# Providing Regulatory Submissions in Electronic and Non-Electronic Format – Promotional Labeling and Advertising Materials for Human Prescription Drugs

Final Guidance for Industry

Jason Cober – FDA/OPDP
Josephine Secnik – Eli Lilly

May 20, 2020

DIA

# Disclaimer

The views and opinions expressed in the following PowerPoint slides are those of the individual presenter and should not be attributed to DIA, its directors, officers, employees, volunteers, members, chapters, councils, Communities or affiliates, or any organization with which the presenter is employed or affiliated.

These PowerPoint slides are the intellectual property of the individual presenter and are protected under the copyright laws of the United States of America and other countries. Used by permission. All rights reserved. DIA and the DIA logo are registered trademarks or trademarks of Drug Information Association Inc. All other trademarks are the property of their respective owners.

© 2020 DIA, Inc. All rights reserved.

# Timeline

- June 24, 2019 – FDA Published the 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
  - Contains both Binding Requirements and Nonbinding Recommendations
- 24 months after the publication of the Final Guidance, required submissions described in the guidance must be submitted in eCTD format
  - Required submissions will be mandatory starting June 24, 2021
- Firms are not required—but are STRONGLY encouraged to—submit electronically other types of promotional material submissions
  - NOTE: Complaints should only be submitted as **paper copies** and cannot be accepted in eCTD

© 2020 DIA, Inc. All rights reserved.

# Purpose

- Outlines requirements and recommendations for firms on how to make submissions pertaining to promotional materials for human prescription drugs to FDA

- Describes specific aspects of submitting promotional materials using mocule 1 (M1) of the electronic Common Technical Document (eCTD) using version 3.3 or higher of the *us-regional-backbone file*

© 2020 DIA, Inc. All rights reserved.

# Binding Requirements vs. Nonbinding Recommendations

- Binding
  - The portion of this guidance that establishes the requirement for electronic submission pursuant to section 745A(a) of the FD&C Act has binding effect
- Nonbinding
  - All other suggestions and recommendations for electronic submissions of promotional-related materials

© 2020 DIA, Inc. All rights reserved.

# Promotional Materials Under Section 745A(a)

- Two types of promotional material-related submissions are subject to the requirements of section 745A(a)
  - Promotional materials submitted in fulfillment of the postmarketing reporting requirements (i.e., Form FDA 2253 submissions of "2253 submissions')
  - Presubmissions of promotional materials for accelerated approval products and other products where such submissions are required for approval (i.e., products approved when human efficacy studies are not ethical or feasible)

© 2020 DIA, Inc. All rights reserved.

# Scope

## Submissions pursuant to section 745A(a)

- 2253 submissions
- Presubmissions of promotional materials for accelerated approval products where such submissions are required for approval (i.e., products approved when human efficacy studies are not ethical or feasible)

## Other promotional material-related submissions

- Voluntary advisory submissions
- Resubmissions
- General correspondences
- Amendments
- Withdrawl requests
- Responses to notice of violation or warning letters
- Responses to information requests
- Reference documents
- Complaints

© 2019 DIA, Inc. All rights reserved.

# Resources

- OPDP has developed multiple resources to assist submitters both during and after the 24-month transition period
  - OPDP eCTD Mailbox- OPDPeCTD@fda.hhs.gov
  - OPDP eCTD Webpage – www.fda.gov/OPDPeCTD
  - How-To Videos
    - Form 2253
    - Accelerated Approval
    - Advisory
  - Webinar Series
    - What's New in the OPDP eCTD Guidance
    - OPDP Electronic Submissions - Common Errors in eCTD
  - Test Submission Process

© 2020 DIA, Inc. All rights reserved.

