

**eCTD Next Major Release Business Requirements Collation (9-JUN-10)**

| ICH Req No. | TOPIC                 | Requirement   | Comment  |
|-------------|-----------------------|---|--|
| ICH001      | APPLICATION LIFECYCLE | A regulated product application may have one or more regulatory activities associated with it   |  |
| ICH002      | APPLICATION LIFECYCLE | It must be possible to define a 'Regulatory Activity' to which a group of sequences will belong   |  |
| ICH003      | APPLICATION LIFECYCLE | A regulatory activity may have one or more sequences associated with it   |  |
| ICH004      | APPLICATION LIFECYCLE | The message should support the ability to provide one sequence to multiple regulatory activities which may span more than one application.  | sequence number values would need to be unique to each application |
| ICH005      | APPLICATION LIFECYCLE | Each sequence should have a unique identifier   |  |
| ICH006      | APPLICATION LIFECYCLE | Capability to identify which eCTD sequences were used at which step of agency review.   |  |
| ICH007      | APPLICATION LIFECYCLE | The message should not restrict adoption/implementation of the standard at any point in a product's lifecycle.  | principle  |
| ICH008      | APPLICATION LIFECYCLE | Compatible both to US/EU product-wise lifecycle and to Japan application-wise lifecycle.  | principle  |
| ICH009      | ARCHIVE               | It must be possible to review and to archive the sequence without need for transformation   | principle  |
| ICH010      | AUTHOR-REVIEW         | It should be possible to review the eCTD  | principle  |
| ICH011      | AUTHOR-REVIEW         | The specification should not restrict the types of file formats which can be submitted for use with the standard (allowed file formats are defined by each implementation and are not defined by the exchange specification). | principle  |
| ICH012      | AUTHOR-REVIEW         | It should be possible for the reviewer to have access to the entire application from any part of the application.   | principle  |
| ICH013      | AUTHOR-REVIEW         | Clear definition of views across multiple sequences (cumulative, current)   | viewer/implementation requirement                                  |

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| ICH014 | BACKWARD COMPATIBLE | Elements and attributes defined by V3.x should be able to be mapped to v4.0 constructs (and not the reverse)  |   |
| ICH016 | BACKWARD COMPATIBLE | The message should support continued use of the information and documentation provided with previous regional implementations, e.g., Module 1, STF. | principle   |
| ICH017 | DATASETS            | It should be possible to provide data definitions for data sets.  | principle   |
| ICH018 | DOCUMENT FORMATTING | It should be possible to support the inclusion of scanned documents, primarily for legacy documents   | principle   |
| ICH019 | DOCUMENT METADATA   | It must be possible to describe, in free text, the titles of the files being submitted  | Title can be different per usage (e.g., context)  |
| ICH020 | DOCUMENT METADATA   | Every submitted file will have a unique identifier  |   |
| ICH021 | DOCUMENT METADATA   | It must be possible for a Submitter to provide user defined information or identifier for a file  | For each file submitted by the Sponsor, a data field is present in the message for the Sponsor to include Sponsor-specified meta data (e.g., Sponsor internal version number or tracking information or OID). This requirement is currently provided by the "version" attribute in the ICH eCTD v3.2.2 leaf element and should continue as an option in the eCTD NMV. As this free text field refers to the actual content file, it should be an attribute of the "file" element in the message. It is proposed the field be called something like "owners-version-number" or "senders-identifier" (note wording to account for two way communication). This field would be optional. |

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| ICH024 | DOCUMENT REUSE | It must be possible to include by reference, a file that physically resides in the same or another sequence within the same regulatory activity, different regulatory activity within the same application or in a different application (e.g., cross-product submission support) | A file has been submitted to a dossier as part of an application's supportive documentation. The file is assigned a unique identifier in an eCTD submission. The information contained in the file is later required to be available for use in the review of a supplement/additional application. The applicant wishes to include the previously submitted file in the supplement/additional application by referring to the file by its unique identifier rather than submitting the file for a second time. A reviewer viewing the supplement/additional application would view the file as though it was submitted to the supplement/additional application along with the other supportive documentation that was actually submitted. |
| ICH025 | DOCUMENT REUSE | It must be possible to include, by reference, a file that has been submitted in a previous sequence and to be able to identify that this is not new but is being used in a different context  | implementation-Reviewer Capability   |

