ANDA FILING CHECKLIST

(CTD or eCTD FORMAT)

FOR COMPLETENESS AND ACCEPTABILITY of an APPLICATION

ANDA:
APPLICANT:
RELATED APPLICATION(S):

DRUG NAME:
DOSAGE FORM:

LETTER DATE:
RECEIVED DATE:

☐ P-IV
☐ FIRST GENERIC
☐ EXPEDITED REVIEW REQUEST (Approved/Denied)
☐ PEPFAR
☐ PET

Electronic or Paper Submission: Type II DMF#

BASIS OF SUBMISSION:
NDA/ANDA:
FIRM:
RLD:

****Document Room Note: for New Strength amendments and supplements, if specific reviewer(s) have already been assigned for the original, please assign to those reviewer(s) instead of the default random team(s).**

Review Team:

CHEM Team**:** ☐**Activity**	Bio Team**:** ☐**Activity**
CHEM Team Leader**:** ☐ **No Assignment Needed in DARRTS**	Bio PM: ☐ **FYI**
CHEM RPM**:** ☐ **FYI**	Clinical Endpoint Team**: (No)** ☐**Activity**
DMF Review Team Leader**:** ☐ **FYI**	
Labeling Reviewer**:** ☐**Activity**	Micro Review**: (No)** ☐**Activity**
SPECIAL INSTRUCTIONS FOR DOCUMENT ROOM (applicable only for a response to a refuse to receive):	

Regulatory Reviewer: Date:	Recommendation: ☐ **FILE** ☐ **REFUSE to RECEIVE**

Comments:
Therapeutic Code:
On Cards:
Archival copy:
Sections:

- **For More Information on Submission of an ANDA in Electronic Common Technical Document (eCTD) Format please go to:** http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm153574.htm
- **For a Comprehensive Table of Contents Headings and Hierarchy please go to: http://www.fda.gov/cder/regulatory/ersr/5640CTOC-v1.2.pdf**
- **For more** CTD and eCTD informational links **see the final page of the ANDA Checklist**

1. Edit Application Property Type in DARRTS where applicable for

a. First Generic Received
☐ Yes ☐ No
b. Market Availability
☐ Rx ☐ OTC
c. Pepfar
☐ Yes ☐ No
d. Product Type
☐ Small Molecule Drug
e. USP Drug Product (at time of filing review)
☐ Yes ☐ No

2. Edit Submission Patent Records
   ☐ Yes
3. Edit Contacts Database with Bioequivalence Recordation where applicable
   ☐ Yes
4. EER (in Draft)
   ☐ Yes

ADDITIONAL COMMENTS REGARDING THE ANDA:

MODULE 1: ADMINISTRATIVE

		COMMENT (S)
1.1	**1.1.2** **Signed and Completed Application Form (356h)** (Rx/OTC Status) (original signature) **Establishment Information:** 1. Drug Substance Manufacturer 2. Drug Product Manufacturer 3. Outside Testing Facility(ies) Establishment information **must** include the following: ▪ Contact name at the manufacturing site and testing laboratories ▪ US Agent's name for each site (if applicable) ▪ Address of the manufacturing site for the drug substance and finished product ▪ Address of all outside contract testing laboratories ▪ Phone and fax numbers, email address of contact for each site ▪ **Detailed** description of function(s) or responsibility(ies) of each site, specify if the function/responsibility is for the Drug Substance, Drug Product or Excipient ▪ CFN/FEI/DUNS number of each site (if available)	
1.2	**Cover Letter**	
1.2.1	**Form FDA 3674 (PDF)**	
*	**Table of Contents** (paper submission only)	
1.3.2	**Field Copy Certification** (N/A for E-Submissions) (original signature)	
1.3.3	**Debarment Certification-GDEA** (Generic Drug Enforcement Act)/Other: (no qualifying statement) 1. Debarment Certification (original signature) 2. List of Convictions statement (original signature)	
1.3.4	**Financial Certifications** Bioavailability/Bioequivalence Financial Certification (Form FDA 3454) Disclosure Statement (Form FDA 3455)	
1.3.5	**Patent Information** Patents listed for the RLD in the Electronic Orange Book Approved Drug Products with Therapeutic Equivalence Evaluations **Patent Certification** 1. Patent number(s) 2. Paragraph: (Check all certifications that apply) MOU ☐ PI ☐ PII ☐ PIII ☐ PIV ☐ (Statement of Notification) ☐ 3. Expiration of Patent(s): a. Pediatric exclusivity submitted? b. Expiration of Pediatric Exclusivity? 4. Exclusivity Statement: State marketing intentions?	
1.4.1	**References** Letters of Authorization 1. DMF letters of authorization a. Type II DMF authorization letter(s) or synthesis for Active Pharmaceutical Ingredient b. Type II DMF# c. Type III DMF authorization letter(s) for container closure 2. US Agent Letter of Authorization (U.S. Agent [if needed, countersignature on 356h])	
1.12.4	**Request for Comments and Advice** - Proprietary name requested If Yes, did the firm provide the request as a separate electronic amendment labeled "Proprietary Name Request" at initial time of filing 1. Yes 2. No - contact the firm to submit the request as a separate electronic amendment.	