# Grouped Submissions

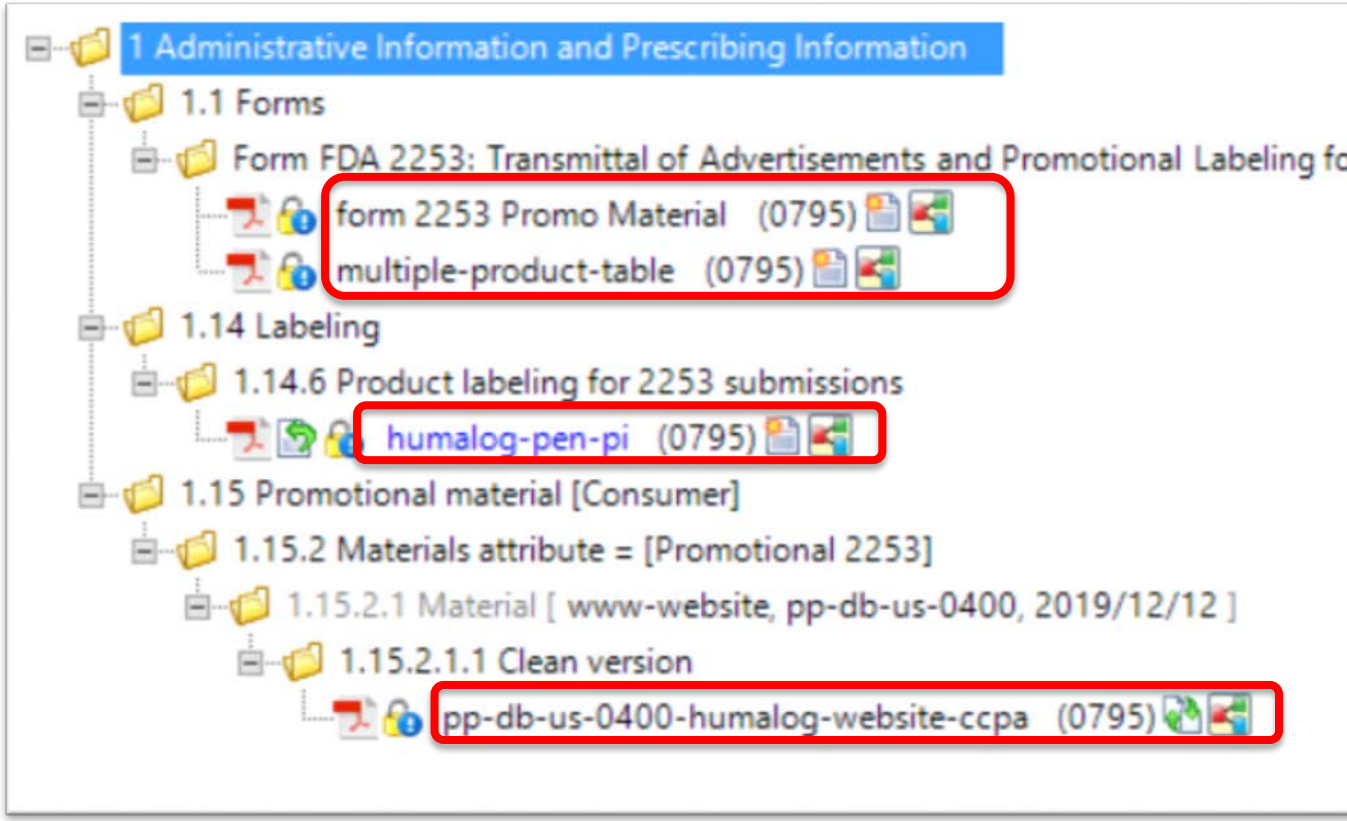
- FDA encourages Submitters to use the Grouped Function when submitting promotional materials that promote more than one Product
  - Discussed in Section VI-J of the Guidance

- How does it work and how do groups appear in the FDA Viewing Tool?
  - Demonstration

© 2020 DIA, Inc. All rights reserved.

# Grouped Submission Example

- In section 1.1
  - A ‘lead’ application is selected for Form 2253
  - A ‘multi-product table’ is included to list the remaining applications associated with the submission
- In section 1.14.6
  - Product labeling for ‘lead’ application is included
- In section 1.15.2.1.1
  - Promotional material is provided




© 2020 DIA, Inc. All rights reserved.

# Grouped Submission Example (con't)

- Metadata for grouped submissions
  - the 'lead' application is 'true
  - the other applications are 'false'


© 2020 DIA, Inc. All rights reserved.

