CTP ELECTRONIC SUBMISSIONS STANDARDS AND ACTIVITIES

ELECTRONIC TOBACCO TECHNICAL DOCUMENT

A presentation to TSRC
by CTP Office of Science, Division of Reg. Science Informatics

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Disclaimer: This is not a formal dissemination of information by FDA and does not represent Agency position or policy.

TOPICS

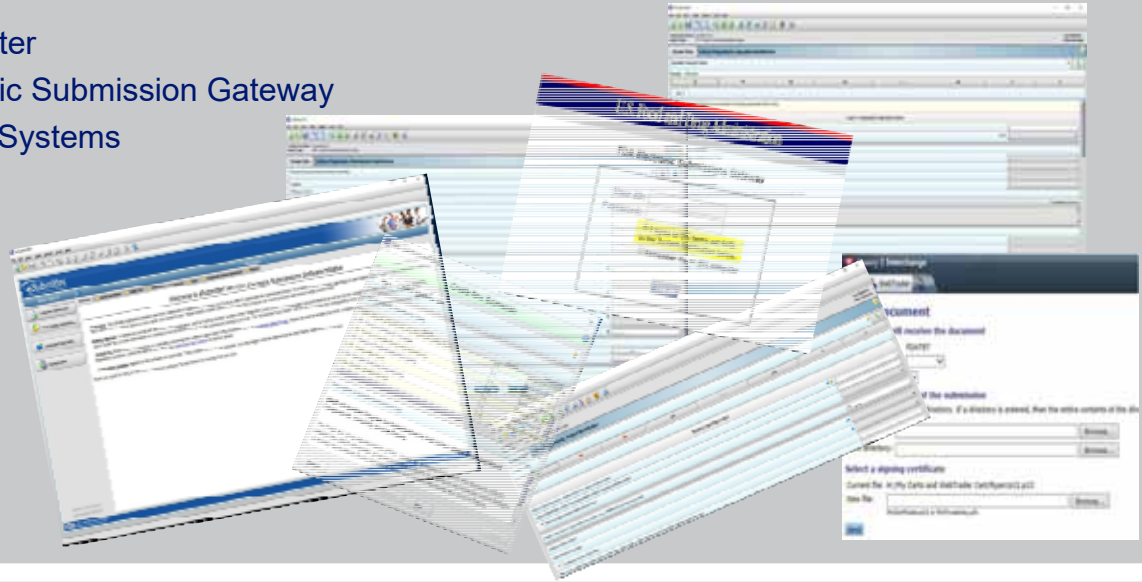
- In the Beginning
- CTP Portal
- Technical Considerations
- Expanding on an existing eSubmission Standard, the eCTD
- Conclusion

THE BEGINNING

- The Tobacco Control Act necessitated capability to receive data and submissions within 6 months, *e.g., 904(a)(1), 905(b)*
- Registration of Establishments
- Registration of Products
- Report of Ingredients

CTP ADAPTED TOOLS FROM OTHER FDA CENTERS TO MEET IMMEDIATE NEEDS

- eSubmitter
- Electronic Submission Gateway
- Internal Systems



CTP PORTAL

- Easy upload of eSubmitter submission files
- Ability to view submission administrative information
- Link to CTP Portal:

  https://ctpportal.fda.gov/ctpportal/login.jsp

- Account management performed by an Industry Account Manager (IAM)
- Link to IAM Request info:

