CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22548Orig1s000

OTHER REVIEW(S)

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications

Memorandum

*****Pre-Decisional Agency Information *****

Date: April 12, 2010

To: Constantine Markos, Project Manager
Division of Anti-Infective and Ophthalmology Products

From: Nisha Patel, Pharm.D., Regulatory Review Officer
Sheila Ryan, Pharm.D., Group Leader
Division of Drug Marketing, Advertising, and Communications (DDMAC)

Subject: Zymaxid™ (gatifloxacin ophthalmic solution) 0.5%
NDA 22548

DDMAC has reviewed the proposed product labeling, including the package insert (PI), draft carton label, and draft container label for Zymaxid™ (gatifloxacin ophthalmic solution) 0.5%, dated 4/6/2010, and we offer the following comments. We have also taken into consideration the labeling for Zymar® (gatifloxacin ophthalmic solution) 0.3%. Please feel free to contact me at (301) 796-3715 with any questions or clarifications.

PACKAGE INSERT

HIGHLIGHTS OF PRESCRIBING INFORMATION

DOSAGE FORMS AND STRENGTHS

- To ensure consistency among ophthalmic fluoroquinolones and since this medication is dosed based on the amount of drops instead of mg, please considering modifying the Dosage Forms and Strengths sentence to the following:

    - o "5 mL size bottle filled with 2.5 mL of gatifloxacin sterile topical ophthalmic solution, 0.5%" or similar as stated in the FULL PRECRIBING INFORMATION section.

6 pages of draft labeling has been withhed in full as B(4) CCI/TS immediately following this page

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22548	ORIG-1	ALLERGAN	GATIFLOXACIN OPHTHALMIC SOLUTION 0.5%

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

/s/

NISHA J PATEL
04/20/2010

RPM FILING REVIEW

(Including Memo of Filing Meeting)

To be completed for all new NDAs, BLAs, and Efficacy Supplements (except SE8 and SE9)

Application Information		
NDA# **022548** BLA#	NDA Supplement#:S- BLA STN#	Efficacy Supplement Type SE-
Proprietary Name: **ZYMAXID** Established/Proper Name: **Gatifloxacin** Dosage Form: **Ophthalmic Solution** Strength(s): **0.5%**		
Applicant: **Allergan, Inc.** Agent for Applicant (if applicable):		
Date of Application: **07/30/2009** Date of Receipt: **07/30/2009** Date clock started after UN:		
PDUFA Goal Date: **05/28/2010**	Action Goal Date (if different): **03/26/2010**	
Filing Date: **09/28/2009**	Date of Filing Meeting: **09/02/2009**	
Chemical Classification: (1,2,3 etc.) (original NDAs only) **3**		
Proposed indication(s)/Proposed change(s): **Bacterial Conjunctivitis**		

Type of Original NDA: AND (if applicable) Type of NDA Supplement: ***If 505(b)(2): Draft the "505(b)(2) Assessment" form found at:*** ***http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/ucm027499.html*** ***and refer to Appendix A for further information.***	**X** 505(b)(1) ☐ 505(b)(2) ☐ 505(b)(1) ☐ 505(b)(2)
Review Classification: ***If the application includes a complete response to pediatric WR, review classification is Priority.*** ***If a tropical disease priority review voucher was submitted, review classification is Priority.***	**X** Standard ☐ Priority ☐ Tropical 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***	☐ Drug/Biologic ☐ Drug/Device ☐ Biologic/Device
☐ Fast Track ☐ 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*):				
List referenced IND Number(s): **059408**				
Goal Dates/Names/Classification Properties	**YES**	**NO**	**NA**	**Comment**
PDUFA and Action Goal dates correct in tracking system? ***If not, ask the document room staff to correct them immediately. These are the dates used for calculating inspection dates.***	**X**			
Are the proprietary, established/proper, and applicant names correct in tracking system? ***If not, 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.***	**X**			
Are all classification properties [e.g., orphan drug, 505(b)(2)] entered into tracking system? ***If not, ask the document room staff to make the appropriate entries.***			**X**	
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***		**X**		
If yes, explain in comment column.				
If affected by AIP, has OC/DMPQ 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?	**X**			

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 UN letter and contact user fee staff.***	Payment for this application: **X** 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: **X** Not in arrears ☐ In arrears
Note: *505(b)(2) applications are no longer exempt from user fees pursuant to the passage of FDAAA. All 505(b) applications, whether 505(b)(1) or 505(b)(2), require user fees unless otherwise waived or exempted (e.g., small business waiver, orphan exemption).*	

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?			**X**	
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 less than that of the reference listed drug (RLD)? (see 21 CFR 314.54(b)(1)).			**X**	
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))? ***Note:*** *If you answered yes to any of the above questions, the application may be refused for filing under 21 CFR 314.101(d)(9).*			**X**	
Is there unexpired exclusivity on the active moiety (e.g., 5-year, 3-year, orphan or pediatric exclusivity)? ***Check the Electronic Orange Book at:*** ***http://www.fda.gov/cder/ob/default.htm*** **If yes**, please list below:			**X**	

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 108(b)(2).Unexpired, 3-year exclusivity will only block the approval, not the submission of a 505(b)(2) application.

Exclusivity	**YES**	**NO**	**NA**	**Comment**
Does another product have orphan exclusivity for the same indication? ***Check the Electronic Orange Book at:*** ***http://www.fda.gov/cder/ob/default.htm***		**X**		
If another product has orphan exclusivity, is the product considered to be the same product according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]? ***If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007)***			**X**	
Has the applicant requested 5-year or 3-year Waxman-Hatch exclusivity? ***(NDAs/NDA efficacy supplements only)*** **If yes**, # years requested: **3 years** ***Note:*** *An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.*	**X**			

Is the proposed product a single enantiomer of a racemic drug previously approved for a different therapeutic use (***NDAs only***)?		**X**		
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 Mary Ann Holovac, Director of Drug Information, OGD/DLPS/LRB.***			**X**	

Format and Content				
Do not check mixed submission if the only electronic component is the content of labeling (COL).	☐ All paper (except for COL) **X** All electronic ☐ Mixed (paper/electronic) **X** 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).	**X**			
Index: Does the submission contain an accurate comprehensive index?	**X**			
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: **X** legible **X** English (or translated into English) **X** pagination **X** navigable hyperlinks (electronic submissions only) **If no**, explain.	**X**			
Controlled substance/Product with abuse potential: Is an Abuse Liability Assessment, including a proposal for scheduling, submitted? ***If yes,*** *date consult sent to the Controlled Substance Staff:*			**X**	
BLAs only: Companion application received if a shared or divided manufacturing arrangement? **If yes**, BLA #			**X**	

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? ***If foreign applicant, <u>both</u> the applicant and the U.S. agent must sign the form.***	**X**			
Are all establishments and their registration numbers listed on the form/attached to the form?	**X**			
Patent Information **(NDAs/NDA efficacy supplements only)**	**YES**	**NO**	**NA**	**Comment**
Is patent information submitted on form FDA 3542a?	**X**			
Financial Disclosure	**YES**	**NO**	**NA**	**Comment**
Are financial disclosure forms FDA 3454 and/or 3455 included with authorized signature? ***Forms must be signed by the APPLICANT, not an Agent.*** ***Note:*** *Financial disclosure is required for bioequivalence studies that are the basis for approval.*	**X**			
Clinical Trials Database	**YES**	**NO**	**NA**	**Comment**
Is form FDA 3674 included with authorized signature?	**X**			
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.*** ***Note:*** *Debarment Certification should use wording in FD&C Act section 306(k)(l) 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…"*	**X**			

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.***			**X**	

Pediatrics	YES	NO	NA	Comment
PREA Does the application trigger PREA? ***If yes, notify PeRC RPM (PeRC meeting is required)*** ***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.*	**X**			
If the application triggers PREA, are the required pediatric assessment studies or a full waiver of pediatric studies included?		**X**		
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***	**X**			
If a request for full waiver/partial waiver/deferral is included, does the application contain the certification(s) required under 21 CFR 314.55(b)(1), (c)(2), (c)(3)/21 CFR 601.27(b)(1), (c)(2), (c)(3) ***If no, request in 74-day letter***	**X**			
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)***		**X**		