# Grouped Submission Example (con't)

- The Form 2253 lists the 'lead' application and indicates 'multiple products'

Form Approved: OMB No. 0910-0001, Expiration Date: March 31, 2021; see PRA Statement on last page.

| DEPARTMENT OF HEALTH AND HUMAN SERVICES<br>Food and Drug Administration<br>**TRANSMITTAL OF ADVERTISEMENTS AND PROMOTIONAL LABELING FOR DRUGS AND BIOLOGICS FOR HUMAN USE** | 1. Date Submitted<br>12/12/2019<br><br>2. Label Review Number (Biologics) | 3. NDA/ANDA/AADA or BLA/PMA<br>Type: NDA Number: 020563<br>☐ Single product ☒ Multiple products<br>For multiple products, submit completed form and specimen of advertising/promotional materials to one application of choice, and attach separate sheet addressing items 3-5 for remainder of products. Refer to No. 3 on instruction sheet. |
|---|---|---|
| **NOTE: Form FDA 2253 is required by law. Reports are required for approved NDAs and ANDAs (21 CFR 314.81).** | | |
| 4. Proprietary Name<br>HUMALOG | 5. Established Name<br>(insulin lispro injection)<br>Product Code No.: | |
| 6. Package Insert Date and ID Number (Latest final printed labeling)<br>LOG-0009-USPI-20191115 | 7. Manufacturer Name<br>Eli Lilly and Company<br>License No. (Biologics): | |

© 2020 DIA, Inc. All rights reserved.

# Grouped Submission Example (con't)

- On multi-product table
  - All other applications associated with the promotional material are listed
  - Links to the PI are provided in the table

**FDA 2253 – Other Referenced Products NDAs**

| NDA# | Trade Name | Established Name | PI # | Business Entity |
|---|---|---|---|---|
| 020928 | Glucagon | glucagon for injection | GLU-0003-USPI-20180706 | Eli Lilly and Company |
| 021017 | Humalog Mix75/25 | insulin lispro protamine and insulin lispro injectable suspension | LOG7525-0005-USPI-20191115 | |
| 021018 | Humalog Mix50/50 | insulin lispro protamine and insulin lispro injectable suspension | LOG5050-0006-USPI-20191119 | |
| 205747 | Humalog U-200 | insulin lispro injection | LOG-0009-USPI-20191115 | |

© 2020 DIA, Inc. All rights reserved.

# Grouped Submission Example (con't)

- If grouped submission include NDA and BLA applications
  - Prepare separate Form 2253 and multi-product tables to separate NDA and BLA applications
  - Cross reference submissions to each other in comment section of Form 2253

| NDA020563 Form 2253 Comment Field | BLA125521 Form 2253 Comment Field |
|---|---|
| Cross reference to bla125521 seq 0995 | Cross reference to nda020563 seq 0794 |

© 2020 DIA, Inc. All rights reserved.

# Lifecycle Operators

- What does the guidance say about the use of lifecycle Operators when submitting Promotional Materials?
- Lifecycle Operators inform the reviewer that the Promotional Material has been revised and represents an update from a previously submitted Material
- Discussed in the following locations of the Guidance
  - Section VI-L; Footnote 47; Lines 953 & 967
- “Replace” Operator used when Promotional Materials have been revised
- “Delete” Operator used when Promotional Materials have been Withdrawn

© 2020 DIA, Inc. All rights reserved.

# Website Submissions

- How do Firms submit websites in eCTD?
  - Discussed in Section VII-E of the Guidance
  - Website submission should clearly display and communicate how the promotional material will convey messages to the end user
  - Preferably will allow reviewers to interact with the piece in the same manner as the end user
  - Websites must be submitted in their entirety prior to first use
    - If a single page is added or revised, only the updated page needs to be submitted
    - Substantial updates and revisions to the website will require submission of the website in its entirety prior to dissemination
- When submitting updates to a Website, minor revisions should be submitted with the “New” Operator
    - Use the “Replace” Operator when the Website has been substantially revised or updated

© 2020 DIA, Inc. All rights reserved.

