CTP ELECTRONIC SUBMISSIONS STANDARDS AND ACTIVITIES

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TOPICS

- Introduction
- 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

- eSubmitter
- Electronic Submission Gateway
- Internal Systems
- FDA Unified Registration & Listing *(FURLS)*

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

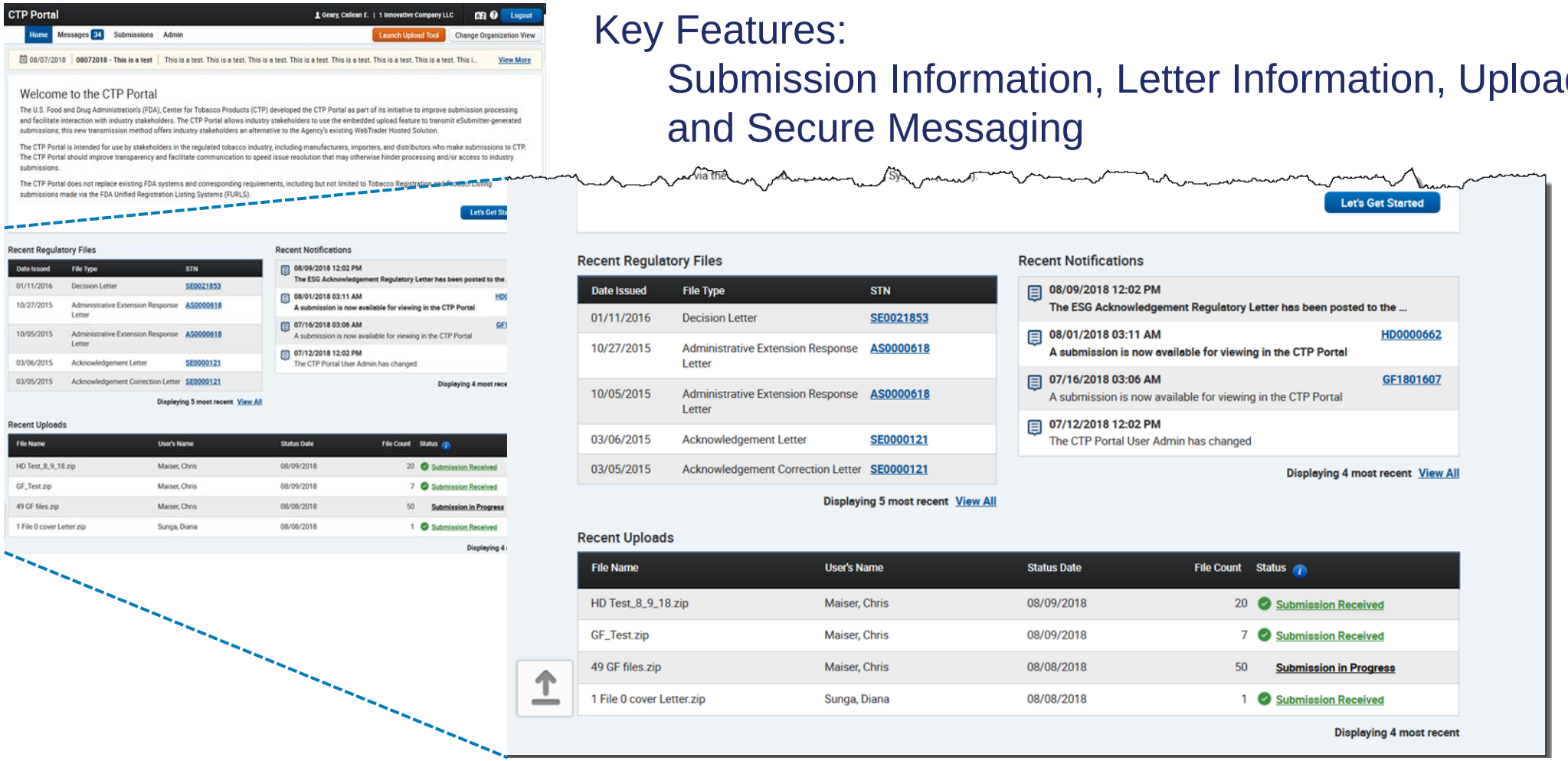
- Account management performed by an Industry Account Manager (IAM)

