CDER eSubmission Update

Regulated Product Submission (RPS) Update

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Outline

• FDA and RPS Goals
• RPS Message
• FDA Implementation Planning
FDA Electronic Submission and Review

• FDA’s goal is to implement a standards-based end-to-end fully electronic receipt, review, dissemination, and archival environment

• PDUFA IV Performance Goals
  • FDA is committed to achieve the long-term goal of an automated standards-based information technology (IT) environment for the exchange, review, and management of information supporting the process for the review of human drug applications throughout the product life cycle.

Regulated Product Submission (RPS) Goal

• Create one standard (exchange message) that can be used for the submission of any regulated product
  – Release 1
    • Provide a flexible framework that will allow sponsors to send regulatory information using predefined parameters to identify and catalog their content
    – Reviewers will be able to consistently locate discipline specific information and data
    – Allows for the cross-reference of previously submitted material
  – Release 2
    • Standardize Submission Response (i.e., two-way communication)
    • Facilitate the processing of submissions and correspondence

FDA Electronic Submission and Review

• To meet Agency and PDUFA objectives RPS will be use to;
  – Standardize submission format/structure
  – Facilitate processing of the submissions
  – Allow sponsors to cross-reference previously submitted material
  – Standardize communication format/structure with sponsors
Regulated Product Submission

- Health Level Seven (HL7) exchange standard
- Scope
  - Animal and Human products
    - Including but not limited to food additives, human therapeutics, veterinary products, and medical devices
  - Worldwide use
    - Same model for all product types to all regulatory authorities
  - Out of Scope - Document content

Regulated Product Submission

- Currently working on release 2 of the RPS message
- Next Version of the eCTD will use the RPS exchange message
  - ICH Draft Requirements Review
    - HL7 RPS R2 Development and Requirement Team
    - Leads review draft ICH requirements
    - Most ICH requirements met by RPS R1 & R2
  - ICH meeting the week of June 8th — Next Steps

Regulated Product Submission

- Release 1
  - Leveraged Human Pharmaceuticals experience (ICH/eCTD)
  - Draft Standard for Trial Use (DSTU) - May 2006
  - HL7 Normative Standard – May 2007
  - ANSI Standard – March 2008
  - Implementation Guide – May 2008
RPS Message Capabilities

• RPS Release 1 provides the capability to;
  – Standardize submission format/structure
  – Cross-reference previously submitted material owned by the sponsor
  – Handle Submission/Document Lifecycle (e.g.; append, replace, delete)
  – Handle bundled supplements/trans-BLA
  – Correct/modify attributes

Regulated Product Submission

• Release 2
  – RPS Project Kick off meeting July 24, 2008
  – Sub-Teams Identified
  – Phased and Iterative Approach
    • Lifecycle 1 DSTU January 2010
    • HL7 RPS 2 documentation and activities posted on RPS HL7 wiki
        • Username: wiki Password: wikiwiki

RPS HL7 Release 2 Status

• Lifecycle One – September 2008 through January 2010
  – Iteration #1 – Two-way communication / Submission Information
    • Requirements complete
    • Development complete
    • Test planning and execution – Reviewing test case comments
  – Iteration #2 – Multi-regulator / Multi-Product
    • Requirements
      – Multi-regulator complete
    – Multi-product ongoing – plan is to complete requirements by June 30th
    • Development – Multi-regulator complete
    – Test planning and execution – complete by 8/24/09
  – Iteration #3 – Rework of Iteration #1 and #2 based on testing
    – Iteration 1 & 2 modifications – 8/25/09 – 10/05/09
    – Draft Standard for Trial Use (DSTU) – January 2010
      • Ballot Discussions and Prep – 10/06/09 – 11/27/09
      • Ballot and Reconciliation – 12/28/09 – 1/15/10
RPS Message Capabilities

- RPS Release 2 will provide the capability to:
  - Handle two-way communication: The regulatory authority (e.g., FDA) will use RPS to send correspondence (e.g., request for additional information, meeting minutes, application approval) to the submitter.
  - Exchange contact information.
  - Associate to the submission/submission unit.
  - Multiple contacts (e.g., Technical, CMC).
  - Classify submission content/purpose.
  - From Sponsor/Applicant (e.g., Meeting Request, New Protocol, Response to Hold).
  - From Regulator (e.g., Information Request, Response to Meeting Request, Approval).
  - Handle Multi-regulator submissions.
  - Capture basic product information.