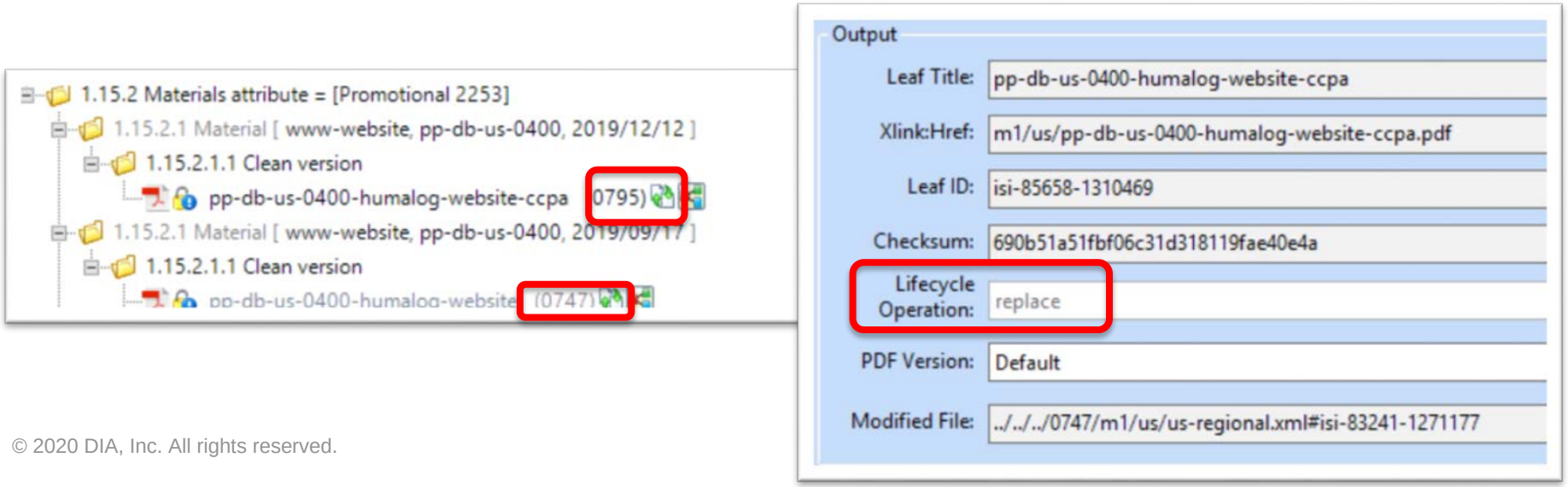
# Lifecycle Operators Example (con't)

- Each firm will need to define for themselves what 'substantially revised' criteria to apply
- Things to consider include:
  - Update to safety information for a product – likely impacts most pages of a website – even if the safety language change is minor
  - Addition of a consumer or professional section to a website
  - Re-design of a website with new imagery, layout, information
- Minor changes would include adding a webpage, adding content/revisions to an existing webpage, updates to logo
- In the example below, website submitted in seq 0795 replaced website submitted in seq 0747

© 2020 DIA, Inc. All rights reserved.

# Lifecycle Operators Example

- If a website is ‘substantially revised’, submit the revised website in it’s entirety
  - The *submission-sub-type* should be ‘original’
  - The ‘*replace*’ operator attribute should be used
- In the example below, website submitted in seq 0795 replaced website submitted in seq 0747




© 2020 DIA, Inc. All rights reserved.

# Social Media Updates

- How should firms submit a 2253 in eCTD format containing the list of all non-restricted sites that include real-time or interactive communications?
  - Discussed at Line 246 of the Draft Guidance titled *"Fulfilling Regulatory Requirements for Postmarketing Submission of Interactive Promotional Media for Prescription Human and Animal Drugs and Biologics"*
  - Submission should include all required components of a Form 2253 Submission in eCTD format
    - Form 2253, Current PI, and Materials
  - Monthly social media update should be submitted with either a file or reference link under the materials section
    - When submitting a file, the document should include the same name, URL/handle, date range, and data of the most recent social media update for that site
    - A reference link to a previous submission may also be used
      - The site name, URL, date range, and date of most recent social media update should be included in the 2253 comments

