CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

206307Orig1s000

OTHER REVIEW(S)

NDA 206-307 PMC Development: Product Quality (CMC-Biopharmaceutics)

This template should be completed by ONDQA's Biopharmaceutics or CMC reviewer. For *each* type of CMC or Biopharmaceutics PMC in the Action Package (See #4 for a list of PMC types).

NDA Product Name:	NDA 206-307 Finafloxacin Otic Suspension
PMC # 1 Description:	The dissolution method development report with the complete data should be submitted within 6 months from NDA's action date. The report should include the following information: a. Solubility and pH data for the drug substance in the proposed dissolution medium; b. Detailed description of the dissolution test being proposed for the evaluation of the proposed drug product and the developmental parameters used to select the proposed dissolution method as the optimal test for the proposed product (i.e., selection of the equipment/ apparatus, in vitro dissolution media, agitation/rotation speed, pH, assay, sink conditions, etc.). The dissolution profile should be complete (i.e., 10, 15, 20, 30, 45, & 60 minutes) and cover at least (b)(4)% of drug release of the label amount or whenever a plateau (i.e., no increase over 3 consecutive time-points) is reached. The use of USP Apparatus 2 with mini-vessels (50-200 ml volume) should be considered for the dissolution testing of this otic suspension drug product. c. Provide the complete dissolution profile data (individual, mean, SD, profiles) for the proposed drug product. The dissolution data should be reported as the cumulative percentage of drug dissolved with time (the percentage is based on the product's label claim); and d. Include the complete dissolution data for the testing conducted to demonstrate the discriminating capability of the selected dissolution test as well as the supportive validation data for the dissolution method (i.e., method robustness, etc.) and analytical method (precision, accuracy, linearity, stability, etc.).
	Final Report Submission: 05/2015
PMC # 2 Description:	A proposal for the dissolution acceptance criterion and the complete supportive data should be submitted within 12 months from NDA's action date. The selection of the proposed acceptance criterion should be based on the dissolution profile data (i.e., 10, 15, 20, 30, 45, and 60 minutes; N=12) from a minimum of 12 commercial batches and the stability data for registration batches. It is noted that the selection of the specification time point should be where Q = (b)(4)% dissolution occurs.

Proposal Submission:	08/2015
NA Final Report Submission	11/2015

1. During application review, explain why this issue is appropriate for a PMC instead of a pre-approval requirement. Check reason below and describe.

   ☐ Need for drug (unmet need/life-threatening condition)
   ☐ Long-term data needed (e.g., stability data)
   ☐ Only feasible to conduct post-approval
   ☐ Improvements to methods
   ☐ Theoretical concern
   ☐ Manufacturing process analysis
   ☒ Other (Dissolution acceptance criteria)

   Resolution of interim dissolution acceptance criteria are generally handled as PMCs and not PMRs

2. Describe the particular review issue and the goal of the study.

   The objective of the PMC is to ensure that the appropriate dissolution method and acceptance criterion have been established for this drug product.

3. What type of study is agreed upon (describe and check type below)?

   Select only one. Fill out a new sheet for each type of PMC study.

   ☒ Dissolution testing (dissolution acceptance criteria)
   ☐ Assay
   ☐ Sterility
   ☐ Potency
   ☐ Product delivery
   ☐ Drug substance characterization
   ☐ Intermediates characterization
   ☐ Impurity characterization
   ☐ Reformulation
   ☐ Manufacturing process issues
   ☐ Other

Describe the agreed-upon study:

4. To be completed by ONDQA/OBP Manager:

   ☒ Does the study meet criteria for PMCs?
   ☒ Are the objectives clear from the description of the PMC?
   ☒ Has the applicant adequately justified the choice of schedule milestone dates?
   ☒ Has the applicant had sufficient time to review the PMCs, ask questions, determine feasibility, and contribute to the development process?

PMR/PMC Development Coordinator:

☒ *This PMC has been reviewed for clarity and consistency, and is necessary to further refine the safety, efficacy, or optimal use of a drug, or to ensure consistency and reliability of drug quality.*

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/s/

BANU S ZOLNIK
11/21/2014

ANGELICA DORANTES
11/21/2014

FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion

****Pre-decisional Agency Information****

Memorandum

Date: October 10, 2014

To: Mike Puglisi, Regulatory Project Manager
Division of Transplant and Ophthalmic Products (DTOP)

From: Christine Corser, PharmD, RAC, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

Subject: NDA 206307
Finafloxacin otic suspension 0.3%

As requested in your consult dated August 21, 2014, the Office of Prescription Drug Promotion (OPDP) has reviewed the proposed labeling for Finafloxacin otic suspension 0.3%.

OPDP's comments are based on the substantially complete version of the labeling titled, "NDA 206307 Draft PI.doc" which was received via email from DTOP on October 6, 2014. OPDP's comments are provided in the attached, clean version of the labeling.

OPDP notes that a proprietary name has not been approved at this time. OPDP further notes that proposed carton and container labeling have not been submitted by the drug sponsor at this time. Please inform OPDP once this labeling is ready for review.

Thank you for the opportunity to provide comments on this PI.

If you have any questions about OPDP's comments, please contact Christine Corser at 6-2653 or at christine.corser@fda.hhs.gov.

