Content and Format for Accurate ANDA Submissions

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Commander, United States Public Health Service
Regulatory Affairs Coordinator
Generic Drug Regulatory Affairs Team
Office Of Generic Drugs

REdI Generic Drug Forum
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Disclaimer

- This presentation reflects the views of the speaker and do not reflect official FDA, HHS, or other government opinion or policy.

- I have nothing to disclose.

Outcome

Provide guidance, strategies, and examples of how to properly complete and communicate submissions related to ANDA files to increase the efficiency of routing and proper identification by review staff.

Outline

- Point of Contact for Industry
- 356h Form and Cover Letters
- eCTD Requirements
- Patent & Exclusivity Amendment Submissions
- Wrap up

Point of Contact for Industry

Regulatory Project Manager

- Oversee the review of ANDAs
  - Provide oversight across all review disciplines
  - Work to ensure all reviews are complete
  - Work to ensure OGD meets GDUFA goal dates
- Triage all amendments from receipt of ANDA to approval
  - Assign received amendments to the applicable disciplines
- Communicate key events in the approval process
  - MAPP 5200.3 Rev. 1
- Serve as point of contact (POC)
  - All communications will go through RPM
  - Exception: responding directly, as requested by a discipline

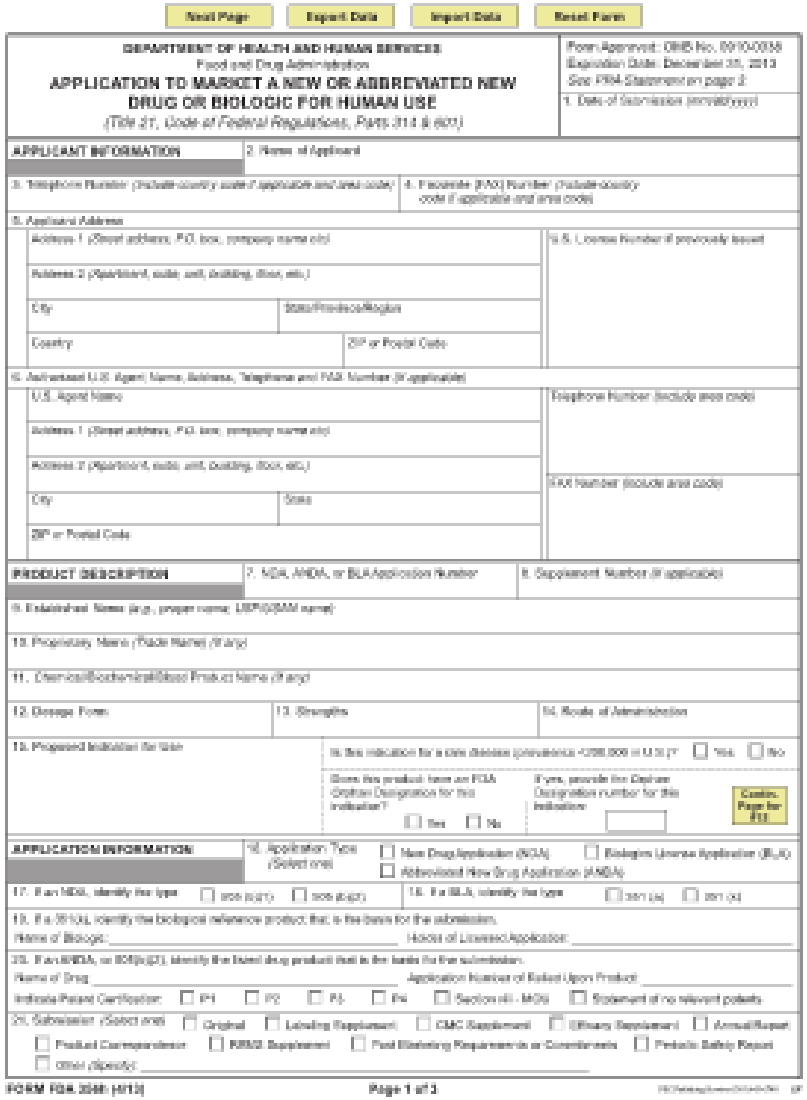
Point of Contact for Industry

- Industry will know who to contact based on the *RPM Introductory Call, Information Request Letter, or Complete Response Letter*.
- Firms should contact the designated OGD Regulatory Project Manager (RPM) for ALL matters on ANDA and Supplements.
- When calling or emailing, always clearly state the nature of the contact.
  - ANDA/Supplement/DMF #, reason for call (status, patent expiration date, forfeiture date, etc.)