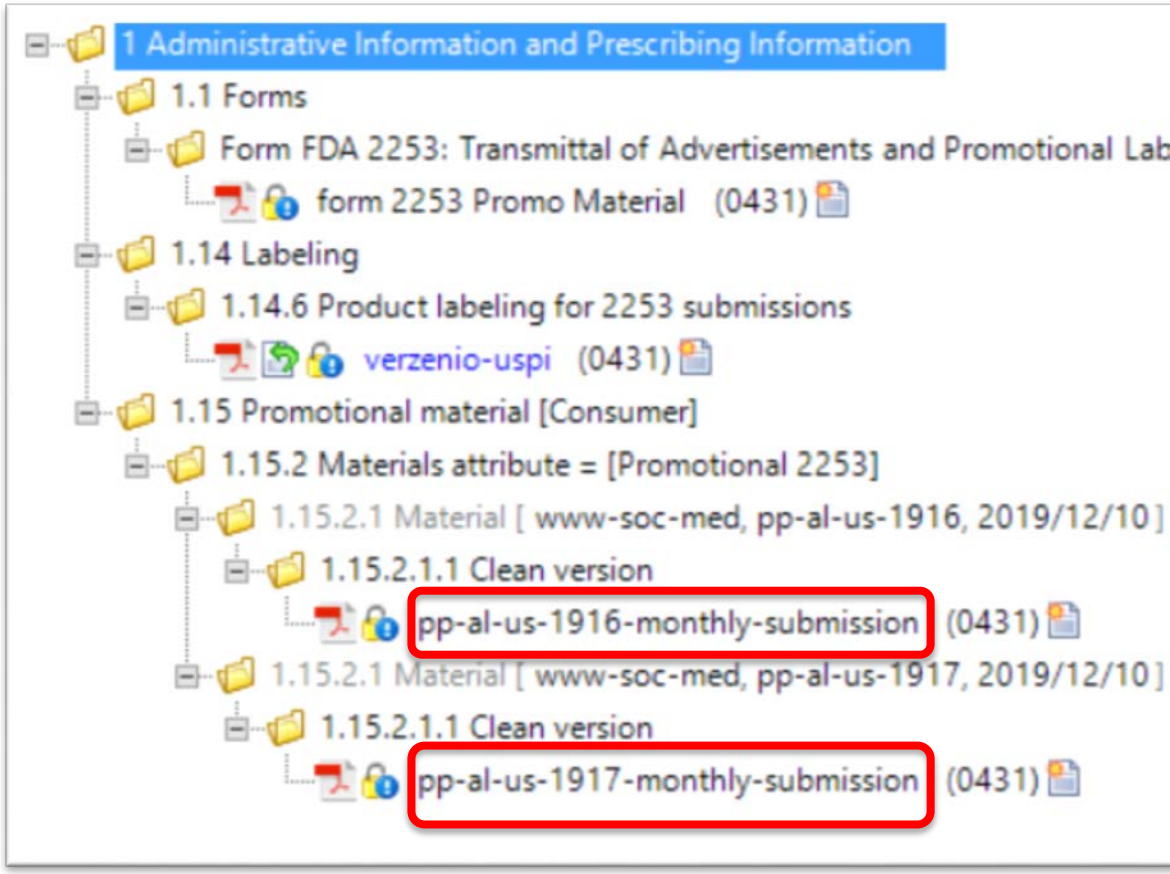
© 2020 DIA, Inc. All rights reserved.

# Interactive Social Media Example

- For interactive social media sites, submit a monthly update on Form 2253
  - Include a PDF with each monthly submission to avoid manual processing at OPDP

  OR

  - use reference link to the original social media tactic submission




© 2020 DIA, Inc. All rights reserved.

# Interactive Social Media Example

- As the submission file, include URL/handle, dates the site was active and date of last monthly submission

Monthly Submission Information Social Media Account

THIS DOCUMENT TO BE SUBMITTED WITH FORM 2253

| Material Type | Publication Date | Material ID Code | Material Description |
|---|---|---|---|
| www-soc-med | 12/11/2019 | PP-AL-US-1916 | Facebook @verzenio account active November 1 - November 30 (most recent submission for the account is Nov 07, 2019) |

© 2020 DIA, Inc. All rights reserved.

