

# 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.*

Sept. 18, 2018

CENTER FOR TOBACCO PRODUCTS

The FDA logo is a blue square with the white letters "FDA" inside. It is positioned in the top right corner of the slide, overlapping the image of the columns.

FDA

2018\_TSRC98\_Sholtes.pdf

TSRC2018(72) - Document not peer-reviewed

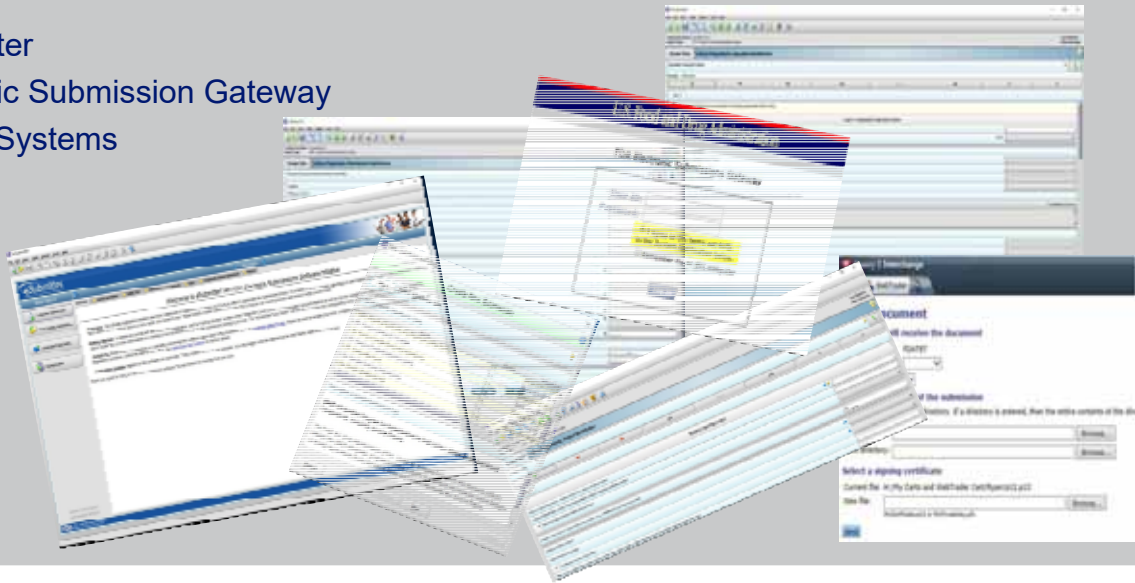
- In the Beginning
- CTP Portal
- Technical Considerations
- Expanding on an existing eSubmission Standard, the eCTD
- Conclusion

# 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://ctportal.fda.gov/ctportal/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

The screenshot displays the CTP Portal Home Screen with the following sections:

- Recent Regulatory Files:** A table listing regulatory files with columns for Date Issued, File Type, and ID.
- Recent Notifications:** A list of notifications with timestamps and brief descriptions.
- Recent Uploads:** A table listing uploaded files with columns for File Name, User's Name, Submission Date, File Count, and Status.

| Date Issued | File Type                                  | ID       |
|-------------|--|----------|
| 01/11/2016  | Decision Letter                            | 00001001 |
| 10/21/2015  | Administrative Enforcement Response Letter | A0000018 |
| 10/06/2015  | Administrative Enforcement Response Letter | A0000018 |
| 03/06/2015  | Acquiescence Letter                        | 00000113 |
| 03/05/2015  | Acquiescence Connected Letter              | 00000113 |

|                     |   |
|---------------------|---|
| 06/04/2018 12:02 PM | The FDA Acknowledgment Regulatory Letter has been posted to the ... |
| 06/01/2018 08:11 AM | A submission is now available for viewing in the CTP Portal.        |
| 05/16/2018 05:08 AM | A submission is now available for viewing in the CTP Portal.        |
| 05/12/2018 12:02 PM | The CTP Portal User Admin has changed.                              |

| File Name                   | User's Name   | Submission Date | File Count | Status                 |
|-----------------------------|---------------|-----------------|------------|------------------------|
| 140_Test_A_8.78.zip         | Melvin, Ching | 08/07/2018      | 20         | Submission Successful  |
| 02_Test.zip                 | Melvin, Ching | 08/07/2018      | 1          | Submission Successful  |
| 01-02_Test.zip              | Melvin, Ching | 08/07/2018      | 10         | Submission In Progress |
| 1 File @ Connect Letter.zip | Tanya, Chane  | 08/08/2018      | 1          | Submission Successful  |

