Practical Tips on eCTD

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April 3, 2019

FDA Disclaimer

The views and opinions presented here represent those of the speaker and should not be considered to represent advice or guidance on behalf of the U.S. Food and Drug Administration.

Poll

How would you characterize your ability to submit your ANDA in proper eCTD format?

- ❑ I'm an experienced expert
- ❑ I'm pretty good at it
- ❑ Somebody else in my company handles the eCTD
- ❑ I am a beginner
- ❑ Wait. What is eCTD?

Topics Covered

- Guidance
- eCTD Metrics (FY 2018)
- Electronic Submission Processing
- Preparing to Submit Electronically and Points to Consider

Guidance – eCTD Required

- **ANDAs, NDAs, BLAs, DMFs*** and **Commercial INDs** must be in eCTD format

- Paper and/or non-eCTD submissions are no longer accepted for above application types

- Study information in modules 4 or 5 must include the Study Tagging File (STF)

- Please see the eCTD web page www.fda.gov/ectd for further information and guidance

*Type III DMFs deadline extended to May 5, 2020

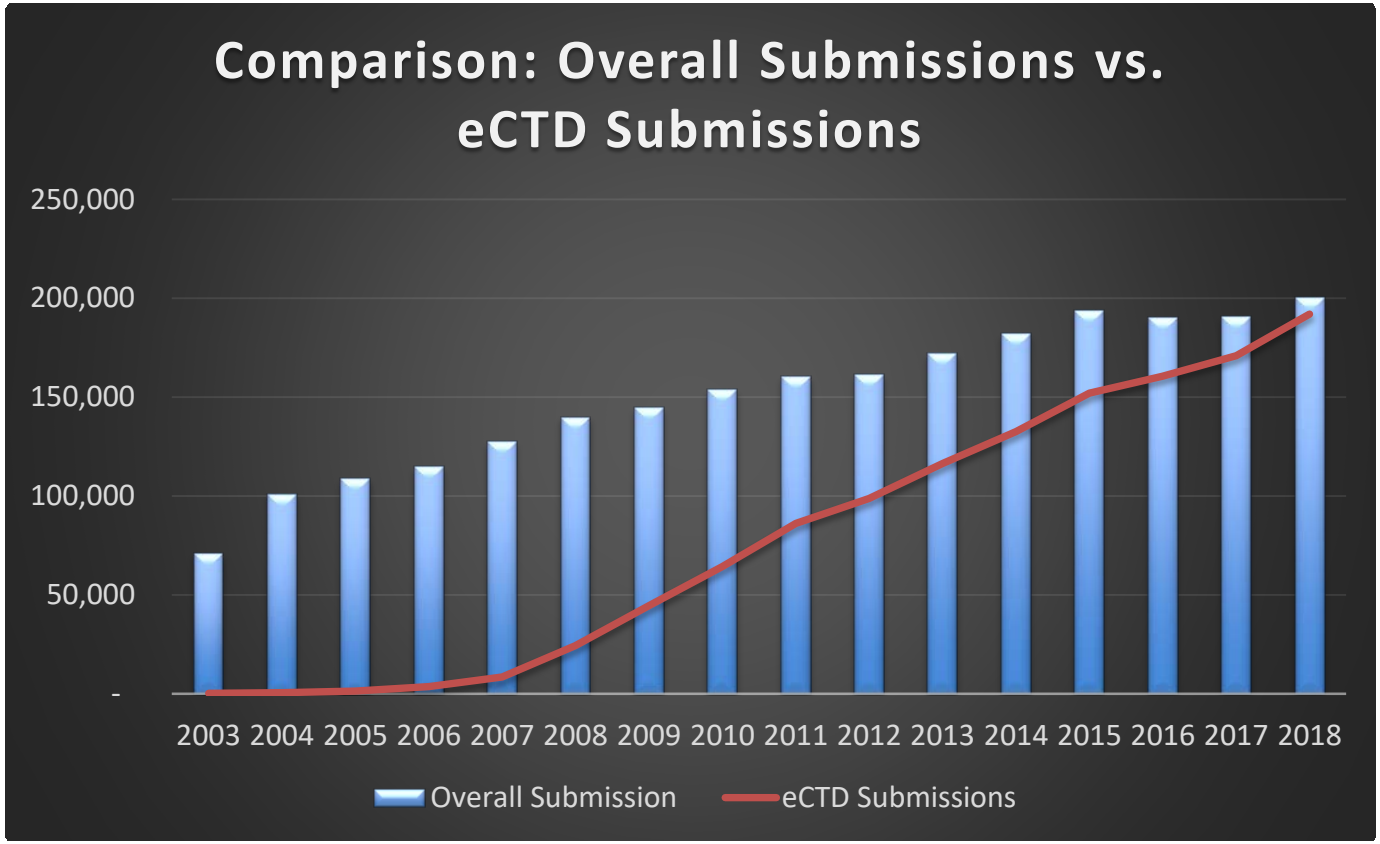
Guidance - Standardized Study Data in Electronic Format