# Social Media Example (con't)

- Form 2253
  - Use 'www-soc-med' for material type
  - Otherwise prepare as typical Form 2253 submission

Form Approved: OMB No. 0910-0001, Expiration Date: March 31, 2021; see PRA Statement on last page.

| DEPARTMENT OF HEALTH AND HUMAN SERVICES<br>Food and Drug Administration<br>**TRANSMITTAL OF ADVERTISEMENTS AND PROMOTIONAL LABELING FOR DRUGS AND BIOLOGICS FOR HUMAN USE** | 1. Date Submitted<br>12/10/2019<br>2. Label Review Number (Biologics) | 3. NDA/ANDA/AADA or BLA/PMA<br>Type: NDA Number: 208716<br>☒ Single product ☐ Multiple products<br>For multiple products, submit completed form and specimen of advertising/promotional materials to one application of choice, and attach separate sheet addressing items 3-5 for remainder of products. Refer to No. 3 on instruction sheet. |
|---|---|---|

**NOTE: Form FDA 2253 is required by law. Reports are required for approved NDAs and ANDAs (21 CFR 314.81).**

| 4. Proprietary Name | 5. Established Name<br>Product Code No.: |
|---|---|
| VERZENIO | abemaciclib |
| 6. Package Insert Date and ID Number (Latest final printed labeling)<br>VER-0005-USPI-20190909 | 7. Manufacturer Name<br>Eli Lilly and Company<br>License No. (Biologics): |

8. **Advertisement / Promotional Labeling Materials**

a. **Please check only one:** ☐ Professional ☒ Consumer

| Material Type (use FDA codes)<br>b. | Dissemination/ Publication Date<br>c. | Material ID Code<br>d. | Material Description<br>e. | |
|---|---|---|---|---|
| www-soc-med | 12/10/2019 | pp-al-us-1916 | FDA_Submission Verzenio Facebook Monthly | Delete Row |
| www-soc-med | 12/10/2019 | pp-al-us-1917 | FDA_Submission Verzenio Twitter Monthly | Delete Row |

*To delete a row, click the "Delete Row" button for that row (or press the enter key if you've tabbed into the button). You cannot delete the last remaining row.* Add New Row

© 2020 DIA, Inc. All rights reserved.

