

# ***IRISS-Forum***

## **eCTD Tool Interoperability Group**

**July 15, 2009 - 7:30am EDT**

### **Attendees**

Laura Barrett, Terri Booth-Genthe, Mike Estrem, Joel Finkle, Gary Gensinger, Carl Hackett, Claire Holmes, Jill Iacopi, Stephan Jaermann, Barbara Jentges, Leah Kleylein, Shy Kumar, Matthew Lukela, Raj Maitra, Harv Martens, Deanna Murden, Alistair Nixon, Lenore Palma, Connie Robinson-Kuiperi, John-Paul Smith, Phyllis Thomas, Hector Trestini, Ken VanLuvanee

### **IRISS Updates**

- Life Cycle Management - [Shy Kumar](#) announced that the topic group will have its first open teleconference on August 5th, 8:30-10:00am EDT. If you are interested in attending, please send him an email and he will respond with the details of the meeting.

### **Agency Updates and Specific Questions:**

- FDA
  - Ginny Ventura has confirmed that CBER does make the general recommendation that PDFs should open to the first page of a TOC. At this time, CDER does not have a stated preference but they'll discuss it at an upcoming eCTD change control meeting. Ginny will provide updates in the future.
  - Ginny has provided a follow up from last month's discussion on a list of allowable characters for attribute values
    - Most eCTD tools create a folder based on the attribute values, and the ICH specification does include a list of allowable characters in folder and file names. If sponsors use characters other than those listed for attributes, which carry over to the folder name, it can create issues.
    - References to allowable characters are:
      - Page 2-3 and 2-4 in the [ICH specs](#)
      - Page 7 in the [Final Guidance for Industry: Providing Regulatory Submissions in Electronic Format--Human Pharmaceutical Applications and Related Submissions Using the eCTD Specifications \[PDF\] \(June 2008\)](#)
    - Ginny also provided information that according to Jason Rock of GlobalSubmit, the only characters not allowed in files are the typical /, \, |, %, :, \*, ?, ", <, >, . as these are the characters that Windows does not allow.
    - Discussion during the teleconference pointed out that these references are specific to folder/file names and not attribute values. Harv Martens confirmed that there is nothing in the ICH M2 specification regarding allowable characters for attribute values. Gary Gensinger stated that he is working with Ginny Ventura to produce a document to clarify allowable

# ***IRISS-Forum***

## **eCTD Tool Interoperability Group**

characters for attribute values. A timeframe for release of this document is not yet known.

- EMEA
  - EU Regional Specs - Will the EU agencies provide feedback on any upcoming regional specification version updates and support for the new variation regulation that goes into effect beginning 2010? (Andy Capella)
    - Claire Holmes stated that v1.4 of the EMEA's Module 1 specification will be released the 1st week of August which includes changes to the handling of variations. Transition guidance as well as validation criteria will also be provided. It is highly recommended to follow this new specification version beginning February 2010 and will be mandatory 6 months after its release. All new submissions are expected to use v1.4 as of February. There will not be a formal testing phase.
    - Post meeting update: The eSubmissions website was updated on July 16th as follows: "The EU M1 will be updated to support the new Variation Regulation coming into force 1st January 2010. The new EU M1 v1.4 has been drafted together with stakeholders from EMEA, MS and industry, and will be published on this website and by NTA in early August. EU M1 v1.4 is highly recommended from 1st January 2010, and will be mandatory for all eCTDs for all procedures by February 2010."
  - Phyllis Thomas asked for clarification regarding file naming. In v1.0 (May 2009) of

**DRAFT FOR TESTING**

### **Guidance for Industry on Providing Regulatory Information in Electronic Format: eCTD electronic Submissions**

This document is published under the auspices of the  
EU Telematic Implementation Group - electronic submissions (TIGes)

it states

#### **2.5.2 File Naming**

The eCTD file naming conventions described in the ICH M2 eCTD Specification and EU Module 1 Specification are highly recommended. If an applicant wishes to submit multiple files in one section, where only one highly recommended name is available, this can be achieved using a suffix to the filename, using the file name-*var*.pdf convention as described in the EU Module 1 Specification, where the -*var* component has no dashes or illegal characters (e.g. pharmaceutical-development-container.pdf).

Would any EU member state fail any eCTD, regardless of procedure type, during validation as a result of this? Claire Holmes responded "no".

