Timeline for Commercial IND Application Submission — Including eCTD Compliance and Publishing Activities

Below is a high-level overview of the steps for preparing and submitting an IND application, starting from document development, through eCTD assessment/formatting and publishing, to final submission to the FDA.

Commercial* IND applications can vary in size (e.g., 20 documents or less, up to 100+ documents) and typically include the following:

- **Module 1:** IB/package insert, GIP, pre-IND correspondence, labeling, and administrative documents
- **Module 2:** Summaries (Intro, Quality, Nonclinical)
- **Module 3:** CMC documentation
- **Module 4:** Non-Clinical Study Reports
- **Module 5:** Protocol, ICF/assent, and investigator information

Refer to the eCTD Templates and Resources document located on the DMID-CROMS website and the IND application tracking worksheet provided by the RAM for further details on IND content.

**The FDA has determined that any IND sponsored by DMID is a commercial IND, not research.*

Timelines for IND Document eCTD Formatting Compliance Assessment (*Prior to IND Finalization and Submission*)

IND documents are provided to the RAM at different times throughout the IND compilation process by several different stakeholders (e.g., CPM, Program, OCRA, Company Partners, etc.) and are reviewed by the ORA contractor, TRI, for eCTD compliance and corrected, as needed.

These assessments are done on a rolling basis as documents are being finalized and are ready for inclusion within the IND application. This occurs prior to the last final IND document being received (timeline for IND submission below).

Step 1: Ensure eCTD Compliance of IND Documents Before Sending them to TRI for an eCTD Compliance Assessment

- Stakeholders (including CPMs and/or document authors) should ensure that the IND and protocol documents* (protocol, ICF/assent, IB/pkg insert, summary of changes, track changes versions, as applicable) are eCTD compliant (i.e., formatted properly) prior to providing them to the RAM.

- Please send to the RAM as documents are finalized, rather than batching, so that the assessment can start as soon as possible.

  ***Note:** Step 1 occurs after the documents have gone through the protocol review tool and are considered final (e.g., version 1.0, 2.0, etc.).*

- **Resources:** Refer to the eCTD resource documents provided on the DMID-CROMS website to ensure final IND documents are properly formatted and compliant.
- **Contact Information:** Questions on eCTD formatting can be addressed by contacting the following email address and cc'ing the RAM: DMID-RASeCTD@tech-res.com.

Step 2: TRI has 5 to 10 business days to Complete an eCTD Assessment and Correct Formatting, as Necessary

- TRI will perform compliance checks and corrects IND and protocol documents, as necessary, to ensure proper formatting and compliance. These activities include, but are not limited to the following:
  - Font Styles Application
  - Table and Figure Captioning and Formatting (i.e., ensuring proper table dimensions)
  - Table of Contents, List of Tables, and List of Figures Updates
  - Inserting Cross References and Link Application (in-text references to sections, appendices, tables and/or figures)
  - Setting PDF Specifications (adding required settings, embedding fonts, etc.)
  - Navigation Pane/Bookmarking
  - Page Number Application

Factors that Impact Timelines:

The **total number of documents**, and the timing of receipt (all at once vs. on a rolling basis), the **number of pages per document**, and the **quality of documents received** (i.e., if they are formatted properly). If extensive corrections are required, extra time is needed to ensure compliance.

Step 3: eCTD-Compliant Protocol Documents are Returned to the CPM Other IND documents are added to the IND submission

- Once the assessment is complete, TRI sends an email to the RAM with the attached eCTD-compliant protocol documents and ***a list of eCTD formatting changes that were needed to correctly format each document to ensure eCTD compliance.***
- The RAM then sends the eCTD-compliant protocol documents and the list of changes made to ***the CPM to share with the site and/or document author.***

Note: *The document file names will end in eCTD (to ensure version control).*

Training Available:

TRI is available to provide eCTD training or answer any questions. Requests can be made using the following email address and cc'ing the RAM: DMID-RASeCTD@tech-res.com.

Timelines for IND Finalization, Compilation, Publishing Activities and Submission

After receipt of the final IND document, TRI has up to 10 business days to complete finalizing the IND documents, publishing, compiling, and submitting the IND application to the FDA

- Once the final IND document is received, it will be assessed for eCTD compliance, and the 10-day timeline for IND submission to the FDA starts.
- After all IND documents have been assessed and corrected, as necessary, to ensure eCTD compliance, they are considered final and ready for submission.
- TRI compiles the final documents into the respective eCTD Module of the IND in the regulatory document management system.
- The RAM completes their review and approval of these documents in the system.
- TRI pulls each document from the system into the publishing software and starts compiling the IND application.
- **Publishing Activities**
    - During compilation, TRI ensures the following:
        - Each document is placed within the correct eCTD Module.
        - Attributes are set on each document.
        - External hyperlinking is included (links to other documents within the IND).
        - Bookmarks are edited as needed.

Factors that Impact Timelines:

The number of IND documents in the application, and the overall number of hyperlinks that need to be placed within the documents.

- TRI then validates the submission, publishes the compilation, and generates the validation report. TRI reviews the final submission and sends the IND application to the FDA via the Electronic Submissions Gateway (ESG).

Protocol Amendments and Changes to IND documents

When drafting protocol amendments please use the final eCTD-compliant protocol documents (protocol, ICF/assent, IB/pkg insert, summary of changes, track changes versions, as applicable). In addition, if making any changes to other IND documents, please make them to the versions that have already been formatted for compliance, as applicable.