FDA Regulatory and Technology Trends and Their Impact On The Life Sciences "Ecosystem"

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Trusted advisors to Life-Science Executives

Research Study

- Over the Summer, Axendia coducted a research study identifying key shifts in FDA's Organizational and Technology infrastructures aimed at Facilitating Electronic Interactions with Regulated Companies.

- Acknowledgement
  - **This study was underwritten by Master Control**
  - **To learn more about the underwriter, please visit http://www.mastercontrol.com/index.html**

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Study Approach:

- Axendia gathered information from proprietary and published sources
- Axendia conducted 1 on 1 interviews with the following FDA personnel to gather information for this study:
  - Dr. Armando Oliva –FDA Deputy Director for Bioinformatics
  - Donna-Bea Tillman, Ph.D, Director, Office of Device Evaluation CDRH
  - Don St. Pierre – Director of the Office of Post-market Transformation
  - Paul Fisher, Senior Policy Analyst - Pre-Market Initiatives
  - Stephen Sykes, Deputy Director, Office of Surveillance and Biometrics - Pre-Market Initiatives
  - John Murray, Part 11 Lead

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What is the Transport Protocol for Interactions with FDA?

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FDA Interactions

- Historically, interactions between FDA and Life-Science Manufacturers have required the creation and dissemination of reams of paper documents for review, approval and audit.
- Over the last few years, FDA has recognized the need foster electronic interactions with the organizations it regulates.

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FDA Initiatives at a glance

FDA Initiatives	A 1. b Implement new systems consistently across divisions	A.1.c Update Tech Specifications as needed	A.1.d Extend single entry to two way transmission	A.1.e Electronic IND, NDA and BLA with automated links	A.1.f Human drug labeling modular system/exchange	A.1.g Standards based postmarket systems							D 1. Enhanced adverse event reporting system and surveillance tools	D 2. IT infrastructure to support access and analyses of externally-linked databases	D 3. Workflow tracking system
E-Platform Initiatives															
Firebird	✓	✓													
Collaboration Portal	✓	✓			✓										
Pre-market Initiatives															
Regulated Product Submission (RPS)	✓	✓	✓	✓											
Electronic Submissions Gateway (ESG)	✓	✓	✓	✓											
eCTD Review System	✓	✓	✓	✓											
Workflow Tracking and Information Management System (DARRTS)	✓			✓											✓
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						✓							✓	✓	✓

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Should I Stop or Should I Go?

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FDA Shifts to Agency-wide IT Model

- Due to a variety of external pressures, the FDA is conducting studies to determine a strategy for modernizing IT infrastructure and services.
- FDA is working to shift its IT decision-making and governance to an Agency-wide, less de-centralized model.
- This governance structure will institute an enterprise approach to automating common or special purpose IT solutions by defining roadmaps for each business process area that will be further refined into discrete IT solutions.
- FDA must resolve technical and policy issues in order to establish standard, Agency-wide solutions for secure exchange of information with Industry.

Source: PDUFA IV Information Technology Plan

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The Path to e

The real promise of
"Electronic Review"
lies beyond simply receiving
submissions in electronic format

"We don't want to pave the cow-path"

Donna-Bea Tillman, Ph.D
Director, Office of Device Evaluation CDRH

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Future State

- FDA is actively pursuing a future world where all regulated product information comes in electronically

- Active discussion are underway to move to an all electronic submission environment for all regulated product information, whether it be product quality, manufacturing, pre market, post market.

Dr. Armando Oliva

FDA Deputy Director for Bioinformatics

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FDA's IT Vision

- The FDA is committed to achieve the 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.

- The FDA vision is a fully electronic submission and review environment of all regulatory documents and data; and the elimination of future paper-based submissions.

Source: PDUFA IV Information Technology Plan

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The BioInformatics Board

IT Governance at the Agency

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FDA Bioinformatics Board

- The FDA Bioinformatics Board (BiB) in coordination with the Office of Information Management (OIM) determines the agency information management (IM) strategy.
- The formation of the BiB in February 2006 addressed a growing number of business automation challenges facing FDA, and was intended to ensure that Agency planning for future business automation meets the needs of FDA programs while satisfying external demands on the Agency.
- The BiB works under a strategic framework for automation established by the Commissioner and implemented by the FDA Management Council.
- The BiB coordinates and oversees all activities and decisions related to business automation planning, acquisition, and implementation throughout FDA, and ensure that the activities related to its charge are communicated to all levels of the Agency.
- The BiB also ensures coordination of activities among FDA representatives to the Federal Health Architecture program and other federal health informatics initiatives, the FDA Regulation Policy Council, the FDA Data Standards Council, and the Enterprise Architecture Review Board, particularly with regard to business process planning and regulatory policies.
- The BiB reports directly to the FDA Management Council.