Proprietary Name	**YES**	**NO**	**NA**	**Comment**
Is a proposed proprietary name submitted? ***If yes, ensure that it is submitted as a separate document and routed directly to OSE/DMEPA for review.***	**X**			
Prescription Labeling	☐ **Not applicable**			
Check all types of labeling submitted.	**X** Package Insert (PI) ☐ Patient Package Insert (PPI) ☐ Instructions for Use (IFU) ☐ Medication Guide (MedGuide) **X** Carton labels **X** Immediate container labels ☐ Diluent ☐ Other (specify)			
	YES	**NO**	**NA**	**Comment**
Is Electronic Content of Labeling (COL) submitted in SPL format? ***If no, request in 74-day letter.***	**X**			
Is the PI submitted in PLR format?	**X**			
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 PLR format in 74-day letter.***			**X**	
All labeling (PI, PPI, MedGuide, IFU, carton and immediate container labels) consulted to DDMAC?	**X**			
MedGuide, PPI, IFU (plus PI) consulted to OSE/DRISK? (*send WORD version if available*)			**X**	
REMS consulted to OSE/DRISK?			**X**	
Carton and immediate container labels, PI, PPI sent to OSE/DMEPA?	**X**			
OTC Labeling	**X 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? ***If no, request in 74-day letter.***				
All labeling/packaging, and current approved Rx PI (if switch) sent to OSE/DMEPA?				
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:***		**X**		

Meeting Minutes/SPAs	**YES**	**NO**	**NA**	**Comment**
End-of Phase 2 meeting(s)? **Date(s):** ***If yes, distribute minutes before filing meeting***		**X**		
Pre-NDA/Pre-BLA/Pre-Supplement meeting(s)? **IND 059408** **Date(s): 11/26/2001** ***If yes, distribute minutes before filing meeting***	**X**			
Any Special Protocol Assessments (SPAs)? **IND 059408** **Date(s): 05/11/2007** ***If yes, distribute letter and/or relevant minutes before filing meeting***	**X**			

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

ATTACHMENT

MEMO OF FILING MEETING

DATE: **09/02/2009**

NDA #: **022548**

PROPRIETARY NAME: **ZYMAXID**

ESTABLISHED/PROPER NAME: **Gatifloxacin**

DOSAGE FORM/STRENGTH: **Ophthalmic Solution/0.5%**

APPLICANT: **Allergan, Inc.**

PROPOSED INDICATION(S)/PROPOSED CHANGE(S): **Bacterial Conjunctivitis**

BACKGROUND: **Please see IND 059408.**

REVIEW TEAM:

Discipline/Organization	Names		Present at filing meeting? (Y or N)
Regulatory Project Management	RPM:	**Constantine J. Markos**	**Y**
	CPMS/TL:	**Maureen P. Dillon-Parker**	**N**
Cross-Discipline Team Leader (CDTL)	**William M. Boyd**		**Y**
Clinical	Reviewer:	**Rhea Lloyd**	**Y**
	TL:	**William M. Boyd**	**Y**
Social Scientist Review (*for OTC products*)	Reviewer:	**N/A**	
	TL:	**N/A**	
OTC Labeling Review (*for OTC products*)	Reviewer:	**N/A**	
	TL:	**N/A**	
Clinical Microbiology (*for antimicrobial products*)	Reviewer:	**Kerry Snow**	**Y**
	TL:	**Fred Marsik**	**Y**

Clinical Pharmacology	Reviewer:	**Ryan Owen**	**Y**
	TL:	**Charles Bonapace**	**N**
Biostatistics	Reviewer:	**Yunfan Deng**	**Y**
	TL:	**Yan Wang**	**Y**
Nonclinical (Pharmacology/Toxicology)	Reviewer:	**Amy Ellis**	**Y**
	TL:	**Wendy Schmidt**	**Y**
Statistics (carcinogenicity)	Reviewer:	**N/A**	
	TL:	**N/A**	
Immunogenicity (assay/assay validation) *(for BLAs/BLA efficacy supplements)*	Reviewer:	**N/A**	
	TL:	**N/A**	
Product Quality (CMC)	Reviewer:	**Lin Qi**	**Y**
	TL:	**Linda L. Ng**	**Y**
Quality Microbiology *(for sterile products)*	Reviewer:	**Robert Mello**	**Y**
	TL:	**N/A**	
CMC Labeling Review *(for BLAs/BLA supplements)*	Reviewer:	**N/A**	
	TL:	**N/A**	
Facility Review/Inspection	Reviewer:	**N/A**	
	TL:	**N/A**	
OSE/DMEPA (proprietary name)	Reviewer:	**Denise Baugh**	**Y**
	TL:		
OSE/DRISK (REMS)	Reviewer:	**N/A**	
	TL:	**N/A**	
Bioresearch Monitoring (DSI)	Reviewer:	**Kassa Ayalew**	**Y**
	TL:	**Tejashri Purohit-Sheth**	**N**

Other reviewers		**N/A**
Other attendees		

FILING MEETING DISCUSSION:

GENERAL • 505(b)(2) filing issues? **If yes,** list issues:	 **X** Not Applicable ☐ YES ☐ NO
• Per reviewers, are all parts in English or English translation? **If no**, explain:	**X** YES ☐ NO
• Electronic Submission comments **List comments**:	**X** Not Applicable
CLINICAL **Comments**: **Please see 74-Day Letter and multiple IRs e-mailed to the sponsor.**	☐ Not Applicable **X** FILE ☐ REFUSE TO FILE **X** Review issues for 74-day letter
• Clinical study site(s) inspections(s) needed? **If no,** explain:	**X** YES ☐ NO
• Advisory Committee Meeting needed? **Comments**: ***If no, for an original NME or BLA application, include the reason. For example:*** o ***this drug/biologic is not the first in its class*** o ***the clinical study design was acceptable*** o ***the application did not raise significant safety or efficacy issues*** o ***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: **X** NO ☐ To be determined Reason:

• 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**:	**X** Not Applicable ☐ YES ☐ NO
CLINICAL MICROBIOLOGY **Comments**: **Please see multiple IRs e-mailed to the sponsor.**	☐ Not Applicable **X** FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
CLINICAL PHARMACOLOGY **Comments**:	☐ Not Applicable **X** FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
• Clinical pharmacology study site(s) inspections(s) needed?	☐ YES **X** NO
BIOSTATISTICS **Comments**:	☐ Not Applicable **X** FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
NONCLINICAL (PHARMACOLOGY/TOXICOLOGY) **Comments**:	☐ Not Applicable **X** FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
IMMUNOGENICITY (BLAs/BLA efficacy supplements only) **Comments**:	**X** Not Applicable ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
PRODUCT QUALITY (CMC) **Comments**: **Please see IR e-mailed to the sponsor.**	☐ Not Applicable **X** 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**:	☐ Not Applicable **X** 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 **X** YES ☐ NO
Facility Inspection • Establishment(s) ready for inspection? ▪ Establishment Evaluation Request (EER/TBP-EER) submitted to DMPQ? **Comments**:	☐ Not Applicable **X** YES ☐ NO **X** YES ☐ NO
Facility/Microbiology Review (BLAs only) **Comments**:	**X** Not Applicable ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
CMC Labeling Review (BLAs/BLA supplements only) **Comments**:	☐ Review issues for 74-day letter

REGULATORY PROJECT MANAGEMENT	
Signatory Authority: Acting Division Director—Wiley A. Chambers **21st Century Review Milestones (see attached)** (optional): **Comments**:	
REGULATORY CONCLUSIONS/DEFICIENCIES	
☐	The application is unsuitable for filing. Explain why:
X	The application, on its face, appears to be suitable for filing. Review Issues: ☐ No review issues have been identified for the 74-day letter. **X** Review issues have been identified for the 74-day letter. List (optional): **Please see 74-Day Letter.** Review Classification: **X** Standard Review ☐ Priority Review
ACTIONS ITEMS	
X	Ensure that the review and chemical classification properties, as well as any other pertinent properties (e.g., orphan, OTC) are correctly entered into tracking system.
☐	If RTF, notify everybody who already received a consult request, OSE PM, and Product Quality PM (to cancel EER/TBP-EER).
☐	If filed, and the application is under AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
☐	BLA/BLA supplements: If filed, send 60-day filing letter
☐	If priority review: • notify sponsor in writing by day 60 (For BLAs/BLA supplements: include in 60-day filing letter; For NDAs/NDA supplements: see CST for choices) • notify DMPQ (so facility inspections can be scheduled earlier)
X	Send review issues/no review issues by day 74
☐	Other

Appendix A (NDA and NDA Supplements only)

NOTE: The term "original application" or "original NDA" as used in this appendix denotes the NDA submitted. It does not refer to the reference drug product or "reference listed drug."