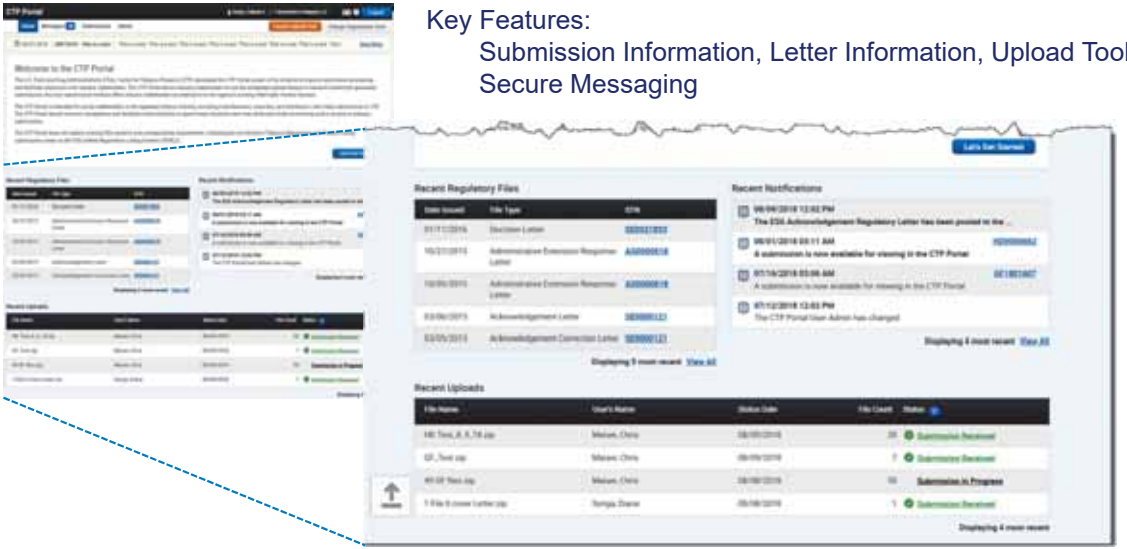
  From the Manufacturing page on CTP Site-

  https://www.fda.gov/TobaccoProducts/GuidanceComplianceRegulatoryInformation/Manufacturing/ucm515185.htm

PORTAL HOME SCREEN

Key Features:

Submission Information, Letter Information, Upload Tool and Secure Messaging

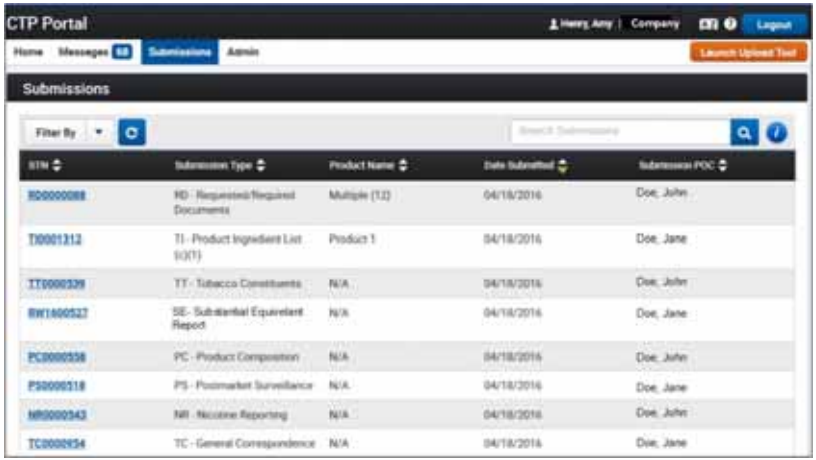


Test data displayed

PORTAL SUBMISSIONS

Key Features:

- Listing of submissions received and assigned a Submission Tracking Number (STN) with high-level information



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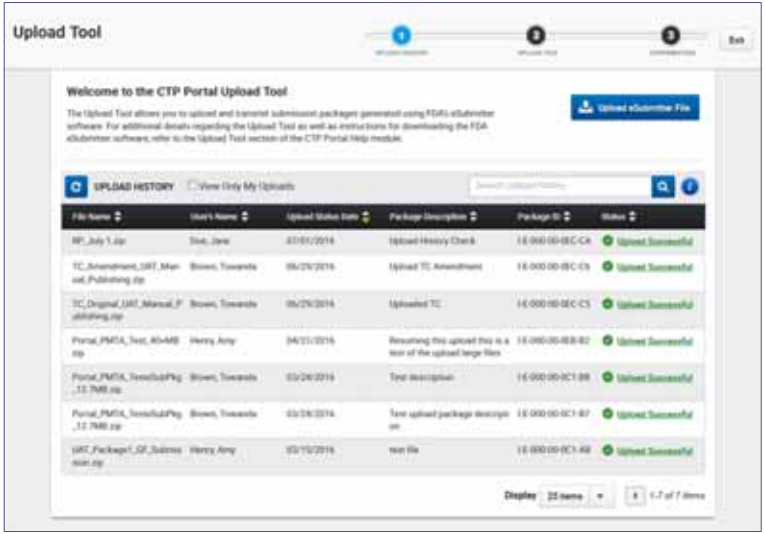
PORTAL UPLOAD TOOL



Key Features:

Listing of uploads with date and user who uploaded

Test data displayed

ENSURE SUBMISSION CAN BE…
PROCESSED, REVIEWED AND ARCHIVED

FDA

Legibility/Usability

- ✓ Create PDF files directly from source file
- ✓ For scanned documents, resolution ≥ 300 dpi, optical character recognition (OCR) helps ensure legibility and usability
- ✓ Include table of contents, hypertext links and bookmarks

Integrity and Security

- ✓ Test the submission by installing onto another location and opening
- ✓ Virus scan all files to be submitted to the FDA
- ✓ Avoid use of security settings in files, *e.g., encryption, password protection, printing restrictions*

ENSURE SUBMISSION CAN BE…
PROCESSED, REVIEWED AND ARCHIVED

"We cannot review what we cannot process, open, and read."

File Formats

- ✓ PDF, DOC, DOCX, TXT, XPT, CSV, XLS, XLSX, XML, JPG, GIF
- ✓ Some formats are appropriate for data, others appropriate for images and
- ✓ Retain extension in the filename to specify the file format type

Filenaming

- ✓ Short, descriptive, unique filenames and file path, *e.g., "MainTOC.pdf", "study1.xpt"*,
- ✓ Special characters and foreign characters cause problems
- ✓ Use lower case and avoid special characters, e.g., #, %, ., &, ><
- ✓ Deep subfolders cause problems, limit path < 180
- ✓ SaS transport file (.xpt) for analysis datasets recommended
  http://www.fda.gov/ForIndustry/DataStandards/StudyDataStandards

Further details available in Electronic Submission File Formats and Specifications, listed on the CTP Manufacturer's Page: https://www.fda.gov/TobaccoProducts/GuidanceComplianceRegulatoryInformation/Manufacturing

CTP REFERENCES FOR FILE AND DATA STANDARDS

- Common Errors and Questions that Delay Submission Processing
  Frequently Asked Questions (FAQ) & Common Errors That Delay Submission Processing
- Electronic Submission File Formats and Specifications
  Provides a reference of file formats, data standards useful for submittal and review
- Overview of the Electronic Submissions Process for Industry
  Basic info about the documents and data needed to successfully create and submit an eSubmitter package

All three available on the CTP Manufacturer's page and CTP's eSubmitter page,

https://www.fda.gov/TobaccoProducts/GuidanceComplianceRegulatoryInformation/Manufacturing

https://www.fda.gov/ForIndustry/FDAeSubmitter

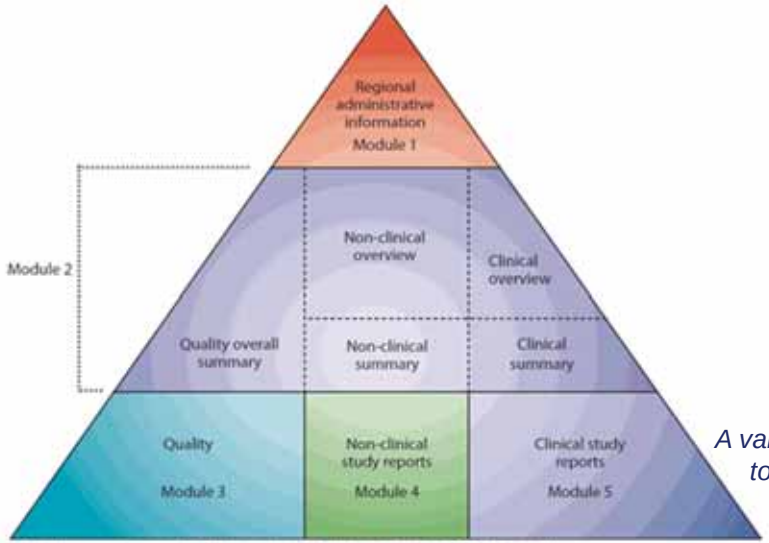
PREPARING FOR YOUR ELECTRONIC SUBMISSION

1. Download the FDA eSubmitter tool to your desktop
   - FDA provides instructions, video tutorials and helpdesk assistance *[eSubmitter@fda.hhs.gov or 1-877-CTP-1373]*
2. Assemble and package your submission using the FDA eSubmitter tool
3. Create a CTP Portal account for transmitting your eSubmitter package
4. CTP Portal: An Industry Account Manager *(IAM)* is needed to create and maintain user accounts for your company

