

# ***IRISS-Forum***

## **eCTD Tool Interoperability Group**

**June 17, 2009 - 7:30am EDT**

### **Attendees**

Laura Barrett, Bernadette Billet, Terri Booth-Genthe, Andy Capella, Kelli Case, Ian Child, Joe Cipollina, Kathy Clark, Damien Daulon, James Errico, Mike Estrem, Gary Gensinger, Brent Jones, Leah Kleylein, Shy Kumar, Alex Lawrence, Raj Maitra, Harv Martens, Deanna Murden, Tracy Naughton, Lenore Palma, Don Palmer, Anita Phadnis, Robin Shibish, Tom Smith, Mindy Sperling, Phyllis Thomas, Hector Trestini, Peggy Zorn

### **IRISS Updates:**

- Life Cycle Management is now an official topic group
  - Shy Kumar is leading this topic group and has a leadership subteam consisting of 2 members from the U.S., 2 members from EU and 1 member from Canada.
  - Concept paper is available on the IRISS website with a list of prioritized discussion topics.
  - If interested in joining this topic group or if you have comments on the concept paper or additional discussion topics, send an email to [Shy@DatafarmInc.com](mailto:Shy@DatafarmInc.com)

### **Agency Updates:**

- FDA (Gary Gensinger)
  - *They will be rolling back the Validate software to v4 this weekend for testing*
  - *ICH M2 meeting*
    - *There was much discussion at last week's meeting around harmonizing the administrative portion of Module 1, but with limited success*
    - *Additional discussion around Next Major Version (NMV) – 32 new requirements defined.*
    - *Discussion about Acrobat and the ISO 32000 PDF version. ICH M2 is considering a recommendation for a restricted subset of ISO 32000 (e.g. no Adobe packages allowed).*
  - *Revised validation criteria has been put on hold due to the rollback of Validate*
  - *FDA Website has been updated*
  - *No update available regarding the CBER requirement for PDFs to open to first page of TOC.*
- Australia
  - Bernadette Billet has not received a response yet to her email requesting participation in IRISS
- Swiss Medic
  - Stephan Järmann has indicated an interest in attending IRISS ETIG.

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#### **Usage of doc-content file-tags and their impact of review (James Errico)**

- Customers have received validation reports from the FDA with a low priority issue description stating that the STF <doc-content> <title> and the leaf title (leaf referencing the file) must match. If <doc-content> <title> is optional (according to the DTD), is this really an error? Should there be a best practice to make them match or not?
- The DTD states that the <doc-content> <title> is optional, however the DTD rules may be overridden by the regional specifications.
- Shy stated that the FDA told him that the <doc-content> <title> is not displayed to the Reviewer; they only see the leaf title.
- Bernadette stated that she has received the same feedback
- Gary Gensinger clarified by saying that the leaf title is displayed to the FDA Reviewer. Vendors and sponsors should keep in mind though that it is not known what the Reviewers at other Health Authorities will see, so it might be best to have them match. He also stated that many of the low priority warnings are to make sponsors aware that a better practice might be used.

#### **EU Electronic Signature Pilot Program Update (Tracy Naughton)**

Rich Furr ([rfurr@safe-biopharma.org](mailto:rfurr@safe-biopharma.org)) provided the following update:

- This Pilot 2 will prove the successful submission of digitally signed documents (MAA & Cover Letters) to the EMEA, including testing the ability to create, publish, submit and manage these documents as part of the eCTD submission process flow. These documents will be submitted with both fully active and flattened digital signatures to allow the EMEA staff to gain familiarity with both formats. Participating companies will, if their infrastructures are properly configured, submit digitally signed eCTD formatted dossiers (Type 1A variations only) via the EMEA e-submissions gateway. Otherwise, companies may submit using current hard media means, e.g., DVD.
- Prove the ability of:
  - eCTD review and publishing tools to accept digitally signed documents without invalidating the signature
  - Industry to prepare eCTD electronic submissions and to incorporate digitally signed documents without invalidating the signature
  - EMEA to receive, process and handle SAFE-BioPharma digitally signed submission documents with both active and flattened signatures
- Provide SAFE-BioPharma digital identity credentials to members of the EMEA staff
- Prove the ability of EMEA staff to generate digital signatures from within the properly configured EMEA infrastructure
- Participating companies include
  - Astra Zeneca, Pfizer, Schering Plough/Organon, sanofi-aventis, GSK, Roche
- Participating tool vendors include:
  - ISI, Thomson Reuters (Liquent), Datafarm, Virtify, Extedo, Lorenz

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**Points to Consider Document Update (Terri Boothe-Genthe)**

- draft TOC is underway
- How big of an impact are broken links to Reviewers? It is believed to be minimal, however experience with life cycle is maturing and the impact may increase over time. There is no single rule of thumb that fits all situations. Further discussion on this topic will take place in the IRISS Life Cycle Topic Group.

**ICH M2 Meeting Update (Harv Martens)**

- Results of Change Requests
  - Shy's delete leaf title request resulted in no actual change other than clarification that the <title> is not required by ICH, but may be required by regional specifications. For example, it is mandatory for the EMEA. See updated Q&A spreadsheet attached – Q&A 36, item 20.
  - Deanna Murden's 2 requests will be addressed by the NMV:
    - CR1 - The lifecycle operation of delete should be allowed at the heading element level in Module 3 (3.2.S, 3.2.P, 3.2.A.1), in addition to the individual leaf element level.
    - CR2 - Cross referencing of identical information contained in multiple applications is difficult to achieve in the eCTD. Though it is technically possible to do so in the US region, the references only apply to individual leaf elements. For Quality data, it is often most useful to refer to entire contents of heading elements 3.2.S, 3.2.P, 3.2.A.1 as a whole entity across applications. The concept could further be expanded to apply to heading elements 3.2.P.4 and 3.2.P.7 where common information could be maintained in one dossier, and referenced or "used" as applying to multiple applications. To realize true benefit of e-working and to minimize newly created redundant activities in the name of eCTD, a change to the DTD is requested to allow referencing or "pointing to" entire heading elements that have been previously reviewed and accepted by a health authority under another marketing application.
  - Terri Boothe-Genthe's PDF Security request (on behalf of IRISS) resulted in recognition that there is a problem, but there needs to be additional information gathered and presented at the next ICH M2 meeting.
    - CR: Many times references are received from publishing vendors with security applied to deny changing pdf documents. As there are copyright laws that support the use of security in this manner we are requesting that the specification be changed to align.
    - There were discussions with Adobe about PDF/A format with the result being that the format is not a viable option because external hyperlinks and digital signatures are not supported.
  - Kevin Wing's request to change the M2 stylesheet to display M3 elements differently was rejected. This will be addressed with the NMV.
  - EFPIA request regarding PDF hyperlinks to URLs resulted in a Q&A stating that there should not be a hyperlink to any websites (see Q&A #64).

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- There will be no update to the DTD until NMV. Specification may be updated prior to NMV, but no changes are currently planned. RPS r2 and NMV are anticipated to become a reality in 2011/2012.

**Miscellaneous:**

- Is there a limit to the length of attribute values? Consideration in regards to the tool's ability to produce a folder name which differs from the displayed attribute value is needed. For tools that require the output folder to match the attribute value, overall path length needs to be considered. For tools that allow the two to differ, the impact is far less.
- Is there a list of allowable characters for attribute values? FDA validation rules state that the leaf title should only use allowable characters as per the ICH specification, however the ICH spec does not specify anything about this.
  - Clarification from the FDA on this issue would be appreciated.

**Next meeting**

- The meetings in 2009 will be held on the 3rd Wednesday of each month ... the next meeting is scheduled for **July 15th @ 7:30am EDT**.