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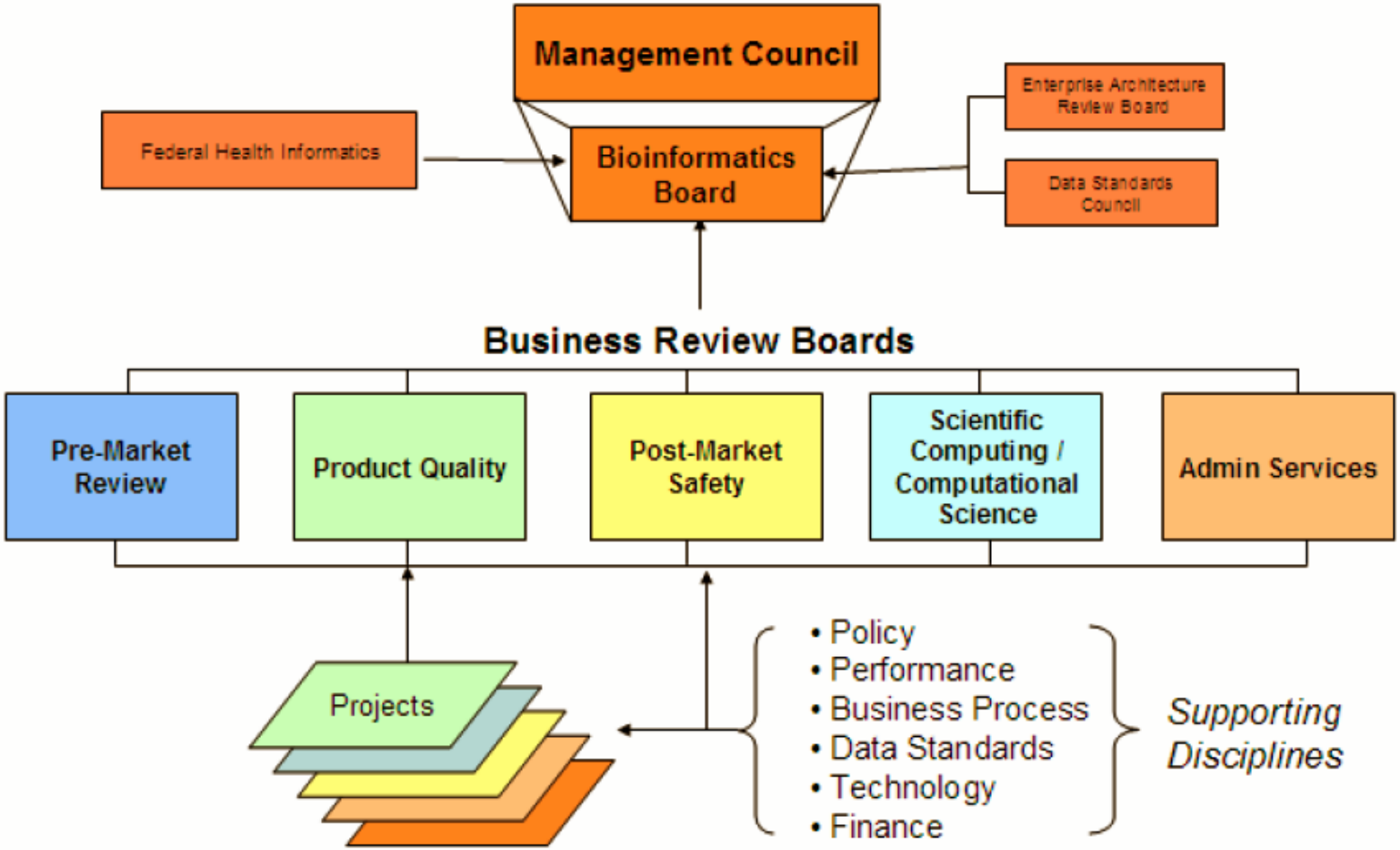
BIB Organizational Chat



http://www.fda.gov/OHRMS/DOCKETS/98fr/FDA-2008-N-0352-bkg.pdf

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Business Review Boards

- Five Business Review Boards (BRBs) set business needs for specific cross-agency business processes
  - Pre-Market Review : electronic submission, tracking and review processes (Paul Fisher)
  - Post-Market Safety : electronic adverse event reporting and database management (Stephen Sykes)
  - Product Quality and Compliance : manufacturing regulation and tracking inspections, product movement (Joanna Weitershausen)
  - Scientific Computing/Computational Science: needs of laboratories and quantitative scientists (Gerry Gray)
  - Administrative Services

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Key Initiatives for BIB and BRBs

- Pre-Market Safety
  - Common Electronic Document Room (EDR)
  - Regulatory Product Submissions (RPS)
- Product Quality and Compliance
  - Harmonized inventory of FDA related entities (registration and listing)
- Post Market Review
  - MedWatchPlus – FDA wide AERS (FAERS)
- Scientific Computing
  - Information Computer Technology for the 21st Century (ICT21)

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FDA's Enterprise Architecture

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FDA Enterprise Architecture

- The Target Enterprise Architecture (EA) for the FDA 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.

- 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 the FDA managers and staff to define a vision, develop strategies and plans for achieving the vision, make resource decisions, 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 those business processes will be supported by a common set of technologies.

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SOA at FDA

- The FDA has numerous information systems, executes overlapping business and information processes, and relies on a number of technologies that are expensive to maintain.
- To reduce costs and streamline operations, the FDA is migrating toward a more service-oriented and component-based approach to architecture.
- This approach, consistent with government and industry best practice, will enable the FDA to "build once, use often."
- By separating out the functionality or capabilities of a business process or application into discrete pieces, components can be shared and reused across the enterprise.

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Enterprise Architecture Objectives

- **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 in support of the business, and applications and technology solutions are driven by business needs. It also allows 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 and operation and maintenance costs by eliminating duplicative investments, promoting 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 be able to more quickly assess the relative value of initiatives, and to identify duplicative and misaligned initiatives.

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Data Standards

The FDA recognizes the importance of, and is committed to using open-consensus based data standards for regulatory submissions wherever possible.

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Data Standards

- FDA divides data standards into two broad categories: exchange standards and terminology standards.
  - 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. For example, Structured Product Labeling (SPL) is an exchange standard for product information.
  - Terminology standards, on the other hand, provide a consistent way to describe concepts. For example, the Unique Ingredient Identifiers (UNII), developed by FDA, provides a consistent way to describe substances in foods and drugs.

