Promotional Submissions in eCTD Format - Grouped Submissions

Jason Cober
Lead Project Manager
Office of Prescription Drug Promotion (OPDP)
CDER | US FDA

Outline

- Background
- eCTD Structure
- Contents of a Grouped Submission
- Common Errors

Background

- June 24, 2019 – FDA Published Final Guidance titled "*Providing Regulatory Submissions in Electronic and Non-Electronic Format – Promotional Labeling and Advertising Materials for Human Prescription Drugs*"
- Guidance describes the structure and format for promotional submissions in eCTD format
- Grouped Submissions are discussed in Section VI.J of the guidance

How does a grouped submission work?

- The contents of the grouped submission are distributed to all member Applications included in the group
- A record is created under each Application in the group
  - Sequence Number submitted in US-Regional file is used to create the submission record
  - A link to the shared location of the submission contents are added to each record
- Reviewer sees one submission linked to multiple Applications

What is a Grouped Submission?

- Single submission in eCTD format
- Contains promotional materials that promote more than one Product
- Contains the current labeling for each promoted Product
  - Can contain draft labeling when submitted for Accelerated Approval or Advisory
- Promoted products must be of the same Application Type
  - If the promoted products are not the same Application Type, the materials must be submitted separately
    - Either a Single-Product Submissions or grouped submissions batched by Application Type

Technical Considerations

- US-Regional.xml file must include all member Applications in the Application Set section
- Each member Application must include a Sequence Number
  - Must be unique to the respective Application
  - Must not have been previously submitted under its respective Application
  - If any grouped submission includes an Application Number and Sequence Number combination that has been previously submitted, the entire group will be rejected

Technical Considerations

- <Application-Set> section may contain one or multiple <Application> elements
- The <Application-Containing-Files> attribute is used to indicate the Lead Application
  - <Application-Containing-Files> = True is the Lead
  - <Application-Containing-Files> = False are non-Lead Member(s)
- Lead Application should be listed first in the Application Section
- Grouped Submission may only contain one Lead Application

Example


Application Information
Application Containing Files: true
Application Type: New Drug Application (NDA)
Application Number: 456789
Submission Type: Promotional Labeling Advertising
Submission Id: 0017
Submission Sub-Type: Original
Sequence #: 0017
Application Containing Files: false
Application Type: New Drug Application (NDA)
Application Number: 567890
Submission Type: Promotional Labeling Advertising
Submission Id: 0020
Submission Sub-Type: Original
Sequence #: 0020
Application Containing Files: false
Application Type: New Drug Application (NDA)
Application Number: 678901
Submission Type: Promotional Labeling Advertising
Submission Id: 0014
Submission Sub-Type: Original
Sequence #: 0014

Grouped Submission Contents

2253 Grouped Submissions

- Same required submission contents as a Single-Product 2253
  - Completed Form FDA 2253
  - Current PI for all members of the group
  - Clean copy of Promotional Material(s)

Form FDA 2253

- The Application listed as the Lead Application in the US-Regional.xml file should match the Application Listed on the Form FDA 2253
- Form FDA 2253 should indicate it is a Multi-Product Submission
- Non-Lead members should be listed on a separate Supplemental Application List
  - Supplemental Application List should include
    - Application Type & Number
    - Product Name
    - Date and File Name of Current PI
- Supplemental Application list should be submitted in the same section as the completed Form FDA 2253

Example


m1-1-forms
Form FDA 2253: Transmittal of Advertisements and Promotional Labeling for Drugs and Biologics for Human Use
Form 2253 Multiple Product Prof 20120430 [new]
+
-
Application Version =
Checksum = 49e154b9bee094a2dm83c459affd63e4
Checksum Type = md5
Filename = 2253-20120430.pdf
Font Library =
ID = a11383b1215558nfdf8a81em95237f796
Keywords =
Operation = new
Version =
Form 2253 Attachment List of Additional Applications [new]
+
-
Application Version =
Checksum = 49e154b9bee094a2dm83c459affd63e4
Checksum Type = md5
Filename = form-attachment.pdf
Font Library =
ID = a11389b1215558nfdf8a81em95237f796
Keywords =
Operation = new
Version =

2253 Labeling

- Grouped 2253 must be accompanied by Current Product Labeling for each member of the group
- Labeling must be placed under Heading 1.14.6
- Submitters may submit a separate PDF copy of each Label under 1.14.6
- Alternately, if the Current Product Label has been submitted previously, a cross-reference to the Product Labeling may be used

Example


m1-14-6-product-labeling-for-2253-submissions
acetyl salicylic acid PI Rev20120130 [new]
+
-
Application Version =
Checksum = 49e154b9nww061v8de43c459affd53e4
Checksum Type = md5
Filename = labeling-accompanying-material.pdf
Font Library =
ID = a11383x9845892nfdf8a81em95237f796
Keywords =
Operation = new
Version =
Drug X PI Rev20120215 [new]
+
-
Application Version =
Checksum = 49e154b9nww061v8de43c459affd63e4
Checksum Type = md5
Filename = labeling-accompanying-material-drug-x.pdf
Font Library =
ID = a11384x9845892nfdf8a81em95237f796
Keywords =
Operation = new
Version =
Drug Z PI Rev20120228 [new]
+
-
Application Version =
Checksum = 49e154b9nww061v8de43c459affd65e4
Checksum Type = md5
Filename = labeling-accompanying-material-drug-z.pdf
Font Library =
ID = a11389x9845892nfdf8a81em95237f796
Keywords =
Operation = new
Version =