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| ICH026 | ENVELOPE    | It must be possible to assign an identifier to a sequence   | to imply an order, to enable sorting (e.g., chronology or review order) or just to assign uniqueness within an application<br>[unique identifier for the sequence within the application and a friendly identifier] |
| ICH027 | ENVELOPE    | It must be possible to identify the regulatory agency for which a specific sequence is intended   |   |
| ICH028 | ENVELOPE    | It must be possible to identify the applicant submitting a sequence   |   |
| ICH029 | ENVELOPE    | It must be possible to unambiguously associate a sequence to the application(s) to which it belongs                                     |   |
| ICH030 | ENVELOPE    | It must be possible to assign a submission type being used for the sequence   |   |
| ICH031 | ENVELOPE    | It must be possible to describe, in free text, the sequence (include a short description of the sequence in the administrative section) |   |
| ICH032 | ENVELOPE    | It must be possible to identify the Procedure type being used for the application   |   |
| ICH033 | ENVELOPE    | It must be possible to assign an invented name (trade name) for the product covered by the application                                  | Not just EU Regional  |
| ICH034 | ENVELOPE    | It must be possible to assign an international non-proprietary name(s) (inn) for the drug substance(s) covered by the application       | Not just EU Regional  |
| ICH035 | EU REGIONAL | It must be possible to identify to which specific country a file is relevant  |   |
| ICH036 | EU REGIONAL | It must be possible to identify that a file is relevant to all countries  |   |

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| ICH037 | EU REGIONAL   | It must be possible to identify for which country(ies) a specific sequence is intended  |  |
| ICH038 | HARMONISATION | The message should support ICH-harmonized content (documentation and metadata) and ICH-regional content   |  |
| ICH039 | HARMONISATION | Need to provide a structure that supports all terminologies for dossier (all regulatory activity related to a product) and regulatory activity (collection of sequences that lead to a decision by the regulatory agency (NDS, SNDS)) which can be mapped to individual ICH-regional regulatory processes                 | controlled vocabularies / Implementation Guide |
| ICH040 | HARMONISATION | Files should only need to be submitted once to a Health Authority and can be included by reference in multiple sequences to support multiple regulatory actions even across applications  | Clarify meaning of application                 |
| ICH041 | HARMONISATION | Ability to reuse of eCTD submitted in other regions. e.g. reuse of leaf files, XML instance by module, eCSR. To achieve this, it is critical to distinguish global part and regional part even in Module2-5, not only in Module1.   | Industry building tool need                    |
| ICH042 | HARMONISATION | When the same documentation is provided, it should be submitted in the same way across HAs. For example, when a study report is submitted in US it is submitted using the STF which is not acceptable in other HAs. This minimizes reuse capabilities and adds to Industry costs to prepare globally harmonized dossiers. | principle                                      |
| ICH043 | HYPERLINKING  | It should be possible for the applicant to include hyperlinks between information   |  |
| ICH044 | HYPERLINKING  | It should be possible to utilise relative addressing for all links.   |  |
| ICH046 | HYPERLINKING  | Need to support relative links across the product lifecycle   |  |