An original application is likely to be a 505(b)(2) application if:

(1) it relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application,
(2) it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval, or
(3) it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations (see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

(1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies),

(2) No additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application, and.

(3) All other “criteria” are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely

for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

(1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2),

(2) The applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement, or

(3) The applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your OND ADRA or OND IO.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22548	ORIG-1	ALLERGAN	GATIFLOXACIN OPHTHALMIC SOLUTION 0.5%

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

/s/

CONSTANTINE J MARKOS
04/09/2010

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: Monday, March 29, 2010

TO: Constantine Markos, Regulatory Health Project Manager Division of Anti of Anti-Infective and Ophthalmology Products
Rhea Lloyd, Medical Officer, DAIOP

FROM: Kassa Ayalew, M.D.
Good Clinical Practice Branch 2
Division of Scientific Investigations

THROUGH: Tejashri Purohit-Sheth, M.D.
Branch Chief Good Clinical Practice Branch 2
Division of Scientific Investigations

SUBJECT: Evaluation of Clinical Inspections.

NDA or BLA: NDA 22-548

APPLICANT: Allergan, Inc.
2525 Dupont Drive
Irvine, CA 92612
Phone (714) 246-5844

DRUG: Gatifloxacin 0.5% Ophthalmic Solution

NME: No

THERAPEUTIC CLASSIFICATION: Standard

INDICATIONS: Treatment of treatment of bacterial conjunctivitis

CONSULTATION REQUEST DATE: August 18, 2009

DIVISION ACTION GOAL DATE: April 28, 2010

PDUFA DATE: May 27, 2010

I. BACKGROUND:

The sponsor, Allergan, submitted supplemental a new drug application under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for gatifloxacin ophthalmic solution 0.5%. (NDA: 22-548) on July 30, 2009 to support a labeling claim for the treatment of bacterial conjunctivitis. The sponsor requests approval of a reformulated gatifloxacin ophthalmic solution at a higher dosage strength of 0.5% with intent to improve microbial kill and allow for reduced dosing frequency "for the treatment of bacterial conjunctivitis." Gatifloxacin has been previously characterized and information regarding the nonclinical pharmacology, pharmacokinetics and toxicology is referenced in NDA 21-493 ZYMAR (gatifloxacin ophthalmic solution) 0.3% which was approved in the US in March 2003 for the indication of bacterial conjunctivitis in adults and pediatric patients above the age of 1 year.

The two formulations (0.3% and 0.5%) are claimed to be the same with the exception of increased drug concentration, a reduction in pH to ensure solubility of the drug substance, and slightly lower sodium chloride concentration for tonicity. To support approval, the Applicant has provided data from 2 identically-designed studies: a 6 day, phase 3 multicenter, double-masked, randomized, 2-arm, vehicle controlled, parallel-group studies comparing gatifloxacin ophthalmic solution 0.5% with gatifloxacin vehicle for the treatment of acute bacterial conjunctivitis in patients (b) (4) 1 year of age.

Protocols inspected:

The protocols inspected were Protocol 198782-004 and Protocol 198782-005. Both protocols were similar in design. **Study 198782-004** was conducted in the United States (US) and **Study 198782-005** was conducted in the US and India. In both trials, the study medication was administered to the qualified eye(s) up to 8 times on the first day, and twice daily on Days 2 through 5 and a comparison of the Safety and Efficacy of Gatifloxacin 0.5% Ophthalmic Solution with that of Vehicle in the treatment of acute bacterial conjunctivitis was conducted. Patients were treated on Days 1 (baseline) through 5, and were evaluated at Day 4 and Day 6.

Both studies were a 6-day, multicenter, double-masked, randomized, 2-arm, vehicle controlled, parallel-group study comparing gatifloxacin 0.5% ophthalmic solution with that of gatifloxacin vehicle for the treatment of acute bacterial conjunctivitis in subjects (b) (4) year of age.

A total of 1437 patients were randomized in the two studies. All 578 patients from Study 198782-004 and 89 patients from Study 198782-005 were from the US, representing 46.4% (667/1437). The sponsor excluded seventy two patients from Site 13020 in India for Study 198782-005, from all efficacy analyses reportedly due to significant data integrity issues. The details of the data integrity issues were not provided

Patients were included in the study if they were at least 1 year of age with a clinical diagnosis of acute bacterial conjunctivitis (or blepharoconjunctivitis), defined as the presence of moderate or severe conjunctival hyperemia and mild to severe discharge, in 1 or both eyes.

Patients with other ocular infections or who had used antibiotics in the previous week, or corticosteroids in the previous 2 weeks, were to be excluded. According to the protocol, prior to initiation of study treatment, each subject who qualified for entry, was to be assigned a subject number that was to be recorded in the source documents and then on the appropriate eCRF. Qualified subjects were to be randomly assigned by an automated Interactive Voice Response System (IVRS) / Interactive Web Response System (IWRS) to either gatifloxacin 0.5% or gatifloxacin vehicle in an even allocation (1:1).

At baseline (Day 1), subjects in both treatment groups were to be instructed to dose with 1 drop of study medication in each qualified eye every two hours (q2h) up to 8 times total. Day 2 to Day 5, subjects in both treatment groups were to be instructed to dose with 1 drop of the assigned study medication in each qualified eye BID. If an unqualified eye (an eye that was not clinically diagnosed on Day 1) became clinically diagnosed with bacterial conjunctivitis prior to the Day 6 visit, the subject was to be assigned a new bottle of identically masked study medication for which to treat the unqualified eye with 1 drop every 2 hours up to 8 times on Day 1 and BID thereafter.

The primary efficacy variable was clinical success, defined as clearing (i.e., score = 0) of both conjunctival hyperemia and conjunctival discharge in the study eye from Day 1. Conjunctival hyperemia and conjunctival discharge were to be measured on a 4-point scale (0=none, 1=mild, 2=moderate, 3=severe). The primary outcome measure or efficacy endpoint in the studies was clinical success at the Day 6 time point. Clinical success at the Day 4 time point as well as microbiological cure, clinical improvement in ocular signs, and clinical improvement in ocular symptoms were secondary efficacy end points. Microbiological response was also a secondary efficacy variable.

Safety measurements included adverse events and physical examination.

This was a routine audit request to assess data integrity and human subject protection for clinical trials submitted in support of this application.

Field inspections of this study were important as verification of data for safety and efficacy for evaluation of conduct of pivotal studies was vital. The sites requested for inspection were the centers with the largest numbers of enrolled subjects in the study. Dr Daniel Long's site was also selected due to high enrollment and inspectional history in 1988.

II. RESULTS (by Site):

Name of CI, IRB, or Sponsor Location	**Protocol #: and # of Subjects:**	**Inspection Date**	**Field Classification/Final Classification**
Yasmin Rusi Bhagat, M.D. Head of Ophthalmology Department St. George's Hospital Fort, Mumbai , India	Protocol 198782-005 Site # 13008 84 Subjects	11/09/2009-11/11/2009	NAI/VAI
Nita Shanbhag, M.D. Omkar Eye Care Center 302/303 Koteshwar Plaza Junc of Jawaharlal Nehru road and RHB road, Mulund (West) Mumbai – 400080, India	Protocol 198782-005 Site # 13014 90 Subjects	11/16/2009-11/17/09	NAI/NAI
Daniel A. Long, MD Dr. Daniel A Long – A Professional Medical Corporation 120 Meadowcrest St. #330 Gretna, LA 70056	Protocol 198782-004 Site # 10008 50 Subjects	10/19/2009-10/21/2009	OAI/OAI-Untitled

Key to Classifications
NAI = No deviation from regulations.
VAI = Deviation(s) from regulations.
OAI = Significant deviations from regulations. Data unreliable.
Pending = Preliminary, letter has not yet issued to the CI.

1. Dr. Nita Shanbhag, M.D.

Omkar Eye Care Center
302/303 Koteshwar Plaza
Junc of Jawaharlal Nehru road and RHB road,
Mulund (West)
Mumbai – 400080, India

a. What was inspected?