7 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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/s/

CHRISTINE G CORSER
10/10/2014

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

CLINICAL INSPECTION SUMMARY

DATE: October 6, 2014

TO: Michael Puglisi, Regulatory Project Manager
Rhea Lloyd, M.D., Medical Officer
William Boyd, M.D., Medical Team Leader
Division of Transplant and Ophthalmology Products

FROM: Roy Blay, Ph.D.
Good Clinical Practice Assessment Branch
Division of Good Clinical Practice Compliance
Office of Scientific Investigations

THROUGH: Janice Pohlman, M.D., M.P.H
Team Leader
Good Clinical Practice Assessment Branch
Division of Good Clinical Practice Compliance
Office of Scientific Investigations

Kassa Ayalew, M.D., M.P.H.
Branch Chief
Good Clinical Practice Assessment Branch
Division of Good Clinical Practice Compliance
Office of Scientific Investigations

SUBJECT: Evaluation of Clinical Inspections

NDA: 206307

APPLICANT: Alcon Research, Ltd.

DRUG: Finafloxacin otic suspension, 0.3%

NME: Yes

THERAPEUTIC CLASSIFICATION: Standard Review

INDICATION: Treatment of acute otitis externa in subjects (b) (4) of age or older.

CONSULTATION REQUEST DATE: May 6, 2014
CLINICAL INSPECTION SUMMARY DATE: October 8, 2014
DIVISION ACTION GOAL DATE: November 21, 2014
PDUFA DATE: December 25, 2014

I. BACKGROUND:

The Applicant submitted this NDA to support the use of finafloxacin otic suspension, 0.3% for the treatment of acute otitis externa in subjects (b) (4) of age or older.

The identical pivotal studies C-10-018 and C-10-019 entitled, "Safety and Efficacy Evaluation of Topical AL-60371 Otic Suspension, 0.3% in the Treatment of Acute Otitis Externa", were inspected in support of this application.

Drs. Calcagno's and Schwartz's clinical sites were selected for inspection because they were among the highest enrolling sites.

II. RESULTS (by Site):

Name of CI, Location	Protocol #/ Site #/ # of Subjects (enrolled)	Inspection Dates	Final Classification
Frank A. Calcagno CYn3ergy Research 24850 Southeast Stark Street, Suite #180 Gresham, OR 97030	C-10-018/ 5019/ 39	6-13 Aug 2014	NAI
Richard H. Schwartz, M.D. Advanced Pediatrics 100 East Street South East, Suite #301 Vienna, VA 22180	C-10-019/ 2234/ 43	18-19 Aug 2014	NAI

Key to Classifications
NAI = No deviation from regulations.
VAI = Deviation(s) from regulations.
OAI = Significant deviations from regulations. Data unreliable.
Pending = Preliminary classification based on information in Form FDA 483 or preliminary communication with the field; EIR has not been received from the field or complete review of EIR is pending.

1. Frank A. Calcagno
   CYn3ergy Research
   24850 Southeast Stark Street, Suite #180
   Gresham, OR 97030

   a. **What was inspected:** At this site for Protocol C-10-018, 42 subjects were screened, 39 subjects were randomized to treatment, and 23 subjects completed the study. Of the 16 subjects discontinuing the study, seven were treated with finafloxacin and nine were treated with vehicle. All informed consent documents for all enrolled subjects were reviewed. Other records reviewed included FDA 1572s, financial disclosure forms, IRB approvals, training certifications, eligibility criteria, adverse events, and drug accountability.

b. General observations/commentary: Dr. Calcagno did not insert otowicks into Subjects 1440, 1443, 1446, and 1455, despite these subjects having an ear canal patency of 50% or less and the protocol's requirement that otowicks be inserted in such cases. Dr. Calcagno's understanding was that insertion of otowicks was at the investigator's discretion. The monitor provided re-education on this protocol requirement. A Form FDA 483 was not issued at the conclusion of the inspection. Review of the records noted above revealed no significant discrepancies or regulatory violations.

c. Assessment of data integrity: The study appears to have been conducted adequately, and the data generated by this site appear acceptable in support of the respective indication.

2. Richard H. Schwartz, M.D.
   Advanced Pediatrics
   100 East Street South East, Suite #301
   Vienna, VA 22180

a. What was inspected: At this site for Protocol C-10-019, 43 subjects were enrolled, 24 subjects discontinued the study early, and 19 subjects completed the study. Of the 24 subjects discontinuing, seven were treated with finafloxacin and the remaining 17 subjects were treated with vehicle. Informed consent forms were reviewed for all 43 enrolled subjects. The complete records for 22 randomly selected enrolled subjects were reviewed. Records reviewed included FDA 1572s, financial disclosure forms, delegation of responsibilities, training certifications, sponsor, monitor and IRB correspondence, subject eligibility, source records, study procedures, visit dates, protocol deviations, progress notes, dosing records, test article accountability and storage documentation, and primary and secondary efficacy endpoints. Source records were compared against sponsor line listings.

b. General observations/commentary: A Form FDA 483 was not issued at the conclusion of the inspection Review of the records noted above revealed no significant discrepancies or regulatory violations.

c. Assessment of data integrity: The study appears to have been conducted adequately, and the data generated by this site appear acceptable in support of the respective indication.

III. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

The clinical sites of Drs. Calcagno and Schwartz were inspected in support of this NDA. Neither Dr. Calcagno nor Dr. Schwartz was issued a Form FDA 483, and the final classification of these inspections was No Action Indicated (NAI). The data generated by these clinical sites appear adequate in support of the respective indication.