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| ICH047 | ICH PROCEDURE | For validation purposes,<br><ul style="list-style-type: none"> <li>- It should be able to uniquely identify: <ul style="list-style-type: none"> <li>- where in CTD a leaf belongs</li> <li>- the relationship between leafs</li> <li>- the lifecycle relationship (append, delete, or replace) between files</li> <li>- the relationship between sequences</li> <li>- the relationship of a sequence to a regulatory activity</li> <li>- the relationship between applications</li> <li>- the type of relationship (parent-child, reference, etc)</li> </ul> </li> </ul> | Principle                                  |
| ICH048 | JP-REGIONAL   | Message should support the ability to provide second and subsequent sequences which contain only additional information in XML Instance  | Implementation Guide                       |
| ICH049 | LANGUAGE      | It must be possible to assign a language to a document   |  |
| ICH050 | LANGUAGE      | It must be possible to (incorporate unicode character sets) to deal with languages such as Bulgarian and Greek   | Deal with greek and cyrillic               |
| ICH051 | LANGUAGE      | It must be possible to include files with 1 or 2 byte characters, or a mixture of both   |  |
| ICH052 | LANGUAGE      | eCTD viewer should recognize section titles defined in CTD, e.g. "2.5 Clinical Overview". It should have an interface capable to show CTD section titles in any languages by switching standard dictionary provided by regional agencies.  | viewer requirement / controlled vocabulary |
| ICH053 | LIFECYCLE     | The message should provide the ability to assign new metadata to update information previously submitted e.g., related sequences, submission type, operation attribute, manufacturer name, etc.  | Delete examples                            |
| ICH054 | LIFECYCLE     | The message should provide the ability to unassign metadata previously submitted, e.g., related sequences, submission type, operation attribute, manufacturer name, etc.   |  |
| ICH055 | LIFECYCLE     | The message should provide the ability to revise metadata previously submitted, e.g., related sequences, submission type, operation attribute, manufacturer name, etc.   |  |

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| ICH056 | LIFECYCLE           | Information provided in the message ( i.e., metadata) used to categorize documentation (e.g., attributes of drug substance, manufacturer, etc) or supplied in the regional envelope (e.g., Company Name, Sponsor) can be modified (i.e., added, edited, removed) during the life cycle of the application. |                                     |
| ICH057 | LIFECYCLE           | Replacement of multiple leafs with single leaf and vice versa should be supported in eCTD.   |                                     |
| ICH058 | LIFECYCLE           | The process for concatenating individual sequences into a combined sequence view (i.e., the current view and the cumulative view) must be unambiguously defined  | viewer requirement / implementation |
| ICH059 | LOGICAL GROUPINGS   | Provide ability to group a collection (or set) of files that together represent a document or reviewable grouping (e.g., all files related to a study report, all files related to a labeling document, all files related to a manufacturer or manufacturing component (e.g., container closure))          |                                     |
| ICH060 | LOGICAL GROUPINGS   | Provide ability to treat a grouping of files as a single entity and to be treated as if it were a single file (complete with all descriptive attributes e.g., title) for all life cycle operations and relationship management and reuse needs   |                                     |
| ICH061 | PHYSICAL FILE RULES | Filenames can include underscores  |                                     |
| ICH062 | PHYSICAL FILE RULES | It should be possible to constrain the contents to ensure there are no security settings, such as passwords.   | Implementation Guide                |
| ICH063 | PHYSICAL FILE RULES | The physical file structure. (file/folder structure) should be minimal   |                                     |
| ICH064 | PHYSICAL FILE RULES | The technical message should not restrict the types of files that may be transferred. However, implementation guides may restrict the types of files and versions of file formats to be transferred or may specify unique file formats for that region.  | principle                           |
| ICH065 | PHYSICAL FILE RULES | It should be possible to support file systems of different operating systems   | principle                           |
| ICH066 | PHYSICAL FILE RULES | It must be possible to constrain the maximum size of any file (reword to reflect ICH minimum standard)   | Implementation issue                |