Test data displayed

# PORTAL SUBMISSIONS

## Key Features:

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

| STN       | Submission Type                    | Product Name  | Date Submitted | Submission POC |
|-----------|------------------------------------|---------------|----------------|----------------|
| SD0000088 | SD - Required/Required Documents   | Multiple (12) | 04/18/2016     | Doe, John      |
| TI0001312 | TI - Product Ingredient List (PIL) | Product 1     | 04/18/2016     | Doe, Jane      |
| TT0000329 | TT - Tobacco Constituents          | N/A           | 04/18/2016     | Doe, John      |
| SE1600523 | SE - Substantial Equivalent Report | N/A           | 04/18/2016     | Doe, Jane      |
| PC0000538 | PC - Product Comparison            | N/A           | 04/18/2016     | Doe, John      |
| PS0000218 | PS - Postmarket Surveillance       | N/A           | 04/18/2016     | Doe, Jane      |
| NR0000343 | NR - Nicotine Reporting            | N/A           | 04/18/2016     | Doe, John      |
| TC0000454 | TC - General Correspondence        | N/A           | 04/18/2016     | Doe, Jane      |

*Test data displayed*

# PORTAL UPLOAD TOOL

The screenshot shows the 'Upload Tool' interface. At the top, there is a progress bar with three steps: 1. UPLOAD PACKAGE, 2. UPLOAD FILE, and 3. SUBMIT PACKAGE. Below this is a 'Welcome to the CTP Portal Upload Tool' section with a 'Upload eSubmitter File' button. The main area is titled 'UPLOAD HISTORY' and contains a table of uploads. The table has columns for File Name, User's Name, Upload Status Date, Package Description, Package ID, and Status. All uploads shown are 'Upload Successful'.

| File Name                              | User's Name    | Upload Status Date | Package Description  | Package ID        | Status            |
|--|----------------|--------------------|--|-------------------|-------------------|
| NP_July 1.zip                          | Stev, Jane     | 07/01/2016         | Upload Henry's Check   | 16-000-00-02C-04  | Upload Successful |
| TC_Amendment_007_Manual_Publishing.zip | Brown, Towards | 06/29/2016         | Upload TC Amendment  | 16-000-00-02C-03  | Upload Successful |
| TC_Original_007_Manual_Publishing.zip  | Brown, Towards | 06/29/2016         | Upload TC  | 16-000-00-02C-03  | Upload Successful |
| Portal_PMTA_Test_40-MB.zip             | Henry, Amy     | 04/21/2016         | Resulting this upload this is a test of the upload large files | 16-000-00-02B-02  | Upload Successful |
| Portal_PMTA_TestUploadPkg_127MB.zip    | Brown, Towards | 03/26/2016         | Test description   | 16-000-00-02C1-08 | Upload Successful |
| Portal_PMTA_TestUploadPkg_127MB.zip    | Brown, Towards | 03/26/2016         | Test upload package description                                | 16-000-00-02C1-07 | Upload Successful |
| 007_Package7_OF_Submitter.pdf          | Henry, Amy     | 03/10/2016         | test file  | 16-000-00-02C1-06 | Upload Successful |

## Key Features:

Listing of uploads with date and user who uploaded

Test data displayed



# ENSURE SUBMISSION CAN BE... *PROCESSED, REVIEWED AND ARCHIVED*

## Legibility/Usability

- ✓ Create PDF files directly from source file
- ✓ For scanned documents, resolution  $\geq 300$  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

## File Naming

- ✓ 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](https://www.fda.gov/TobaccoProducts/GuidanceComplianceRegulatoryInformation/Manufacturing), 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>