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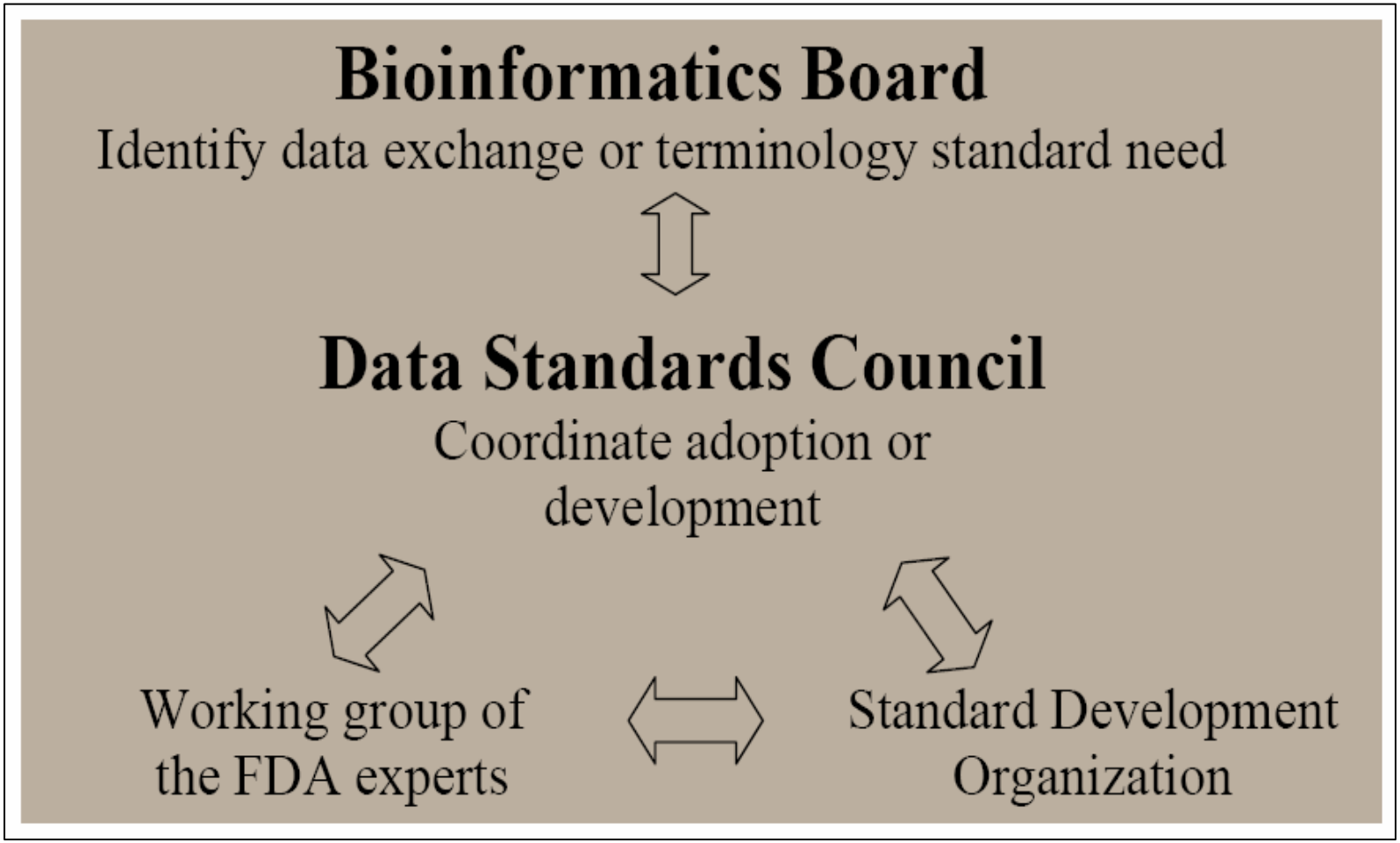
Standards Development and Adoption



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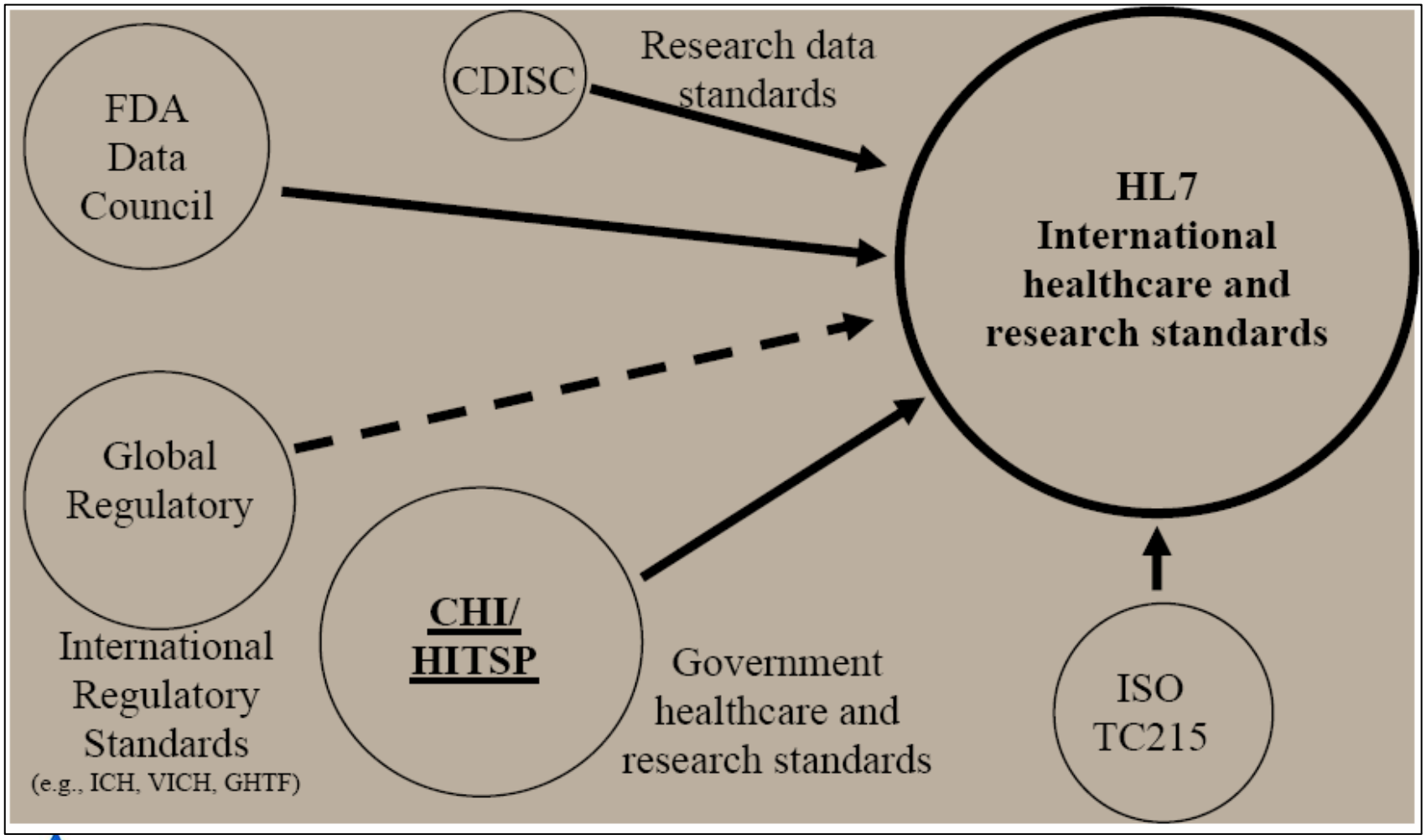
FDA Works Within HL7



