What's New in the OPDP Electronic Submissions Final Guidance?

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Publication of Final Guidance

- On June 24, 2019, FDA published the Final Guidance for Industry titled *Providing Regulatory Submissions in Electronic and Non-Electronic Format – Promotional Labeling and Advertising Materials for Human Prescription Drugs*
  - Referred to as the OPDP eSub Guidance
- No earlier than 24 months after the publication of the OPDP eSub Guidance, the following promotional submissions will be required to be submitted in eCTD format:
  - Promotional Materials Submitted in Fulfillment of the Postmarketing Reporting Requirements (FDA Form 2253 Submissions)
  - Presubmission of Promotional Materials for Accelerated Approval Products
- The 24-month transition period will end on June 24, 2021

Changes between Draft and Final Guidance

- The revisions between the Draft and Final Guidance fall into the following categories:
  - Changes to provide greater clarity
  - Changes to address technical considerations
  - Changes to create consistency between terms used
  - Clarification of expectations for using specific Correspondence headings (Section 1.15)
  - Clarification of format for subsequent submissions after the 24-month transition period
  - Request for paper submissions to include electronic copy of submission on CD

Changes to Provide Greater Clarity

- Section III: General Considerations
  - For OPDP, address submissions that require correspondence to the attention of “OPDP Project Manager”
- Section IV-A: Form 2253
  - Firms are also encouraged, **but not required**, to submit annotated versions
  - Firms may choose to communicate the Indication being promoted in the promotional materials in the Comments section of the Form 2253
- Section IV-D: Promotional Materials Submitted Voluntarily for Advisory Comments
  - Clarified that annotated version of the storyboard for proposed TV ad should clearly identify the source of support for each claim (e.g., specific page and lines of the PI or specific page and column/paragraph from other references)
  - Clarified that websites are limited to 12 printed, **legible** pages
  - Clarified that FDA may determine that materials submitted do not meet the definition of Core Materials if they exceed content or page limitations

Changes to Provide Greater Clarity

- Section VI-J: Grouped Submissions
  - Firms are encouraged to submit multi-product submissions using the grouped submission function
- Section VI-L: Complaints
  - Clarified that Complaints may be submitted in either paper or non-eCTD electronic format

Changes to Address Technical Considerations

- Changed “hypertext links should be provided to the page/specific lines” to “hypertext links should be provided to the **specific page**”
  - Change appears in multiple locations
- Clarification of lifecycle operators
  - Section VI-L: If a material previously submitted on 2253 is revised and resubmitted, use the “Replace” operator to replace the previously submitted files
  - Section VII-E footnote: If a web page or section is updated, use the “New” operator. If the website is substantially revised, the “Replace” operator should be used.
- Clarified that the correct date format in eCTD is yyyymmdd (four-digit year, two-digit month, two-digit day)
  - E.g., January 1, 1900 should be formatted as “19000101”

Changes to Create Consistency between Terms Used

- The following updates were made throughout the document:
  - Changed “Request for Advisory Comments” to “Voluntary Request for Advisory Comments”
  - Removed reference to 503C Submissions
  - Removed “Draft” from references to Guidance
  - Changed “piece(s)” to “material(s)”
  - Changed “paper hard copies” to “paper copies”
  - Minor grammatical edits

Clarification of Expectations for Using Specific Correspondence Headings (Section 1.15)

- Section IV-G: Amendments
  - Amendments are used to submit one or multiple clean materials to a previously submitted 2253, Voluntary Request for Comment, or Accelerated Approval submission
    - Includes cases where a material was rejected, unreviewable due to technical reasons, omitted from the submission, or the incorrect file was submitted
    - Cover letter should be placed under Heading 1.15.1.8 (Correspondence accompanying materials previously missing or rejected)
    - Clean materials should be placed under Section 1.15.2.1
    - Amendments must include at least one clean material but may also include Annotated Materials, Annotated Labeling, and/or Annotated References

Clarification of Expectations for Using Specific Correspondence Headings (Section 1.15)

- Section IV-G: Amendments
  - Reference Documents are used to submit Annotated Materials, Annotated Labeling, and/or Annotated References
    - Includes cases where the non-clean version of the material was rejected, unreviewable due to technical reasons, omitted from the submission, or the incorrect file was submitted
    - Cover letter should be placed under Heading 1.15.1.10 (Submission of Annotated References)
    - Submission should NOT include a Clean Material

Clarification of Expectations for Using Specific Correspondence Headings (Section 1.15)

- Section IV-H: Withdrawals
  - Added Example 4 which discusses withdrawal of Materials from Form 2253
  - Clarified that firms should only use Heading 1.15.1.9 (Withdrawal Request) when materials will not be disseminated publicly
  - If a firm plans to disseminate or publish promotional materials for Accelerated Approval products without waiting for comments from FDA, the firm should notify FDA in a General Correspondence.
    - The cover letter should be placed under Heading 1.15.1.11 (General Correspondence)

Format for Submissions After the 24-month Transition Period

- Submission history is defined by the format through which the original submission was made
  - If a Form 2253 was received in paper format (or on a CD in non-eCTD format), the entire submission is considered paper
  - All subsequent submissions related to the original 2253 (e.g., Amendments, Reference Documents, General Correspondence, Withdrawal, etc) made prior to June 24, 2021 should be in paper format
  - FDA will work with firms to determine the appropriate format for subsequent submissions made after June 24, 2021 to submissions originally made in paper format
  - If a submission is received in eCTD format, all subsequent submissions related to the submission should be made in eCTD

Request to Include CD Copy

- Form 2253 and Accelerated Approval Submissions may continue to be submitted in paper format until June 24, 2021
  - 2253 Submissions in paper format do not require a paper copy of the entire submission
    - Only a signed copy of the paper Form 2253 is required
    - All other materials may be submitted in non-eCTD format on an attached CD
- Non-2253 Submissions in non-eCTD format should follow the recommendations in Table 1 of the Guidance (Page 18)
  - Non-2253 submissions in paper format must still include paper copies of the entire submission
  - When paper copy materials are submitted, sponsors are encouraged, but not required, to include one non-eCTD copy of the contents of the submission on a CD
  - When submitting a CD copy, the cover letter should include a statement verifying that the contents of the CD match the contents of the paper submission

Outreach Efforts

- Questions related to the OPDP eSub Guidance or the submission of test files should be directed to the OPDP eCTD email mailbox
  - OPDPeCTD@fda.hhs.gov