

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-262

ADMINISTRATIVE DOCUMENTS

1.4 PATENT INFORMATION AND CERTIFICATION

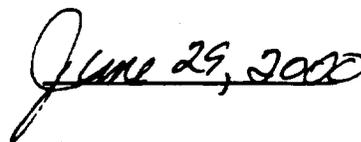
The following patents are currently in effect for Chlorine Dioxide (Purite) containing ophthalmic preparations. A copy of each patent is enclosed.

Patent Number	Patent Title	Expiration Date
U.S. Patent No. 5,424,078	Aqueous Ophthalmic Formulations and Methods for Preserving Same	June 13, 2012
U.S. Patent No. 5,736,165	In-the-Eye Use of Chlorine Dioxide Containing Compositions	April 7, 2015

I, the undersigned, hereby declare that Patent Nos. 5,424,078 and 5,736,165 covers the formulation, composition, and/or method of use of Chlorine Dioxide. This product that is the subject of this application for which approval is being sought is covered by these patents.



Peter A. Kresel, MS, MBA



(Date)

Sr. Vice President, Global Regulatory Affairs

Allergan, Inc.

1.5 CERTIFICATION FOR EXCLUSIVITY

Allergan, Inc. (the applicant) is submitting information in support of a request for three-year exclusivity per Sections 505 (c)(3)(D) and 505 (j)(4)(D) of the Federal Food, Drug and Cosmetic Act for Brimonidine Purity™ Ophthalmic Solution 0.15% NDA. The results of the following two controlled clinical studies demonstrate that Brimonidine-Purite™ Ophthalmic Solution 0.15% is safe and efficacious for the lowering of intraocular pressure in patients with open-angle glaucoma or ocular hypertension. In the applicant's opinion these studies are essential to the approval of the new drug application for Brimonidine-Purite™ Ophthalmic Solution 0.15%. The applicant is the sponsor of [REDACTED] under which these clinical studies were conducted:

190342-007

A Multicenter, Double-Masked, Randomized, Active-Controlled, Parallel-Group Study of the Safety and Efficacy of Brimonidine-Purite™ Ophthalmic Solution 0.15% used three times daily for up to one year for the lowering of intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

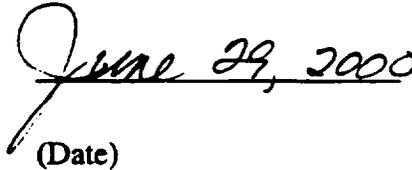
190342-008

A Multicenter, Double-Masked, Randomized, Active-Controlled, Parallel-Group Study of the Safety and Efficacy of Brimonidine-Purite™ Ophthalmic Solution 0.15% used three times daily for up to one year for the lowering of intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

Allergan, Inc., hereby certifies that to the best of our knowledge, the clinical investigations listed herein have not formed part of the basis of a finding of substantial evidence of effectiveness for a previously approved new drug application or supplement. Furthermore, no other drug product containing all of the same ingredients with the same conditions of approval has been previously approved for human use. The scientific literature has been thoroughly searched and in the applicant's opinion there are no published studies or publicly available reports of clinical investigations (other than those sponsored by the applicant) to support the approval of the new drug application for Brimonidine-Purite™ Ophthalmic Solution 0.15%. The applicant is not aware of any approvals of this product for human use.



Peter A. Kresel, MS, MBA



(Date)

Sr. Vice President, Global Regulatory Affairs

Allergan, Inc.

EXCLUSIVITY SUMMARY for NDA # 21-262 SUPPL #

Trade Name Alphagan P 0.15%
Generic Name brimonidine tartrate ophthalmic solution
Applicant Name Allergan Inc. HFD-550
Approval Date March 16, 2001

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete Parts II and III of this Exclusivity Summary only if you answer "YES" to one or more of the following questions about the submission.

- a) Is it an original NDA? YES / X / NO / /
- b) Is it an effectiveness supplement? YES / / NO / X /
- c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "NO.")

YES / X / NO / /

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

- d) Did the applicant request exclusivity?

YES / X / NO / /

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

3 years

e) Has pediatric exclusivity been granted for this Active Moiety?

YES /___/ NO /_X_/

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use? (Rx to OTC Switches should be answered No - Please indicate as such).

YES /___/ NO /_X_/

If yes, NDA # _____ Drug Name _____

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

3. Is this drug product or indication a DESI upgrade?

YES /___/ NO /_X_/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9 (even if a study was required for the upgrade).

PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES
(Answer either #1 or #2, as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES / / NO / /

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # 20-613 Brimonidine tartrate 0.2%

NDA # 20-490 Brimonidine tartrate 0.5%

NDA # _____

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES / / NO / /

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # _____
NDA # _____
NDA # _____

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9. IF "YES," GO TO PART III.

PART III: THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2, was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /_X_/ NO /___/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis

for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

- (a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES / / NO / /

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval **AND GO DIRECTLY TO SIGNATURE BLOCK ON Page 9:**

- (b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES / / NO / /

- (1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES / / NO / /

If yes, explain: _____

- (2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES / / NO / /

If yes, explain: _____

- (c) If the answers to (b) (1) and (b) (2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Investigation #1, Study # 190342-007

Investigation #2, Study # 190342-008

Investigation #3, Study # _____

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

- (a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES /___/ NO /_X_/

Investigation #2 YES /___/ NO /_X_/

Investigation #3 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

NDA # _____ Study # _____
NDA # _____ Study # _____
NDA # _____ Study # _____

- (b) For each investigation identified as "essential to the approval," does the investigation duplicate the results of another investigation that was relied on by the agency

to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /_X_/

Investigation #2 YES /___/ NO /_X_/

Investigation #3 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:

NDA # _____ Study # _____

NDA # _____ Study # _____

NDA # _____ Study # _____

- (c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Investigation # 1, Study # 190342-007

Investigation # 2, Study # 190342-008

Investigation # , Study # _____

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

(a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1

IND # YES /_X_/ NO /___/ Explain: _____

Investigation #2

IND # YES /_X_/ NO /___/ Explain: _____

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1

YES /___/ Explain _____ NO /___/ Explain _____

Investigation #2

YES /___/ Explain _____ NO /___/ Explain _____

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /___/

If yes, explain: _____

/S/

Jennifer Harris, M.D.
Signature of Preparer
Title: Medical Officer

12/22/00
Date

/S/

Wiley A. Chambers, M.D.
Signature of ~~Office of~~ Deputy Division Director

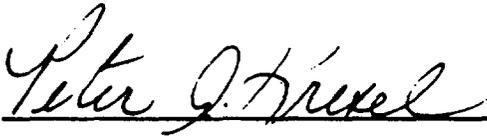
3/16/01
Date

cc:
HFD-093/Mary Ann Holovac
HFD-104/PEDS/T. Crescenzi

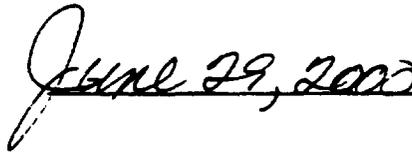
Form OGD-011347
Revised 8/7/95; edited 8/8/95; revised 8/25/98, edited 3/6/00

1.6 DEBARMENT CERTIFICATION

Allergan, Inc., 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.



Peter A. Kresel, MS, MBA



(Date)

Sr. Vice President, Global Regulatory Affairs

ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Attachment 3

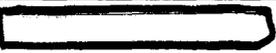
Application: **NDA 21262/000**
Stamp: **30-JUN-2000** Regulatory Due: **30-APR-2001**
Applicant: **ALLERGAN**
2525 DUPONT DR
IRVINE, CA 926239534

Priority: **3S** Org Code: **550**
Action Goal: District Goal: **01-MAR-2001**
Brand Name: **BRIMONIDINE TARTRATE 0.15%
TOPICAL SOLUT**
Established Name:
Generic Name: **BRIMONIDINE TARTRATE 0.15%
TOPICAL SOLUT**
Dosage Form: **SOL (SOLUTION)**
Strength: **0.15%**

FDA Contacts: **L. GORSKI (HFD-550) 301-827-2090 , Project Manager**
L. RODRIGUEZ (HFD-830) 301-827-2069 , Review Chemist
L. NG (HFD-830) 301-827-2511 , Team Leader

Overall Recommendation:

Establishment: **1643525**
ALLERGAN INC
8301 MARS DR
WACO, TX 76712

DMF No: 
AADA No:

Profile: **SNI** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **11-JUL-2000**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: **FINISHED DOSAGE
MANUFACTURER**

Establishment: **9610728** DMF No:
ALLERGAN PHARMACEUTICALS IR AADA No:
WESTPORT, COUNTY MAYO, EI