2253 Materials

- Only include one set of materials under section 1.15.2
- Each material included in the group will be linked to all members of the group

Example

m1-15-promotional-material (Professional)

m1-15-2-materials (Promotional 2253)

m1-15-2-1-material (Catalog) material-id 12PC35482 issue-date 20120430

m1-15-2-1-1-clean-version

CATALOG 12PC35482 Product price catalog 20120430 [new]
+
-
Application Version =
Checksum = 49e158f4bee040a2de43c459affd6304
Checksum Type = md5
Filename = clean-catalog.pdf
Font Library =
ID = b21383b1861534dfdf8a81df05237f704
Keywords =
Operation = new
Version =

Non-2253 Grouped Submissions

- One cover letter should be placed under the appropriate cover letter heading
- Cover letter should include a list of all member Applications
  - Include Application Type & Number and Product Name
- It is not necessary to submit a Supplemental Application list if the cover letter lists all members of the group
- Subject line should reference the Lead Application Number and clearly identify the submission as a group

Common Errors

Batched Materials

- Submitting promotional materials for multiple products when the materials do not promote all members of the group
- Ex: Grouped 2253 contains 3 member Applications and 15 Promotional Materials
  - 5 Materials promote Product A, 5 Materials promote Product B, 5 Materials promote Product C
  - None of the Materials promote Products A, B, *and* C
- Promotional materials must promote all Products listed in the Group

Application References

- Using Application References instead of Application Set
- Including one or multiple Applications in the References section of the US-Regional.xml file does not create a grouped submission
  - References only create a link between the Applications
  - References do not require or include a Sequence Number
- Including Application References will not distribute the submission to the Referenced Applications

Example

Application Information	Application Containing Files: true Application Type: New Drug Application (NDA) Application Number: 456789 Submission Type: Original Application Submission Id: 0001 Submission Sub-Type: Application Sequence #: 0003 Cross Reference Number: 012345 Cross Reference Type: Drug Master File (DMF) Cross Reference Number: 543210 Cross Reference Type: Drug Master File (DMF)

Missing Additional Applications

- Structuring a Single Product submission as a Grouped Submission
  - Submission includes all files required for a Grouped Submission
  - 2253 indicates Multi-Product submission
- US-Regional.xml file indicates submission is a single-product submission
- Submission will only be processed using the data included in the US-Regional file
- FDA cannot add Additional Applications that are not listed in the US-Regional.xml file even if the submission includes a Supplemental Application list

Single Product Submissions

- Structuring a Grouped Submission as a Single Product Submission
  - Submission includes all files required for a Grouped Submission
  - 2253 indicates Multi-Product submission
- US-Regional.xml file indicates submission is a single-product submission
- Same submission is submitted multiple times
  - Submitter changes the Application Number listed in the US-Regional.xml file and submits individually
- Appears to be a grouped submission submitted separately to multiple Applications

Test Submission Process

Test Submissions

- Test Submission Process provides Submitters with an opportunity to validate eCTD submission structure prior to submitting to Production Environment
- OPDP Project Management Team will review the structure of the submission and provide feedback
  - Will provide instructions for corrections, if necessary

Test Submissions - Process

- Begin by viewing the available presentations on the OPDP eCTD webpage
  - Prepare any questions you may have for the OPDP eCTD Team
- Contact the OPDP eCTD Mailbox and send the following items:
  - Questions to be answered
  - Types of Submissions (Accelerated Approval, Advisory, 2253, etc)
  - Availability (Dates & Times) for a 30-minute meeting
- OPDP eCTD Team will schedule a planning meeting
  - Will provide answers during the meeting
  - Assist with planning test cases
- Submit Test Files
  - Notify OPDP eCTD Mailbox of results (either accepted or rejected)
  - Be sure to provide the COR ID when the file is accepted
- OPDP eCTD Team will review test submission(s) and provide feedback

Resources

- OPDP eCTD Mailbox- OPDPeCTD@fda.hhs.gov
- OPDP eCTD Webpage - www.fda.gov/OPDPeCTD
- eCTD Test Submission Instructions - https://www.fda.gov/industry/create-esg-account/setting-webtrader-account-checklist
- OPDP Electronic Submissions Guidance - https://www.fda.gov/media/128163/download
- eCTD Validation Criteria - https://www.fda.gov/media/87056/download
- Comprehensive Table of Headings – https://www.fda.gov/media/76444/download
- eCTD Submission Standards – https://www.fda.gov/media/93301/download
- eCTD Sample Submissions - https://www.fda.gov/media/83809/download


FDA
U.S. FOOD & DRUG
ADMINISTRATION