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| ICH067 | SCOPE       | Allow the capacity to modify the ICH CTD organizational structure (ToC) without modifying or changing the eCTD message structure                                |   |
| ICH068 | SCOPE       | It should be possible to compile an eCTD equivalent to the CTD  | principle   |
| ICH069 | STANDARDS   | The message should interoperate with other healthcare standards, e.g. use controlled vocabularies from established standard-based vocabularies                  | principle   |
| ICH070 | STANDARDS   | It should be possible to restrict the technology utilized to use open (ISO, W3C, IETF) standards when ever possible.  | Principle   |
| ICH071 | STRUCTURE   | It must be possible to constrain the inclusion of documents at inappropriate locations in the submission structure (e.g.. at highest levels of eCTD)            |   |
| ICH072 | STRUCTURE   | The message should allow for the control/enforcement of document/structural granularity.  |   |
| ICH073 | STRUCTURE   | It must be possible to assign 'attributes' to the contents of specific sections to support the ICH CTD organizational structure (e.g., repeating section 3.2.S) |   |
| ICH074 | STRUCTURE   | It must be possible to ensure that all files submitted are defined and referenced   |   |
| ICH075 | STRUCTURE   | It must be possible to validate the contents of a sequence against the CTD (e.g., module 6 is invalid)  |   |
| ICH076 | STRUCTURE   | It should be possible to identify all of the files relevant to a specific section of the CTD  |   |
| ICH077 | STRUCTURE   | It should be possible to review the sequence in its entirety or in sections.  | Method of transmission should support the consumption |
| ICH078 | TECHNOLOGY  | The standard must not be constrained by the need for delivery via a particular medium   | principle   |
| ICH079 | TECHNOLOGY  | It should be possible to include colour and black & white images  | principle   |
| ICH080 | TECHNOLOGY  | It should be possible to support the introduction of new technology to aid in the review process.   | principle   |
| ICH081 | TERMINOLOGY | The message should support the use of controlled vocabularies for harmonized metadata   |   |



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| ICH082 | TERMINOLOGY           | The message should support the use of controlled vocabularies for regional metadata.  |                      |
| ICH083 | TERMINOLOGY           | It should be possible to specify date values in an unambiguous manner.  |                      |
| ICH084 | TRANSFER/SECURITY     | The message should support a means to enable the validation of the integrity of the electronic files within an instance   |                      |
| ICH085 | TRANSFER/SECURITY     | The message standard should not restrict the mechanism for transmitting the message (e.g., media type, network)   | principle            |
| ICH086 | TRANSFER/SECURITY     | The message standard should not restrict or prevent regionally implemented secure electronic message delivery standards   | Implementation Guide |
| ICH087 | TWO-WAY COMMUNICATION | The message should support submission of a sequence from a regulator to a regulated party.  |                      |
| ICH090 | TWO-WAY COMMUNICATION | It should be possible to define the security methods to be used for transmission to the agencies and acknowledgement from the agency.                                   | principle            |
| ICH091 | US-REGIONAL           | The message should support the identification of the role of the instance within the identified regulatory activity, e.g. presubmission, application, amendment, etc.   |                      |
| ICH092 | US-REGIONAL           | The message should support the identification of the regulatory activity associated with the instance, e.g. original-application, labeling-supplement, etc.             |                      |
| ICH093 | VALIDATION            | It must be possible to define unambiguously, the validation criteria for a sequence   | Principle            |
| ICH094 | VALIDATION            | Message should contain sufficient information to unambiguously identify which version(s) of the DTD/Schema and controlling vocabularies was used to create the instance |                      |
| ICH095 | VALIDATION            | The message should not require the submission of the DTD/Schema and controlling vocabularies with each instance   |                      |
| ICH097 | COMPATIBILITY         | It should be possible for an applicant to build on an eCTD lifecycle started using the eCTD 3.2.x specification and continued using the eCTD NMV specification          |                      |