- **What** is the requirement?
  - Studies that start after **December 17, 2016** must be in standardized format for ANDA, NDA, and BLA submissions. *Commercial IND (December 17, 2017)*
  - See the Study Data for Submission to CDER and CBER website for more information
- **How** will it be enforced?
  - Technical Rejection Criteria for Study Data
  - Specifications for eCTD Validation Criteria
- **Where** can I find *The Guidance*?

Have Questions? Contact eData@fda.hhs.gov

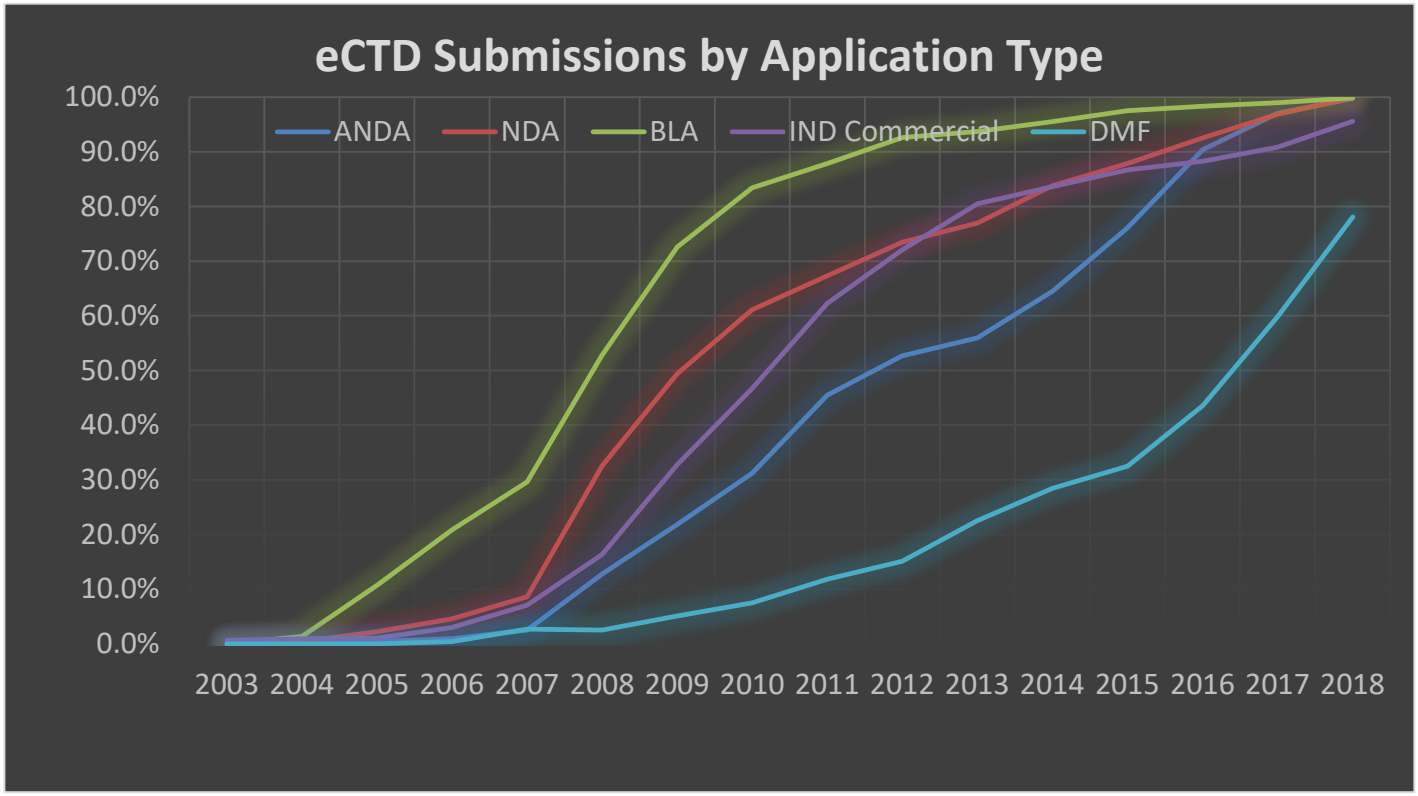
eCTD Submission Metrics

CDER receives approximately 200,000 electronic submissions via ESG annually. Nearly 192,000 were in eCTD in FY 2018.



eCTD Submission Metrics

In FY 2018, nearly 100% of the regulatory submissions for NDA, BLA, and ANDA were in eCTD. For Commercial IND and DMF, 96% and 78% (Type II, IV, V).



Electronic Submission Processing: Increasing Automation

Submission Processing: 2018

All CDER regulatory submissions received are processed by Document Room

Document Room Process:

Staff reads the Cover Page of every submission (Approx. 850 per day) to categorize and route to correct Review Divisions

Submission Processing: 2019

Automate process to identify Submission Category

Process:

1. Determine Submission Category based on structured data in eCTD sequence
2. Route to Review Division based on Submission Category

Benefit:

Reviewer gets submission faster

Submission Processing Challenges

- To efficiently and effectively process the increased number of submissions and leverage the submitted structured eCTD and study data, FDA is in the process of automating inbound submissions by using structured data from the eCTD backbone files and FDA Forms. **However, data submitted in eCTD backbone files (e.g. us-regional.xml file) and regulatory form (e.g., Form 356h) are not always consistent.**

