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eCTD

Simonetta Conti, Regulatory Affairs Manager
Euticals S.p.A. part of AMRI

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What is this presentation?

- An overview of some important features of eCTD
- A quick guide to navigation

What is **NOT**?

- A comprehensive guide to using eCTD

- Why eCTD?
- Roadmap of eCTD for EU and US
- eCTD around the world
- What is eCTD?
- How does it work?
- What does it look like?
- Module 1 in eCTD
- Some tips
- Useful Guidelines and Links

Why eCTD?

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- Lack of space at Agencies.
- Electronic Submissions give more accountability.
- Efficient and secure storage and transfer of electronic data.
- Standard and harmonised electronic format for all filed dossiers.
- Searchable and allows a faster review of the documents.
- Better version control and change management.
- User friendliness for a faster and more efficient revision.
- Life-cycle management of dossiers.
- Cross-linking within data.

eCTD Roadmap for EU and US

EDQM

- **January 2018** Require eCTD submissions for new applications.
- **January 2018** Stop accepting PDF submissions for revisions and renewals. Therefore, all such submissions need to be in NeeS or eCTD format.
- **January 2020** Require eCTD submissions for all applications.

IMPORTANT: Once eCTD has been adopted coming back to a previous submission format is **not** allowed.

NOT applicable to TSE only submissions and for submissions for substances for veterinary use only.

FDA

- **May 5, 2017** New Drug Applications (NDAs), Abbreviated NDAs (ANDAs), Biologics Licence Applications (BLAs) must be submitted using eCTD format.
- **May 5, 2018** Commercial Investigational New Drug Applications (INDs) and Master Files must be submitted using eCTD format.
- **May 5, 2018** Referral Letters, Responses to Deficiency Letters, Annual Reports and any communication with US Agency must be submitted using eCTD format.

NOT Applicable to noncommercial INDs, to devices that are regulated by CBER as biological products, to submissions for blood and blood components, to INDs for devices that are regulated by CBER as biological products.

eCTD Around the World

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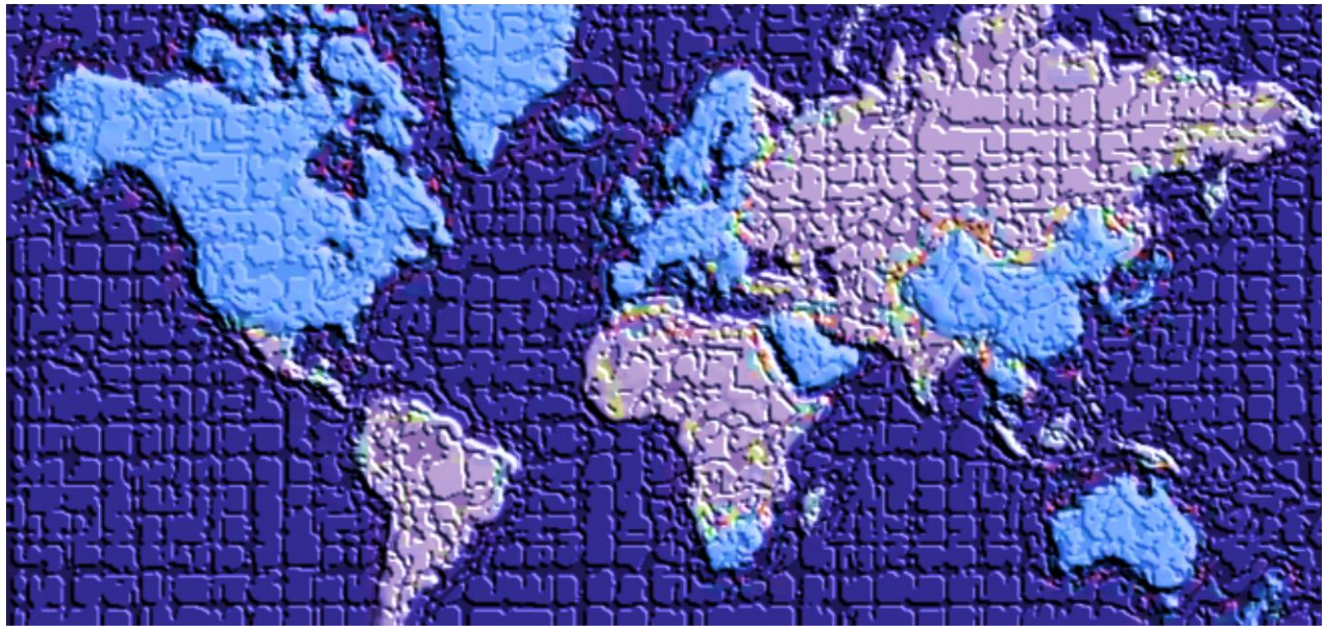
- Besides USA and EMA EEA Member States, eCTD is officially accepted by Canada, Australia, New Zealand, Gulf Cooperation Council Member States, South Africa, China, Japan, South Korea, Taiwan, Hong Kong, Singapore and Thailand.
- eCTD in Japan accepted by PMDA only for finished dosage forms but not for API documentation.
- CIS (Commonwealth of Independent States) countries want to keep nation specific dossiers in native languages. Therefore little applicability.
- ASEAN (Association of Southeast Asian Nations) countries have adopted ACTD. Little talk about AeCTD. Only exceptions are Singapore and Thailand.