{See appended electronic signature page}

Roy Blay, Ph.D.
Good Clinical Practice Assessment Branch
Division of Good Clinical Practice Compliance
Office of Scientific Investigations

CONCURRENCE:

{See appended electronic signature page}

Janice Pohlman, M.D., M.P.H.
Team Leader
Good Clinical Practice Assessment Branch
Division of Good Clinical Practice Compliance
Office of Scientific Investigations

{See appended electronic signature page}

Kassa Ayalew, M.D., M.P.H.
Acting Branch Chief
Good Clinical Practice Assessment Branch
Division of Good Clinical Practice Compliance
Office of Scientific Investigation

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/s/

ROY A BLAY
10/07/2014

JANICE K POHLMAN
10/07/2014

KASSA AYALEW
10/07/2014

LABEL AND LABELING REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	September 12, 2014
Requesting Office or Division:	Division of Transplant and Ophthalmology Products (DTOP)
Application Type and Number:	NDA 206307
Product Name and Strength:	Finafloxacin Otic Suspension, 0.3%
Product Type:	Single Ingredient
Rx or OTC:	Rx
Applicant/Sponsor Name:	Alcon Laboratories
Submission Date:	May 8, 2014
OSE RCM #:	2014-942
DMEPA Primary Reviewer:	Rachna Kapoor, PharmD
DMEPA Team Leader:	Yelena Maslov, PharmD

1 REASON FOR REVIEW

This review evaluates the proposed container label, carton labeling, patient instructions for use and prescriber information labeling for Finafloxacin Otic Suspension, NDA 206307, for areas of vulnerability that could lead to medication errors.

2 MATERIALS REVIEWED

We considered the materials listed in Table 1 for this review. The Appendices provide the methods and results for each material reviewed.

Table 1. Materials Considered for this Label and Labeling Review

Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
FDA Adverse Event Reporting System (FAERS)	B (N/A)
Previous DMEPA Reviews	C
Human Factors Study	D (N/A)
ISMP Newsletters	E (N/A)
Other	F (N/A)
Labels and Labeling	G

N/A=not applicable for this review

3 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

DMEPA did not identify any major issues with container label, carton labeling, patient instructions for use or prescriber information labeling. As a result, we will be providing routine recommendations regarding the route of administration and ancillary statements placement in our conclusion and recommendations section.

4 CONCLUSION & RECOMMENDATIONS

DMEPA concludes that the proposed container label and carton labeling can be improved to increase the prominence of important information on the label to promote the safe use of the product.

Additionally, DMEPA concludes that the patient instructions for use and prescriber information labeling are acceptable. We have no additional comments for the patient instructions for use or prescriber information labeling at this time.

Based on this review, DMEPA recommends the following be implemented prior to the approval of this NDA:

4.1 RECOMMENDATIONS FOR THE APPLICANT/SPONSOR

A. Container Label (sample only)
    i. Add the statement "For Topical Use in the Ear Only" to highlight the correct route of administration. We recommend this revision to help prevent wrong route of administration errors.

B. Carton Labeling (including sample)
    i. Relocate the statement "Shake well before using" to the principal display panel as this statement provides important information regarding the correct use of the product.

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Finafloxacin that Alcon Laboratories submitted on May 8, 2014.

Table 2. Relevant Product Information for Finafloxacin	
Active Ingredient	Finafloxacin
Indication	Treatment of acute otitis externa, with or without an otowick, in pediatric (age (b) (4) and older), adult and elderly patients
Route of Administration	Otic
Dosage Form	Otic suspension
Strength	0.3%
Dose and Frequency	Instill four drops into the affected ear twice daily for seven days. For patients requiring use of an otowick, the initial dose can be doubled (to eight drops), followed by four drops instilled into the affected ear twice daily for seven days
How Supplied	5 mL fill in an 8 mL bottle; 0.5 mL fill in a 4 mL bottle (sample)
Storage	Store at 2° – 25°C (36° – 77°F). Do not freeze. Shake well before use

APPENDIX C. PREVIOUS DMEPA REVIEWS

C.1 Methods

We searched the L:Drive on September 9, 2014 using the term Finafloxacin to identify reviews previously performed by DMEPA.

C.2 Results

A proprietary name review was completed on July 24, 2014 for Finafloxacin under the same NDA 206307 (Panorama#2014-17319).

APPENDIX G. LABELS AND LABELING

G.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[1] along with postmarket medication error data, we reviewed the following Finafloxacin labels and labeling submitted by Alcon Laboratories on May 8, 2014.

- Container Label
- Carton Labeling
- Patient Instructions for Use
- Package Insert (no image included)

G.2 Label and Labeling Images

Container Label

(b) (4)

Container Label (sample)

(b) (4)

[1] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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/s/

RACHNA KAPOOR
09/12/2014

YELENA L MASLOV
09/15/2014

PEDIATRIC EXCLUSIVITY DETERMINATION CHECKLIST

PART I - TO BE COMPLETED BY THE REVIEWING DIVISION.