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Consolidated Health Informatics

Messaging Standards

- **Imaging-** DICOM®
- **Medical Devices -** IEEE™ 1073
- **Pharmacy-** NCPDP-SCRIPT
- **Clinical –** HL7®

Vocabulary Standards

LOINC®
- Laboratory Result Names
- Laboratory Test Order Names

SNOMED CT®
- Laboratory Result Contents
- Non-Laboratory Interventions/Procedures
- Nursing
- Diagnosis/Problem Lists
- Anatomy - National Cancer Institute's Thesaurus *

Federal Drug Terminologies
- Medications

HL7®
- Demographics
- Immunizations
- Clinical Encounters
- Text-based Reports (CDA)
- Units

HUGN
- Genes

EPA
- Chemicals

HIPAA Approved Code Sets
- Billing/Financial - HIPAA Transactions and Code Sets

No Standards Designation
- Supplies, History & Physical, Population Health,
- Disability, Physiology, Proteins, Multimedia

*To support more specific research programs and clinical trials, the National Cancer Institute's Thesaurus maybe used in conjunction with SNOMED CT. The two terminologies will be related through mapping.

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FDA Data Standards Activities

- Activities associated with this phase of data standards management include:
  - Interaction with standards development and standards maintenance organizations
  - Exchange standards development
    - Data standards requirements gathering / use case development
    - Modeling requirements and use cases (e.g., modeling to HL7 Reference Information Model)
    - Testing model against requirements and use cases to include development of visualization tools (e.g., stylesheets, XForm) documentation and coordination assistance
    - Balloting (e.g., ballot preparation, presentation and reconciliation)
    - Accreditation
    - Conformance specifications (implementation guide)
  - Terminology standards development
  - Standards maintenance (e.g. Unique Ingredient Identifier, NCI Enterprise Vocabulary Services)
  - Training and implementation support
    - Support for training or other related IT development activities associated with standards adoption and implementation (e.g. data type specification, message instance examples or data standards harmonization)

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The Janus Initiative

In Roman mythology, Janus (or Ianus) was the god of gates, doors, doorways, beginnings and endings.

He was frequently used to symbolize change and transitions such as the progression of past to future, of one condition to another, of one vision to another.

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The Janus Initiative

- Janus is designed to improve 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 that facilitate the integration of structured scientific 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 life-cycle 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 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;
  - Make 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.

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Janus Solution Components

- **Janus Data Model (JDM)**
  - a comprehensive logical data model for the scientific data needed to evaluate the safety and efficacy and quality of FDA regulated products.
- **Janus Database (JDB)**
  - a physical database (or multiple physical databases forming a virtual database) that instantiates all or part of the Janus data model.
- **Janus Data Importer (JIM)**
  - a set of software tools that can be used to extract, validate, transform, and load scientific data into the Janus database.
- **Janus Data Exporter and Data Mart (JEM)**
  - a set of tools that support the creation and maintenance of views or materialized views of standard analytical data sets for use by review tools.
- **Janus Analytical Tools (JAM)**
  - a set of review tools that are capable of using JDB data either through JEM data views or by direct access to the JDB.