- FDA reviewers use the state-of-the-art review tools (e.g. JMP Clinical) to support analyzing submitted study data. **However, study data submitted do not always conform with the published FDA Data Standards Catalog.**

eCTD Data Discrepancy Example: 1

Can you guess the correct regulatory activity in this submission?

us-regional.xml (DTD V2.01)

```
<submission submission-type="original-application">
  <sequence-number>0022</sequence-number>
</submission>
```

Indicating "Original Application"

Form 356h

21. Submission *(See instructions)* ☐ Original ☐ Labeling Supplement ☐ CMC Supplement ☐ Efficacy Supplement ☐ Annual Report
☐ Product Correspondence ☐ REMS Supplement ☐ Postmarketing Requirements or Commitments ☑ Periodic Safety Report
☐ Request for Proprietary Name Review ☐ Other *(Specify)*: _____

Indicating "Periodic Safety Report"

This submission was a periodic safety report.
The appropriate eCTD "**submission-type**" would have been "**other**".

eCTD Data Discrepancy Example: 2

Can you guess the correct regulatory activity in this submission?

us-regional.xml (DTD V3.3)

```
<submission-information>
  <submission-id submission-type="fdast3" supplement-effective-date-type="fdasedt2">[redacted]</submission-id>
  <sequence-number submission-sub-type="fdasst3">[redacted]</sequence-number>
```

Indicating "CBE"

Form 356h

21. Submission *(See instructions)*	☐ Original	☐ Labeling Supplement	☑ CMC Supplement	☐ Efficacy Supplement	☐ Annual Report
☐ Product Correspondence	☐ REMS Supplement	☐ Postmarketing Requirements or Commitments	☐ Periodic Safety Report		
☐ Request for Proprietary Name Review	☐ Other *(Specify)*: _____				
22. Submission Sub-Type	☐ Presubmission	☐ Amendment	23. If a supplement, identify the appropriate category.	☐ CBE	☑ Prior Approval (PA)
	☑ Initial Submission	☐ Resubmission		☐ CBE-30	

Indicating "Prior Approval"

This submission was an Initial CMC Supplement CBE.
The appropriate "**Supplement Category**" on Form 356h would have been "**CBE**"