Date of Written Request from FDA: **02/22/2013**
Application Written Request was made to: **IND 110,576**
Timeframe Noted in Written Request for Submission of Studies: **On or before June 30, 2016**
NDA: **206307 SDN-001**
Sponsor: **Alcon Research, Ltd.**
Generic/Non-proprietary Name: **finafloxacin otic suspension** Tradename: **To be determined**
Strength: **0.3%** Dosage Form/Route: **otic suspension/ topical**
Date of Receipt of Reports of Studies: **04/25/2014**
Pediatric Exclusivity Determination Due Date (90 or 180 days from the date of studies receipt): **10/22/14**

Was a formal Written Request made for the pediatric studies submitted?	Y _X__	N ___
Were the studies submitted after the Written Request?	Y _X_	N ___
Were the reports submitted as a supplement or amendment to an NDA/BLA, or original NDA/BLA?	Y _X__	N ___
Was the timeframe noted in the Written Request for submission of studies met?	Y _X_	N ___
Were the studies reported in accordance with the requirements for filing? (If No, then the next two questions may not apply and should remain unanswered)	Y _X_	N ___
Were the studies conducted in accordance with commonly accepted scientific principles and protocols?	Y _X__	N ___
Did the studies fairly respond to the Written Request?	Y _X__	N ___

SIGNED _____ **DATE** 8/11/14
(Reviewing Medical Officer)

SIGNED _____ MD **DATE** 8/11/14
(Deputy Division Director)

Do not enter in DARRTS - FORWARD TO PEDIATRIC EXCLUSIVITY BOARD via Pediatric and Maternal Health Staff PM

PART II - TO BE COMPLETED BY THE PEDIATRIC EXCLUSIVITY BOARD

Pediatric Exclusivity ✓ **Granted*** ___ **Denied**

*Additional Information

1. Pediatric Exclusivity was granted to:	Single Moiety X	Combination ___
2. The period of Pediatric Exclusivity granted:	First X	Second ___
3. Was Written Request originally issued since FDAAA (9/27/07)?	Yes X (see 21 U.S.C. 355a(c)(2))	No ___

SIGNED _____ **DATE** 8/25/2014

(Revised October 3, 2013)

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/s/

MATTHEW A BACHO
08/25/2014

LYNNE P YAO
08/25/2014

RPM FILING REVIEW

(Including Memo of Filing Meeting)

To be completed for all new NDAs, BLAs, and Efficacy Supplements [except SE8 (labeling change with clinical data) and SE9 (manufacturing change with clinical data]

Application Information		
NDA # 206307 BLA#	NDA Supplement #:S- BLA Supplement #	Efficacy Supplement Type SE-
Proprietary Name: to be determined Established/Proper Name: finafloxacin Dosage Form: otic suspension Strengths: 0.3%		
Applicant: Alcon Research, Ltd. Agent for Applicant (if applicable):		
Date of Application: April 25, 2014 Date of Receipt: April 25, 2014 Date clock started after UN: N/A		
PDUFA Goal Date: December 25, 2014	Action Goal Date (if different):	
Filing Date: June 24, 2014	Date of Filing Meeting: June 3, 2014	
Chemical Classification: (1,2,3 etc.) (original NDAs only) 1		
Proposed indication: Treatment of acute otitis externa		

Type of Original NDA: AND (if applicable) Type of NDA Supplement: ***If 505(b)(2): Draft the "505(b)(2) Assessment" review found at:*** ***http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/UCM027499.***	☒ 505(b)(1) ☐ 505(b)(2) ☐ 505(b)(1) ☐ 505(b)(2)
Type of BLA ***If 351(k), notify the OND Therapeutic Biologics and Biosimilars Team***	☐ 351(a) ☐ 351(k)
Review Classification: ***If the application includes a complete response to pediatric WR, review classification is Priority.*** ***If a tropical disease priority review voucher or pediatric rare disease priority review voucher was submitted, review classification is Priority.***	☐ Standard ☒ Priority ☐ Tropical Disease Priority Review Voucher submitted ☐ Pediatric Rare Disease Priority Review Voucher submitted
Resubmission after withdrawal? ☐	Resubmission after refuse to file? ☐
Part 3 Combination Product? ☐ ***If yes, contact the Office of Combination Products (OCP) and copy them on all Inter-Center consults***	☐ Convenience kit/Co-package ☐ Pre-filled drug delivery device/system (syringe, patch, etc.) ☐ Pre-filled biologic delivery device/system (syringe, patch, etc.) ☐ Device coated/impregnated/combined with drug ☐ Device coated/impregnated/combined with biologic ☐ Separate products requiring cross-labeling ☐ Drug/Biologic ☐ Possible combination based on cross-labeling of separate products ☐ Other (drug/device/biological product)

☐ Fast Track Designation ☐ Breakthrough Therapy Designation ***(set the submission property in DARRTS and notify the CDER Breakthrough Therapy Program Manager)*** ☐ Rolling Review ☐ Orphan Designation ☐ Rx-to-OTC switch, Full ☐ Rx-to-OTC switch, Partial ☐ Direct-to-OTC Other:	☐ PMC response ☐ PMR response: ☐ FDAAA [505(o)] ☐ PREA deferred pediatric studies [21 CFR 314.55(b)/21 CFR 601.27(b)] ☐ Accelerated approval confirmatory studies (21 CFR 314.510/21 CFR 601.41) ☐ Animal rule postmarketing studies to verify clinical benefit and safety (21 CFR 314.610/21 CFR 601.42)