REMINDER

DO NOT contact individual reviewers, team leaders, directors (includes not cc'ing them on emails), etc.

356h Form and Cover Letters



Next Page | Export Data | Import Data | Reset Form

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

APPLICATION TO MARKET A NEW OR ABBREVIATED NEW DRUG OR BIOLOGIC FOR HUMAN USE

(Title 21, Code of Federal Regulations, Parts 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: December 31, 2013
See PRA Statement on page 2.

1. Date of Submission (mm/dd/yyyy)

APPLICANT INFORMATION

2. Name of Applicant

3. Telephone Number (Include country code if applicable and area code)

4. Facsimile (FAX) Number (Include country code if applicable and area code)

5. Applicant Address

Address 1 (Street address, P.O. box, company name c/o)

Address 2 (Apartment, suite, unit, building, floor, etc.)

City

State/Province/Region

Country

ZIP or Postal Code

6. U.S. License Number if previously issued

6. Authorized U.S. Agent Name, Address, Telephone and FAX Number (If applicable)

U.S. Agent Name

Address 1 (Street address, P.O. box, company name c/o)

Address 2 (Apartment, suite, unit, building, floor, etc.)

City

State

ZIP or Postal Code

Telephone Number (Include area code)

FAX Number (Include area code)

PRODUCT DESCRIPTION

7. NDA, ANDA, or BLA Application Number

8. Supplement Number (If applicable)

9. Established Name (e.g., proper name, USP/USAN name)

10. Proprietary Name (Trade Name) (If any)

11. Chemical/Biochemical/Blood Product Name (If any)

12. Dosage Form

13. Strengths

14. Route of Administration

15. Proposed Indication for Use

16. Is this indication for a rare disease (prevalence <200,000 in U.S.)? ☐ Yes ☐ No

Does this product have an FDA Orphan Designation for this indication? ☐ Yes ☐ No

If yes, provide the Orphan Designation number for this indication

Continue Page for #15

APPLICATION INFORMATION

17. Application Type (Select one) ☐ New Drug Application (NDA) ☐ Biologics License Application (BLA) ☐ Abbreviated New Drug Application (ANDA)

17. If an NDA, identify the type ☐ 505 (b)(1) ☐ 505 (b)(2)

18. If a BLA, identify the type ☐ 351 (a) ☐ 351 (k)

19. If a 351(k), identify the biological reference product that is the basis for the submission.
Name of Biologic: _____ Holder of Licensed Application: _____

20. If an ANDA, or 505(b)(2), identify the listed drug product that is the basis for the submission.
Name of Drug: _____ Application Number of Listed Drug Product: _____
Indicate Patent Certification: ☐ P1 ☐ P2 ☐ P3 ☐ P4 ☐ Section viii - 505j ☐ Statement of no relevant patents

21. Submission (Select one) ☐ Original ☐ Labeling Supplement ☐ CMC Supplement ☐ Efficacy Supplement ☐ Annual Report
☐ Product Correspondence ☐ REMS Supplement ☐ Post Marketing Requirements or Commitments ☐ Periodic Safety Report
☐ Other (Specify): _____

FORM FDA 3580 (4/12) Page 1 of 3

356h: FDA's Point of Contact to Industry

- Designate one Point-of-Contact (POC) for the ANDA on the 356h.
- FDA will **only** communicate with the person identified/autorized on the 356h regarding your application.
- If point of contact changes, need to update ANDA with updated 356h AND Cover Letter

356h Form

- Every 356h should have the following:
  - Current **Applicant** and **U.S. Agent** (if applicable) phone, fax and email.
  - Responsible **Official/Agent's** current phone, fax, and email.
  - Complete **Facility** address, FEI, DUNS, and contact information
  - Listing of all facilities

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

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(Title 21, Code of Federal Regulations, Parts 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: December 31, 2017
See PRA Statement on page 3.