Countries Accepting eCTD



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What is eCTD?

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- It is an acronym for Electronic Common Technical Document.
- It is an XML backbone that is assembled around the documents placed into the publishing software.

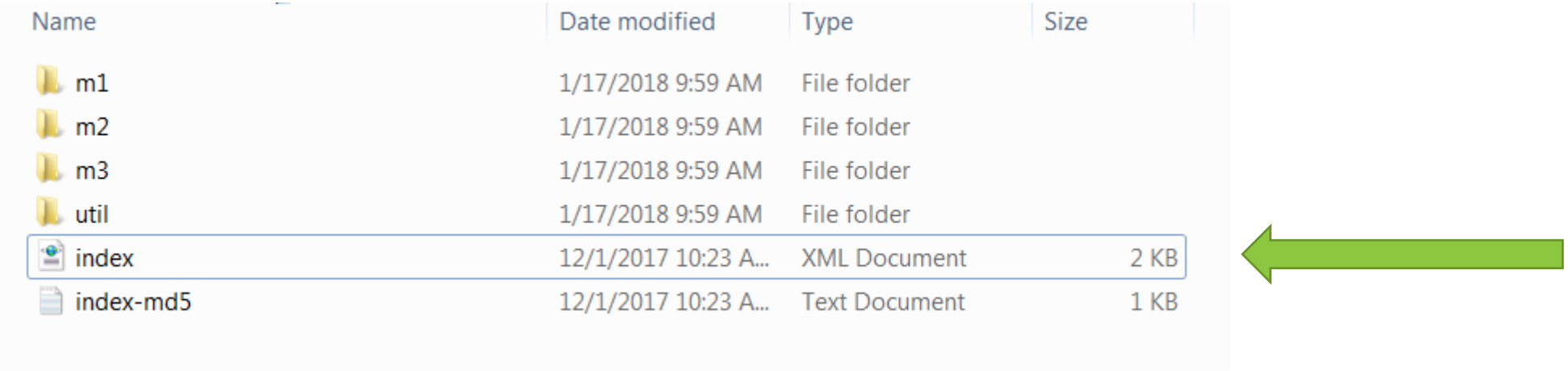
- It allows for:
  - Easy navigation between sections of the submission utilizing hyperlinks.
  - Quick to reference Meta-Data that tells the reviewer basic information about your submission.
  - Lifecycle management of documents, allowing the reviewer to see what documents are new, what documents are replacing a previous revision and what are appending already submitted documents.

eCTD ….. how does it work?

- The first submission should be the baseline 0000.
- Baseline should be submitted at the start of a procedure
  - ✓ as a separate sequence - preferred option
  - ✓ or as a revision/renewal application
  - ✓ a baseline won't be accepted during the course of a procedure (e.g. as a response to deficiency letter)
- For each update a new sequence 000(X+1) should be provided.
- For each new sequence updated Module 1 and 3 should be included as appropriate.
- A new sequence is issued not only when updated DMFs or Sections are submitted, but also whenever a letter of access is issued and sent to Health Authorities.
- Before being submitted to Health Authorities, the submission should be technically validated with an appropriate validation tool.

What does it look like?

Always open the Index file to navigate the eCTD sequence, it presents you with the rendered XML backbone.