This inspection was conducted in accordance with Compliance Program 7348.811 between November 16 and 17, 2009.

A total of 93 subjects were screened and 90 were enrolled and randomized into the study. All 90 subjects completed the study. There were no Serious Adverse Events (SAEs) or Deaths during the study. The inspection evaluated informed consent and included review of source documents and hard copy reporting for 100% of subjects randomized. Study subject files were reviewed for verification of: 1) entry criteria, 2) diagnosis of target disease, 3) efficacy variables, 4) adequate adverse experience reporting, and 5) handling of pharmacokinetic samples. In addition, drug accountability records, IRB approval and dates, and sponsor monitoring records were reviewed. There were no limitations to the inspection.

b. General observations/commentary:

The inspection of **Nita Shanbhag**'s site revealed that the study was conducted in accordance with the investigational plan. A Form FDA 483, Inspectional Observations, was not issued to this investigator.

c. Assessment of data integrity:

Based on inspectional findings, efficacy and safety data obtained from this site are considered reliable.

2. Yasmin Rusi Bhagat, M.D.
Head of Ophthalmology
Department
St. George's Hospital
Fort, Mumbai – 400 001

a. **What was inspected**:

This inspection was conducted in accordance with Compliance Program 7348.811 Between November 9 and 11, 2009

A total of 85 subjects were screened and 84 were enrolled and randomized the study. Of the 84 subjects randomized, 83 subjects completed the study. One subject who was found to be pregnant did not receive study drug. The inspection included review of records for 84 subjects who were randomized. There were no Serious Adverse Events (SAEs) or Deaths during the study. The following items were reviewed for verification: 1) entry criteria, 2) diagnosis of target disease, 3) efficacy variables, 4) adequacy of adverse experience reporting. In addition, drug accountability records, IRB approval and dates, and sponsor monitoring records were reviewed. There were no limitations to the inspection.

b. **General observations/commentary**:

The inspection of Dr. Bhagat's site revealed that the study was not conducted in accordance with the investigational plan. However, a Form FDA 483, Inspectional Observations, was not issued to this investigator. The following regulatory violations were observed during the inspection:

- Failure to conduct the study according to the signed investigator statement and the investigational plan [21 CFR 312.60]. For example:
    - the eCRF did not document all AEs on the eCRF as required by the protocol:
        - Subject # 1541 had a negative culture of the conjunctival right eye on Day 1 and Day 4. However, the Day 6 culture laboratory report documented a growth of Yeast. This should have been documented in the eCRF; however, the eCRF did not document any AEs.
        - Subject # 1576 had a negative culture of the conjunctival right eye on Day 1 and Day 4. However, the Day 6 culture laboratory report documented a growth of "Staphylococcus warneri". This should have been documented in the eCRF; however, the eCRF did not document any AEs.

- Subject # 1577 had a negative culture of the conjunctival right eye on Day 1 and Day 4. However, the Day 6 culture laboratory report documented a growth of "Staphylococcus". This should have been documented in the eCRF; however, the eCRF did not document any AEs.

c. **Assessment of data integrity**:

Although regulatory violations were noted above, it is unlikely based on the nature of the violations that they significantly affect overall reliability of safety and efficacy data from the site, as they appear to be isolated findings. Based on the provided EIR for this site and Dr. Bhagat's responses regarding the regulatory violations during the inspection, which were documented in the EIR, data derived from Dr. Bhagat's site are considered reliable.

3. Daniel A. Long, MD
A Professional Medical Corporation
120 Meadowcrest St. #330
Gretna, LA 70056
Phone #: (504) 391-7560

a. What was inspected:

This inspection was conducted in accordance with Compliance Program 7348.811 between 10/19/2009-10/21/2009.

At this site a total of 50 subjects were screened and 50 completed the study. The inspection included review of records for 34 subjects who were randomized. There were no Serious Adverse Events (SAEs) or Deaths during the study. The following items were reviewed for verification: 1) entry criteria, 2) diagnosis of target disease, 3) efficacy variables, 4) adequacy of adverse experience reporting. In addition, drug accountability records, IRB approval and dates, and sponsor monitoring records were reviewed. There were no limitations to the inspection.

a. **General observations/commentary**:

The inspection of Dr. Long's site revealed that the study was not conducted in accordance with the investigational plan. A Form FDA 483, Inspectional Observations, was issued to this investigator, mainly for:

- Failure to conduct the study according to the signed investigator statement and the investigational plan [21 CFR 312.60]. Specifically, for
    - Administering study medications to 14 of the 34 subjects (40%)

(prior to randomization and study drug treatment kit identification through the Interactive Voice Response System (IVRS). The reported time that study subjects received **the first dose** of study drug **before randomization** ranged from 17 minutes to 157 minutes.

Reviewer Comment:

The investigator failed to ensure the correct times were recorded on the source document for 14 or the 34 subjects reviewed. However, the review of the Drug Accountability records indicated that all subjects may have received the correct investigational product as assigned by the IVRS system. Dr Long's response also states that all subjects were first randomized in the IVRS system before receiving the IVRS assigned kit of investigational product. Based on the review of the EIR and the Drug accountability records, even though the investigator failed to ensure the correct times were recorded on the source document, all subjects appear to have received the correct investigational product as assigned by the IVRS system.

- **Enrolling and randomizing** 12 of 34 subjects (35%) into the study prior to completion of the tests to determine eligibility for enrollment (i.e prior to collection of the conjunctival sample for the adenovirus antigen)

Reviewer Comment:

The adenovirus antigen test was one of screening tests to enroll subjects into the study. According to the exclusion criteria listed in the protocol (page 24) if the adenovirus antigen test revealed a positive result, the subject was not supposed to qualify for the study. If the adenovirus test revealed a negative result and all other eligibility criteria were met, the site telephoned the Interactive Voice Response System (IVRS) to receive a randomization number and a medication treatment kit number.

In the review of 11 of 34 subjects records that were enrolled in the study, there were however instances where subjects (Subject # 1027,1046,1050, 1078,1161,1162,1301,1316,1463,1479,1504) appeared to be dosed prior to the collection of the sample for the adenovirus antigen screening test and before revealing the test results.

Despite the above instances, all referred subjects who had been enrolled into the study had a negative adenovirus antigen screening tests. Even though the investigator appears to have failed to collect the conjunctival sample for the adenovirus antigen screening test and administered study medications before revealing the adenovirus

antigen test results, based on the review of the EIR there were no subjects who had adenoviral conjunctivitis who should have been excluded from the study.

Therefore, the above protocol violations do not appear to impact study data.

- Administering study medication to one subject prior to completion of the tests to determine eligibility for (i.e the collection of the conjunctiva sample)

    - Subject #1005 was dosed with the study medication (16:30) prior to the collection of the conjunctiva sample for the bacterial culture (17:00). The conjunctiva samples for the bacterial culture should have been collected prior to dosing with the study medication.

- Failure to obtain adenovirus antigen test to one subject prior to the conjunctiva bacterial culture

    - The Investigator failed to follow the protocol in that the conjunctiva sample for the adenovirus antigen test (10:35) was collected prior to the conjunctiva sample (11:00) for Subject #1110. The conjunctiva sample for the adenovirus antigen test should have been collected prior to the conjunctiva sample for the bacterial culture.

- Failure to analyze the adenovirus antigen test at least 10 minutes after the sample was loaded into the test kit

    - Subjects (Subject # 1027, #1046,# 1050,#1076,# 1301) were dosed less than 10 minutes after the sample collection time recorded in the source documents for the adenovirus antigen test. The results of the adenovirus antigen test should have been analyzed at least 10 minutes after the sample is loaded into the test kit.
- Failure to prepare or maintain accurate case histories with respect to the observations and data pertinent to the investigation.

    - Specifically, study source documents and clinic charts contained unexplained and uncorroborated changes in the data.

        Examples include:

        - **Subject #1001:** The protocol specifies that the

conjunctiva sample for the bacterial culture is to be collected prior to the conjunctiva sample for the adenovirus antigen test. The adenovirus antigen conjunctiva sample collection time was initially recorded as 09:35 and the culture sample collection time as 10:00. The conjunctiva sample collection time for the adenovirus antigen was written over several times with 10:05, which would comply with the protocol.