1.12.11	**Basis for Submission** NDA#: Ref Listed Drug: Firm: **ANDA suitability petition required?** If Yes, provide petition number and copy of approved petition **ANDA Citizen's Petition Required?** If Yes, provide petition number and copy of petition	
1.12.12	**Comparison between Generic Drug and RLD-505(j)(2)(A)** 1. Conditions of use 2. Active ingredients 3. Inactive ingredients 4. Route of administration 5. Dosage Form 6. Strength	
1.12.14	**Environmental Impact Analysis Statement** **(**cite 21CFR 25.31, if applicable)	
1.12.15	**Request for Waiver** Request for Waiver of In-Vivo BA/BE Study(ies)	
1.14.1	**Draft Labeling** (Multi Copies N/A for E-Submissions) **1.14.1.1** 4 copies of draft for paper submission only (each strength and container) **1.14.1.2** 1 side by side labeling comparison of containers and carton with all differences visually highlighted and annotated **1.14.1.3** 1 package insert (content of labeling) and SPL submitted electronically	
1.14.3	**Listed Drug Labeling** **1.14.3.1** 1 side by side labeling (package and patient insert) comparison with all differences visually highlighted and annotated **1.14.3.3** RLD package insert, 1 RLD label and 1 RLD container label	

MODULE 2: Quality Overall Summary

		COMMENT (S)
2.3	**Quality Overall Summary (QOS)** **E-Submission: PDF** **Word Processed e.g., MS Word** A model Quality Overall Summary for an immediate release tablet and an extended release capsule can be found on the OGD webpage http://www.fda.gov/cder/ogd/ **Question based Review (QbR)** **2.3.S Drug Substance (Active Pharmaceutical Ingredient)** 2.3.S.1 General Information 2.3.S.2 Manufacture 2.3.S.3 Characterization 2.3.S.4 Control of Drug Substance 2.3.S.5 Reference Standards or Materials 2.3.S.6 Container Closure System 2.3.S.7 Stability **2.3.P Drug Product** 2.3.P.1 Description and Composition of the Drug Product 2.3.P.2 Pharmaceutical Development 2.3.P.2.1 Components of the Drug Product 2.3.P.2.1.1 Drug Substance 2.3.P.2.1.2 Excipients 2.3.P.2.2 Drug Product **Oral Solids**: Immediate Release or Modified Release (Matrix Technology or Compressed Film Coated Components) tablet scoring data per Draft *Guidance for Industry, Tablet Scoring: Nomenclature, Labeling and Data for Evaluation* (if applicable) 2.3.P.2.3 Manufacturing Process Development 2.3.P.2.4 Container Closure System 2.3.P.3 Manufacture 2.3.P.4 Control of Excipients 2.3.P.5 Control of Drug Product 2.3.P.6 Reference Standards or Materials 2.3.P.7 Container Closure System 2.3.P.8 Stability	

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MODULE 2.7: Clinical Summary

