eCTD IV:
It's Almost As Fun As Super Bowl XLIX

DIA eRegulatory and Intelligence Annual Conference

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Pre-Game Warmup

- Regulated Product Submission
  - Health Level Seven (HL7) standard
    - Exchange standard that can be used for the submission of any regulated product
    - Major International Stakeholders
      - International Conference on Harmonisation (ICH)
      - International Medical Device Regulators Forum (IMDRF)
- What does this mean in relation to eCTD v4?
  - *Will use the HL7 RPS exchange message to implement the eCTD v4 ICH and regional requirements*
    - The eCTD hierarchy is not changing
    - Some additional headings, based on change requests
    - New “group title” keyword

RPS Playbook Terminology

- Application – Dossier/Application
- Submission – Regulatory Activity
- Submission Unit – Sequence
- Context of Use
  - Placement of a document within a TOC (eCTD) heading/section
- Keyword
  - Additional information (e.g., manufacturer) used to organize files within a TOC heading/section

RPS Basics

Application

Submission - Original


Original


Amendment


Amendment

Submission Unit

Submission - Supplement


Supplement


Amendment


Amendment

Accomplishments to Roar About

- Successful HL7 RPS Normative ballot – September 2014
- ICH Step 2 signoff – January/February 2015
  - ICH eCTD v4.0 Implementation Guide (Draft)
  - Controlled Vocabulary
  - Submission Format Specification
- Posting of ICH & Regional Specifications for Public Comment

I Kissed eCTD v4.0 and I Liked It

- ICH Comment & Regulatory Consultation (February 2015 – May 2015)
  - ICH information posted on; http://estri.ich.org/new-eCTD/index.htm
  - Comment Period
    - ICH comment period closes on May 22, 2015
    - FDA comment period closes on May 27, 2015
- FDA regional information (e.g., FDA M1 IG) posted on;

  http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm309911.htm

eCTD v4.0 Enhancements

- ***Message is managed through the use of controlled vocabularies***
  - Currently: requires modification of the eCTD DTD
  - RPS:
    - Headings are a controlled vocabulary and would not require modification of the standard or review tool
    - Capability to tailor requirements based on application type (e.g., NDA, MF)
- ***Complete standard***
  - Regional model/xml
    - Currently: handled separately by each region
    - RPS incorporates regional requirements to enable harmonization
  - Simplified submission management
    - Currently: requires sending numerous messages per submission
    - RPS combines all submission information into a single message

eCTD v4.0 Enhancements

- ***Enhanced control of dossier***
  - Simple reuse of previously submitted files
    - Currently: possible but it's not well understood and CBER does not allow
    - RPS greatly simplifies reuse using a unique reference id
  - Document Ordering
    - Currently: defined by each review tool; may not be the same between tools
    - RPS allows the submitter to explicitly define the display order for files in a specific section

eCTD v4.0 Enhancements

- ***Enhanced control of dossier***
  - Keyword/attribute modifications
    - Currently: a slight misspelling in eCTD attributes (e.g., manufacturer) creates separate eCTD sections
    - RPS keywords/attributes are managed and corrections are allowed simplifying the modification process
  - Enhanced Life-cycle control
    - Currently: life-cycle only allows for one-to-one
    - RPS life-cycle allows one-to-one, one-to-many, many-to-one
  - New eCTD v4 Keyword “Group Title”
    - Sponsors can use group titles based on M4 Granularity Document where “One or multiple documents can be submitted”

eCTD v4.0 Enhancements

- ***Enhanced identification of information contained within a submission***
  - Identify certain content (e.g., datasets) for additional processing
  - Currently: By folder or leaf title
  - RPS applies this to the document metadata

- ***Support for two-way communication***
  - Currently: one-way communication
  - The regulatory authority can use RPS to send correspondence to the submitter

Get Ur Regional Freak On

- Application Information
  - Applicant
  - Application Type & Number
  - References to related applications (e.g., NDA to a DMF)
  - *Keyword Definition for user-defined keywords (e.g., manufacturer)*
- Submission Information
  - Submission Type (e.g., Original Application, Efficacy Supplement)
  - Contact information
  - Regulatory Review Time: Designate supplement type (e.g., CBE30)
  - *Regulatory Status & Effective Date*
    - Used by FDA for correspondence to the sponsor/applicant
- Submission Unit
  - Submission Unit Id is the unique identifier
  - Sequence Number: *Will expand to six digits*
  - Submission Unit Title/Description
  - *Categorization of Submission Unit*
    - From Sponsor/Applicant (e.g. Meeting Request, Response to Clinical Hold)
    - From Regulator (e.g. Information Request / Advice, Complete Response, Approval)

Work It FDA M1

	M1 DTD 2.01	M1 DTD 3.3	M1 eCTD v4.0
Applicant Id	N	Y	Y
Applicant Name	Y	Y	Y
Application Type/Number	Y	Y	Y
Related Applications	N	Y	Y
Keyword Management	N	N	Y
Submission Id	N	Y	Y
Submission Type	Y*	Y	Y
Regulatory Review Time	N	Y	Y
Regulatory Status/Date	N	N	FDA Only
Contact Information	N	Y	Y
Sequence Number	Y	Y	Y
Submission Sub-Type	N	Y	Y
Submission Description	N	Y	Y
Submission Categorization	N	N	Y

* Submission Type and Subtype values

Don’t forget the World Cup

(Additional Regional Information)

- Application Information
  - For EU, includes
    - Review Procedure (Centralised, Decentralised, Mutual Recognition Procedure, National Procedure)
    - Territorial Authorities (e.g., EMA, Germany – BfArM, France – ANSM)
- Submission Information
  - For EU, Submission Mode (e.g., single, grouped, workshare)
- Product information
  - EU and Japan requesting product information

"Ignite the light/ And let it shine"

(Two-way Communication)

- FDA correspondence to the sponsor/applicant
- Current thinking on the eCTD v4.0 FDA message
  - Application Type & Number
  - Submission
    - Submission Type
    - Regulatory Status & Effective Date, for status change correspondence
    - RPM Contact Information
  - Submission Unit
    - Submission Unit Type = "Correspondence"
    - FDA Sequence Number
    - Categorization, examples are;
      - Acknowledgement
      - Meeting Request Granted
      - Information Request / Advice
      - Complete Response
  - Context of Use & Document
    - Using "m1.25 fda to industry correspondence"

Don’t Be Deflated about the Implementation Challenges

- eCTD vs. RPS Terminology
- XML changes
  - HL7 V3 Messaging - Based on HL7 Reference Information Model (RIM)
  - Use of controlled vocabularies
- Forward Compatibility with eCTD v3.2.2
  - Administrative message to transition to eCTD v4 capabilities
    - Submit Current View, not including documents
    - Transition message will contain minimum set of information to complete the transition
  - Purpose of the transition message
    - Enable Context of Use lifecycle
    - Enable reuse of documents
    - Want to retire 3.2.2 in the future

Don’t Pass On Implementation Planning

- ICH will review IG comments during the June ICH meeting
- ICH Step 4 Signoff (December 2015)
  - Update Step 2 Implementation Guide (June 2015 – November 2015)
- Finalize FDA eCTD v4.0 M1 Implementation Guide (December 2015)
- 2015 - 2017
  - Training of technical staff on HL7 RPS standard and eCTD implementation guides
  - Update automated submission processes and systems
  - Conduct pilot with industry
  - FDA Guidance
  - FDA acceptance of eCTD v4.0 submissions