Collaborative Review Division (*if OTC product*): N/A

List referenced IND Number(s): IND 110576

Goal Dates/Product Names/Classification Properties	**YES**	**NO**	**NA**	**Comment**
PDUFA and Action Goal dates correct in tracking system? ***If no, ask the document room staff to correct them immediately. These are the dates used for calculating inspection dates.***	☒	☐		
Are the proprietary, established/proper, and applicant names correct in tracking system? ***If no, ask the document room staff to make the corrections. Also, ask the document room staff to add the established/proper name to the supporting IND(s) if not already entered into tracking system.***	☒	☐		
Is the review priority (S or P) and all appropriate classifications/properties entered into tracking system (e.g., chemical classification, combination product classification, 505(b)(2), orphan drug)? ***For NDAs/NDA supplements, check the New Application and New Supplement Notification Checklists for a list of all classifications/properties at:*** ***http://inside.fda.gov:9003/CDER/OfficeofBusinessProcessSupport/ucm163969.htm*** ***If no, ask the document room staff to make the appropriate entries.***	☒	☐	☐	
Application Integrity Policy	**YES**	**NO**	**NA**	**Comment**
Is the application affected by the Application Integrity Policy (AIP)? ***Check the AIP list at:*** ***http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm***	☐	☒		
If yes, explain in comment column.				
If affected by AIP, has OC/OMPQ been notified of the submission? **If yes,** date notified:	☐	☐		
User Fees	**YES**	**NO**	**NA**	**Comment**
Is Form 3397 (User Fee Cover Sheet) included with authorized signature?	☒	☐		

User Fee Status ***If a user fee is required and it has not been paid (and it is not exempted or waived), the application is unacceptable for filing following a 5-day grace period. Review stops. Send Unacceptable for Filing (UN) letter and contact user fee staff.***	Payment for this application: ☒ Paid ☐ Exempt (orphan, government) ☐ Waived (e.g., small business, public health) ☐ Not required
If the firm is in arrears for other fees (regardless of whether a user fee has been paid for this application), the application is unacceptable for filing (5-day grace period does not apply). Review stops. Send UN letter and contact the user fee staff.	Payment of other user fees: ☒ Not in arrears ☐ In arrears

505(b)(2) **(NDAs/NDA Efficacy Supplements only)**	**YES**	**NO**	**NA**	**Comment**
Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA?	☐	☐	☐	
Is the application for a duplicate of a listed drug whose only difference is that the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action is less than that of the reference listed drug (RLD)? **[see 21 CFR 314.54(b)(1)].**	☐	☐	☐	
Is the application for a duplicate of a listed drug whose only difference is that the rate at which the proposed product's active ingredient(s) is absorbed or made available to the site of action is unintentionally less than that of the listed drug **[see 21 CFR 314.54(b)(2)]?** ***If you answered yes to any of the above questions, the application may be refused for filing under 21 CFR 314.101(d)(9). Contact the 505(b)(2) review staff in the Immediate Office of New Drugs***	☐	☐	☐	
Is there unexpired exclusivity on any drug product containing the active moiety (e.g., 5-year, 3-year, orphan, or pediatric exclusivity)? ***Check the Electronic Orange Book at:*** ***http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm*** **If yes**, please list below:	☐	☐	☐	

Application No.	Drug Name	Exclusivity Code	Exclusivity Expiration

If there is unexpired, 5-year exclusivity remaining on the active moiety for the proposed drug product, a 505(b)(2) application cannot be submitted until the period of exclusivity expires (unless the applicant provides paragraph IV patent certification; then an application can be submitted four years after the date of approval.) Pediatric exclusivity will extend both of the timeframes in this provision by 6 months. 21 CFR 314.108(b)(2). Unexpired, 3-year exclusivity may block the approval but not the submission of a 505(b)(2) application.

Exclusivity	**YES**	**NO**	**NA**	**Comment**
Does another product (same active moiety) have orphan exclusivity for the same indication? ***Check the Orphan Drug***	☐	☒		

Designations and Approvals list at: *http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm*				
If another product has orphan exclusivity, is the product considered to be the same product according to the orphan drug definition of sameness **[see 21 CFR 316.3(b)(13)]**? ***If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy***	☐	☐	☒	
Has the applicant requested 5-year or 3-year Waxman-Hatch exclusivity? ***(NDAs/NDA efficacy supplements only)*** **If yes**, # years requested: 5 years ***Note:*** *An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.*	☒	☐	☐	
Is the proposed product a single enantiomer of a racemic drug previously approved for a different therapeutic use (***NDAs only***)?	☐	☒	☐	
If yes, did the applicant: (a) elect to have the single enantiomer (contained as an active ingredient) not be considered the same active ingredient as that contained in an already approved racemic drug, and/or (b): request exclusivity pursuant to section 505(u) of the Act (per FDAAA Section 1113)? ***If yes, contact the Orange Book Staff (CDER-Orange Book Staff).***	☐	☐	☒	
For BLAs: Has the applicant requested 12-year exclusivity under section 351(k)(7) of the PHS Act? ***If yes, notify Marlene Schultz-DePalo, OBP Biosimilars RPM*** ***Note****: Exclusivity requests may be made for an original BLA submitted under Section 351(a) of the PHS Act (i.e., a biological reference product). A request may be located in Module 1.3.5.3 and/or other sections of the BLA and may be included in a supplement (or other correspondence) if exclusivity has not been previously requested in the original 351(a) BLA. An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.*	☐	☐	☐	

Format and Content	
Do not check mixed submission if the only electronic component is the content of labeling (COL).	☐ All paper (except for COL) ☒ All electronic ☐ Mixed (paper/electronic) ☒ CTD ☐ Non-CTD ☐ Mixed (CTD/non-CTD)
If mixed (paper/electronic) submission, which parts of the application are submitted in electronic format?	