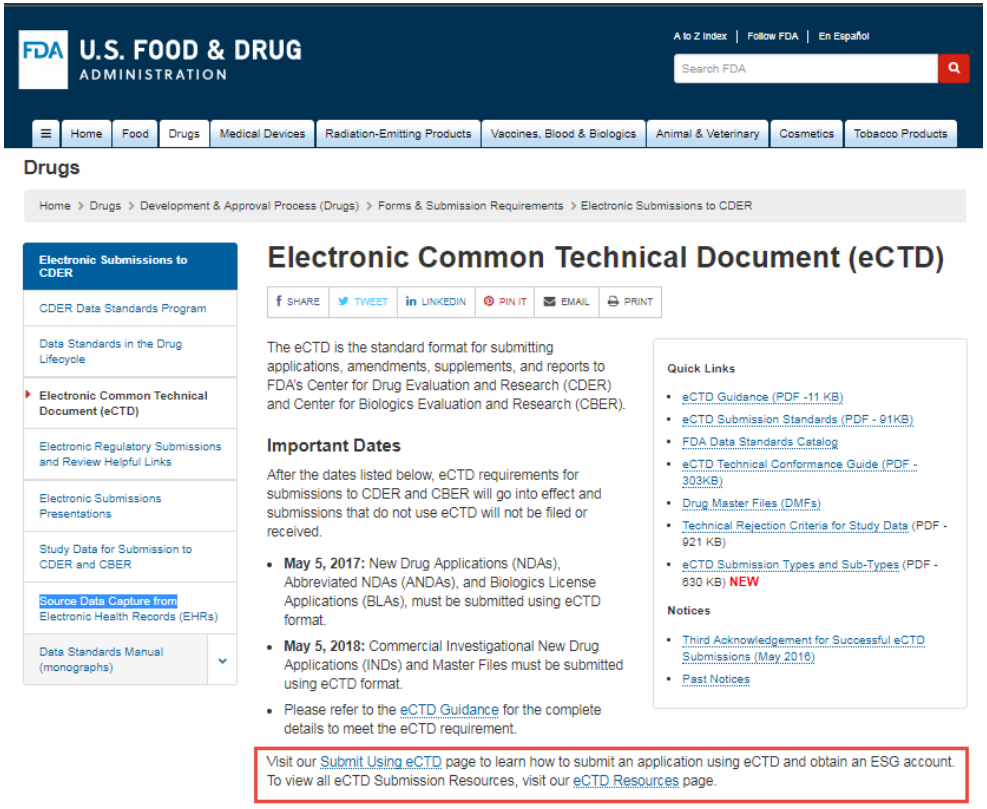
eCTD Data Discrepancy Impact

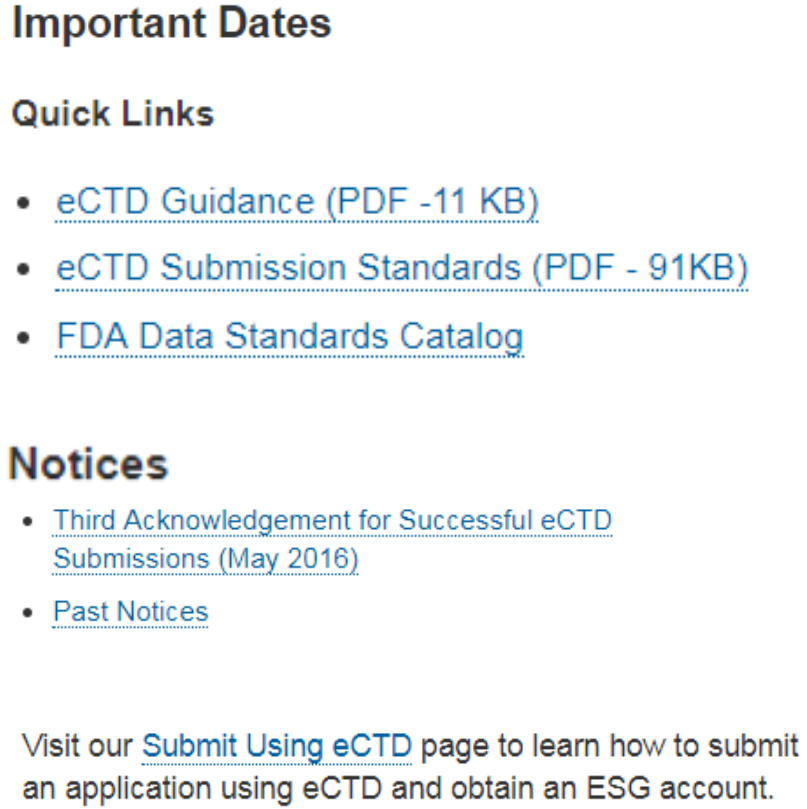
- When data is submitted correctly in eCTD backbone files (e.g. us-regional.xml file) and regulatory form (e.g., Form 356h), submission can be efficiently routed to the assigned review division and/or reviewer(s)