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

PORTAL HOME SCREEN

Key Features:

Submission Information, Letter Information, Upload Tool and Secure Messaging

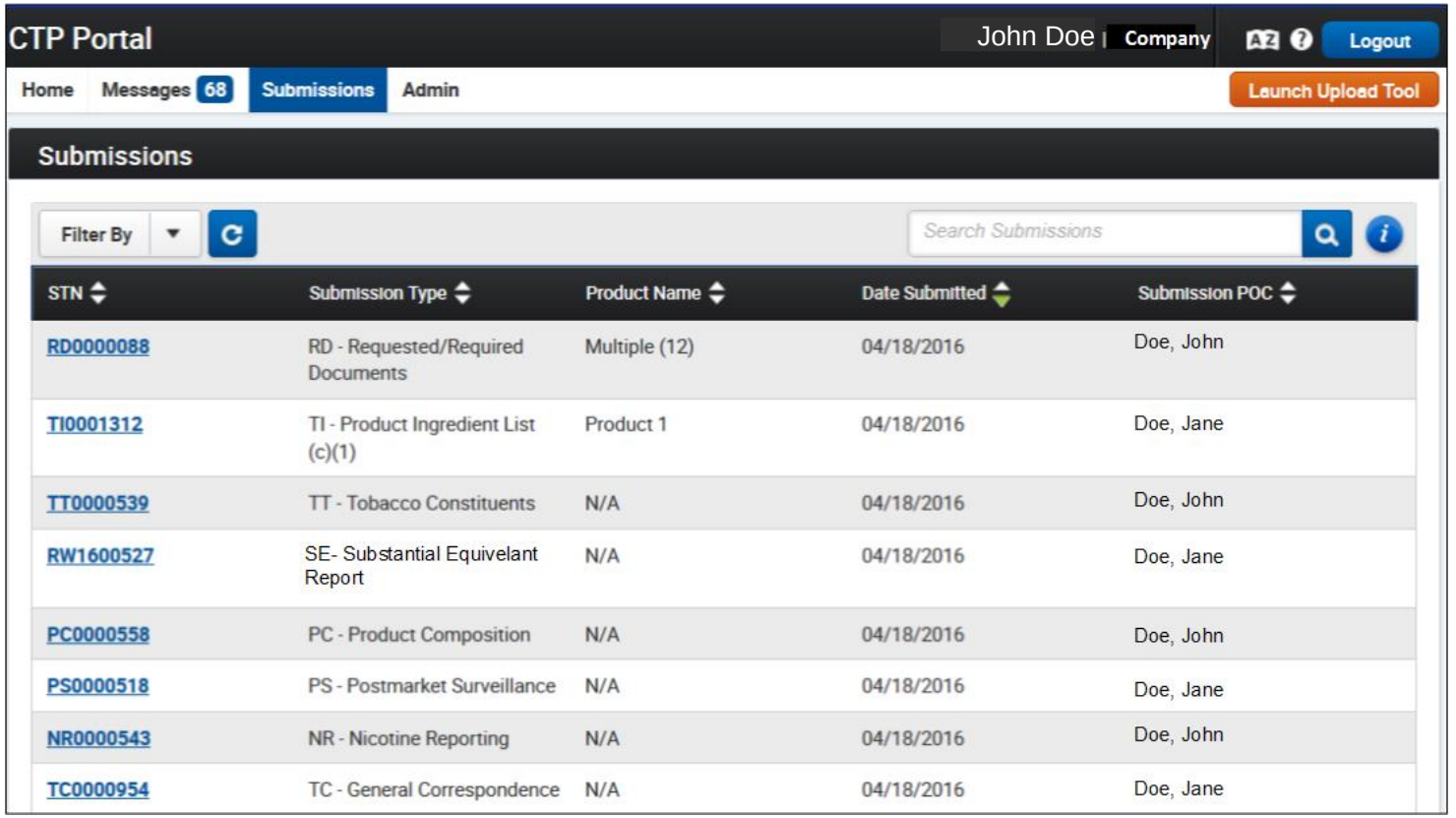


Test data displayed

PORTAL SUBMISSIONS

Key Features:

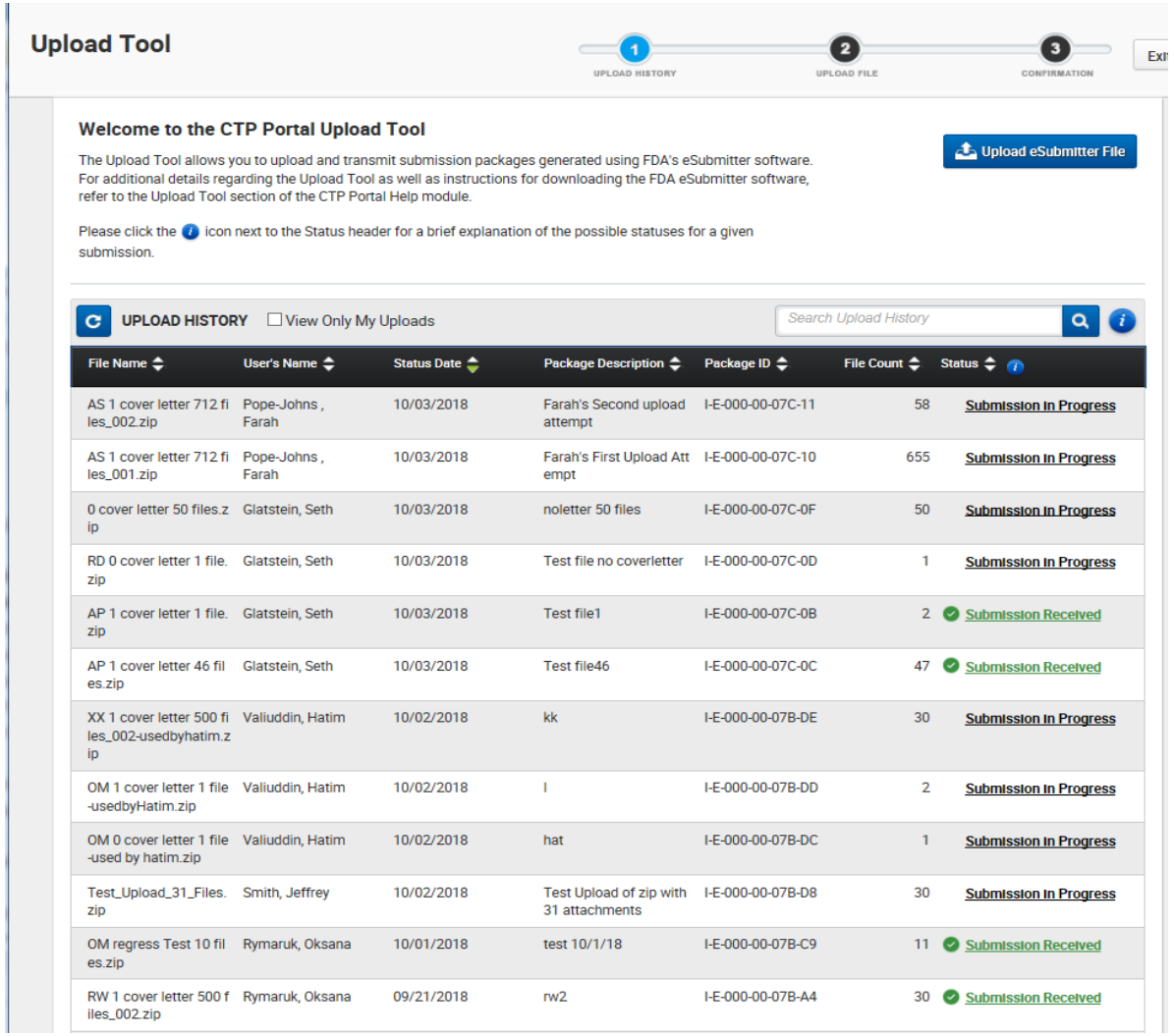
- Listing of received submissions
- Assigned Submission Tracking Number (STN)
- High-level submission information