Submission Hierarchy

Reviewable Unit
The collection of files provided to the Regulatory Authority at one time

Keywords are used to further define the context of documentation. Types defined by regulatory authority (e.g. manufacturer, study), value defined by business (e.g. Acme, Study 12345)

Controlled vocabulary
- Defines the structure and values
  - Submission Format – Table of Contents
  - Submission Information
    - Contact Type
    - Submission Unit Category/Subcategory
- Can be different based on application type, regulatory authority, and international agreements
  - Application
    - Human pharmaceuticals (NDA, BLA)
    - Devices (PMA, 510K)
  - Submission (original, supplement, etc.)
  - Submission units (original, amendment, etc.)
  - Documentation (synopsis, protocol, summary of clinical, etc.)
Keywords are used to further refine the table of contents.

## Submission Hierarchy

- **Application**
  - All submissions that are grouped together for regulatory purposes
  - Original NDA and Supplements
  - Original IND and Amendments

- **Submission**
  - What gets approved (e.g. NDA, NDA Supplement)

- **Submission Unit**
  - What is being sent to the FDA
  - Can probably does contain many documents
  - Equivalent to a set of paper binders/volumes
  - Equivalent to an eCTD sequence

- **Reviewable Unit**
  - A mechanism to organize Submission Units for the purpose of a modular review (e.g. CMC, Pharm Tox)

- **Context of Use**
  - Pointer to a file
  - Places a document in the table of contents
  - File can be reused
    - Files in investigational application can be reused in marketing application
    - Version control

- **Keyword**
  - Keywords are used to further define the context of documentation.
Current FDA Implementation Planning

- RPS 2 DSTU - January 2010

- Integration Testing
  - Planning & Industry Coordination 1/2010 – 10/2010

- Production (Dependent on testing outcomes)
  - Production 9/2011

RPS Release 2 Testing

- HL7 Requirements/Development phase – “Paper” testing

- DSTU Phase
  - Planning (through 10/2010)
    - Work with industry to identify testing partners
    - Identify test scenarios and processes
    - Ensure vendor tools are available
    - Perform internal vendor tool selection and testing
    - Perform testing
    - Identify issues/questions for implementation
    - Determine if modifications are required to the RPS message

Reference Slide
PDUFA IV Cross-reference & two-way communication (transmission) goals

**XIV Information Technology Goals**

**A. Objectives**

1. FDA is committed to achieving the long-term goal of an automated standards-based information technology (IT) environment for the exchange, review, and management of information supporting the process for the review of human drug applications throughout the product life cycle. Toward this goal, FDA plans to work to achieve the following objectives by the end of FY 2012:

   a) Extend the capability of the secure electronic single point of entry to include two-way communication of regulatory correspondence.

   b) Establish an automated standards-based electronic submission and review environment for INDs, NDAs, and BLAs and their supplements, that enables the following functions over the life cycle of the product:

      1. Electronic IND, NDA, and BLA submissions received by FDA can be archived to enable retrieval through standardized automated links.

      2. Electronic IND, NDA, and BLA submissions can include cross-references to previously submitted electronic materials through standardized automated links.

      3. Archived electronic IND, NDA, and BLA submissions can be retrieved through standardized automated links.

PDUFA IV Performance Goals (http://www.fda.gov/oc/pdufa4/pdufa4goals.html)