Overall Format/Content	YES	NO	NA	Comment
If electronic submission, does it follow the eCTD guidance?[1] **If not,** explain (e.g., waiver granted).	☒	☐	☐	
Index: Does the submission contain an accurate comprehensive index?	☒	☐		
Is the submission complete as required under 21 CFR 314.50 (*NDAs/NDA efficacy supplements*) or under 21 CFR 601.2 (*BLAs/BLA efficacy supplements*) including: ☒ legible ☒ English (or translated into English) ☒ pagination ☒ navigable hyperlinks (electronic submissions only) **If no**, explain.	☒	☐		
BLAs only: Companion application received if a shared or divided manufacturing arrangement? **If yes**, BLA #	☐	☐	☐	

Forms and Certifications
Electronic *forms and certifications with electronic signatures (scanned, digital, or electronic – similar to DARRTS, e.g., /s/) are acceptable. Otherwise,* ***paper*** *forms and certifications with hand-written signatures must be included.* ***Forms*** *include: user fee cover sheet (3397), application form (356h), patent information (3542a), financial disclosure (3454/3455), and clinical trials (3674);* ***Certifications*** *include: debarment certification, patent certification(s), field copy certification, and pediatric certification.*

Application Form	YES	NO	NA	Comment
Is form FDA 356h included with authorized signature per 21 CFR 314.50(a)? ***If foreign applicant, a U.S. agent must sign the form [see 21 CFR 314.50(a)(5)].***	☒	☐		
Are all establishments and their registration numbers listed on the form/attached to the form?	☒	☐	☐	
Patent Information (NDAs/NDA efficacy supplements only)	**YES**	**NO**	**NA**	**Comment**
Is patent information submitted on form FDA 3542a per 21 CFR 314.53(c)?	☒	☐	☐	
Financial Disclosure	**YES**	**NO**	**NA**	**Comment**
Are financial disclosure forms FDA 3454 and/or 3455	☒	☐		

[1] http://www fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072349.pdf

included with authorized signature per 21 CFR 54.4(a)(1) and (3)? ***Forms must be signed by the APPLICANT, not an Agent [see 21 CFR 54.2(g)].*** ***Note:*** *Financial disclosure is required for bioequivalence studies that are the basis for approval.*				
Clinical Trials Database	**YES**	**NO**	**NA**	**Comment**
Is form FDA 3674 included with authorized signature? ***If yes, ensure that the application is also coded with the supporting document category, "Form 3674."*** ***If no, ensure that language requesting submission of the form is included in the acknowledgement letter sent to the applicant***	☒	☐		
Debarment Certification	**YES**	**NO**	**NA**	**Comment**
Is a correctly worded Debarment Certification included with authorized signature? ***Certification is not required for supplements if submitted in the original application; If foreign applicant, <u>both</u> the applicant and the U.S. Agent must sign the certification [per Guidance for Industry: Submitting Debarment Certifications].*** ***Note:*** *Debarment Certification should use wording in FD&C Act Section 306(k)(1) i.e., "[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application." Applicant may not use wording such as, "To the best of my knowledge…"*	☒	☐	☐	
Field Copy Certification (NDAs/NDA efficacy supplements only)	**YES**	**NO**	**NA**	**Comment**
For paper submissions only: Is a Field Copy Certification (that it is a true copy of the CMC technical section) included? ***Field Copy Certification is not needed if there is no CMC technical section or if this is an electronic submission (the Field Office has access to the EDR)*** ***If maroon field copy jackets from foreign applicants are received, return them to CDR for delivery to the appropriate field office.***	☐	☐	☒	
Controlled Substance/Product with Abuse Potential	**YES**	**NO**	**NA**	**Comment**
<u>For NMEs:</u> Is an Abuse Liability Assessment, including a proposal for scheduling, submitted per 21 CFR 314.50(d)(5)(vii)? ***If yes,*** *date consult sent to the Controlled Substance Staff:* <u>For non-NMEs</u>: *Date of consult sent to Controlled Substance Staff*:	☐	☐	☒	

Pediatrics	YES	NO	NA	Comment
PREA Does the application trigger PREA? ***If yes, notify PeRC RPM (PeRC meeting is required)***[2] ***Note**: NDAs/BLAs/efficacy supplements for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration trigger PREA. All waiver & deferral requests, pediatric plans, and pediatric assessment studies must be reviewed by PeRC prior to approval of the application/supplement.*	☒	☐		
If the application triggers PREA, are the required pediatric assessment studies or a full waiver of pediatric studies included?	☒	☐	☐	
If studies or full waiver not included, is a request for full waiver of pediatric studies OR a request for partial waiver and/or deferral with a pediatric plan included? ***If no, request in 74-day letter***	☐	☐	☒	
If a request for full waiver/partial waiver/deferral is included, does the application contain the certification(s) required by FDCA Section 505B(a)(3) and (4)? ***If no, request in 74-day letter***	☐	☐	☒	
BPCA (NDAs/NDA efficacy supplements only): Is this submission a complete response to a pediatric Written Request? ***If yes, notify Pediatric Exclusivity Board RPM (pediatric exclusivity determination is required)***[3]	☒	☐		
Proprietary Name	**YES**	**NO**	**NA**	**Comment**
Is a proposed proprietary name submitted? ***If yes, ensure that the application is also coded with the supporting document category, "Proprietary Name/Request for Review."***	☒	☐	☐	
REMS	**YES**	**NO**	**NA**	**Comment**
Is a REMS submitted? ***If yes, send consult to OSE/DRISK and notify OC/ OSI/DSC/PMSB via the CDER OSI RMP mailbox***	☐	☒	☐	
Prescription Labeling	☐ **Not applicable**			
Check all types of labeling submitted.	☒ Package Insert (PI) ☐ Patient Package Insert (PPI) ☐ Instructions for Use (IFU) ☐ Medication Guide (MedGuide)			