STN	Submission Type	Product Name	Date Submitted	Submission POC
RD0000088	RD - Requested/Required Documents	Multiple (12)	04/18/2016	Doe, John
TI0001312	TI - Product Ingredient List (c)(1)	Product 1	04/18/2016	Doe, Jane
TT0000539	TT - Tobacco Constituents	N/A	04/18/2016	Doe, John
RW1600527	SE- Substantial Equivelant Report	N/A	04/18/2016	Doe, Jane
PC0000558	PC - Product Composition	N/A	04/18/2016	Doe, John
PS0000518	PS - Postmarket Surveillance	N/A	04/18/2016	Doe, Jane
NR0000543	NR - Nicotine Reporting	N/A	04/18/2016	Doe, John
TC0000954	TC - General Correspondence	N/A	04/18/2016	Doe, Jane

Test data displayed

PORTAL UPLOAD TOOL



Upload Tool

1 UPLOAD HISTORY — 2 UPLOAD FILE — 3 CONFIRMATION

Welcome to the CTP Portal Upload Tool

The Upload Tool allows you to upload and transmit submission packages generated using FDA's eSubmitter software. For additional details regarding the Upload Tool as well as instructions for downloading the FDA eSubmitter software, refer to the Upload Tool section of the CTP Portal Help module.

Upload eSubmitter File

Please click the icon next to the Status header for a brief explanation of the possible statuses for a given submission.

UPLOAD HISTORY ☐ View Only My Uploads — Search Upload History

File Name	User's Name	Status Date	Package Description	Package ID	File Count	Status
AS 1 cover letter 712 files_002.zip	Pope-Johns , Farah	10/03/2018	Farah's Second upload attempt	I-E-000-00-07C-11	58	Submission In Progress
AS 1 cover letter 712 files_001.zip	Pope-Johns , Farah	10/03/2018	Farah's First Upload Attempt	I-E-000-00-07C-10	655	Submission In Progress
0 cover letter 50 files.zip	Glatstein, Seth	10/03/2018	noletter 50 files	I-E-000-00-07C-0F	50	Submission In Progress
RD 0 cover letter 1 file.zip	Glatstein, Seth	10/03/2018	Test file no coverletter	I-E-000-00-07C-0D	1	Submission In Progress
AP 1 cover letter 1 file.zip	Glatstein, Seth	10/03/2018	Test file1	I-E-000-00-07C-0B	2	Submission Received
AP 1 cover letter 46 files.zip	Glatstein, Seth	10/03/2018	Test file46	I-E-000-00-07C-0C	47	Submission Received
XX 1 cover letter 500 files_002-usedbyhatim.zip	Valiuddin, Hatim	10/02/2018	kk	I-E-000-00-07B-DE	30	Submission In Progress
OM 1 cover letter 1 file-usedbyHatim.zip	Valiuddin, Hatim	10/02/2018	l	I-E-000-00-07B-DD	2	Submission In Progress
OM 0 cover letter 1 file-used by hatim.zip	Valiuddin, Hatim	10/02/2018	hat	I-E-000-00-07B-DC	1	Submission In Progress
Test_Upload_31_Files.zip	Smith, Jeffrey	10/02/2018	Test Upload of zip with 31 attachments	I-E-000-00-07B-D8	30	Submission In Progress
OM regress Test 10 files.zip	Rymaruk, Oksana	10/01/2018	test 10/1/18	I-E-000-00-07B-C9	11	Submission Received
RW 1 cover letter 500 files_002.zip	Rymaruk, Oksana	09/21/2018	rw2	I-E-000-00-07B-A4	30	Submission Received

Key Features:

Listing of uploads including upload date and user who uploaded

Test data displayed

TIPS TO 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 the narrative
- ✓ Retain extension in the filename to specify the file format type
- ✓ SaS transport file (.xpt) for analysis datasets recommended
  http://www.fda.gov/ForIndustry/DataStandards/StudyDataStandards

File Naming

- ✓ Short, descriptive, unique filenames and file path, *e.g., "MainTOC.pdf", "study1.xpt"*,
- ✓ Special characters and foreign characters cause problems, *e.g., #, %, ., &, ><, ç, ü*
- ✓ Deep subfolders cause problems, limit path < 180 characters