- **Subject #1016:** The adenovirus antigen sample collection time was initially recorded as 08:40 and the bacterial culture sample collection time as 09:30. The sample collection time for the adenovirus antigen test was written over several times with 09;40, which would comply with the protocol.

- Study source documents for Day 1, Day 4, and Day 6 visits were not available for Subject # 1593

- IVRS confirmation sheets documenting the time of screening, time of randomization, and randomization treatment code were missing for Subject # 1389.

- Source documents contain changes in data made by the Sub-I that were initially recorded by the PI.

  Examples include:

  - Subject #1078, the subject was screened, consented, and observed by Dr. Long on 10/29/07 as documented in the study source documents. Changes to the adenovirus antigen test sample collection time (14:45 changed to 14:35) and time of the first doses of the study medication (14:35 changed to 14:45) were performed by (b) (4) on 12/11/07. These changes show non compliance with the protocol since the sample collection time for the bacterial culture was recorded as 14:30 by Dr. Long.

- Conflicting information was included in study source and clinic documents.

  Examples include:

  Subject # 1001: The progress note dated 8/20/07 (study visit Day 1) located in the subject's clinic chart indicates a conjunctival hyperemia (redness) score of 1+ and a discharge

score of 2+, however the study source documents include a conjunctival hyperemia score of 2 (necessary for inclusion in the study). The progress note in the subject's clinic chart documents the first dose of the study medication as 10:20. The study source document captures the time of the first dose as 10:30.

Subject# 1004: The name represented in the patient clinic chart as RTE (first name, middle name, last name) is represented in the study source documents including a signed informed consent form as ETR (last name, middle initial, first name). The signed patient information sheet included in the patient's clinic chart is signed as first initial, middle initial, last name.

Subject# 1019: Study source documents include the bacterial culture sample collection times as 08:42 (OD) and 08:43 (OS) however the laboratory requisition form and the laboratory report document the collection times as 08:30 (OU).

Subject #1063: The study source document includes the bacterial culture sample collection time as 11 :00 while the laboratory report documents the collection time as 10:00. Additionally, the laboratory requisition form initially had the collection time as 10:00 but this was written over to read 12:00.

b. **Assessment of data integrity**

Although several regulatory violations were noted during the inspection, and a couple were noted in a large proportion of subjects, based on the review of the specific nature of the findings and impact of these findings on the evaluation of safety and efficacy, it is unlikely that these findings would importantly impact data reliability as described above in "Reviewer's comments."

However, the recommended classification is OAI based on the fact that the findings were noted in a large proportion of subjects and for the potential of these findings to have impacted data integrity. An untitled letter is being issued due to the conclusion that although multiple protocol deviations were noted, it is unlikely that the violations would affect data integrity

IV. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

In general, the studies appear to have been conducted adequately and the data in support of the NDA appear reliable. The final classification of the inspection for Dr. Shanbhag is NAI. The final classification of the Clinical Investigator inspection of Dr. Bhagat is VAI. Although regulatory violations were noted at Dr Bhagat's site, it is unlikely that they significantly affect overall data reliability from the site. The data from Dr. Long's clinical site documented several regulatory violations due to the clinical investigator's failure to conduct the study according to the signed investigator statement and the investigational plan. However, the violations are unlikely to affect overall data reliability from the site. The classification of the Clinical Investigator inspection of Dr. Long is OAI-Untitled, based on the conclusion that although there was a potential for these significant findings to impact subject safety and/or efficacy, review of the findings demonstrate that these findings did not result in adverse outcomes that would otherwise impact subject safety and/or efficacy. Dr. Long submitted a written response that provided adequate corrective actions for the violations noted during the inspection. The data in support of the application are considered reliable.

{See appended electronic signature page}

Kassa Ayalew, M.D.
Good Clinical Practice Branch II
Division of Scientific Investigations

CONCURRENCE:

{See appended electronic signature page}

Tejashri Purohit-Sheth, M.D.
Branch Chief
Good Clinical Practice Branch II
Division of Scientific Investigations

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22548	ORIG-1	ALLERGAN	GATIFLOXACIN OPHTHALMIC SOLUTION 0.5%

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/s/

KASSA AYALEW
04/28/2010

TEJASHRI S PUROHIT-SHETH
04/28/2010

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date:	January 27, 2010
To:	Wiley Chambers, MD, Acting Director Division of Anti-infective and Ophthalmology Products
Through:	Todd Bridges, RPh, Team Leader Denise P. Toyer, PharmD, Deputy Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Denise V. Baugh, PharmD, BCPS, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Label and Labeling Review
Drug Name(s):	Zymaxid (Gatifloxacin) Ophthalmic Solution 0.5%
Application Type/Number:	NDA# 022548
Applicant:	Allergan, Inc.
OSE RCM #:	2009-1539

1 INTRODUCTION

This review is written in response to a request from the Division of Anti-infective and Ophthalmology Products for assessment of the label and labeling for Zymaxid (Gatifloxacin) Ophthalmic Solution 0.5% for their vulnerability to medication errors.

2 METHODS AND MATERIALS

The Division of Medication Error Prevention and Analysis (DMEPA) used Failure Mode and Effects Analysis (FMEA) [1] in our evaluation of the container labels and carton labeling (see Appendix A) submitted on November 24, 2009 and the insert labeling submitted on August 20, 2009. Since Zymar and Zymaxid contain the same active ingredient and may be stored in close proximity to one another in the pharmacy, DMEPA reviewed the container labels and carton labeling for Zymar (Gatifloxacin) Ophthalmic Solution 0.3% (NDA# 021493) submitted in the annual report dated July 25, 2007 (Appendix B). The Zymar labels and labeling were assessed for their similarity to the proposed product's labels and labeling and the potential for confusion between the two drug products.

3 CONCLUSIONS AND RECOMMENDATIONS

Our evaluation noted areas where information on the carton and insert labeling can be improved to minimize the potential for medication errors. We provide recommendations on the insert labeling in Section 3.1, *Comments to the Division,* for discussion during the review team's label and labeling meetings. Section 3.2, *Comments to the Applicant,* contains our recommendations for the carton labeling. We request the recommendations in Section 3.2 be communicated to the Applicant prior to approval.

We would be willing to meet with the Division for further discussion, if needed. Please copy the Division of Medication Error Prevention and Analysis on any communication to the Applicant with regard to this review. If you have questions or need clarifications, please contact Brantley Dorch, OSE Regulatory Project manager, at 301-796-0150.

3.1 COMMENTS TO THE DIVISION

We note the use of an abbreviation in Section 2.1 of the Full Prescribing Information Section. Specifically, the Applicant designates the age of the patient as (b) (4) 1 year of age'. The greater than symbol is considered a dangerous abbreviation. As such, it is included on the Institute of Safe Medication Practice's List of Error-Prone Abbreviations, Symbols, and Dose Designations[2]. As part of a national campaign to avoid the use of dangerous abbreviations and dose designations, FDA agreed not to approve such error prone abbreviations in the approved labeling of products. We recommend revising the statement (b) (4) and Adult' to 'Patients 1 year of age or older' which is consistent with the Dosage and Administration section within the Highlights of Prescribing Information.

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

[2] http://www.ismp.org/Tools/errorproneabbreviations.pdf, Last accessed 10/28/2009.

3.2 COMMENTS TO THE APPLICANT

CARTON LABELING

We note the use of a blue diagonal line incorporated into the letter 'x' in the proposed name 'Zymaxid'. The presence of this line decreases the readability of the proprietary name, specifically the letter, 'x'. Revise the letter 'x' so that it is presented in the same font type, size and color as the rest of the name.