		COMMENT (S)
2.7	**Clinical Summary (Bioequivalence)**Model BE Data Summary Tables **E-Submission: PDF** **Word Processed: e.g., MS Word** **2.7.1 Summary of Biopharmaceutic Studies and Associated Analytical Methods** **2.7.1.1 Background and Overview** Table 1. Submission Summary Table 4. Bioanalytical Method Validation Table 6. Formulation Data Table 10. Study Information Table 11. Product Information **2.7.1.2 Summary of Results of Individual Studies** Table 5. Summary of In Vitro Dissolution (include complete comparative In Vitro Dissolution Data (individual) with Certificate of Analysis [CoA] for Test and Reference products including: potency, assay, content uniformity, date of manufacture and lot number) Table 9. Reanalysis of Study Samples Table 12. Dropout Information Table 13. Protocol Deviation Table 14. Summary of Standard Curve and QC Data for Bioequivalence Sample Analysis **2.7.1.3 Comparison and Analyses of Results Across Studies** Table 2. Summary of Bioavailability (BA) Studies Table 3. Statistical Summary of the Comparative BA Data Table 16. Composition of Meal Used in Fed Bioequivalence Study (if the standard meal referenced in the CDER Guidance for Industry Food-Effect Bioavailability and Fed Bioequivalence Studies is used, then provide a statement of compliance to the FDA standard meal. If an alternative meal is used, then complete the summary table with the name of the food item(s), ingredient(s), amount (g), energy (kcal), protein (kcal), fat (kcal) and carbohydrates (kcal). **2.7.1.4 Appendix** Table 15. SOPs Dealing with Bioanalytical Repeats of Study Samples **2.7.4.1.3 Demographic and Other Characteristics of Study Population** Table 7. Demographic Profile of Subjects Completing the Bioequivalence Study **2.7.4.2.1.1 Common Adverse Events** Table 8. Incidence of Adverse Events in Individual Studies	

MODULE 3: 3.2.S DRUG SUBSTANCE

		COMMENT (S)
3.2.S.1	**General Information**) (Do not refer to DMF) **3.2.S.1.1 Nomenclature** **3.2.S.1.2 Structure** **3.2.S.1.3 General Properties**	
3.2.S.2	**Manufacturer** **Drug Substance (Active Pharmaceutical Ingredient)** Must correlate to the establishment information submitted in annex to Form FDA 356h. 1. Name and Full Address(es)of the Facility(ies) 2. Contact name, phone and fax numbers, email address 3. U.S Agent's name (if applicable) 4. Specify Function or Responsibility 5. Type II DMF number for API 6. CFN, FEI or DUNS numbers (if available)	
3.2.S.3	**Characterization** Provide the following in tabular format: 1. Name of Impurity(ies) 2. Structure of Impurity(ies) 3. Origin of Impurity(ies)	
3.2.S.4	**Control of Drug Substance (Active Pharmaceutical Ingredient)** **3.2.S.4.1 Specification** Testing specifications and data from drug substance manufacturer(s) **3.2.S.4.2 Analytical Procedures** **3.2.S.4.3 Validation of Analytical Procedures** (API that is USP or reference made to DMF, must provide verification of USP or DMF procedures) 1. Spectra and chromatograms for reference standards and test samples 2. Samples-Statement of Availability and Identification of: a. Drug Substance b. API lot number(s) **3.2.S.4.4 Batch Analysis** 1. COA(s) specifications and test results from drug substance mfgr(s) 2. Applicant certificate of analysis **3.2.S.4.5 Justification of Specification**	
3.2.S.5	**Reference Standards or Materials (**Do not refer to DMF)	
3.2.S.6	**Container Closure Systems**	
3.2.S.7	**Stability** 1. Retest date or expiration date of API	