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

TIPS TO ENSURE SUBMISSION CAN BE…
PROCESSED, REVIEWED AND ARCHIVED

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
- ✓ Use existing templates

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*

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

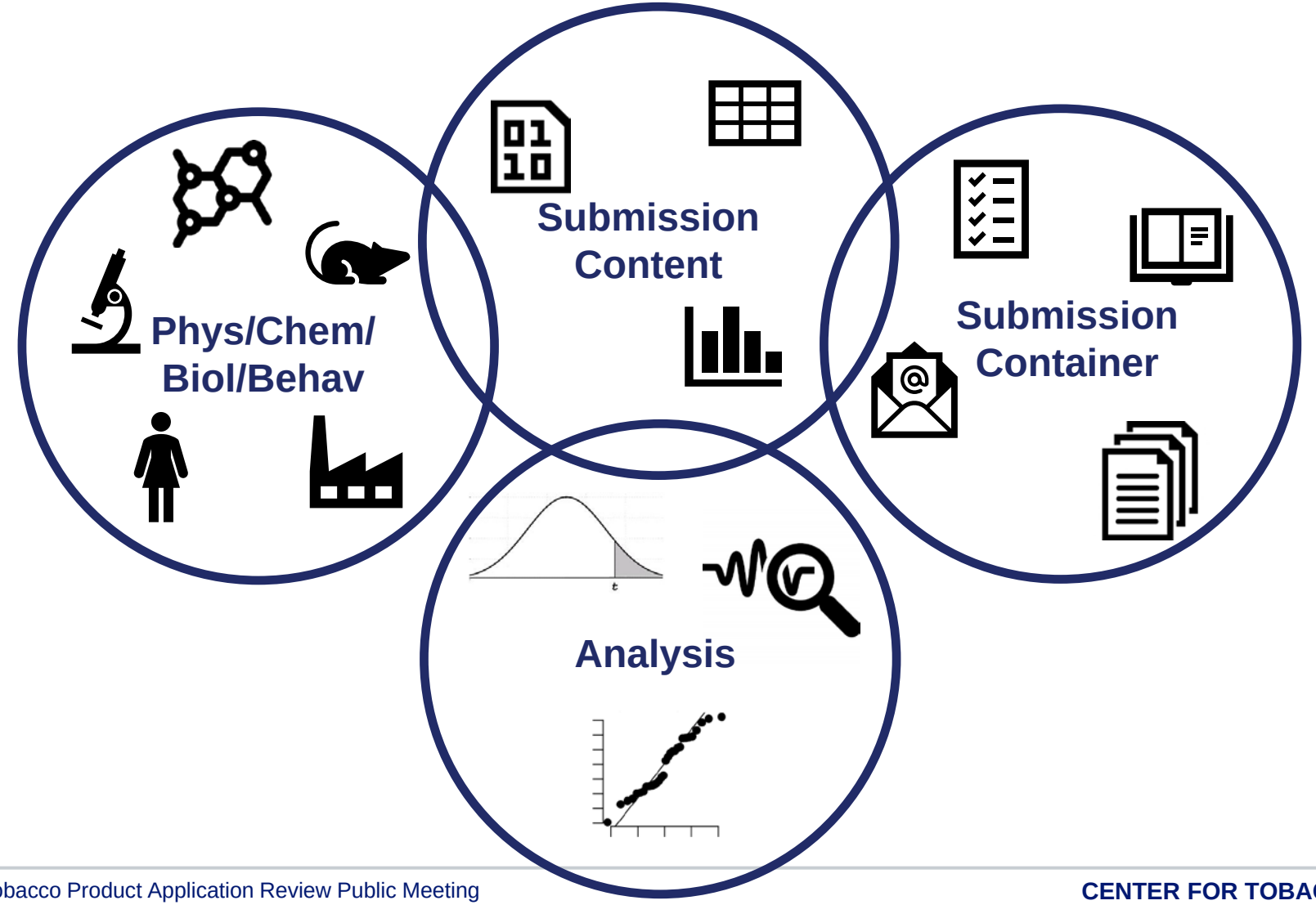
   FDA provides instructions, video tutorials and helpdesk assistance
   [eSubmitter@fda.hhs.gov or 1-877-CTP-1373]