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| ICH098 | COMPATIBILITY   | No applicant should be required to resubmit data in the eCTD NMV specification if it has previously been submitted using the eCTD 3.2.x specification. (It is recognised that in the future, further major versions of the eCTD specification may require data migration guidance to ensure the use of data over the life of a drug product). | principle |
| ICH099 | COMPATIBILITY   | Tools designed to view eCTD NMV sequences must also be able to view a lifecycle started with the eCTD 3.2.x specification. However, the reverse requirement is not needed (i.e. it is not needed that tools for the eCTD 3.2.x specification should be able to view sequences created using the eCTD NMV specification).                      | principle |
| ICH100 | COMPATIBILITY   | It is expected that once an eCTD lifecycle is transitioned to the eCTD NMV specification, then no further submissions/sequences will be made in the eCTD 3.2.x specification.   | principle |
| ICH101 | COMPATIBILITY   | The implementation guide must state how lifecycle relationships can be maintained from eCTD 3.2.x to eCTD NMV.  |           |
| ICH102 | COMPATIBILITY   | Ability to reuse content; files submitted in eCTD sequences can be referenced in eCTD NMV submission units  |           |
| ICH104 | DESIGN CONCEPTS | The file format of the message should be xml-based.   | principle |
| ICH105 | DESIGN CONCEPTS | The message standard should not prevent or restrict the ability to e-sign the message.  | principle |
| ICH106 | DESIGN CONCEPTS | The message standard should not prevent or restrict the ability to encrypt the message for secure transfer purposes   | principle |
| ICH107 | DESIGN CONCEPTS | The message standard must not require encryption  | principle |
| ICH108 | INTEGRITY       | Integrity checks for all files included in the sequence are required.   |           |
| ICH109 | DESIGN CONCEPTS | The message should provide the ability to identify further specific usage of the file<br>(e.g., SPL, SDTM, application format, packaging insert, CTN) beyond that defined by the CTD  |           |
| ICH110 | INTEGRITY       | The ability to specify which algorithm is being used for file integrity checks is required.   |           |

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| ICH112 | TWO-WAY COMMUNICATION | It must be possible to relate any message to a particular message, regulated activity and/or application.  |   |
| ICH113 | TWO-WAY COMMUNICATION | Every eCTD message must be uniquely identifiable.  |   |
| ICH114 | DESIGN CONCEPTS       | In principle, the number of xml files managing content should be kept to a minimum and use a consistent technical design approach even though the content models may differ regionally | principle                                       |
| ICH115 | ENVELOPE              | The message standard must provide the ability to include information required for the processing (e.g., message standard version) and integrity (e.g., checksum) of the message        |   |
| ICH116 | ENVELOPE              | The message standard must provide a three-level hierarchy of application, regulatory activity and submission unit.   | principle                                       |
| ICH117 | ENVELOPE              | The message standard must provide information about the product.   | enumerate data points to be required regionally |
| ICH118 | ENVELOPE              | The message standard must provide enough information to identify the sender.   | enumerate data points to be required regionally |
| ICH119 | ENVELOPE              | The message standard must provide enough information to identify the recipient.  | enumerate data points to be required regionally |
| ICH121 | LIFECYCLE             | The order/sequence of leaf elements within a CTD section must be able to be controlled   |   |
| ICH122 |                       | A file can be displayed in multiple sections of the CTD (preserving the leaf - file concept in the current eCTD specification)   |   |

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| ICH123 |                 | Maintain a similar file-leaf model as in the current eCTD in the eCTD NMV, with the following exception/changes:<br>a. The operation attribute value “append” be removed from the list of allowed values (leaving only new, replace and delete)<br>b. Allow a replace or delete leaf to modify more than one leaf in a previous sequence or sequences<br>c. Allow a single leaf to be “modified” by more than one leaf in later sequences (supports changes in granularity) |           |
| ICH124 |                 | A file can be replaced in one existing eCTD section or context without impacting the use of the file in other eCTD sections or contexts   |           |
| ICH125 |                 | Life cycle operations must occur within the same context as the existing (target) leaf  |           |
| ICH126 |                 | There should be no restrictions on the characters used in controlled vocabularies   | principle |
| ICH127 |                 | There should be a basic ICH stylesheet for presentation purposes  |           |
| ICH128 |                 | STF construct should be integrated into the message standard  |           |
| ICH129 |                 | Cardinality rules of the current eCTD Specification should be retained plus those cited in approved Change Requests (e.g., CR#1490/1500 - Module 3.2.A.3 will be made a repeating attribute in Version 3.2 of the specification based on excipient).  |           |
| ICH130 | DESIGN CONCEPTS | The message standard should allow the ability to e-sign the message.  | principle |