Opening the sequence….

eCTD DTD version 3.2

- m1-administrative-information-and-prescribing-information
  - eu-regional.xml [new]
- m2-common-technical-document-summaries
  - m2-3-quality-overall-summary
    - m2-3-s-drug-substance [manufacturer: Euticals S.p.A.] [substance: Applicant Part -]
      - AP Drug Substance [new]
    - m2-3-s-drug-substance [manufacturer: Euticals S.p.A.] [substance: Restricted Part -]
      - RP Drug Substance [new]
- m3-quality
  - m3-2-body-of-data
    - m3-2-s-drug-substance [manufacturer: Euticals S.p.A.] [substance: Applicant Part -]
      - m3-2-s-1-general-information
        - m3-2-s-1-1-nomenclature
          - AP Nomenclature [new]
        - m3-2-s-1-2-structure
          - AP Structure [new]
        - m3-2-s-1-3-general-properties
          - AP General Properties [new]
      - m3-2-s-2-manufacture
        - m3-2-s-2-1-manufacturer
          - AP Manufacturer [new]
        - m3-2-s-2-2-description-of-manufacturing-process-and-process-controls
          - AP Description of Manufacturing Process and Process Controls [new]

Module 1

Module 2

Module 3

An Example of Lifecycle

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eCTD DTD version 3.2

- m1-administrative-information-and-prescribing-information
  - eu-regional.xml [new]
- m2-common-technical-document-summaries
  - m2-3-quality-overall-summary
    - m2-3-s-drug-substance [manufacturer: Euticals S.p.A.] [substance: Applicant Part -]
      - AP Drug Substance [new]
    - m2-3-s-drug-substance [manufacturer: Euticals S.p.A.] [substance: Restricted Part -]
      - RP Drug Substance [new]

[new] indicates the lifecycle function

More metadata

Other Lifecycle Functions


New

Document is New to the DMF.


Replace

Document is replacing a previous version of the same document.


Delete

Document is deleting the document from the submission (rarely used, and strongly discouraged by Health Authorities).


Append

Document is appending another document. Also this function is discouraged by Health Authorities (EDQM), since it leads frequently to lifecycle difficulties.

Module 1 in eCTD

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EU Module 1

DTD version 3.0.1

Envelope for ES	
Identifier:	74385800-79d3-11e8-adc0-fa7ae01bbebc
Submission:	Type: Active Substance Master File
Procedure Tracking Number(s):	to/be/assigned
Submission Unit:	Type: Initial submission to start any regulatory activity
Applicant:	Euticals S.p.A.
Agency:	Spain - Agencia Española de Medicamentos y Productos Sanitarios (ES-AEMPS)
Procedure:	National Procedure
Invented Name:	Not available
INN:	API NAME
Sequence:	0001
Related Sequence:	0001
Submission Description:	ASMF for API NAME made Euticals S.p.A.