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

AREAS OF STANDARDS DEVELOPMENT

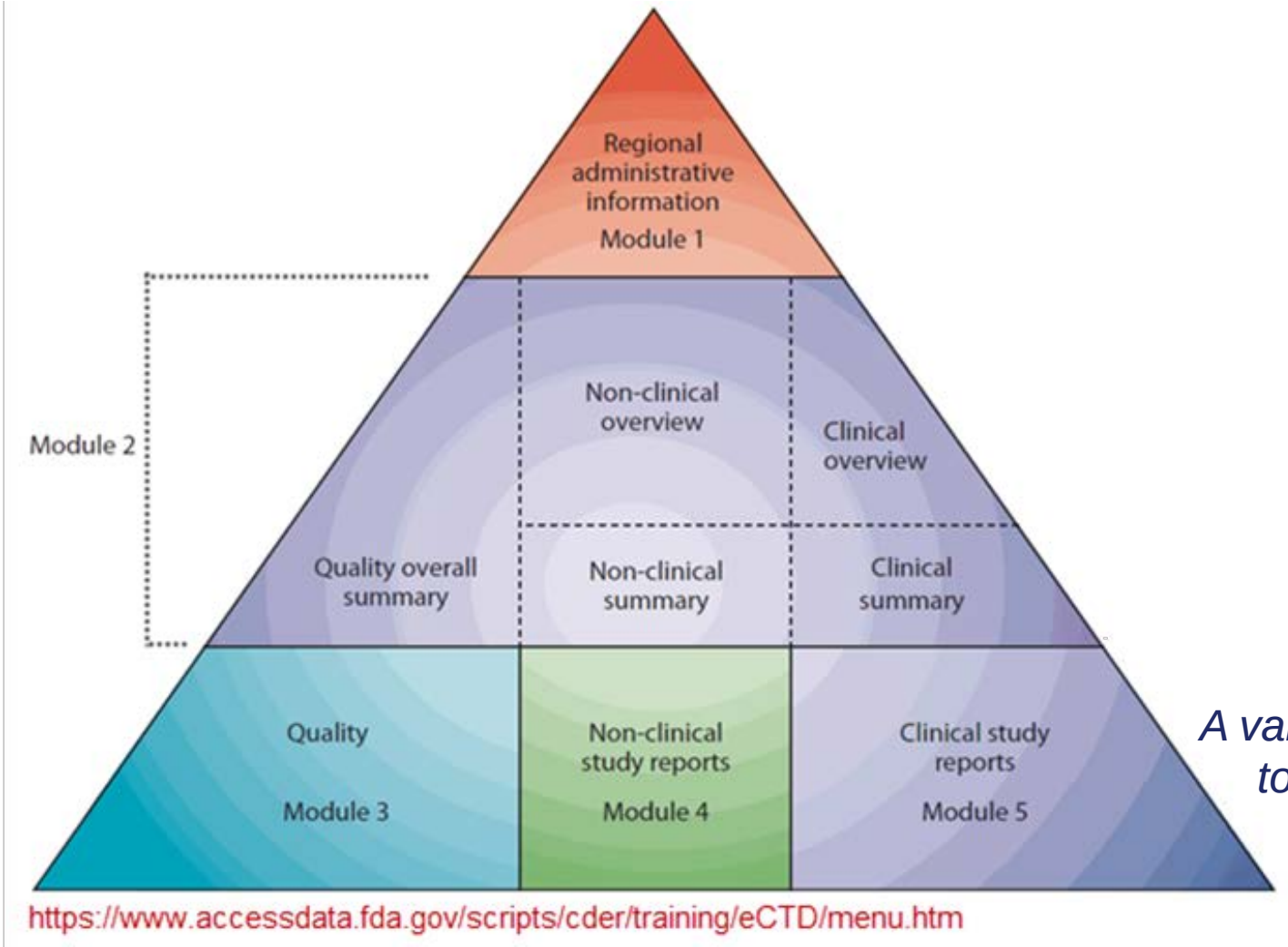


EXPANDING UPON AN EXISTING INTERNATIONAL ELECTRONIC SUBMISSION SPECIFICATION

- 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*"

