouncil/20070917_cdisc_hl7_project.pdf

4. For more information about the RPS initiative, please refer to the following link:
https://gforge.nci.nih.gov/plugins/wiki/index.php?Regulated%20Product%20Submission&id=234&type=g

5. For more information about ICT21, please refer to the following link:
http://www.fda.gov/bbs/topics/NEWS/2008/NEW01893.html

6. For more information about EDR, please refer to the following link:
http://www.fda.gov/cder/regulatory/ersr/

7. For more information about this initiative, please refer to the following link:
http://www.fda.gov/bbs/topics/NEWS/2006/NEW01435.html

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