4 pages of draft labeling has been withheld in full immediately following this page as (B4) CCI/TS

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22548	ORIG-1	ALLERGAN	GATIFLOXACIN OPHTHALMIC SOLUTION 0.5%

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/s/

DENISE V BAUGH
01/27/2010

TODD D BRIDGES
01/27/2010

DENISE P TOYER
01/27/2010

DSI CONSULT: Request for Clinical Inspections

Date: August 18, 2009

To: Leslie Ball, M.D., Branch Chief, GCP2 Constance Lewin, M.D., M.P.H, Branch Chief, GCP1 Division of Scientific Investigations, HFD-45 Office of Compliance/CDER

Through: Rhea Lloyd, M.D., Medical Officer Division of Anti-Infective and Ophthalmology Products

From: Constantine Markos, Regulatory Health Project Manager Division of Anti-Infective and Ophthalmology Products

Subject: Request for Clinical Site Inspections

General Information

Application#: NDA 22-548
Sponsor/Sponsor contact information: Allergan, Inc. Joanne Lemmo, Senior Manager, Global Regulatory

Affairs Phone: 714-246-5844 Fax: 714-246-4051 Email: lemmo_joanne@allergan.com

Drug: (gatifloxacin ophthalmic solution) 0.5% Trade Name: None submitted NME: No
Standard or Priority: Standard Proposed indication: Treatment of bacterial conjunctivitis

PDUFA: May 27, 2010 Action Goal Date: April 28, 2010
Inspection Summary Goal Date: March 28, 2010

Protocol/Site Identification

Site # (Name,Address, Phone number, email, fax#)	Protocol #	Number of Subjects	Indication
DSI choice	Study 198782-004 Study 198782-005	578 859	treatment of bacterial conjunctivitis

An inspection is requested for at least one site for each of these clinical trials as your resources permit.

Note that the highest enrollers in Study198782-004 are Jesse M. De Leon, MD, Daniel A. Long, MD, and Warren H. Heller, MD, who each enrolled 50 subjects. Note that the highest enroller in Study 198782-005 is Dr. Nita Shanbhag (Mumbai, India), who enrolled 90 subjects.

Domestic Inspections:

Reasons for inspections (please check all that apply):

Enrollment of large numbers of study subjects
High treatment responders (specify):
Significant primary efficacy results pertinent to decision-making
There is a serious issue to resolve, e.g., suspicion of fraud, scientific misconduct, significant human subject protection violations or adverse event profiles.
X Other (specify): Routine Inspections

Goal Date for Completion:
We request that the inspections be performed and that the Inspection Summary Results be provided by March 28, 2010**.** We intend to issue an action letter on this application by May 28, 2010. The PDUFA due date for this application is **May 31, 2010.**

Should you require any additional information, please contact Constantine Markos at 301-796-3871 or Rhea Lloyd, MD at 301-796-0753.

Additional Information:

This is an eCTD NDA submission. The clinical portion of the application has been preliminarily reviewed. The applicant reports a data integrity problem with investigator 13020 who enrolled 71 subjects in Section 11.1.1.1.5 of the CSR for 198782-005. Specific information regarding the data integrity issues are not provided within the CSR. The Division has requested more information regarding the data integrity issues.

The List and Description of Investigators for both studies are appended to this request.

16.1.4 List and Description of Investigators

	Investigator Number	Principal Investigator Name (Site Number), Address	Other Important Participants Name, Degree (Role)	N	Patient Numbers
10001	3809	William F. Davitt III, MD Corona Research Consultants, Inc. 8815 Dyer St. Ste 165 El Paso, TX 79904		16	1018, 1033, 1034, 1090, 1108, 1129, 1136, 1154, 1165, 1178, 1272, 1317, 1379, 1392, 1405, 1474
10002	3957	Jesse M. De Leon, MD Center for Clinical Trials, LLC 16660 Paramount Blvd. Suite 301 Paramount, CA 90723	(b) (6)	50	1026, 1032, 1038, 1040, 1042, 1049, 1053, 1057, 1079, 1080, 1111, 1134, 1141, 1142, 1146, 1147, 1148, 1149, 1150, 1152, 1155, 1160, 1167, 1174, 1197, 1199, 1200, 1201, 1207, 1220, 1221, 1225, 1236, 1249, 1250, 1252, 1258, 1260, 1261, 1264, 1265, 1270, 1271, 1273, 1278, 1280, 1282, 1310, 1329, 1330
10006	4666	Michael S. Korenfeld, MD Comprehensive Eye Care, Ltd. 901 East 3rd Street Washington, MO 63090	(b) (6)	1	1357
10007	619	Norman S. Levy, MD Florida Ophthalmic Institute 7106 NW 11th Place, Suite B Gainesville, FL 32605		5	1022, 1093, 1430, 1450, 1481

Site Number	Investigator Number	Principal Investigator Name (Site Number), Address	Other Important Participants Name, Degree (Role)	N	Patient Numbers
10008	356	Daniel A. Long, MD Dr. Daniel A Long – A Professional Medical Corporation 120 Meadowcrest St. #330 Gretna, LA 70056	(b) (6)	50	1001, 1002, 1003, 1004, 1005, 1016, 1019, 1025, 1027, 1043, 1046, 1050, 1063, 1076, 1078, 1091, 1096, 1110, 1126, 1127, 1161, 1162, 1163, 1164, 1180, 1187, 1190, 1195, 1217, 1230, 1237, 1242, 1254, 1262, 1293, 1296, 1301, 1316, 1389, 1427, 1463, 1479, 1480, 1504, 1536, 1544, 1569, 1593, 1608, 1616
10009	3240	Dr. Douglas C. Lorenz, DO Nevada Eye & Ear 2598 Windmill Pkwy. Henderson, NV 89074	(b) (6)	7	1044, 1064, 1086, 1097, 1176, 1527, 1632
10010	1187	Kenneth W. Olander, MD University Eye Surgeons 622 Smithview Drive Maryville, TN 37803		1	1235

Site Number	Investigator Number	Principal Investigator Name (Site Number), Address	Other Important Participants Name, Degree (Role)	N	Patient Numbers
10011	3858	Bernard R. Perez, MD International Eye Center 4506 Wishart Blvd Tampa, FL 33603	(b) (6)	21	1029, 1045, 1048, 1052, 1055, 1059, 1061, 1256, 1259, 1291, 1345, 1409, 1423, 1425, 1433, 1440, 1496, 1511, 1514, 1573, 1576
10012	2429	Howard I. Schenker, MD Rochester Ophthalmological Group, P.C. 2100 S. Clinton Ave Rochester, NY 14618		15	1035, 1070, 1089, 1107, 1123, 1132, 1153, 1192, 1297, 1302, 1307, 1340, 1549, 1613, 1638
10013	5082	John D. Sheppard, MD Virginia Eye Consultants 241 Corporate Blvd. Norfolk, VA 23502		3	1008, 1168, 1169
10014	3255	Steve S. Spector, MD Presidential Eye Center, PA 1501 Presidential Way, Suite #11 West Palm Beach, FL 33401		4	1193, 1244, 1384, 1590
10019	10378	Yue-Kong Au, MD Yue-Kong Au MD, LLC 2539 Viking Drive, Suite 103 Bossier City, LA 71111		13	1006, 1015, 1020, 1021, 1023, 1031, 1037, 1039, 1058, 1073, 1098, 1099, 1182
10021	10380	Tomas Coronado, MD Sun Research Institute 303 E. Quincy St., Suite 101 San Antonio, TX 78215		9	1009, 1011, 1072, 1075, 1102, 1458, 1459, 1515, 1586

Site Number	Investigator Number	Principal Investigator Name (Site Number), Address	Other Important Participants Name, Degree (Role)	N	Patient Numbers
10026	10382	Warren H. Heller, MD Arizona Center for Clinical Trials, LLC 515 W. Buckeye Road, Suite 203 Phoenix, AZ 85003	(b) (6)	50	1062, 1067, 1068, 1071, 1114, 1115, 1120, 1144, 1172, 1173, 1177, 1203, 1214, 1215, 1216, 1218, 1226, 1231, 1238, 1246, 1248, 1279, 1281, 1299, 1300, 1312, 1332, 1344, 1359, 1364, 1367, 1368, 1372, 1373, 1380, 1381, 1382, 1386, 1429, 1434, 1436, 1437, 1445, 1449, 1476, 1477, 1482, 1488, 1489, 1564
10028	10384	Paul A. Jorizzo, MD Medical Eye Center 2727 Barnett Road Medford, OR 97504		2	1030, 1137
10029	10385	Ranjan P. Malhotra, MD Ophthalmology Associates 12990 Manchester Road, Suite 200 St. Louis, MO 63131		28	1010, 1014, 1028, 1047, 1066, 1069, 1101, 1116, 1117, 1188, 1228, 1232, 1245, 1276, 1353, 1377, 1413, 1416, 1441, 1460, 1508, 1587, 1589, 1597,