Module 1 EU

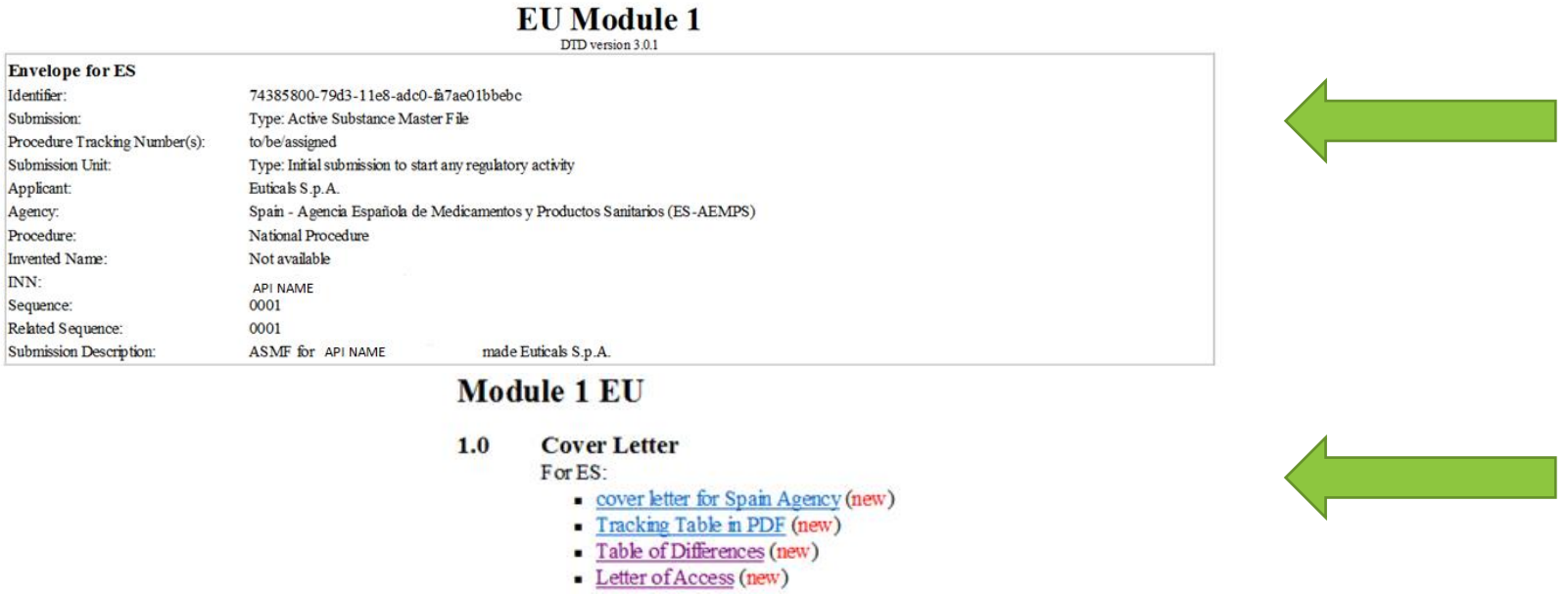
1.0 Cover Letter

For ES:

- cover letter for Spain Agency (new)
- Tracking Table in PDF (new)
- Table of Differences (new)
- Letter of Access (new)

Module 1 in eCTD

- The metadata at the top of Module 1 tells the Health Authority the information they need to know about your submission.



EU Module 1

DTD version 3.0.1

Envelope for ES	
Identifier:	74385800-79d3-11e8-adc0-fa7ae01bbebc
Submission:	Type: Active Substance Master File
Procedure Tracking Number(s):	to/be/assigned
Submission Unit:	Type: Initial submission to start any regulatory activity
Applicant:	Euticals S.p.A.
Agency:	Spain - Agencia Española de Medicamentos y Productos Sanitarios (ES-AEMPS)
Procedure:	National Procedure
Invented Name:	Not available
INN:	API NAME
Sequence:	0001
Related Sequence:	0001
Submission Description:	ASMF for API NAME made Euticals S.p.A.

Module 1 EU

1.0 Cover Letter

For ES:

- cover letter for Spain Agency (new)
- Tracking Table in PDF (new)
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- Letter of Access (new)

- For European countries it is extremely important to apply using the right modules/letters as requested by each National Authority in order to avoid any rejection of the submission.

Some Tips to Avoid Rejections….

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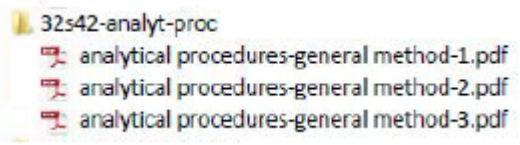
- Relevant analytical procedures and validations should be separated.



- A multiple file approach can be used, however there are limitations to the number of files included in one single section.
- The dossier should be easy to navigate.
- Used titles should be short and easy to understand. Strongly discouraged the use of internal codes or “nicknames”.
- Documents of 5 pages or more must have Table of Contents (TOC’s).
- Tables of Contents must have a Table of Tables and a Table of Figures if applicable.

… And Some Others ….

- Strongly discouraged a more than 4 levels deep on the TOC.

Not allowed

- The embedded items such as chemical structures, chromatograms, spectra etc … must be clearly legible.
- Headers must be oriented the same direction as the text on the page.
- Used font should be 12 for body of document and 9 for footnotes.
- Can not be password protected.

Guidelines and Links Helping Us Out of eCTD Jungle

- Providing Regulatory Submissions in Electronic Format (FDA)
- Portable Document Format (PDF) Specifications (FDA)
- www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ ElectronicSubmissions/ucm153574.htm
- eCTD submission standard
- Guidance for Electronic submissions for Certificates of Suitability applications
- eCTD Technical Conformance Guide

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