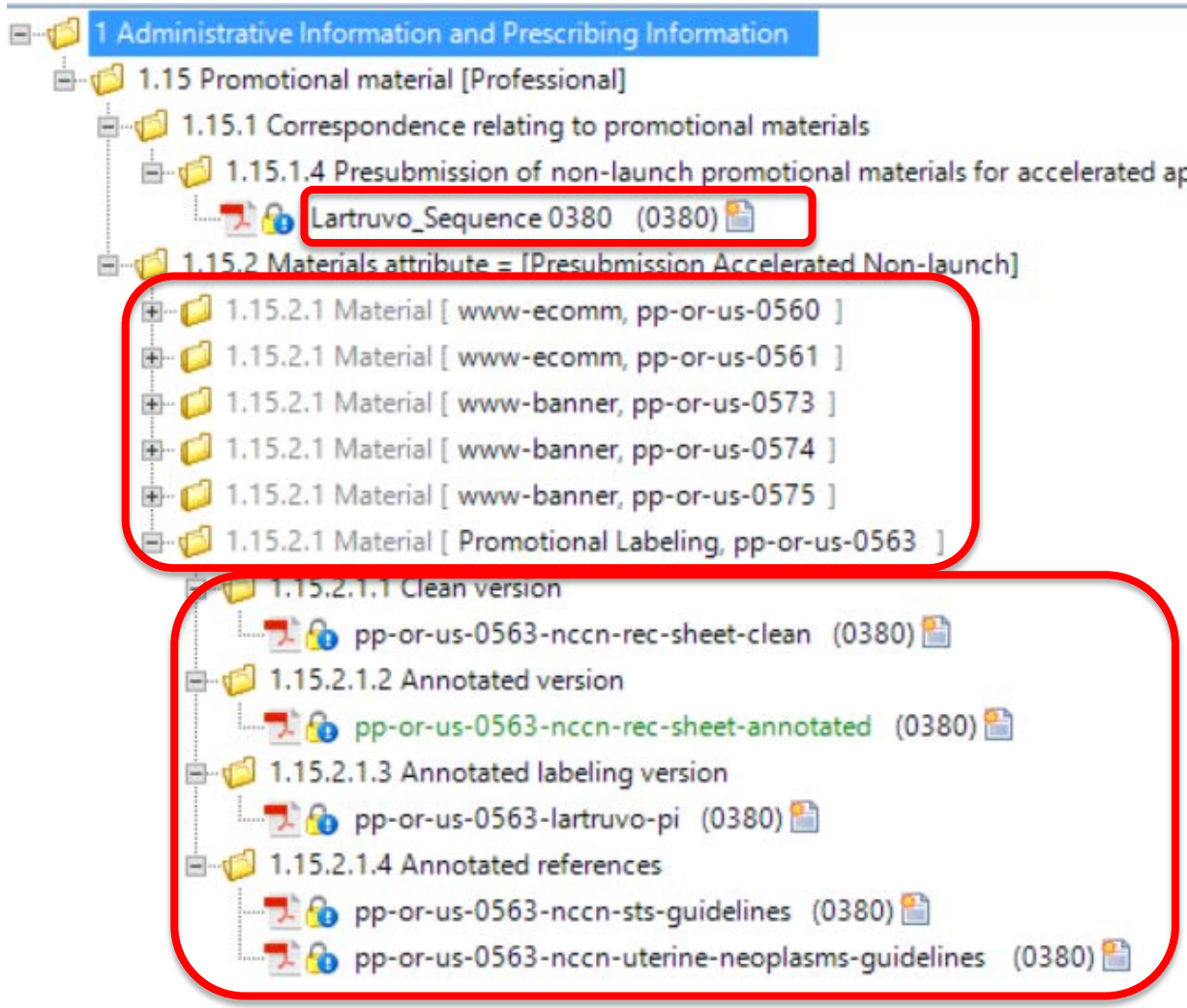
# Accelerated Approval Annotations

- What annotations are required for Accelerated Approval Pre-Submission files?
  - Discussed in Section IV-B of the Guidance
  - Accelerated Approval Pre-Submission files must include annotated materials regardless of whether the Submitter is seeking comments or not
  - All Accelerated Approval Pre-Submissions should include a clean copy of the draft materials and an annotated copy of the materials
  - The annotated copy of the draft material should include links to the annotated PI and/or annotated Reference Documents
    - Hyperlink should redirect to the source of support for the claim in either the PI or Reference
    - Hyperlinks should not redirect to a website or any content outside of either the current or any previous submissions
    - Hyperlink to the Reference Document only needs to link to the page where the source of support for the claim can be found
    - Firms should not send link to external websites

© 2020 DIA, Inc. All rights reserved.