THE ELECTRONIC COMMON TECHNICAL DOCUMENT (eCTD)

- A Tobacco submission standard would be voluntary
- A tobacco variation of eCTD would provide a customized table of contents for tobacco product submissions
- Technical advantages:
  - Fully metadata driven – no folder structure
  - Associates amendments with original information
  - Reference previously submitted documents and data
  - Supports two-way exchange of information
- **Current eCTD is supported by the commercial marketplace**

ELECTRONIC COMMON TECHNICAL DOCUMENT (eCTD)



https://www.accessdata.fda.gov/scripts/cder/training/eCTD/menu.htm

A variation of the eCTD is needed to support tobacco products

eCTD MODULES- LEVEL 2 OF HIERARCHY

FDA

Additions

Module 1 Administrative information
1.1 Forms
1.2 Cover letters
1.3 Administrative information
1.4 References
1.5 Application status
1.6 Meetings
1.7 Fast track
1.8 Special protocol assessment request
1.9 Pediatric administrative information
1.10 Dispute resolution
1.12 Other correspondence
1.13 Annual report
1.14 Labeling
1.15 Promotional material
1.16 Risk management plan
1.17 Postmarketing studies

Module 2 Summaries
2.2 Introduction to summary
2.3 Quality overall summary
2.4 Nonclinical overview
2.5 Clinical overview
2.6 Nonclinical written and tabulated summaries
2.7 Clinical summary
Module 3 Quality
3.2 Body of data
3.2.S Drug substance [name, manuf]
3.2.P Drug product [name, dosage form, manuf]
3.2.A Appendices
3.2.R Regional information
3.3 Literature references
Module 4 Nonclinical Study Reports
4.2 Study reports
4.3 Literature references
Module 5 Clinical Study Reports
5.2 Tabular listing of all clinical studies
5.3 Clinical study reports and related information
5.4 Literature references

Deletions

Changes

EXPANDING UPON AN EXISTING INT'L ELECTRONIC SUBMISSION SPECIFICATION

- FDA makes use of existing standards, *whenever possible*
- FDA uses the eCTD for pharmaceutical products
- FDA pursuing a variation of HL7 **Regulated Product Submission** (RPS) Standard for future submissions; eCTD is the structure and code behind it
- eCTD not suited for Tobacco Products and so CTP is drafting an …

… Electronic Tobacco Technical Document, "*eTTD*"

RPS APPLICATION *(PRODUCT DOSSIER)* SCHEMA

FDA

RPS Application

- An "RPS" Application is the cumulative information exchanged between an industry organization and CTP about a Tobacco Product or Manufacturing Establishment.
- Each Application is characterized by an Application Type, *e.g., Tobacco Product Report and has associated Submissions*.

RPS Submission

- A Submission is a single regulatory activity characterized by a Submission Type, *e.g., Substantial Equivalence (SE) Report.*

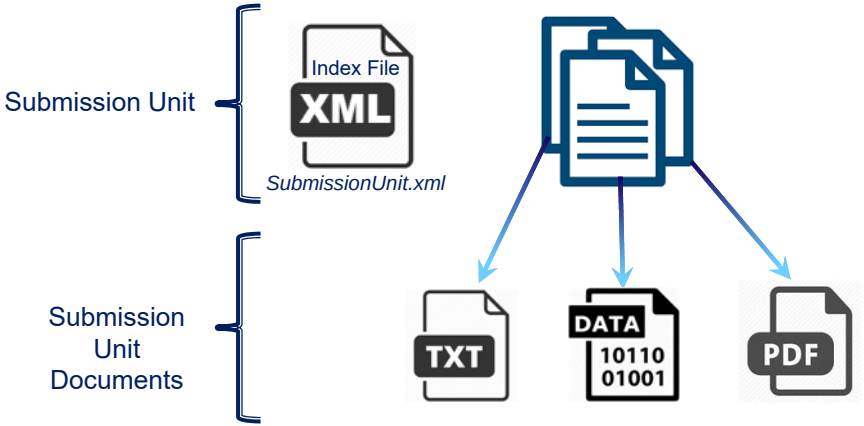
Submission Unit

- A Submission Unit is the delivery to CTP of a set of electronic files or documents. Each Submission Unit has a unique identifier and is characterized by a Submission Unit Type, *e.g., Original or Amendment.*