[2] http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/PediatricandMaternalHealthStaff/ucm027829.htm
[3] http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/PediatricandMaternalHealthStaff/ucm027837.htm

	☒ Carton labels ☒ Immediate container labels ☐ Diluent ☐ Other (specify)			
	YES	**NO**	**NA**	**Comment**
Is Electronic Content of Labeling (COL) submitted in SPL format? ***If no, request applicant to submit SPL before the filing date.***	☒	☐		
Is the PI submitted in PLR format?[4]	☒	☐		
If PI not submitted in PLR format, was a waiver or deferral requested before the application was received or in the submission? **If requested before application was submitted**, what is the status of the request? ***If no waiver or deferral, request applicant to submit labeling in PLR format before the filing date.***	☐	☐	☒	
All labeling (PI, PPI, MedGuide, IFU, carton and immediate container labels) consulted to OPDP?	☒	☐	☐	
MedGuide, PPI, IFU (plus PI) consulted to OSE/DRISK? (*send WORD version if available*)	☐	☐	☒	
Carton and immediate container labels, PI, PPI sent to OSE/DMEPA and appropriate CMC review office (OBP or ONDQA)?	☒	☐	☐	
OTC Labeling	☒ **Not Applicable**			
Check all types of labeling submitted.	☐ Outer carton label ☐ Immediate container label ☐ Blister card ☐ Blister backing label ☐ Consumer Information Leaflet (CIL) ☐ Physician sample ☐ Consumer sample ☐ Other (specify)			
	YES	**NO**	**NA**	**Comment**
Is electronic content of labeling (COL) submitted? ***If no, request in 74-day letter.***	☐	☐		
Are annotated specifications submitted for all stock keeping units (SKUs)? ***If no, request in 74-day letter.***	☐	☐	☐	
If representative labeling is submitted, are all represented SKUs defined?	☐	☐	☐	

[4] http://inside fda.gov:9003/CDER/OfficeofNewDrugs/StudyEndpointsandLabelingDevelopmentTeam/ucm025576.htm

If no, request in 74-day letter.				
All labeling/packaging, and current approved Rx PI (if switch) sent to OSE/DMEPA?	☐	☐	☐	
Other Consults	**YES**	**NO**	**NA**	**Comment**
Are additional consults needed? (e.g., IFU to CDRH; QT study report to QT Interdisciplinary Review Team) ***If yes, specify consult(s) and date(s) sent:***	☐	☒	☐	
Meeting Minutes/SPAs	**YES**	**NO**	**NA**	**Comment**
End-of Phase 2 meeting(s)? **Date(s):** ***If yes, distribute minutes before filing meeting***	☐	☒		
Pre-NDA/Pre-BLA/Pre-Supplement meeting(s)? **Date(s):** 9/27/13 ***If yes, distribute minutes before filing meeting***	☒	☐		
Any Special Protocol Assessments (SPAs)? **Date(s):** ***If yes, distribute letter and/or relevant minutes before filing meeting***	☐	☒		

ATTACHMENT

MEMO OF FILING MEETING

DATE: June 3, 2014

BLA/NDA/Supp #: NDA 206307

PROPRIETARY NAME: to be determined

ESTABLISHED/PROPER NAME: finafloxacin

DOSAGE FORM/STRENGTH: otic suspension, 0.3%

APPLICANT: Alcon Research, Ltd.

PROPOSED INDICATION: Treatment of acute otitis externa

REVIEW TEAM:

Discipline/Organization	Names		Present at filing meeting? (Y or N)
Regulatory Project Management	RPM:	Puglisi, M.	Y
	CPMS/TL:	Milstein, M.	Y
Cross-Discipline Team Leader (CDTL)	Boyd, W.		Y
Clinical	Reviewer:	Lloyd, R.	Y
	TL:	Boyd, W.	Y
Social Scientist Review (*for OTC products*)	Reviewer:		
	TL:		
OTC Labeling Review (*for OTC products*)	Reviewer:		
	TL:		
Clinical Microbiology (*for antimicrobial products*)	Reviewer:	Shurland, S.	Y
	TL:	Snow, K.	Y