- Indicating different Submission Type and/or Submission Sub-Type in us-regional.xml and Form 356h could:
  - Impact FDA's ability to automate the submission process
  - Require additional effort to read the Cover Letter in order to resolve the discrepancy
  - May require Request(s) for Information that may otherwise not be necessary

Preparing to Submit Electronically and Points to Consider

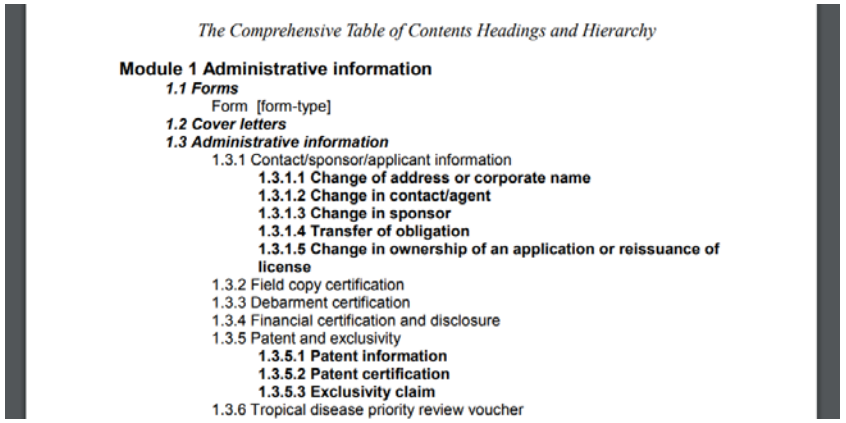
Become familiar with the eCTD website





Submission Hierarchy

- Organize content to follow Common Technical Document (CTD) structure
- Resources
  - The Comprehensive Table of Contents Headings and Hierarchy
  - M4 Organization of the Common Technical Document for the Registration of Pharmaceuticals for Human Use Guidance for Industry



The Comprehensive Table of Contents Headings and Hierarchy

Module 1 Administrative information
1.1 Forms
Form [form-type]
1.2 Cover letters
1.3 Administrative information
1.3.1 Contact/sponsor/applicant information
1.3.1.1 Change of address or corporate name
1.3.1.2 Change in contact/agent
1.3.1.3 Change in sponsor
1.3.1.4 Transfer of obligation
1.3.1.5 Change in ownership of an application or reissuance of license
1.3.2 Field copy certification
1.3.3 Debarment certification
1.3.4 Financial certification and disclosure
1.3.5 Patent and exclusivity
1.3.5.1 Patent information
1.3.5.2 Patent certification
1.3.5.3 Exclusivity claim
1.3.6 Tropical disease priority review voucher

File Format and PDF Specifications

- When creating content, follow the Specifications for File Format Types Using eCTD Specifications for guidance on file formats FDA expects under the different CTD headings

- Follow FDA's PDF Specifications and communicate to vendors the need to follow these specifications

Study Data

- If submitting study data, please see the Study Data for Submission to CDER and CBER website.
- Key Study Data Resources:
  - Providing Regulatory Submissions In Electronic Format — Standardized Study Data Guidance for Industry
  - Technical Rejection Criteria for Study Data
  - Study Data Technical Conformance Guide
  - ANDA Forms and Submission Requirements Website