Site Number	Investigator Number	Principal Investigator Name (Site Number), Address	Other Important Participants Name, Degree (Role)	N	Patient Numbers
10030	10386	Eugene B. McLaurin, MD Total Eye Care, PA 6060 Primacy Parkway, Suite 200 Memphis, TN 38119	(b) (6)	19	1013, 1036, 1130, 1196, 1204, 1208, 1298, 1320, 1334, 1431, 1456, 1484, 1500, 1546, 1562, 1565, 1566, 1583, 1639
10032	10388	Stephen E. Smith, MD Eye Associates of Fort Myers 4225 Evans Avenue Fort Myers, FL 33901	(b) (6)	19	1007, 1017, 1054, 1060, 1065, 1084, 1094, 1156, 1157, 1170, 1185, 1194, 1471, 1472, 1475, 1529, 1535, 1541, 1620
10034	9750	William B. Trattler, MD Center for Excellence in Eye Care 8940 N. Kendall Drive, Suite 400-E Miami, FL 33176	(b) (6)	2	1263, 1319
10035	10389	Francis J. Wapner, MD Advanced Eye Care 1250 East 3900 South, Suite 310 Salt Lake City, UT 84124		6	1092, 1166, 1277, 1294, 1468, 1630
10036	2851	Douglas G. Day, MD Omni Eye Services 5505 Peachtree-Dunwoody Road, Suite 300 Atlanta, GA 30342		1	1219

Site Number	Investigator Number	Principal Investigator Name (Site Number), Address	Other Important Participants Name, Degree (Role)	N	Patient Numbers
10038	3212	Michael E. Tepedino, MD Cornerstone Eye Care 307 Lindsay Street High Point NC, 27262	(b) (6)	43	1082, 1113, 1121, 1122, 1124, 1131, 1140, 1151, 1175, 1181, 1202, 1306, 1324, 1347, 1354, 1369, 1374, 1375, 1388, 1390, 1396, 1397, 1403, 1412, 1421, 1439, 1443, 1452, 1453, 1454, 1462, 1464, 1466, 1483, 1492, 1499, 1522, 1523, 1563, 1570, 1571, 1591, 1603
10042	1587	Richard Sturm, MD Ophthalmic Consultants of Long Island 360 Merrick Road, 3rd Floor Lynbrook, MY 11563		2	1223, 1305
10045	1777	Henry Perry, MD Ophthalmic Consultants of Long Island Ryan Medical Arts Building 2000 North Village Avenue, Suite 402 Rockville Centre, NY 11570		4	1109, 1229, 1517, 1542
10046	3238	Stephen E. Pascucci, MD Eye Consultants of Bonita Springs, PLLC 23451 Walden Center Drive Bonita Springs, FL 34135		1	1575

Site Number	Investigator Number	Principal Investigator Name (Site Number), Address	Other Important Participants Name, Degree (Role)	N	Patient Numbers
10048	10643	Sherif M. El-Harazi, MD, MPH Lugene Eye Institute 801 S. Chevy Chase Drive, Suite 103 Glendale, CA 91205	(b) (6)	12	1077, 1081, 1083, 1087, 1088, 1105, 1198, 1205, 1210, 1211, 1234, 1554
10049	10647	Jodi I. Luchs, MD South Shore Eye Care, LLP 2185 W. Wantagh Ave. Wantagh, NY 11793		5	1290, 1358, 1495, 1498, 1605
10050	10650	Barbara J. Arnold, MD, FACS Center for Clinical Trials of Sacramento, Inc. 7600 Hospital Drive Ste. G Sacramento, CA 95823		18	1159, 1206, 1239, 1253, 1350, 1362, 1366, 1402, 1404, 1447, 1469, 1558, 1561, 1567, 1579, 1602, 1624, 1642
10052	10660	Bruce Kanengiser, MD Clinical Research Laboratories, Inc. 371 Hoes Lane, Suite 100 Piscataway, NJ 08854		9	1118, 1189, 1303, 1322, 1339, 1391, 1510, 1526, 1629
10053	10664	Lincoln Manzi, MD Southland Clinical Research Center 11100 Warner Avenue, Suite 214 and 352 Fountain Valley, CA 92708	(b) (6)	4	1171, 1341, 1400, 1417
10055	10704	Shachar Tauber, MD St. John's Clinic – Eye Specialists 1229 East Seminole, Suite 430 Springfield, MO 65804		8	1289, 1311, 1328, 1352, 1383, 1426, 1572, 1609
10058	2037	Michael Howard Rotberg, MD Charlotte Eye, Ear, Nose, and Throat Associates, PA 6035 Fairview Road Charlotte, NC 28210		1	1095
10059	11080	Scott M. Corin, MD Advanced Eye Centers, Inc 500 Faunce Corner Road, Suite 110 Dartmouth, MA 02747		5	1128, 1138, 1139, 1183, 1191

Site Number	Investigator Number	Principal Investigator Name (Site Number), Address	Other Important Participants Name, Degree (Role)	N	Patient Numbers
10061	3225	James D. Branch, MD James D. Branch, MD 224 Town Run Lane Winston-Salem, NC 27101	(b) (6)	4	1292, 1304, 1370, 1568
10062	11160 1458	W. Colby Stewart, MD (Start date: 2008.05.13) Robert H. Stewart, MD (End date: 2008.05.13) Houston Eye Associates 2855 Gramercy St. Houston, TX 77025		0 8	1212, 1257, 1321, 1355, 1371, 1385, 1387, 1473
10064	10290	Jung Dao, MD Cornea Consultants of Arizona 3815 East Bell Road, Suite 2500 Phoenix, AZ 85032		9	1104, 1326, 1346, 1398, 1444, 1487, 1493, 1494, 1534
10065	2897	Mark Rubin, MD International Eye Associates 550 Memorial Circle, Suite N Ormond Beach, FL 32174		1	1448
10066	11088	Scott Portnoy, MD Allegheny Ophthalmology Associates 2853 Freeport Road Natrona Heights, PA 15065	(b) (6)	4	1269, 1288, 1376, 1548
10067	11095	Phillip Lee Shettle, DO Shettle Eye Center 670 North Clearwater-Largo Road Largo, FL 33770		1	1438
10071	11188	Hope Yongsmith, MD Innovis Health 1702 South University Drive Fargo, ND 58103		4	1233, 1241, 1615, 1637
10072	11183	Jose Luis Perez-Becerra, MD Belle Vue Eye Centre 1327 SW Military Drive San Antonio, TX 78221		7	1112, 1337, 1356, 1365, 1577, 1611, 1612
10073	11314	Barry A. Bohn, MD Gulf Coast Research 314 Audubon Blvd. Lafayette, LA 70503	(b) (6)	2	1313, 1578
10074	11315	Fred J. George, MD NEA Clinic Ophthalmology 416 East Washington Avenue, Suite B Jonesboro, AR 72401		3	1513, 1520, 1555

Site Number	Investigator Number	Principal Investigator Name (Site Number), Address	Other Important Participants Name, Degree (Role)	N	Patient Numbers
10075	11318	William Beck, MD Heartland Research Associates, LLC 700 Medical Center Drive, Suite 210 Newton, KS 67114	(b) (6)	16	1275, 1284, 1308, 1327, 1333, 1338, 1342, 1406, 1410, 1418, 1432, 1521, 1525, 1537, 1584, 1604
10076	11322	Harold E. Reaves, MD Harold E. Reaves, M.D, Inc 1127 Wilshire Blvd. Suite 504 Los Angeles, CA 90017	(b) (6) (b) (6)	4	1343, 1349, 1524, 1617
10077	11709	Belu Allam, MD Northwood Pediatrics 25214 Borough Park Drive The Woodlands, TX 77380	(b) (6)	8	1424, 1435, 1446, 1501, 1502, 1507, 1601, 1636
10084	10698	Kavita Surti, MD Atlantis EyeCare 236 West College	(b) (6) (b) (6))	38	1224, 1227, 1243, 1247,

	Investigator Number	Principal Investigator Name (Site Number), Address	Other Important Participants Name, Degree (Role)	N	Patient Numbers
10087	3727	Jeffrey A. Hirschfield, MD SCORE Physician Alliance, LLC 6499 38th Avenue North, Suite A-2 Saint Petersburg, FL 33710	(b) (6)	31	1240, 1255, 1266, 1274, 1335, 1414, 1419, 1457, 1478, 1486, 1509, 1512, 1516, 1530, 1538, 1545, 1547, 1550, 1553, 1557, 1574, 1592, 1599, 1610, 1614, 1619,

Note: curricula vitae for principal investigators have been truncated and do not include lists of publications (available upon request).