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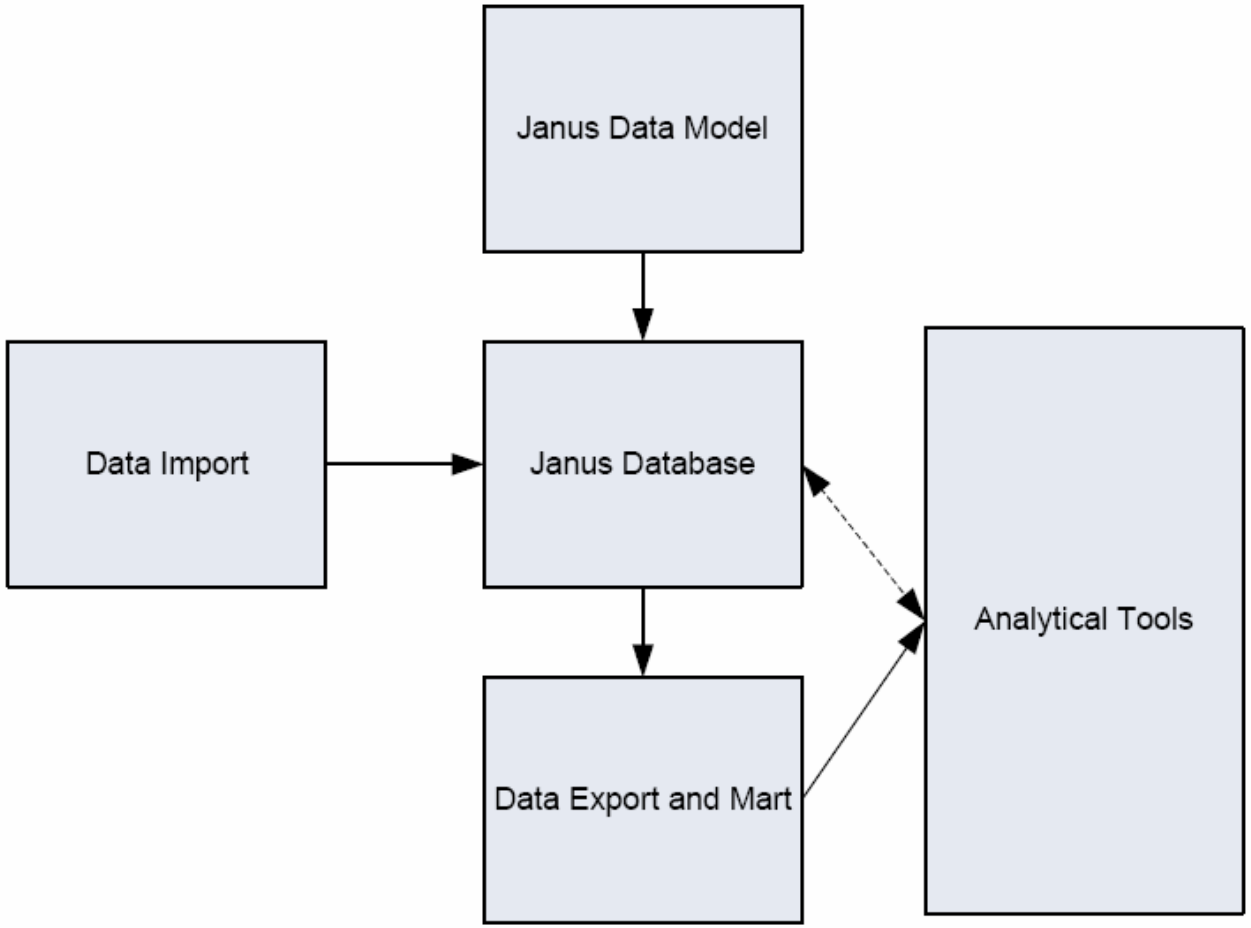
Janus Functional Components



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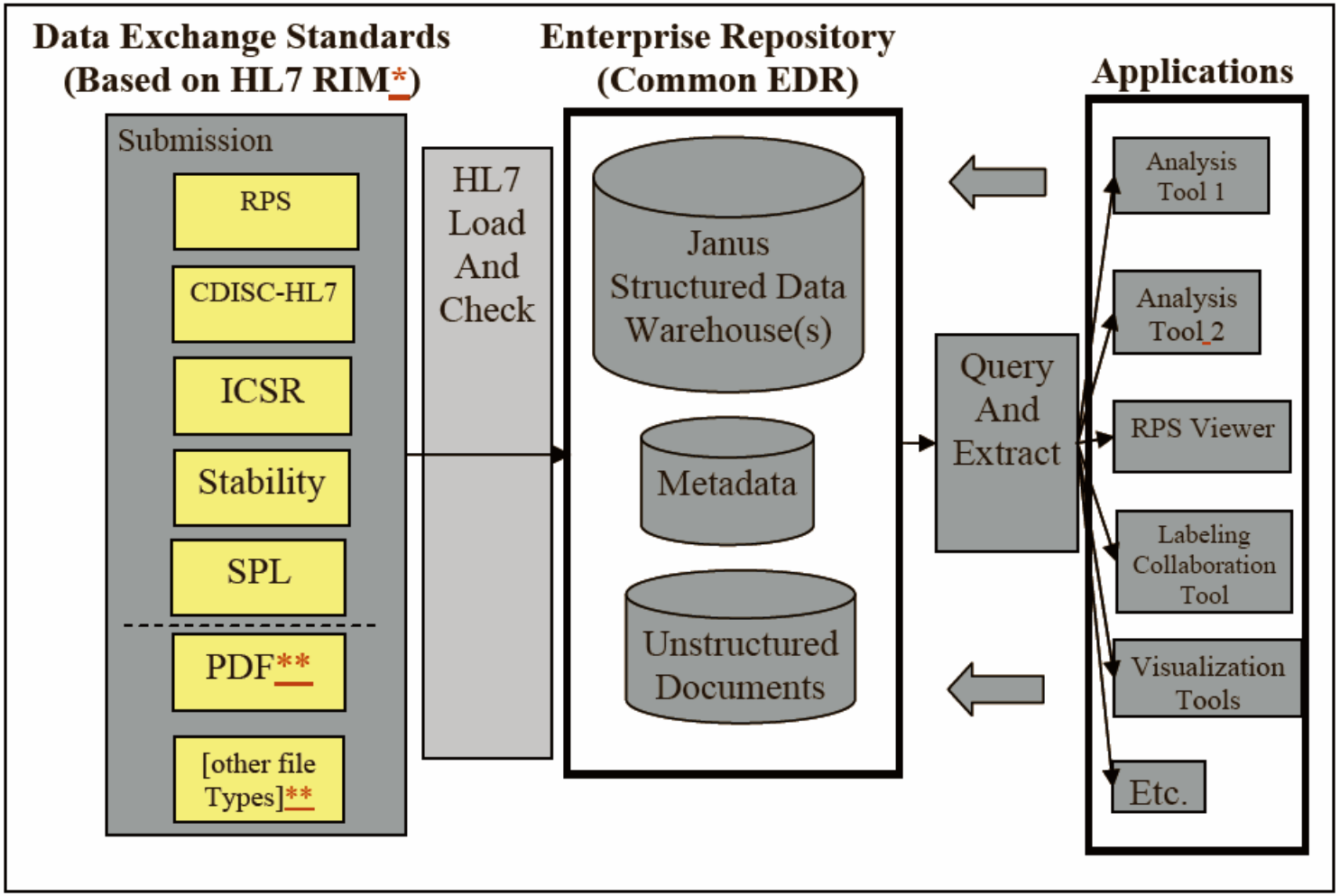
Target Data Flow for Regulated Product Information