MODULE 3: 3.2.P DRUG PRODUCT

		COMMENT (S)
3.2.P.1	**Description and Composition of the Drug Product** 1. Unit composition with indication of the function of the inactive ingredient(s) 2. Inactive ingredients and amounts are appropriate per IIG (per/dose justification) 3. Conversion from % to mg/dose values for inactive ingredients (if applicable) 4. Elemental iron: provide daily elemental iron calculation or statement of adherence to 21CFR73.1200 (calculation of elemental iron intake based on **maximum daily dose (MDD)** of the drug product is preferred if this section is applicable) 5. Injections: If the reference listed drug is packaged with a drug specific diluent then the diluent must be Q1/Q2 and must be provided in the package configuration	
3.2.P.2	**Pharmaceutical Development** 1. Pharmaceutical Development Report	
3.2.P.3	**Manufacture** **3.2.P.3.1 Drug Product** Must correlate to the establishment information submitted in annex to From FDA 356h for the finished dosage manufacturer and all outside contract testing laboratories. 1. Name and Full Address(es)of the Facility(ies) 2. Contact name, phone and fax numbers, email address 3. U.S Agent's name (if applicable) 4. Specify Function or Responsibility 5 CGMP Certification (from both applicant and drug product manufacturer if different entities) 6. CFN, FEI or DUNS numbers (if available) **3.2.P.3.2 Batch Formula** **3.2.P.3.3 Description of Manufacturing Process and Process Controls** 1. Description of the Manufacturing Process 2. Master Production Batch Record(s) for largest intended production runs (no more than 10x pilot batch) with equipment specified 3. Master packaging records for intended marketing container(s) 4. If sterile product 5. Reprocessing Statement (cite 21CFR 211.115, submitted by the drug product manufacturer and the applicant, if different entities) **3.2.P.3.4 Controls of Critical Steps and Intermediates** **3.2.P.3.5 Process Validation and/or Evaluation** 1. Microbiological sterilization validation 2. Filter validation (if aseptic fill)	
3.2.P.4	**Controls of Excipients** (Inactive Ingredients) Source of inactive ingredients identified **3.2.P.4.1 Specifications** 1. Testing specifications (including identification and characterization) 2. Suppliers' COA (specifications and test results) **3.2.P.4.2 Analytical Procedures** **3.2.P.4.3 Validation of Analytical Procedures** **3.2.P.4.4 Justification of Specifications:** 1. Applicant COA	

MODULE 3: 3.2.P DRUG PRODUCT (Continued)

		COMMENT (S)
3.2.P.5	**Controls of Drug Product** **3.2.P.5.1 Specification(s)** **3.2.P.5.2 Analytical Procedures** **3.2.P.5.3 Validation of Analytical Procedures** (if using USP procedure, must provide verification of USP procedure) Samples - Statement of Availability and Identification of: 1. Finished Dosage Form 2. Lot number(s) and strength of Drug Product(s) **3.2.P.5.4 Batch Analysis** Certificate of Analysis for Finished Dosage Form **3.2.P.5.5 Characterization of Impurities** **3.2.P.5.6 Justification of Specifications**	
3.2.P.7	**Container Closure System** 1. Summary of Container/Closure System (if new resin, provide data) 2. Components Specification and Test Data 3. Packaging Configuration and Sizes 4. Container/Closure Testing (recommended additional testing for all plastic) a. Solid Orals: water permeation, light transmission b. Liquids: leachables, extractables, light transmission 5. Source of supply and suppliers address	
3.2.P.8	**3.2.P.8.1 Stability (Finished Dosage Form)** 1. Stability Protocol submitted 2. Expiration Dating Period **3.2.P.8.2 Post-approval Stability and Conclusion** Post Approval Stability Protocol and Commitments **3.2.P.8.3 Stability Data** 1. Accelerated stability data a. four (4) time points 0,1,2,3 **-OR-** b. three (3) time points 0,3,6 (if 3 time points for accelerated stability data are submitted then provide 3 exhibit batches along with 12 months of room temperature stability data –Refer to Guidance for Industry Q1A(R2) Stability Testing of New Drug Substances and Products November 2003, Section B) 2. Batch numbers on stability records the same as the test batch	

MODULE 3: 3.2.R REGIONAL INFORMATION (Drug Substance)

		COMMENT (S)
3.2.R Drug Substance	**3.2.R.1.S Executed Batch Records for drug substance (if available)** **3.2.R.2.S Comparability Protocols** **3.2.R.3.S Methods Validation Package** Methods Validation Package (3 copies for paper and N/A for E-Submissions) (Required for Non-USP drugs)	

MODULE 3: 3.2.R REGIONAL INFORMATION (Drug Product)