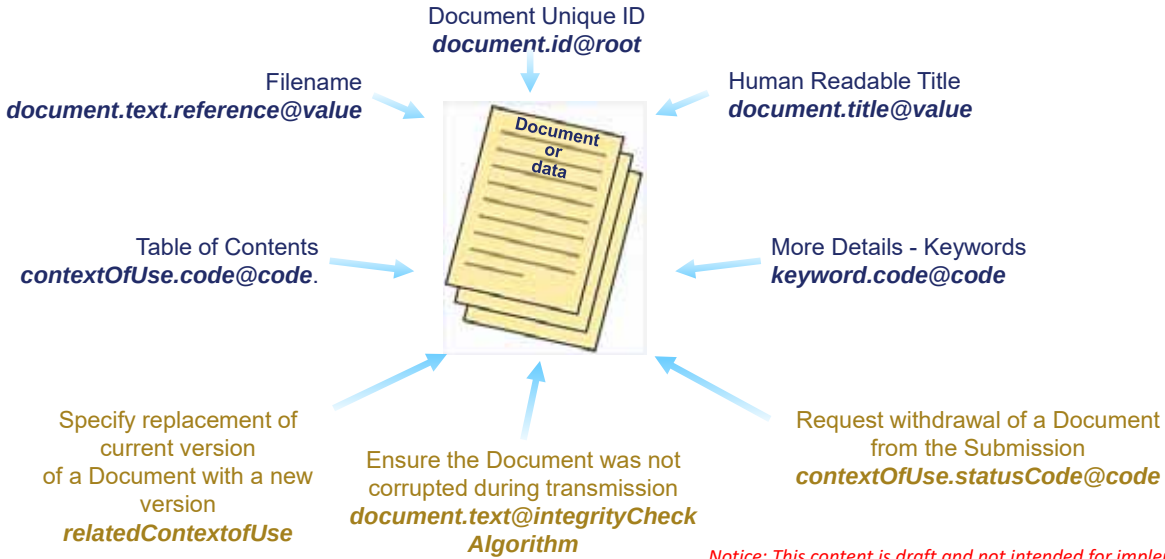
Document

- An electronic file provided as part of a Submission Unit. A Document has a unique identifier and title, *e.g., Product Component Ingredients,* and a file name, e.g., *Ingredients99.pdf.*
- Each document is assigned a Context of Use (CoU) code; Allows both parties to flexibly organize the contents of a Submission to their specific needs or disciplines.
- Additional information about the use of Documents can be provided through Keywords. In addition to CTP-Defined Keywords, eTTD allows Sender-Defined Keywords.

TWO MAIN PIECES OF AN eCTD MESSAGE



XML TAGS WITHIN AN eCTD MESSAGE- *METADATA ABOUT A SUBMISSION DOCUMENT*



Notice: This content is draft and not intended for implementation

CTP WILL TAKE FULL ADVANTAGE OF METADATA

Structure of the Submission is determined by its *Metadata*

Capability	Benefit
The table of contents fully describes the organization of documents in the submission	Complex folder structure eliminated
CTP defined and user-defined keywords	Greater definition of the purpose of submitted documents
Category events	Communicate the purpose of each submission
Application references	Direct identification of related applications, e.g. Predicate Product or Master Files

EXAMPLE eCTD XML SUBMITTED WITH DOCUMENTS

TECHNICAL SPECIFICATION IS BEING DRAFTED

Technical Implementation Guide (TIG)

- ✓ Details the use of XML tags and structures
- ✓ Provides validation rules for mandatory and optional items
- ✓ Identifies which fields require the use of controlled vocabularies
- ✓ Explains user defined keywords to describe documents

Controlled vocabulary (CV) to define valid values for certain fields

Sample Files to illustrate the use of the specification for several common tobacco submission types

CURRENT ACTIVITIES WITHIN CTP

- Developing XML schema that will transmit *fielded* information that can be generated by computer and be processed by CTP
- Developing documentation explaining the creation and use of the electronic submission
- Prototyping parsers to read and load the XML code and associated documents into internal databases
- Initial proof-of-concept test with software companies
- *then…* Provide draft documents for public comment

~~THE END~~ *THE BEGINNING*

We look forward to working with industry to streamline the submission process and…

- *Improve the Fidelity of Input*
- *Facilitate the Overall Process*
- *Communicate Submission Status More Directly*