- Shy asked for clarification regarding the operation attribute to be applied to the Application Form Annexes. Should the Annex leafs always be "new" like the application form or is it possible for those leafs to have a life cycle? Claire

## ***IRISS-Forum***

### **eCTD Tool Interoperability Group**

stated that the Annex leafs should be treated individually and may have life cycle operations applied to them.

- Swiss Medic
  - Stephan Jaermann informed the group that the agency website (<http://www.swissmedic.ch/zulassungen/00933/00937/index.html?lang=en>) would be updated later in the week with draft regional eCTD specification and guidance documentation. As of January 1, 2010 eCTD submissions will become possible. In a first step, new applications (for example, new active substances, generics, known active substances, new indications, new dosage strength and new dosage recommendations) will be accepted. Later, other submission types such as variations will also be accepted. The timelines for this staggered approach will not be defined until October 2009.
    - An attempt was made to keep the regional requirements aligned with EMEA. The final version (1.0) will be published in October 2009 and is applicable from January 1, 2010. New applications may be submitted in eCTD format as of that date. Paper will still be accepted, however NeES is not considered to be an acceptable specification (supportive documentation purposes only). Between July and August 2009, a limited number of pilot submissions (with 2 accompanying paper copies) will be accepted.
      - Post meeting update: The website was updated on July 17th.

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

- A draft version of the document's Table of Contents will be provided and distributed with the minutes of the meeting. Sub-teams will be formed to address the various points with a final published document due by the end of the year. Please email Terri if you are interested in participating on one of the sub-teams.

#### **Are there mandatory requirements for the visual appearance of hyperlinks?**

- Harv Martens stated that ICH does not mandate the look of hyperlinks; it is up to the agency and their respective validation rules as to acceptable hyperlinks.
- Connie Robinson-Kuiperi stated that the FDA expects hyperlinks to be blue text or thin line blue boxes.
  - Post meeting update: Connie provided the following references that specify blue lined boxes and blue text are to be used for hyperlinks:
    - Page 8 of the [Final Guidance for Industry: Providing Regulatory Submissions in Electronic Format--Human Pharmaceutical Applications and Related Submissions Using the eCTD Specifications](#) [PDF] (June 2008)
    - Page 5 of the [Portable Document Format Specifications](#) [PDF] (6/4/2008)
- It should not be assumed that TOCs are hyperlinked, so blue text or blue box should be used.

# ***IRISS-Forum***

## **eCTD Tool Interoperability Group**

### **Is it necessary to change page size and margins so that all documents are able to be printed?**

- Safest approach is to set up templates with the appropriate margins so that page size doesn't matter.

### **Order of XML components**

- Sequence order was discussed early on during RPS requirements gathering and was found to be out of scope for RPS r2. Further discussion on this topic will take place in the Life Cycle Management topic group.
- Deanna Murden stated that a change in the order of elements and leafs within Module 3 can have an impact on the reviewability of a submission. For example, if there were two Drug Substance (3.2.S) elements submitted, it may be critical to display them in a particular order.

3.2.S <contains majority of substance documents>

3.2.S <documents pertaining to a particular process>

3.2.S <documents pertaining to route>

- Do tools allow for XML components to be entered in random order?
  - eCTD Specs state:

```
<!ELEMENT ectd:ectd (m1-administrative-information-and-prescribing-information?, m2-common-technicaldocument-summaries?, m3-quality?, m4-nonclinical-study-reports?, m5-clinical-study-reports?)>
<!ATTLIST ectd:ectd xmlns:ectd CDATA #FIXED "http://www.ich.org/ectd"
xmlns:xlink CDATA #FIXED "http://www.w3c.org/1999/xlink"
xml:lang CDATA #IMPLIED
dtd-version CDATA #FIXED "3.2"
>
```
  - If the code is in a different order, will your tool process it correctly?

```
<!ATTLIST ectd:ectd xmlns:ectd CDATA #FIXED "http://www.ich.org/ectd"
dtd-version CDATA #FIXED "3.2"
xmlns:xlink CDATA #FIXED "http://www.w3c.org/1999/xlink"
xml:lang CDATA #IMPLIED
>
```
  - This was addressed in ETICS and participants were notified of issues.

### **Next meeting**

- The meetings in 2009 will be held on the 3rd Wednesday of each month ... the next meeting is scheduled for **August 19th @ 7:30am EDT**.