# Accelerated Approval Application Example

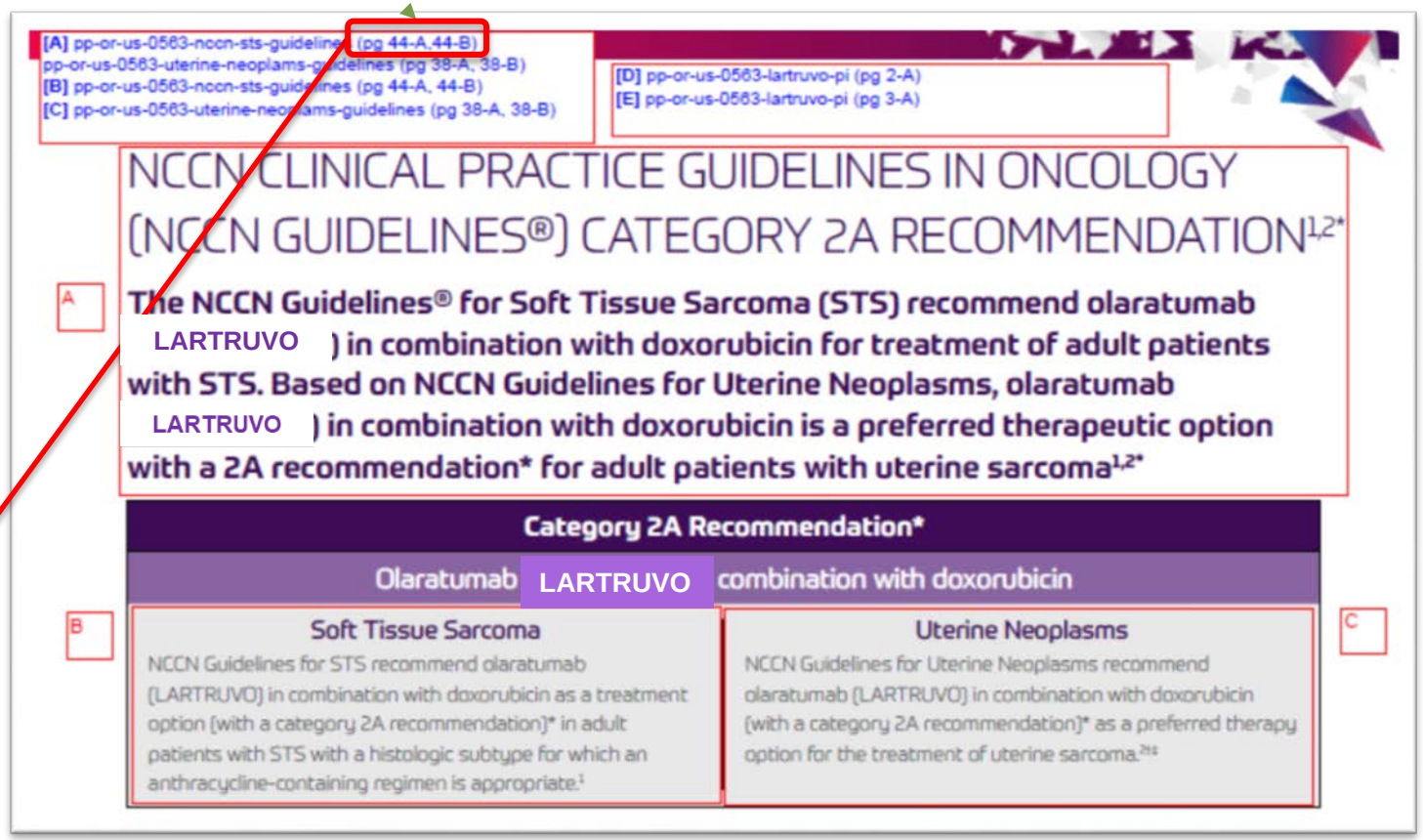
- In section 1.15.1.4
  - Add correspondence letter
- In section 1.15.2.1
  - Add the promotional material(s)
- In sections 1.15.2.1.1 through 1.15.2.1.4
  - Clean promotional material
  - Annotated promotional material
  - Annotated labeling
  - Annotated references




© 2020 DIA, Inc. All rights reserved.

# Accelerated Approval Application Example (con't)

- On annotated tactic
  - Clearly indicate words/graphics within promotional material that is supported by each reference
    - In this example, red boxes labeled as 'A', 'B' and 'C' denote areas supported by subsequent references [A], [B] and [C]
    - Links to the references are created during publishing process so that OPDP reviewers can easily get to information
    - '44-A' and '44-B' become links directly to the reference




© 2020 DIA, Inc. All rights reserved.

# Accelerated Approval Application Example (con't)

- On correspondence
  - Send consumer from professional promotional materials on separate requests
  - Identify all the items being submitted in the same eCTD sequence

**PRESUBMISSION OF NON-LAUNCH MATERIALS FOR ACCELERATED APPROVAL PRODUCT**

**RE: BLA 761038; LARTRUVO® (olaratumab injection); eCTD sequence No. 0380**

Eli Lilly and Company (Lilly) is notifying the Office of Prescription Drug Promotion (OPDP) per 21 CFR 314.550 of the submission of the following Lartruvo® health care professional (HCP) promotional materials intended for dissemination within 30 days following this submission. Lilly is not requesting advisory comments on these materials.

| Document No. | Material Type | Description/Title |
|---|---|---|
| PP-OR-US-0560 | www-ecomm | Lartruvo Target Patient Safety (v0.4) |
| PP-OR-US-0561 | www-ecomm | Lartruvo Target Patient Dosing (v0.3) |
| PP-OR-US-0573 | www-banner | Lartruvo Everyday Health EM DMU 1 TP/Patient Characteristics (v0.3) |
| PP-OR-US-0574 | www-banner | Lartruvo Everyday Health EM DMU_2 TP/Efficacy (v0.3) |
| PP-OR-US-0575 | www-banner | Lartruvo Everyday Health EM DMU_3 Guidelines (v0.3) |
| PP-OR-US-0563 | Promotional Labeling | LARTRUVO NCCN Guidelines Recommendation Sheet (PDF)_update (v0.3) |

© 2020 DIA, Inc. All rights reserved.

DIA