*RIM – Reference Information Model
** non-RIM based information

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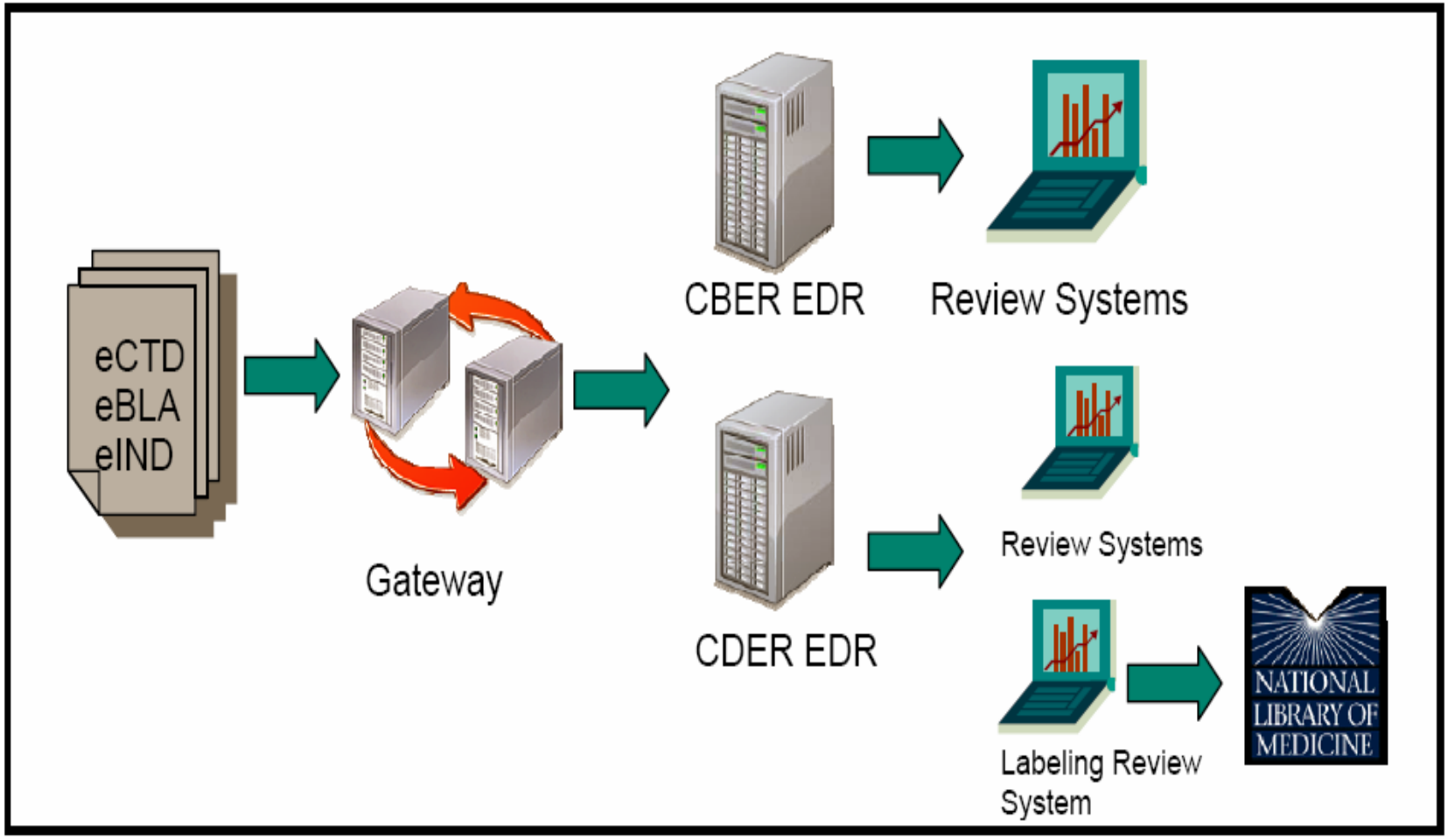
Premarket Current State



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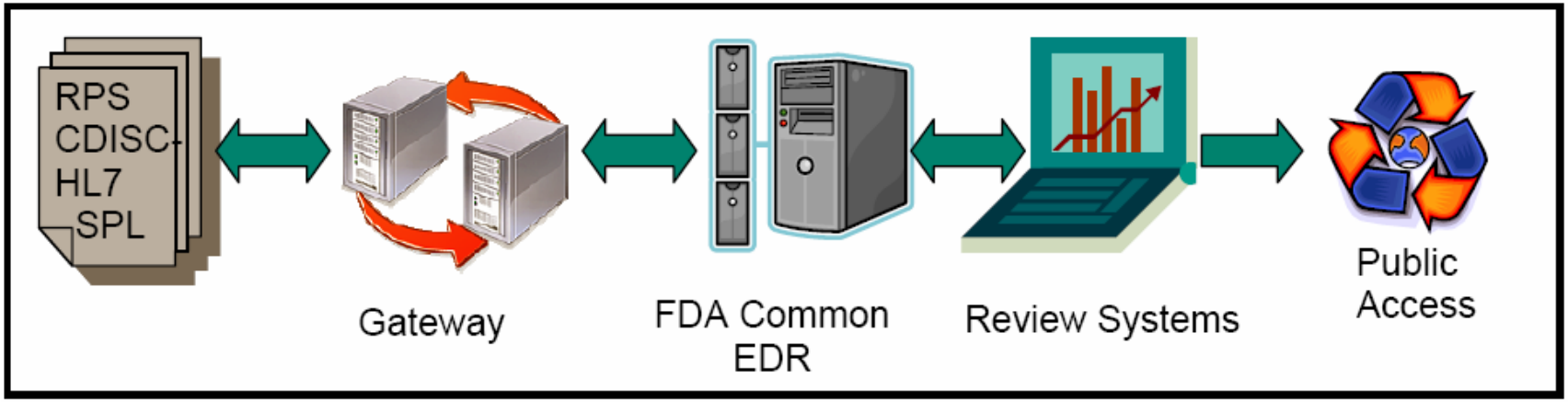
Premarket Target State