1. Date of Submission *(mm/dd/yyyy)*: 01/01/2016

APPLICANT INFORMATION

2. Name of Applicant: GENERIC DURG COMPANY

3. Telephone Number *(Include country code if applicable and area code)*: 91-40-123456789

4. Facsimile (FAX) Number *(Include country code if applicable and area code)*: 91-40-98765430

5. Applicant Address

Address 1 *(Street address, P.O. box, company name c/o)*: HELP ME Unit I Happy Vallry

Address 2 *(Apartment, suite, unit, building, floor, etc.)*: Generic Drug Village, Building 1000

City: Urban City

State/Province/Region: Somewhere Far Away

Country: New Zealand

ZIP or Postal Code: 123456

Email Address: Email@genericcompany.com

U.S. License Number if previously issued:

6. Authorized U.S. Agent *(Required for non-U.S. applicants)*

Authorized U.S. Agent Name: Mr. Joe White, Director, Regulatory Affairs

Address 1 *(Street address, P.O. box, company name c/o)*: Generic Drug Company USA, Inc.

Address 2 *(Apartment, suite, unit, building, floor, etc.)*: 123 Generic Drug Avenue

City: Generic Drug City

State: New Jersey

ZIP Code: 77956

Telephone Number *(Include area code)*: 555-789-5555

FAX Number *(Include area code)*: 555-789-1234

Email Address: usagent@genericdrugsusa.com

PRODUCT DESCRIPTION

7. NDA, ANDA, or BLA Application Number: 200145

8. Supplement Number *(If applicable)*:

9. Established Name *(e.g., proper name, USP/USAN name)*: Generic Drug

10. Proprietary Name *(Trade Name) (If any)*: Not Applicable

11. Chemical/Biochemical/Blood Product Name *(If any)*: 5, 1, 2, 10-triethyl-bisphenol-2-6 hyrdo ether

12. Dosage Form: Tablet

13. Strengths: 10 mg, 15 mg, 20 mg

14. Route of Administration: Oral

15. Proposed Indication for Use: treatment of complicated illnesses that prevent someone from being healthy

Is this indication for a rare disease (prevalence <200,000 in U.S.)? ☐ Yes ☐ No

Does this product have an FDA Orphan Designation for this indication? ☐ Yes ☑ No

If yes, provide the Orphan Designation number for this indication:

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APPLICATION INFORMATION

16. Application Type *(Select one)*: ☐ New Drug Application (NDA) ☐ Biologics License Application (BLA) ☑ Abbreviated New Drug Application (ANDA)

17. If an NDA, identify the type ☐ 505(b)(1) ☐ 505(b)(2)

18. If a BLA, identify the type ☐ 351(a) ☐ 351(k)

19. If a 351(k), identify the biological reference product that is the basis for the submission.

Name of Biologic:

Holder of Licensed Application:

20. If an ANDA, or 505(b)(2), identify the listed drug product that is the basis for the submission.

Name of Drug: Orange Book Durg

Application Number of Relied Upon Product: 024567

Indicate Patent Certification(s): ☐ P1 ☐ P2 ☐ P3 ☑ P4 ☑ Section viii - MOU ☐ Statement of no relevant patents

21. Submission *(See instructions)*: ☐ Original ☐ Labeling Supplement ☐ CMC Supplement ☐ Efficacy Supplement ☐ Annual Report ☐ Product Correspondence ☐ REMS Supplement ☐ Postmarketing Requirements or Commitments ☐ Periodic Safety Report ☑ Other *(Specify)*: Point of Contact Change

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29. Establishment Information *(Full establishment information should be provided in the body of the application.)*

Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, registration number (FEI), MF number, Establishment DUNS number, and manufacturing steps and/or type of testing (e.g., final dosage form, stability testing, container closure) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

Establishment Name
GENERIC DRUGS LIMITED UNIT 10

Address 1 *(Street address, P.O. box, company name c/o)*
Generic Drug Village, Building 1000

Address 2 *(Apartment, suite, unit, building, floor, etc.)*

City
Pharmaceutical City

State/Province/Region
Region All Naturale

Country
My Country

ZIP or Postal Code
123 456

Registration (FEI) Number
9871236549

MF Number

Establishment DUNS Number
987654321

Is the establishment new to the application? ☐ Yes ☑ No

What is the status of the establishment? ☐ Pending ☑ Active ☐ Inactive ☐ Withdrawn

Establishment Contact Information

Name of Contact for the Establishment
Dr. Imake Good Drugs, Director (Pharma)

Address 1 *(Street address, P.O. box, company name c/o)*
GENERIC DRUGS LIMITED UNIT 10

Address 2 *(Apartment, suite, unit, building, floor, etc.)*
Generic Drug Village, Building 1000

City
Pharmaceutical City

State
Region All Naturale

ZIP or Postal Code

Telephone Number *(Include area code)*
91-40-12345678

FAX Number *(Include area code)*
91-40-87654321

Email Address
imakegooddrugs@genericdrugslimited.com

Manufacturing Steps and/or Type of Testing
Manufacturing Steps and/or Type of Testing: All steps of finished dosage form manufacturing and packaging Testing of of finished dosage form including in-process, finished dosage and stability testing .