16.1.4 List and Description of Investigators

	Investigator Number	Principal Investigator Name and Address	Other Important Participants Name, Degree (Role)	N	Patient Numbers
10001	9727	Marilou G. Cruz, MD Premier Health Research Center, LLC 11525 Brookshire Ave. Suite 400 Downey, CA 90241	(b) (6)	32	1183, 1206, 1207, 1252, 1276, 1277, 1278, 1282, 1287, 1289, 1333, 1350, 1382, 1383, 1402, 1403, 1417, 1422, 1445, 1446, 1472, 1562, 1666

Site Number	Investigator Number	Principal Investigator Name and Address	Other Important Participants Name, Degree (Role)	N	Patient Numbers
10010	4615	Gail L. Torkildsen, MD Andover Eye Associates 138 Haverhill Street Andover, MA 01810	(b) (6)	1	1799
10013	12431	John D. Goosey, MD Houston Eye Associates 2855 Gramercy St. Houston, TX 77025	(b) (6)	25	1478, 1492, 1493, 1625, 1665, 1692, 1764, 1815

	Investigator Number	**Principal Investigator Name and Address**	**Other Important Participants Name, Degree (Role)**	**N**	**Patient Numbers**
13001	11134	Dr. Umang Mathur Dr. Shroff's Charity Eye Hospital 5027, Kedarnath Road, Daryaganj, New Delhi – 110002	(b) (6) (b) (6) -	12	1038, 1042, 1052, 1082, 1085, 1356, 1377, 1404, 1421, 1479, 1551, 1653

Site Number	Investigator Number	Principal Investigator Name and Address	Other Important Participants Name, Degree (Role)	N	Patient Numbers	
13004	11110	Dr. Rajesh Parekh Bhagwan Mahaveer Jain Hospital Miller's Road Vasanthnagar Bangalore - 52	(b) (6) (b) (6) (b) (6)r (b) (6)	66	1023, 1030, 1039, 1046, 1050, 1054, 1081, 1113, 1114, 1161, 1162, 1166, 1175, 1196, 1227, 1228, 1241, 1247, 1251, 1286, 1312, 1340, 1367, 1373, 1386, 1430, 1490, 1501, 1507, 1516, 1517, 1531, 1592, 1602, 1610, 1663, 1687, 1690, 1699, 1716, 1718, 1724, 1725, 1731, 1735, 1738, 1740, 1748	

Site Number	Investigator Number	Principal Investigator Name and Address	Other Important Participants Name, Degree (Role)	N	Patient Numbers
13008	11209	Dr. Mrs. Yasmin Rusi Bhagat Head of Ophthalmology Department St. George's Hospital Fort, Mumbai – 400 001	(b) (6)	84	10001, 10002, 10003, 10004, 10005, 10017, 10024, 10026, 10027, 10029, 10031, 10035, 10040, 10041, 10087, 10088, 10089, 11115, 11116, 11117, 11131, 11132, 11

Site Number	Investigator Number	Principal Investigator Name and Address	Other Important Participants Name, Degree (Role)	N	Patient Numbers	
13010	11215	Dr. Kini Kulai Shobha Vasan Eye Care Hospital F 22 Raman road AVK Nagar, Salem -4 Tamil Nadu	(b) (6) (b) (6)	49	1055, 1058, 1059, 1060, 1066, 1068, 1090, 1092, 1095, 1096, 1097, 1107, 1135, 1144, 1145, 1147, 1149, 1152, 1187, 1213, 1217, 1266, 1267, 1270, 1283, 1290, 1299, 1300, 1311, 1314, 1360, 1376, 1416, 1428, 1429, 1482, 1486, 1489, 1504, 1528, 1605, 1622, 1623, 1753, 1774, 1775, 1836,	

Site Number	Investigator Number	Principal Investigator Name and Address	Other Important Participants Name, Degree (Role)	N	Patient Numbers
13014	11130	Dr. Nita Shanbhag Omkar Eye Care Center 302/303 Koteshwar Plaza Junc of Jawaharlal Nehru road and RHB road, Mulund (West) Mumbai - 400080	(b) (6)	90	1230, 1261, 1269, 1271, 1272, 1291, 1292, 1343, 1344, 1349, 1359, 1388, 1389, 1390, 1410, 1432, 1433, 1443, 1481, 1491, 1502, 1509, 1530, 1549, 1550, 1567,

Site Number	Investigator Number	Principal Investigator Name and Address	Other Important Participants Name, Degree (Role)	N	Patient Numbers
13016	11589	Dr. Ganesh Balasubramaniam Jaya Eye Care Centre 12, Norton 3rd Lane Mandavelipakkam, Chennai - 600028	(b) (6)	24	1018, 1019, 1020, 1021, 1025, 1028, 1033, 1053, 1069, 1134

Site Number	Investigator Number	Principal Investigator Name and Address	Other Important Participants Name, Degree (Role)	N	Patient Numbers
13018	11591	Dr. Nelson Jesudasan C.A Institute of Ophthalmology Joseph Eye Hospital Melaputhur Trichy – 620001	(b) (6)	65	1256, 1259, 1260, 1301, 1302, 1309, 1310, 1336, 1348, 1370, 1412, 1413, 1424, 1434, 1437, 1474, 1480, 1496, 1498, 1499, 1553, 1560, 1563, 1566, 1588, 1589, 1700, 1701,

Site Number	Investigator Number	Principal Investigator Name and Address	Other Important Participants Name, Degree (Role)	N	Patient Numbers
13020	11593	Dr. Shanta A Motwane K J Somaiya Medical College & Hospital Near Everord Nagar, Sion, Mumbai – 400 022	(b) (6)	71	1070, 1074, 1075, 1076, 1094, 1098, 1157, 1163, 1165, 1167, 1168, 1202, 1203, 1215, 1234, 1239, 1262, 1293, 1294,

Site Number	Investigator Number	Principal Investigator Name and Address	Other Important Participants Name, Degree (Role)	Patient Numbers
13021	11607	Dr. Kummararaj G. Dr. A. Govindarajan Eye Hospitals, No: 06, Officers Colony, Puthur, Tiruchirappalli – 620017 Tamil Nadu, India	(b) (6)	1086, 1093, 1099, 1108, 1109, 1110, 1111, 1112, 1118, 1122, 1124, 1137, 1138, 1139, 1140, 1148, 1170, 1171, 1178, 1185, 1188, 1189, 1190, 11

Site Number	Investigator Number	Principal Investigator Name and Address	Other Important Participants Name, Degree (Role)	N	Patient Numbers
13023	11595	Prof. K. Vasantha Corneal Department, Regional Institute of Ophthalmology Rukmani Lakshmipati Road, Egmore, Chennai – 600008	(b) (6)	20	1235, 1236, 1237, 1238, 1240, 1243, 1279, 1280, 1296, 1298, 1385, 1391, 1419, 1484, 1485, 1487, 1488, 1584, 1897, 1925
13024	11596	Dr. Sanita Mary George Korah Ophthalmology Department	(b) (6)	6	1032, 1049, 11

Site Number	Investigator Number	Principal Investigator Name and Address	Other Important Participants Name, Degree (Role)	N	Patient Numbers	
13029	11603	Dr. Leslie Ravi Kumar Medisys Clinisearch Bangalore Eye Hospital and Retina Center #426, 4th Cross, 2nd Block Kalyan Nagar Bangalore-560043	(b) (6)	38	1006, 1007, 1008, 1010, 1011, 1012, 1013, 1014, 1015, 1016, 1022, 1036, 1044, 1045, 1047, 1048, 1071, 1078, 1128, 1142, 1233, 1325, 1606, 1607, 1612, 1649, 1651, 1679, 1706, 1715, 1721, 1760, 1782, 1797, 1831, 1909, 1921, 1928	

Note: curricula vitae for principal investigators have been truncated and do not include lists of publications (available upon request).

Linked Applications	Submission Type/Number	Sponsor Name	Drug Name / Subject
NDA 22548	ORIG 1	ALLERGAN	GATIFLOXACIN OPHTHALMIC SOLUTION 0.5%
NDA 22548	ORIG 1	ALLERGAN	GATIFLOXACIN OPHTHALMIC SOLUTION 0.5%

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/s/

RAPHAEL R RODRIGUEZ
08/27/2009