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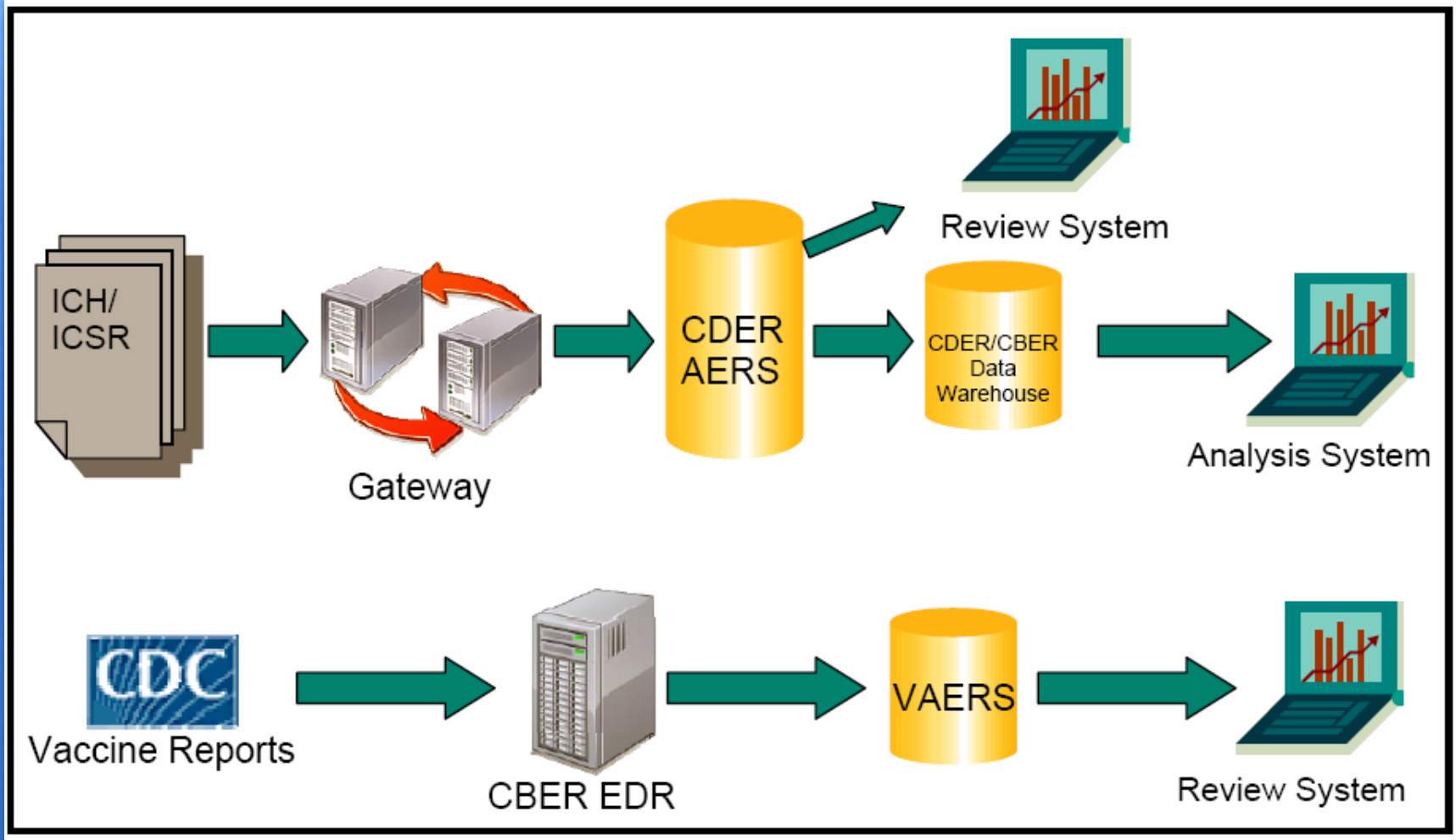
Postmarket Current State