Is the site ready for inspection? ☑ Yes ☐ No

If No, when will site be ready? *(mm/dd/yyyy)*

Continuation Page for #29

356h Form

Extremely Important

Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, registration number (FEI), MF number, Establishment DUNS number, and manufacturing steps and/or type of testing (e.g., final dosage form, stability testing, container closure) conducted at the site. Indicate whether the site is ready for inspection or, if not, when it will be ready.

All facilities involved, must be submitted. For supplements, all new sites, ***as well as all previously approved sites (even inactive and withdrawn ones)*** *must also be included.*

- *New sites are to be flagged as "pending".*
- *Withdrawn sites are to be flagged as "withdrawn".*

356h: Facility Information Hitches

- Ensure 356h (question 29) contains the most current and complete facilities information for your ANDA
  - *Missing/unclear/conflicting facility information and responsibilities cause delays!!!*
  - 356h facility information must match relevant eCTD Sections (3.2.P.3.1 for drug products and 3.2.S.2 for the drug substance)
  - Immediately Identify ANY changes to facilities (additions, withdrawals, etc.) with an amendment with updated 356h and cover letter to the ANDA

Cover Letter

- Every Cover Letter should have the following:
  - Clear statement of what the submission entails (Tier 1 Minor; Amendment - Final Approval Requested; Patent Amendment; Change of Contact Update; etc.)
  - Clear identification of what disciplines are being responded to in the amendment (Quality, Labeling, etc.)
  - Clear identification of changes to facilities, either additions or withdrawals.
- Correct coding ensures timely, accurate triage and that correct goal dates applied.

A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission:

RESUBMISSION
1st/2nd/3rd/4th/5th (if GDUFA) MINOR / MAJOR (TIER 1, 3)
COMPLETE RESPONSE
CHEMISTRY / BIOEQUIVALENCE / CLINICAL / MICROBILOGY / LABELING

Within one year after the date of this letter, you are required to resubmit or take other actions available under 21 CFR 314.110. If you do not take one of these actions, we may consider your lack of response a request to withdraw the ANDA under 21 CFR 314.65. You may also request an extension of time in which to resubmit the ANDA. A resubmission response must fully address all the deficiencies listed.

The drug product may not be legally marketed until you have been notified in writing that this ANDA is approved.

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions with respect to self-identification of facilities and payment of annual facility fees. Your ANDA identifies at least one facility that is subject to the self-identification requirement and payment of an annual facility fee. Self-identification must occur by June 1 of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the Federal Register notice announcing facility fee amounts. All finished dosage forms (FDFs) or active pharmaceutical ingredients (APIs) manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

Food and Drug Adminstration,
Center for Drug Evaluation and Reasearch,
Office of Generic Drugs,
Document Control Room,
Metro Park North VII,
7620 Standish Place,
Rockville, Maryland 20855

"RESUBMISSION
MAJOR
COMPLETE RESPONSE AMENDMENT
CHEMISTRY/LABELLING"

March 30, 2015

Re: [redacted] Tablets 100 mg, ANDA # [redacted], Resubmission – Major Complete Response Ammendment in eCTD format.

Dear Sir/Madam,

This is in reference to Complete Response letter dated January 29, 2015 for [redacted] Tablets 100 mg, ANDA # [redacted]. We are herewith submitting the response to the deficiencies in eCTD format.

In accordance with 21 CFR 314.110 we are amending the application with response to all deficiencies addressed in this 'Resubmission - Major Complete Response Amendment Chemistry/Labeling'.