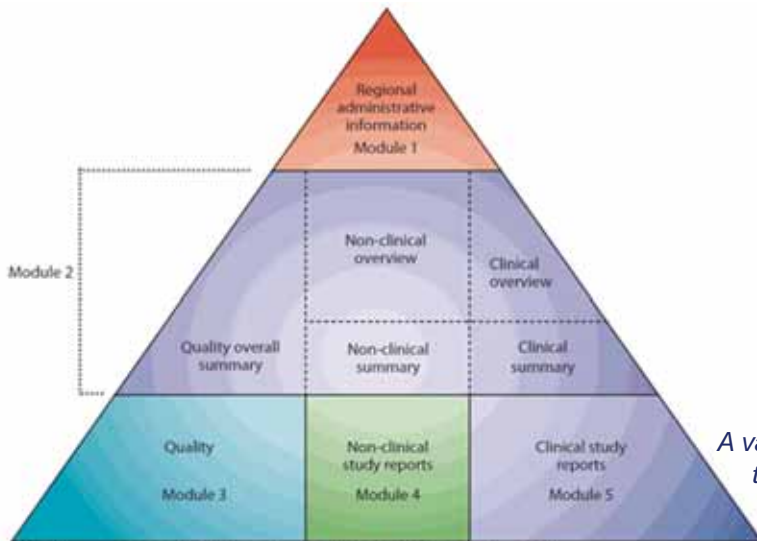
# PREPARING FOR YOUR ELECTRONIC SUBMISSION

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

|  |  |
|--|--|
| <b>Module 1 Administrative information</b> | <b>Module 2 Summaries</b>                          |
| 1.1 Forms                                  | 2.2 Introduction to summary                        |
| 1.2 Cover letters                          | 2.3 Quality overall summary                        |
| 1.3 Administrative information             | 2.4 Nonclinical overview                           |
| 1.4 References                             | 2.5 Clinical overview                              |
| 1.5 Application status                     | 2.6 Nonclinical written and tabulated summaries    |
| 1.6 Meetings                               | 2.7 Clinical summary                               |
| 1.7 Fast track                             | <b>Module 3 Quality</b>                            |
| 1.8 Special protocol assessment request    | 3.2 Body of data                                   |
| 1.9 Pediatric administrative information   | 3.2.S Drug substance [name, manuf]                 |
| 1.10 Dispute resolution                    | 3.2.P Drug product [name, dosage form, manuf]      |
| 1.12 Other correspondence                  | 3.2.A Appendices                                   |
| 1.13 Annual report                         | 3.2.R Regional information                         |
| 1.14 Labeling                              | 3.3 Literature references                          |
| 1.15 Promotional material                  | <b>Module 4 Nonclinical Study Reports</b>          |
| 1.16 Risk management plan                  | 4.2 Study reports                                  |
| 1.17 Postmarketing studies                 | 4.3 Literature references                          |
|  | <b>Module 5 Clinical Study Reports</b>             |
|  | 5.2 Tabular listing of all clinical studies        |
|  | 5.3 Clinical study reports and related information |
|  | 5.4 Literature references                          |

*Additions*

*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

## 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*.

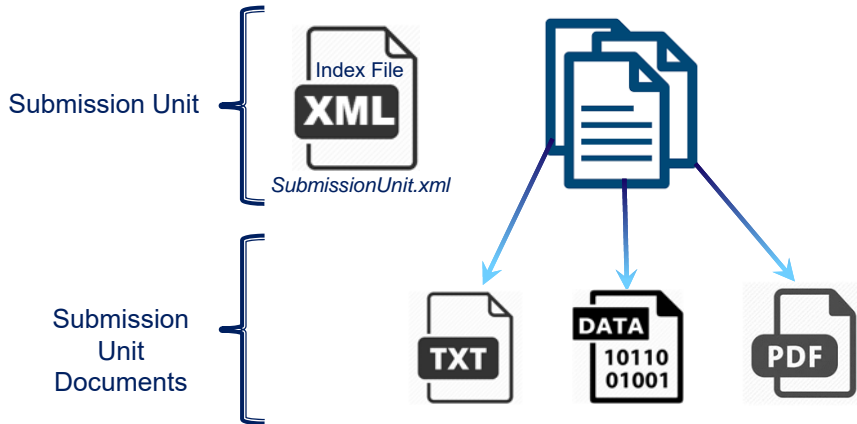
## Submission Unit

- 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*.