		COMMENT (S)
3.2.R Drug Product	**3.2.R.1.P.1** **Executed Batch Records** Copy of Executed Batch Record with Equipment Specified, including Packaging Records (Packaging and Labeling Procedures) Batch Reconciliation and Label Reconciliation a. Theoretical Yield b. Actual Yield c. Packaged Yield Bulk Package Reconciliation required if bulk packaging is used to achieve the minimum package requirement. Provide the following information in their respective sections: a. Bulk Package Label (1.14.1) b. Bulk Package Stability (accelerated stability data [0,1,2,3] **–OR-** room temperature [0,3,6]) (3.2.P.8) c. Bulk Package Container and Closure information (3.2.P.7) **3.2.R.1.P.2 Information on Components** **3.2.R.2.P Comparability Protocols** **3.2.R.3.P Methods Validation Package** Methods Validation Package (3 copies for paper and N/A for E-Submissions) (Required for Non-USP drugs)	

MODULE 5: CLINICAL STUDY REPORTS

		COMMENT (S)
5.2	**Tabular Listing of Clinical Studies**	
5.3.1 (complete study data)	**Bioavailability/Bioequivalence** **1. Formulation data same?** a. Comparison of all Strengths (proportionality of multiple strengths) b. Parenterals, Ophthalmics, Otics and Topicals (21 CFR 314.94 (a)(9)(iii)-(v) **2. Lot Numbers and strength of Products used in BE Study(ies)** **3. Study Type: IN-VIVO PK STUDY(IES)** (Continue with the appropriate study type box below)	
	5.3.1.2 Comparative BA/BE Study Reports **Case Report Forms** should be placed under the study to which they pertain, and appropriately tagged. Refer to The eCTD Backbone File Specification for Study Tagging //www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/UCM163560.pdf See Module 2: 2.7 Clinical Summary for placement of BA/BE Summary Tables 9 – 16.	

5.4	**Literature References**	
	Possible Study Types:	
Study Type	**IN-VIVO BE STUDY(IES) with PK ENDPOINTS (**i.e., fasting/fed/sprinkle) 1. Study(ies) meets BE criteria (90% CI of 80-125, C max, AUC) 2. EDR Email: Data Files Submitted 3. In-Vitro Dissolution	
Study Type	**IN-VIVO BE STUDY with CLINICAL ENDPOINTS** 1. Properly defined BE endpoints (eval. by Clinical Team) 2. Summary results meet BE criteria: 90% CI of the proportional difference in success rate between test and reference must be within (-0.20, +0.20) for a binary/dichotomous endpoint. For a continuous endpoint, the test/reference ratio of the mean result must be within (0.80,1.25) 3. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) 4. EDR Email: Data Files Submitted	
Study Type	**IN-VITRO BE STUDY(IES) (**i.e., in vitro binding assays) 1. Study(ies) meets BE criteria (90% CI of 80-125) 2. EDR Email: Data Files Submitted 3. In-Vitro Dissolution	
Study Type	**NASALLY ADMINISTERED DRUG PRODUCTS** **1. <u>Solutions</u> (Q1/Q2 sameness)** a. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming) **2. <u>Suspensions</u> (Q1/Q2 sameness):** a. In-Vivo PK Study 1. Study(ies) meets BE Criteria (90% CI of 80-125, C max, AUC) 2. EDR Email: Data Files Submitted b. In-Vivo BE Study with Clinical End Points 1. Properly defined BE endpoints (eval. by Clinical Team) 2. Summary results meet BE criteria (90% CI within +/- 20% of 80-125) 3. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) 4. EDR Email: Data Files Submitted c. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming)	
Study Type	**IN-VIVO BE STUDY(IES) with PD ENDPOINTS** (e.g., topical corticosteroid vasoconstrictor studies) 1. Pilot Study (determination of ED50) 2. Pivotal Study (study meets BE criteria 90%CI of 80-125)	
Study Type	**TRANSDERMAL DELIVERY SYSTEMS** 1. <u>In-Vivo PK Study</u> a. Study(ies) meet BE Criteria (90% CI of 80-125, C max, AUC) b. In-Vitro Dissolution c. EDR Email: Data Files Submitted 2. <u>Adhesion Study</u> 3. <u>Skin Irritation/Sensitization Study</u>	

UPDATE FILING CHECKLIST LOG

QUARTER/YEAR	DATE OF POSTING
INITIAL REVISION	1/2011
Q1-2011	3/2011
Q2-2011	6/2011
Q3-2011	9/2011
Q4-2011	12/ 2011