Please find the requested information and documents in accordance with the electronic

☑ Abbreviated New Drug Application (ANDA)

17. If an NDA, identify the type ☐ 505 (b)(1) ☐ 505 (b)(2)

18. If a BLA, identify the type ☐ 351 (a) ☐ 351 (k)

19. If a 351(k), identify the biological reference product that is the basis for the submission.
Name of Biologic: _____ Holder of Licensed Application: _____

20. If an ANDA, or 505(b)(2), identify the listed drug product that is the basis for the submission.
Name of Drug: Smile® Tablets Application Number of Relied Upon Product: 654321
Indicate Patent Certification(s): ☐ P1 ☐ P2 ☑ P3 ☐ P4 ☐ Section viii - MOU ☐ Statement of no relevant patents

21. Submission *(Select one)* ☐ Original ☐ Labeling Supplement ☐ CMC Supplement ☐ Efficacy Supplement ☐ Annual Report
☐ Product Correspondence ☐ REMS Supplement ☐ Postmarketing Requirements or Commitments ☐ Periodic Safety Report
☑ Other *(Specify)*: Resubmission Minor Complete Response Amendment-Chemistry/Labeling

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22. Submission Sub-Type ☐ Presubmission ☑ Amendment ☐ Initial Submission ☐ Resubmission

23. If a supplement, identify the appropriate category. ☐ CBE ☐ Prior Approval (PA) ☐ CBE-30

24. Does this submission contain *only* pediatric data? ☐ Yes ☑ No

25. Reasons for Submission
Resubmission Minor Complete Response Amendment-Chemistry/Labeling

26. Proposed Marketing Status *(Select one)* ☑ Prescription Product (Rx) ☐ Over-The-Counter Product (OTC)

27. This application is *(Select one)* ☐ Paper ☐ Paper and Electronic ☑ Electronic

28. Number of Volumes Submitted N/A

Cover Letter

- Every Cover Letter should clearly identify ANY new (unsolicited/gratuitous) data/facility/review material
- Identify what discipline this unsolicited information pertains to
- Unsolicited data outside of the CR response to the CR Letter may impact any GDUFA goals

356h Form and Cover Letter

- Cover Letters should state the following if applicable:
  - **Expedited Review Requested**
  - **Expedited Review Granted**
  - **Drug Shortage**
  - **PEPFAR**

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to, the following:

1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660, and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202.
5. Regulations on making changes in application in FD&C Act section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.
7. Local, state, and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge, are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

32. Typed Name and Title of Applicant's Responsible Official	33. Date *(mm/dd/yyyy)*
Dr. I'm Somebody, Director-Regulatory Affairs	10/28/2013

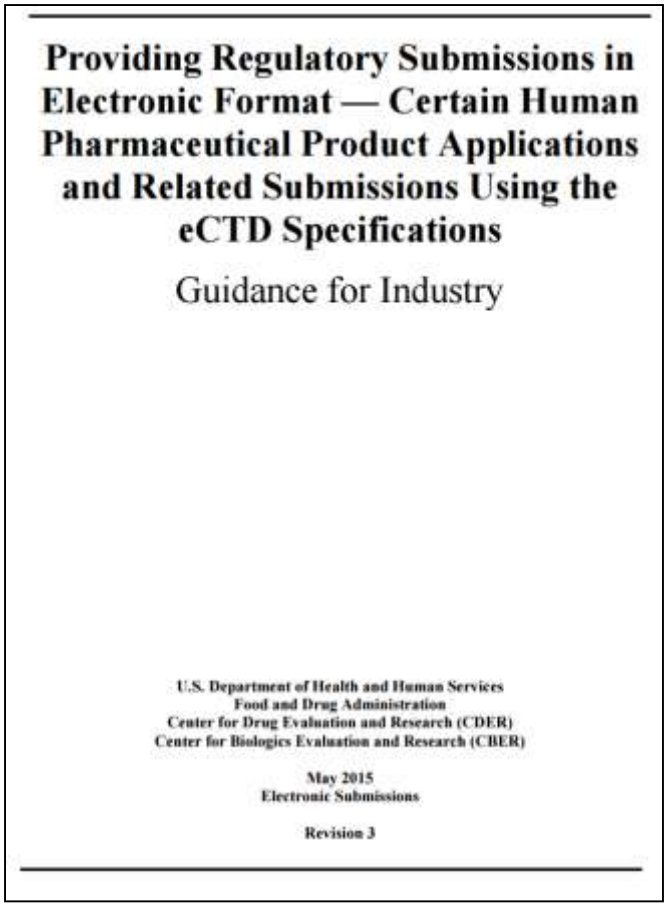
34. Telephone Number *(Include country code if applicable and area code)*	35. FAX Number *(Include country code if applicable and area code)*	36. Email Address
732-529-0423	732-562-8854	imsomebody@genericdrugsusa.com