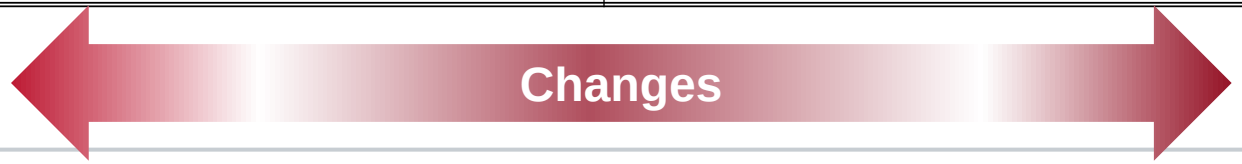
ELECTRONIC COMMON TECHNICAL DOCUMENT (eCTD)



A variation of the eCTD is needed to support tobacco products

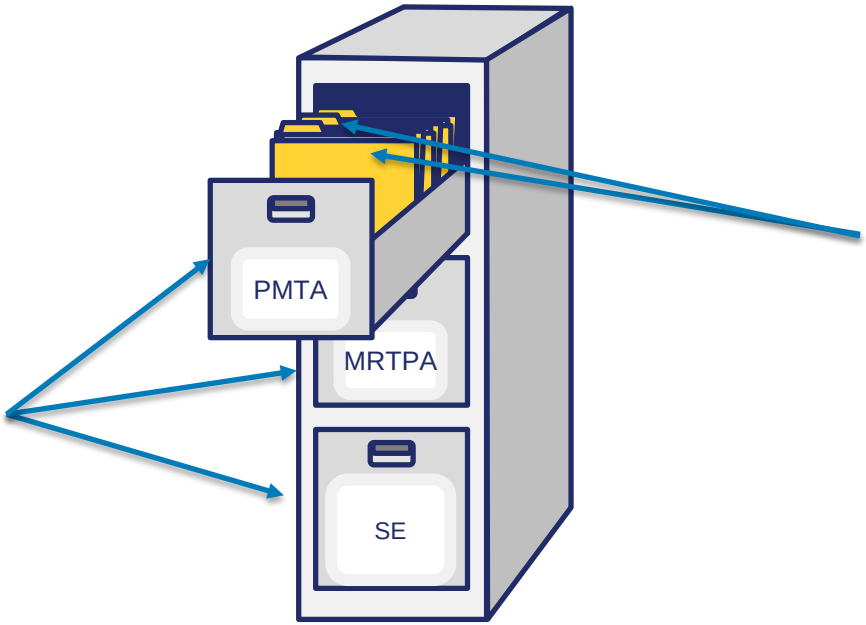
eCTD MODULES- LEVEL 2 OF HIERARCHY

Module 1 Administrative information	Module 2 Summaries
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	**Module 3 Quality**
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	**Module 4 Nonclinical Study Reports**
1.16 Risk management plan	4.2 Study reports
1.17 Postmarketing studies	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



RPS APPLICATION *(PRODUCT DOSSIER)*

Product Dossier
(RPS Application)



Submission Unit Folders

Submission Drawers
(e.g., Marketing Applications)

