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

Final Guidance for Industry

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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

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 module 1 (M1) of the electronic Common Technical Document (eCTD) using version 3.3 or higher of the *us-regional-backbone file*

Binding Requirements vs. Nonbinding Recommendations

- Binding
  - the portion of this guidance that establishes the requirement for electronic submissions 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

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 or "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)

Scope

Submissions pursuant to section 745A(a) of the FD&C Act

- 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

Other promotional material-related submissions

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

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
  - Webinar Series
  - Test Submission Process

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

Sample Submission

Brand	Sequence # Assigned	Application Containing Files
Brand Product A	0020	TRUE
Brand Product B	1003	FALSE
Brand Product C	1564	FALSE
Brand Product D	0271	FALSE
Brand Product E	0268	FALSE
Brand Product F	0987	FALSE
Brand Product G	0333	FALSE
Brand Product H	0851	FALSE

*Submission should include PI for all Products

m1-1-forms

Form FDA 2253: Transmittal of Advertisements and Promotional Labeling for Drugs and Biologics for Human Use

2253 NDA BrandProductA 2019 07 22 (1) [new] +

Other Referenced Products Page test [new] +

m1-14-6-product-labeling-for-2253-submissions

BrandProductA-PI [new] +

BrandProductB-PI [new] +

BrandProductC-PI [new] +

BrandProductD-PI [new] +

BrandProductE-PI [new] +

BrandProductF-PI [new] +

BrandProductG-PI [new] +

BrandProductH-PI [new] +

m1-15-promotional-material (Professional)

m1-15-2-materials (Promotional 2253)

m1-15-2-1-material (www-website) material-id 12US19EXC0002 issue-date 20190830

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

12US19EXC0002 Products Page Corporate Website [new] +

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

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 Submissions 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 a either a file or reference link under the materials section
    - When submitting a file, the document should include the site name, URL, date range, and date 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

Website Submissions

- How do Firms submit websites in eCTD?
  - Discussed in Section VII-E of the Guidance
  - Website submissions 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

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 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 links to external websites

Collaborative Marketing Agreements

- What are the recommendations when a different Firm markets and submits Promotional Materials on behalf of the Application Holder?
  - Discussed in Section III of the Guidance
  - Before submitting promotional materials, the Application Holder should submit a general correspondence to FDA which describes the agreement
  - All subsequent submissions should indicate the business relationship
    - Can be included in the comments section of the 2253
    - Should be included in the cover letter of any correspondence to OPDP
  - Application Holder is still responsible for promotion of the product

Demonstration of a properly-structured 2253 in Viewing Tool


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