37. Address of Applicant's Responsible Official

Address 1 *(Street address, P.O. box, company name c/o)*	
Generic Drugs USA, Inc.	
Address 2 *(Apartment, suite, unit, building, floor, etc.)*	
123 Generic Drug Avenue	
City	State/Province/Region
Generics City	New Jersey
Country	ZIP or Postal Code
United States of America	12345

38. Signature of Applicant's Responsible Official or Other Authorized Official	39. Countersignature of Authorized U.S. Agent
Sign	Sign

Electronic Common Technical Document (eCTD)



Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

May 2015
Electronic Submissions

Revision 3

eCTD Requirements

- Electronic submission of ***ANDAs*** and ***Master Files*** in eCTD format will be required as of May 2017 *(see Guidance for industry Providing Regulatory Submissions in Electronic Format – Certain Human Pharmaceuticals Product Applications and Related Submissions Using the eCTD Specifications)*

- Review metric goals only apply to submissions made electronically following the Electronic Common Technical Document (eCTD) format in effect at the date of submission

- Electronic format must be compete and in a form FDA can process, review and archive (21 CFR 314.94(d)(1)(iii))

- See the FDA web site for guidances and technical specifications to ensure documents are submitted correctly:
  - http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm153574.htm

Patent & Exclusivity Amendment Submissions

Patent Keys for Success

- Address ALL patents and/or exclusivities
  - Submit all required documentation related to *receipt of notice* (21 CFR 314.95(e))
- PIV certifications to 'later-listed' patents
  - Sponsors must still submit documentation that notice was sent to NDA holder and patent assignees
- Inconsistencies between patent certifications or between patent certifications and labeling.
  - Labeling must match manner in which sponsor has addressed listed patents
  - Sponsor must generally address patent(s) which are associated with the same use code(s) in the same manner.
  - Sponsors may need to provide 'split-certifications' for patents to maintain consistency

Patent Keys for Success

- Submit all information required by 21 CFR 314.107(e) and (f)(2)
  - All court decisions/orders MUST be submitted to the application
  - This includes dismissal orders and adverse court decisions
  - Late submission of Court Decisions can impact timing of approvals.
  - Submit Court Orders that resolve litigation within 10 days of issuance
- Convert certifications from PIV to PIII
  - Required by 21 CFR 314.94(a)(12)(viii)(A) when a final judgment has been entered finding the patent infringed

Patent Keys for Success

- Submit of Pediatric Waivers
  - Applicable when ANDA applicant intends to be approved during 6 month period of pediatric exclusivity associated with a patent
  - Pediatric Waivers MUST be provided even with settlement agreements

- Submit Launch notices for applicants eligible for 180 day exclusivity (21 CFR 314.107(c)(4))

Summary

Summary

- Regulatory Project Manager (RPM) is **Point of Contact** for all ANDA inquiries.
- Applicants should designate one **Point of Contact** when interacting with FDA.
- Submit all documents electronically via the Gateway following the eCTD format.

Summary

- Use Cover Letter and 356h with every submission
  - Clearly identify content of each submission
    - CR response
    - IR response
    - Patent Amendment
    - BE studies
    - New facilities
    - Unsolicited Amendment

Summary

Facilities:

- Provide **ALL** facilities on 356h form (new, exiting, withdrawn)
- 356h facility information must match relevant eCTD Sections
- Clearly identify **NEW** facilities in submissions
- Facilities added in IR response are out of scope
- Avoid new facilities added at end of review cycle

Summary

- Continuous and prompt **Patent updates**
- Provide prompt **litigation updates**
  - Critical as submission nears GDUFA goal date or TAD

Summary

- Submit ALL amendment, correspondence, etc. documents via Gateway to **archival ANDA file**
  - NEVER send to OGD Immediate Office, Policy Office, or the RPM
  - Desk copies NOT needed unless requested
  - For paper submissions ONLY:
    - Office of Generic Drugs
      Center for Drug Evaluation and Research
      Food and Drug Administration
      Metro Park North VII
      7620 Standish Place
      Rockville, MD 20855

http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm142112.htm

Summary

Information Response (IR) Amendments:

- Respond ONLY to those issues raised in the IR
- Do NOT include out of scope unsolicited data:
  - New facility
  - Other disciplines
  - Information that is off topic
  - Lots of extraneous information over what was requested
  - Tons of data, 1,000s of pages of reports

Summary

- Stay on top of:
  - RLD labeling changes
  - REMS modifications

- IF there are changes to either of these, ANDA applicant needs to submit revised labeling or REMS

Questions?

surveymonkey.com/r/GDF-D2S2