Documents

POTENTIAL SUBMISSION STANDARD

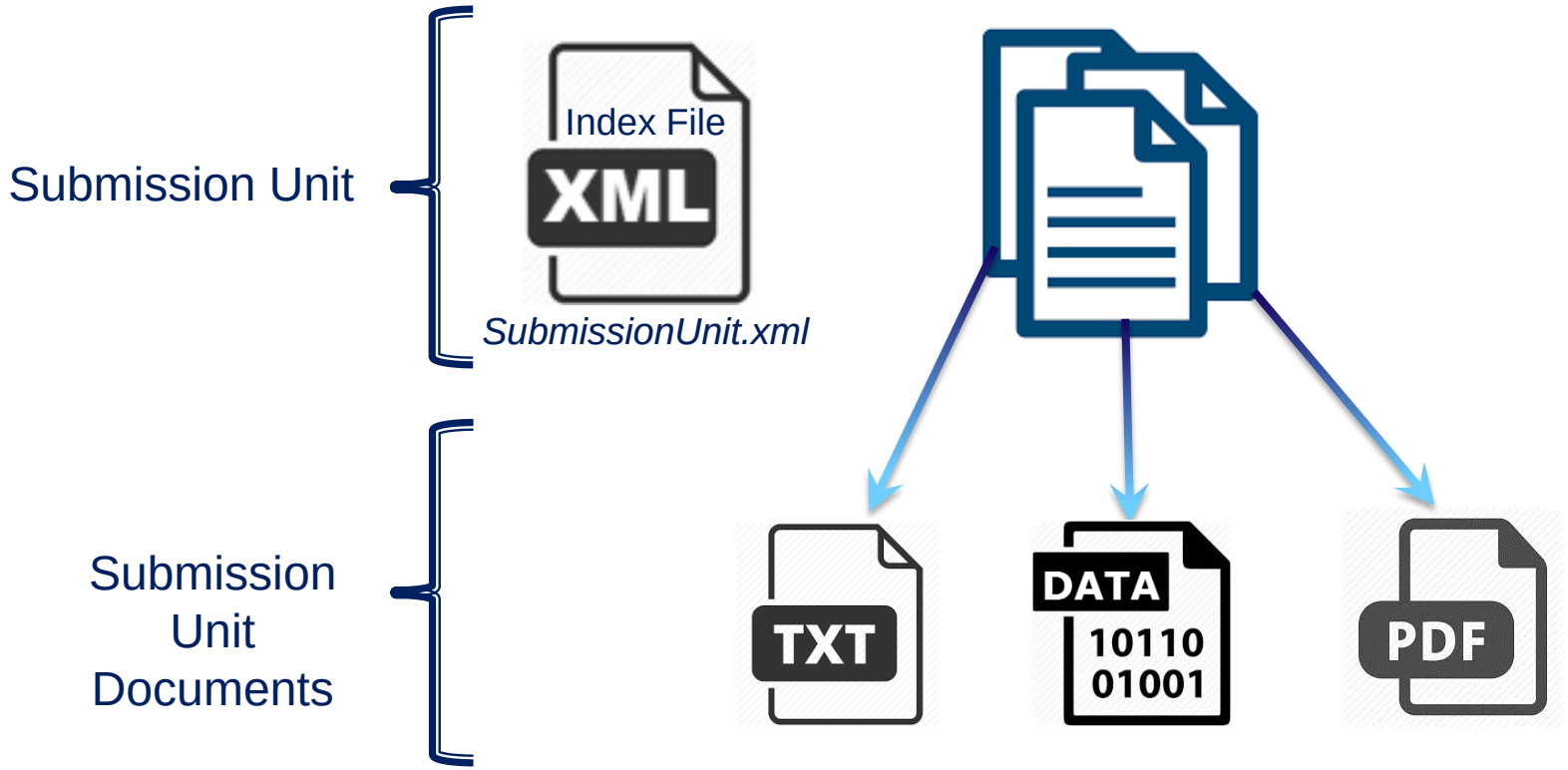
Technical advantages:

- Fully metadata driven – no folder structure to files
- 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

- Commercial support expected for future standards

TWO MAIN PIECES OF AN eCTD MESSAGE



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

Document Unique ID
document.id@root

Filename
document.text.reference@value

Human Readable Title
document.title@value

Table of Contents
contextOfUse.code@code.

More Details - Keywords
keyword.code@code

Specify replacement of current version of a Document with a new version
relatedContextofUse

Ensure the Document was not corrupted during transmission
document.text@integrityCheck Algorithm

Request withdrawal of a Document from the Submission
contextOfUse.statusCode@code

Notice: This content is draft and not intended for implementation

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>45268d0989ab4c403072e9f89376bf9178de1fcfef4ce4468f95c6b3a00f9be1</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 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

… ACTIVITIES CONTINUED

- Building internal technology to accommodate eTTD
- 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*