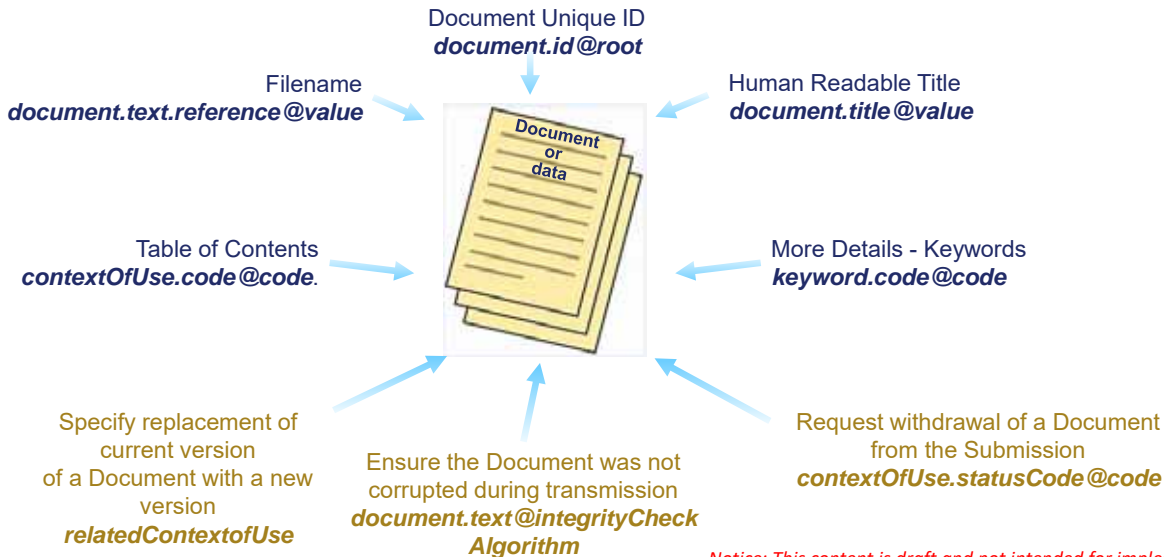
## Document

- 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

```
</component>
- <component>
  - <document>
    <!--document ( Section 7.2.17 )-->
    <id root="9eeb0374-86e7-11e8-adc0-fa7ae01bbebc"/>
    <!--BR061,62,63-->
    <title value="ctp_1.6 meeting"/>
    <!--BR064-->
    - <text integrityCheckAlgorithm="SHA256">
      <reference value="meeting.pdf"/>
      <!--BR067-->
      <integrityCheck>45268d0989ab4c403072e9f89376bf9178d61fcfef4ce4468f95c6b3a00f9be1</integrityCheck>
      <!--BR065,66-->
    </text>
  </document>
</component>
+ <component>
  - <document>
    <!--document ( Section 7.2.17 )-->
    <id root="9eeb05ae-86e7-11e8-adc0-fa7ae01bbebc"/>
    <!--BR061,62,63-->
    <title value="ctp_1.6.2 industry meeting package"/>
    <!--BR064-->
    - <text integrityCheckAlgorithm="SHA256">
      <reference value="meetingpackage.jpg"/>
      <!--BR067-->
      <integrityCheck>bc8ceab0d289741597683a911e30eddc062f7bfa915743414213243f3df7c43f</integrityCheck>
      <!--BR065,66-->
    </text>
  </document>
</component>
+ <component>
  - <document>
    <!--document ( Section 7.2.17 )-->
    <id root="9eeb07de-86e7-11e8-adc0-fa7ae01bbebc"/>
```

## 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

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*