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# *IRISS-Forum Concept Paper*

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## *Topic : eCTD Tool Interoperability*

### **Problem Statement**

The ICH eCTD standard, published in 2002, has made a significant impact on the ability to efficiently manage electronic submission information for both industry and regulators. There are now more than a dozen vendors of software products designed to create, manage, view and review eCTD formatted submissions.

However, as the ICH M2 ETICS I and ETICS II projects in 2006 and 2008 have shown, there are still numerous problems with the interoperability and compliance of these tools. Some common examples:

1. An eCTD which complies with the specification produced by one tool cannot be imported by another tool (necessary to continue to manage application lifecycle when changing to a new tool).
2. An eCTD which is not compliant is imported into another tool without error but the noncompliance causes a cascade of errors as additional submission sequences are built.
3. An eCTD which is not compliant is opened by a viewing tool without error, but the rendered view is incorrect. The user gets no indication that there is a problem.

There is no single, ICH approved, validation test suite against which vendors may test their tools. This results in inconsistent interpretation by software developers in areas where the specification or regional guidance are ambiguous. Furthermore, there is no organization which can independently certify tools as being compliant.

The participation and support for the ETICS project has been strong. But some vendors have expressed a desire to be more involved in the planning of such trials and even to communicate with each other in an open forum about interoperability issues.

### **Issues to Be Addressed**

- Provide an open forum for vendors to share questions and concerns about eCTD tool interoperability via *IRISS*
- Provide an open forum for industry, agencies and vendors to share concerns and knowledge via *IRISS*
- Provide a decision making body and a process whereby the vendor, industry and agency members can reach a consensus agreement on interoperability issues
- Produce a best practices guideline
- Provide a test suite of agreed to and established *IRISS* guidelines and best practices for vendors to test their tools against
- Provide a certification service (future) for tools

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## Background to the Proposal

The ICH M2 ETICS group has served a very useful role in dealing with implementation issues of the eCTD standard. However, as an ICH sub-group, this group is limited in its ability to discuss issues openly with vendors.

Some issues which have been studied by ETICS, such as complex leaf lifecycle, do not have a right or wrong answer. It would benefit interoperability greatly if a consensus view of lifecycle was established by this group.

The ICH M2 group has processed 14 change requests resulting from the ETICS II study. Of these, 10 resulted in new Q&As and 4 were deferred. These 14 issues were recognized by the ETICS team as some of the most pressing problems found during the ETICS II study. They present an excellent starting point for this topic group, particularly those 4 issues for which the ICH M2 has not issued new guidance. The 14 change requests are attached as Appendix A.

## Type of Topic Group Proposed

All eCTD tool vendors should receive a special invitation to join *IRISS*. The group should include more industry representatives. Operation will be by teleconference, email and other internet-enabled technologies.

*The process for coming to a conclusion on issues discussed is not yet determined. There could be, for example, a consensus position published (with some members abstaining), a majority vote or simply a white paper which describes the work done and the different positions taken. This will be discussed in the next teleconference.*

## IRISS Promotion

One goal of the interoperability group should be to promote the value of *IRISS*. It is intended that *IRISS* will be a single voice through which all members (brand and generic drug, biotech, device, and animal health product manufacturers, software vendors, consultants, and regulators) can discuss critical issues and reach consensus opinions.

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## Appendix A – Change Requests from ETICS II

Can additional guidance be provided on the format of the “index-md5.txt” file?	Approved for Q&A	Q&A #48
Can additional guidance be provided on how to handle missing attribute values?	Approved for Q&A	Q&A #49
Question 30 of the ICH eCTD Q&As says that applicants should seek regional guidance on the acceptability of providing their own style sheets. The ICH M2/ESTRI website has published the checksum of the ICH stylesheet and we know that some eCTD validation tools will report issues if the checksum of the provided stylesheet does not match the published value. Is there any further guidance that ICH can give on the acceptability of applicant created stylesheets?	Approved for Q&A	Q&A #50
Is there any restriction on the contents of the util/dtd and util/style folders?	Approved for Q&A	Q&A #51
Should the leaf ID be unique within an eCTD sequence or within an XML instance?	Approved for Q&A	Q&A #52
Is it permissible to refer to a single STF file from more than one leaf in the same backbone instance or in another sequence?	Deferred	Regional Issue
Is it permissible to have references within an STF file to leaf elements in another eCTD element in the same backbone instance or in another sequence?	Deferred	Regional Issue
In order to comply with the STF specification section entitled “Presenting Information from One Study in a Different Subsection of the CTD” is it permissible to provide STF files in 2 different locations in the backbone having the same Study ID?	Deferred	Regional Issue
In order to comply with the STF specification section entitled “Distinguishing Time-Specific Analyses Within the Same Subsection of the CTD” is it permissible to provide 2 STF files in the same location having the same Study ID and use the Study title to differentiate the 2 groups? Is it permissible or advisable to add a suffix to the study ID to differentiate the 2 groups?	Deferred	Regional Issue
Must all PDF files in the eCTD have bookmarks?	Approved for Q&A	Q&A #53
Can an eCTD file folder structure contain empty folders (that is folders that do not contain either another folder or a file)?	Approved for Q&A	Q&A #54
The eCTD specification recommends that the PDF 1.4 is the only acceptable version in all regions. Does the ICH have any recommendations for other PDF Document Properties?	Approved for Q&A	Q&A #55
How should the application version attribute in the leaf description be used?	Approved for Q&A	Q&A #56
Can clarification be provided on the correct usage of the xml:lang attribute?	Approved for Q&A	Q&A #57