Clinical Pharmacology	Reviewer:	Zhang, Y.	Y
	TL:	Colangelo, P.	Y
Biostatistics	Reviewer:	Deng, Y.	Y
	TL:	Wang, Y.	Y
Nonclinical (Pharmacology/Toxicology)	Reviewer:	McDougal, A.	Y
	TL:	Kotch, L.	Y
Statistics (carcinogenicity)	Reviewer:		
	TL:		
Immunogenicity (assay/assay validation) *(for BLAs/BLA efficacy supplements)*	Reviewer:		
	TL:		
Product Quality (CMC)	Reviewer:	Zhang, C.	Y
	TL:	Shanmugam, B.	Y
Quality Microbiology *(for sterile products)*	Reviewer:	Pawar, V	Y
	TL:		
CMC Labeling Review	Reviewer:		
	TL:		
Facility Review/Inspection	Reviewer:		
	TL:		
OSE/DMEPA (proprietary name)	Reviewer:	Kapoor, R.	Y
	TL:	Maslov, Y.	Y
OSE/DRISK (REMS)	Reviewer:		
	TL:		
OC/OSI/DSC/PMSB (REMS)	Reviewer:		
	TL:		

Bioresearch Monitoring (OSI)	Reviewer:		
	TL:		
Controlled Substance Staff (CSS)	Reviewer:		
	TL:		
Other reviewers			
Other attendees			

FILING MEETING DISCUSSION:

GENERAL • 505(b)(2) filing issues: o Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? o Did the applicant provide a scientific "bridge" demonstrating the relationship between the proposed product and the referenced product(s)/published literature? Describe the scientific bridge (e.g., BA/BE studies):	☒ Not Applicable ☐ YES ☐ NO ☐ YES ☐ NO
• Per reviewers, are all parts in English or English translation? **If no**, explain:	☒ YES ☐ NO
• Electronic Submission comments **List comments**:	☒ Not Applicable
CLINICAL **Comments**:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
• Clinical study site(s) inspections(s) needed? **If no,** explain:	☒ YES ☐ NO

• Advisory Committee Meeting needed? **Comments**: ***If no, for an NME NDA or original BLA, include the reason. For example:*** ○ ***this drug/biologic is not the first in its class*** ○ ***the clinical study design was acceptable*** ○ ***the application did not raise significant safety or efficacy issues*** ○ ***the application did not raise significant public health questions on the role of the drug/biologic in the diagnosis, cure, mitigation, treatment or prevention of a disease***	☐ YES Date if known: ☒ NO ☐ To be determined Reason: not first in class, no significant safety or efficacy concerns
• Abuse Liability/Potential **Comments**:	☒ Not Applicable ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
• If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance? **Comments**:	☒ Not Applicable ☐ YES ☐ NO
CLINICAL MICROBIOLOGY **Comments**:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
CLINICAL PHARMACOLOGY **Comments**:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
• Clinical pharmacology study site(s) inspections(s) needed?	☐ YES ☒ NO
BIOSTATISTICS **Comments**:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter

NONCLINICAL (PHARMACOLOGY/TOXICOLOGY) **Comments**:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter

IMMUNOGENICITY (BLAs/BLA efficacy supplements only) **Comments**:	☒ Not Applicable ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
PRODUCT QUALITY (CMC) **Comments**:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
Environmental Assessment • Categorical exclusion for environmental assessment (EA) requested? **If no**, was a complete EA submitted? **If EA submitted**, consulted to EA officer (OPS)? **Comments**:	 ☒ YES ☐ NO ☐ YES ☐ NO ☐ YES ☐ NO
Quality Microbiology (for sterile products) • Was the Microbiology Team consulted for validation of sterilization? (**NDAs/NDA supplements only**) **Comments**:	☐ Not Applicable ☒ YES ☐ NO
Facility Inspection • Establishment(s) ready for inspection? ▪ Establishment Evaluation Request (EER/TBP-EER) submitted to OMPQ? **Comments**:	☐ Not Applicable ☒ YES ☐ NO ☒ YES ☐ NO

Facility/Microbiology Review (BLAs only) **Comments**:	☒ Not Applicable ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
CMC Labeling Review **Comments**: 	 ☐ Review issues for 74-day letter
APPLICATIONS IN THE PROGRAM (PDUFA V) (NME NDAs/Original BLAs) • Were there agreements made at the application's pre-submission meeting (and documented in the minutes) regarding certain late submission components that could be submitted within 30 days after receipt of the original application? • If so, were the late submission components all submitted within 30 days?	☐ N/A ☐ YES ☒ NO ☐ YES ☐ NO
• What late submission components, if any, arrived after 30 days?	
• Was the application otherwise complete upon submission, including those applications where there were no agreements regarding late submission components?	☒ YES ☐ NO
• Is a comprehensive and readily located list of all clinical sites included or referenced in the application?	☒ YES ☐ NO
• Is a comprehensive and readily located list of all manufacturing facilities included or referenced in the application?	☒ YES ☐ NO
REGULATORY PROJECT MANAGEMENT	
Signatory Authority: John Farley, MD	

Date of Mid-Cycle Meeting (for NME NDAs/BLAs in "the Program" PDUFA V): July 28, 2014

21st Century Review Milestones (see attached) (listing review milestones in this document is optional):

Comments:

	REGULATORY CONCLUSIONS/DEFICIENCIES
☐	The application is unsuitable for filing. Explain why:
☒	The application, on its face, appears to be suitable for filing. Review Issues: ☒ No review issues have been identified for the 74-day letter. ☐ Review issues have been identified for the 74-day letter. List (optional): Review Classification: ☐ Standard Review ☒ Priority Review

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This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

MICHAEL J PUGLISI
08/21/2014