Prepare for Submission to FDA

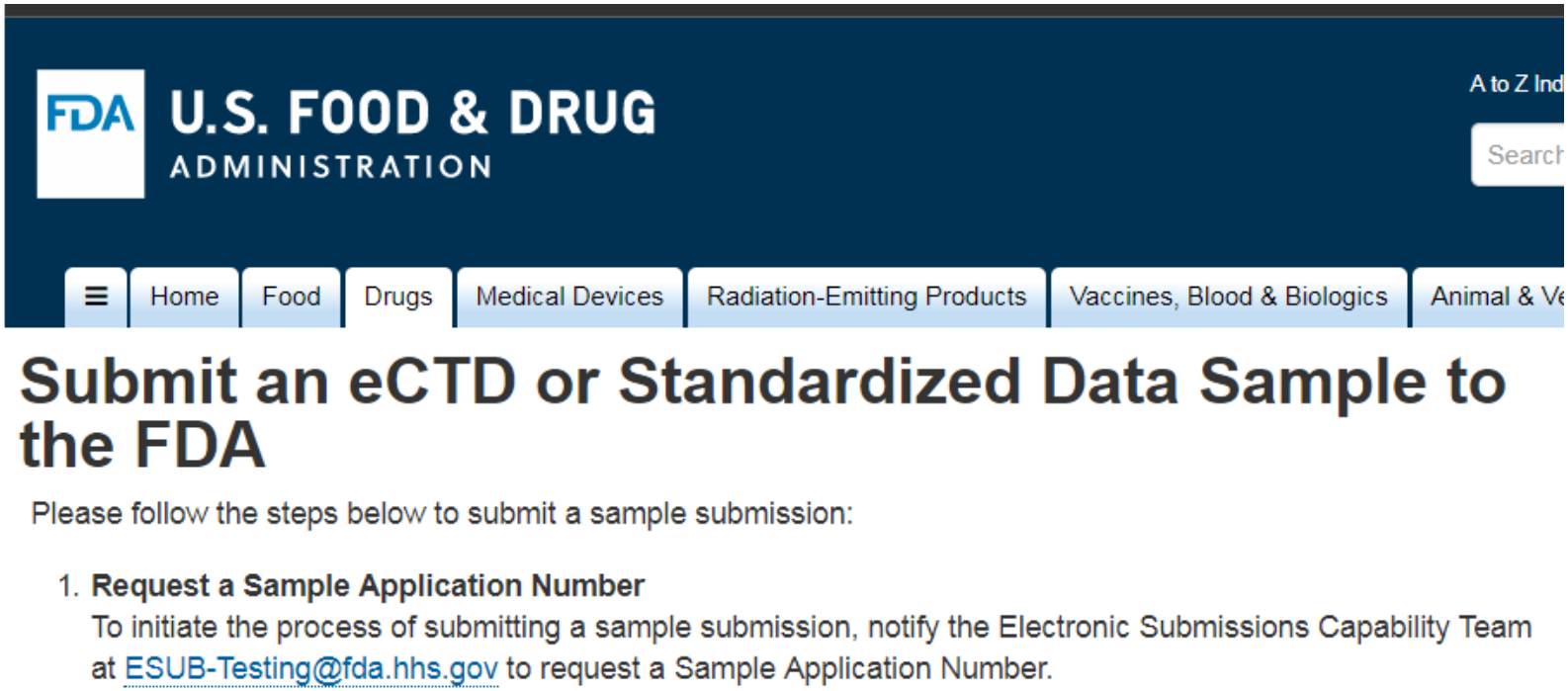
- Request an Application Number from FDA
- Register for an Electronic Submission Gateway

Generate the eCTD for Submission to FDA

- Publish content into eCTD format via eCTD Publishing Tool or eCTD Tool Vendor
  - Utilize eCTD publishing tool to:
    - Capture administrative information
    - Map submission content to CTD section headings
    - Generate final submission in eCTD format including all required technical files/folder structure

Validate eCTD (Optional) and/or Request eSub Feedback

- (Optional) Validate via eCTD Validation Tool
- (Optional) Ask ESUB-Testing@fda.hhs.gov for technical feedback via Sample Submission Process



Summary

- Important Guidance Requirements
  - **ANDAs, NDAs, BLAs, DMFs, and Commercial INDs must be submitted in eCTD**
  - **Technical Rejection Criteria for Study Data**
- Confirm eCTD metadata is consistent with FDA Form
  - **eCTD Submission Type and Subtype align with values on 356h**
- Preparing to Submit Electronically and Points to Consider
  - **Utilize FDA's eCTD Website**
  - **Align Content with CTD**

Thank You

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eSub@fda.hhs.gov

www.fda.gov/ectd


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