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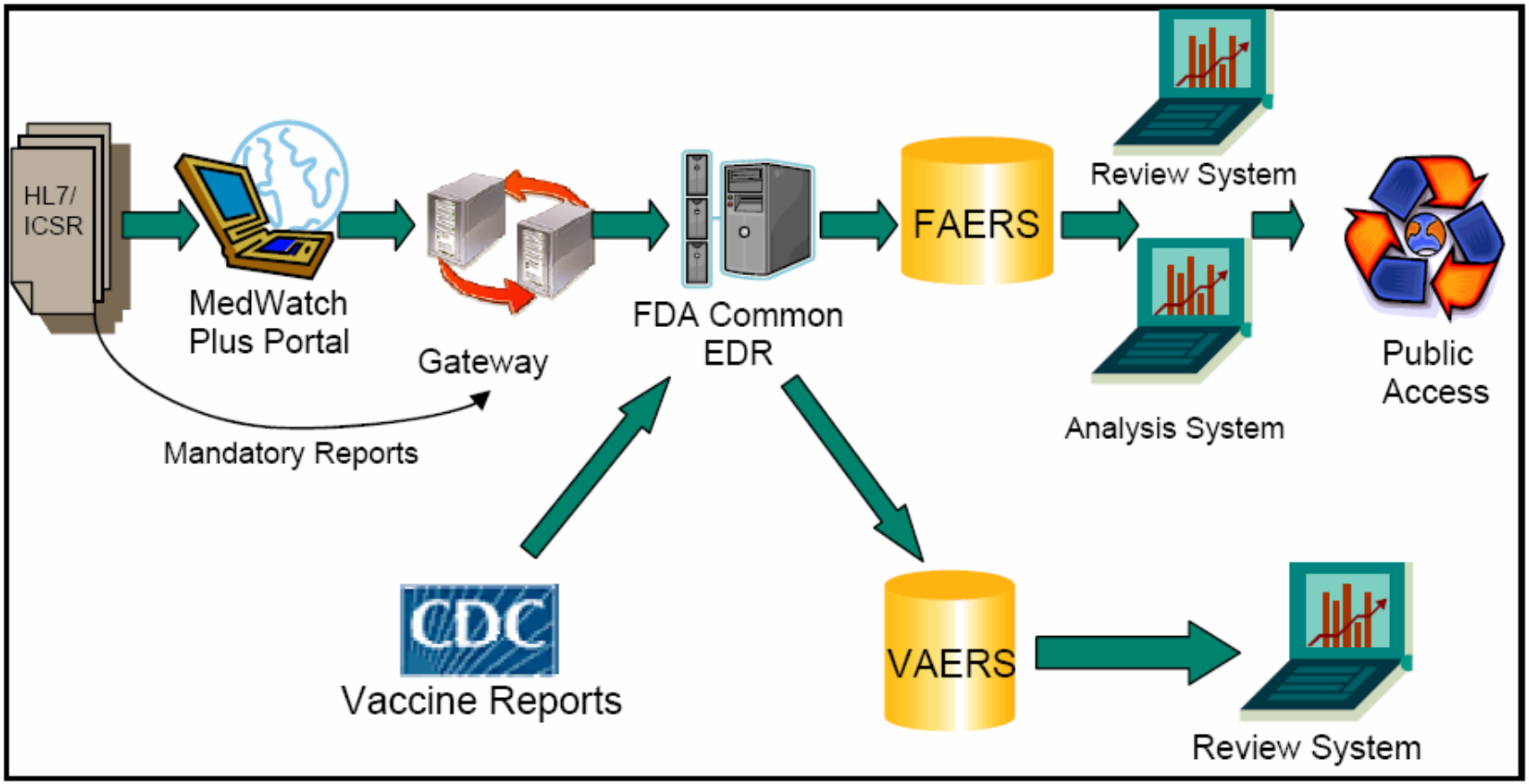
Postmarket Target State



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MedWatch^{Plus}

- The MedWatch^{Plus} initiative will enable the 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.
- The portal will be supported by an Agency-wide repository of adverse event reports (FAERS) with integrated safety signal management and analytical tools.

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Sentinel System

- 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.
- The system will enable FDA to query data sources at remote locations, consistent with strong privacy and security safeguards.
- Data sources will continue to be maintained by their owners.

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21 CFR § 11
Part Two

Coming to Theaters

11/11/11

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Part 11

- Draft proposal submitted for Review to FDA Management and Legal
  - Awaiting feedback

John Murray, FDA Part 11 lead

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Part 11 in a State of Flux

- Where is part 11 going
  - Moving from a prescriptive approach to a wider interpretation
- One of the problems of Part 11is that it is voluntary
  - companies may chose to submit electronically or on paper
    - part 11 applies only applies if electronic
    - Study data submitted on paper is worthless. Cannot be analyzed

Dr. Armando Oliva –FDA Deputy Director for Bioinformatics

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Janus and Part 11

- Part 11 is not adequate to support Janus
- Proposing new regulation to require submission of study data in standard form
- Proposed rule for studies on drugs and biologics
- Long term goal all study data submitted electronically
- Part 11 only provides for voluntary submission of electronic data
- To realize Janus vision, FDA must require all data FDA industry/Agency interactions electronic

Dr. Armando Oliva –FDA Deputy Director for Bioinformatics

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What Does The Future Hold

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FDA Awards up to $2.5 Billion to Modernize Information Technology

Cornerstone of 21st century Bioinformatics Initiative

- The U.S. Food and Drug Administration announced the selection of ten contractors to receive up to a total of $2.5 billion for information technology (IT) and data center management services over the next ten years.
- The contract is the cornerstone of the FDA's Information Technology for the 21st Century (ICT21) bioinformatics initiative, an extensive IT modernization program encompassing data management, data warehousing, IT infrastructure and IT security.
- "This contract sets the stage for the FDA to have IT to acquire, analyze and act on data critical for import protection, food protection and medical product safety plans," said Andrew C. von Eschenbach, M.D., Commissioner of Food and Drugs.
- "We are creating a high-tech, efficient, data management system designed to meet the needs of those who must accomplish our mission -- protecting and promoting the health of the American public."

September 30, 2008

http://www.fda.gov/bbs/topics/NEWS/2008/NEW01893.html

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Future State

- FDA actively pursuing a future world where all regulated product information comes in electronically
- Active discussion underway to move to an all electronic submission environment for all regulated product information
  - Pre market
  - Submissions
  - Product quality
  - Manufacturing
  - Post market

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What The Future Holds

- Electronic Interactions
- Paper Interactions
- Use of Standards (i.e., HL7, CDISC, GHTF and others)
- More structure to submissions
- Controlled vocabularies and nomenclature
- Digital signatures
- Trusted electronic communication and collaboration among healthcare stakeholders

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Thank You

Questions?

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