Profile: **CTL** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **10-JUL-2000**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: **FINISHED DOSAGE STABILITY
TESTER**

Establishment: 

DMF No:
AADA No:

Profile: **CSN** OAI Status: **NONE**
Last Milestone: **ASSIGNED INSPECTION TO IB**
Milestone Date: **29-SEP-2000**

Responsibilities: **DRUG SUBSTANCE
MANUFACTURER**

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Attachment 3

Establishment:

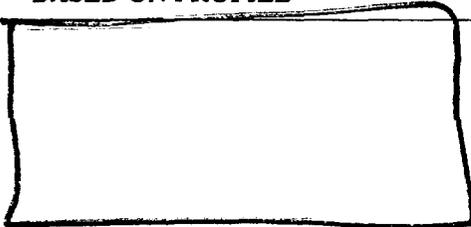


DMF No:
AADA No:

Profile: **GSP** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **24-AUG-2000**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities: **FINISHED DOSAGE STERILIZER**

Establishment:

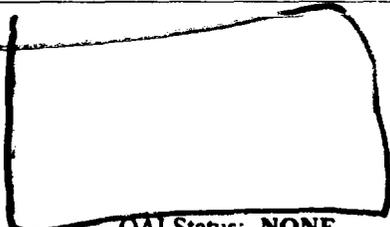


DMF No:
AADA No:

Profile: **RSP** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **24-AUG-2000**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities: **FINISHED DOSAGE STERILIZER**

Establishment:

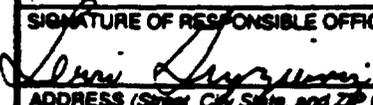


DMF No:
AADA No:

Profile: **CSN** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **10-JUL-2000**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities: **DRUG SUBSTANCE
MANUFACTURER**

DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE <i>(Title 21, Code of Federal Regulations 314 & 601)</i>		Form Approved: OMB No. 0910-0338 Expiration Date: April 30, 2000 See OMB Statement on last page.
		FOR FDA USE ONLY
		APPLICATION NUMBER
APPLICANT INFORMATION		
NAME OF APPLICANT Allergan, Inc.		DATE OF SUBMISSION 4/28/2000
TELEPHONE NO. (Include Area Code) 800/347-4500		FACSIMILE (FAX) Number (Include Area Code) 714/246-4272
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): 2525 Dupont Drive P.O. Box 18534 Irvine, CA 92623-9534		AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE
PRODUCT DESCRIPTION		
NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (if previously issued)		21-262
ESTABLISHED NAME (e.g., Proper name, USP/USAN name) Brimonidine Tartrate (USAN/INN)		PROPRIETARY NAME (trade name) IF ANY
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (if any)		CODE NAME (if any) AGN 190342
DOSAGE FORM: Topical Ophthalmic	STRENGTHS: 0.15%	ROUTE OF ADMINISTRATION: Topical
(PROPOSED) INDICATION(S) FOR USE: Indicated for the lowering of intraocular pressure in patients with open-angle glaucoma or ocular hypertension.		
APPLICATION INFORMATION		
APPLICATION TYPE (check one) <input checked="" type="checkbox"/> NEW DRUG APPLICATION (21 CFR 314.50) <input type="checkbox"/> ABBREVIATED APPLICATION (ANDA, AADA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (21 CFR part 601)		
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE <input checked="" type="checkbox"/> 505 (b) (1) <input type="checkbox"/> 505 (b) (2) <input type="checkbox"/> 507		
IF AN ANDA, OR AADA, IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION Name of Drug: _____ Holder of Approved Application: _____		
TYPE OF SUBMISSION (check one) <input checked="" type="checkbox"/> ORIGINAL APPLICATION <input type="checkbox"/> AMENDMENT TO A PENDING APPLICATION <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT <input type="checkbox"/> SUPAC SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input type="checkbox"/> OTHER		
REASON FOR SUBMISSION Request for marketing approval.		
PROPOSED MARKETING STATUS (check one) <input checked="" type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)		
NUMBER OF VOLUMES SUBMITTED <u>202</u>	THIS APPLICATION IS <input type="checkbox"/> PAPER <input checked="" type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> ELECTRONIC	
ESTABLISHMENT INFORMATION		
Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (construction sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFR), DMF number, and manufacturing steps and/or type of testing (e.g., Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.		
Refer to attachment.		
Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)		
IND 32,292 (Allergan, Inc.); NDA 20-613 Alphagan® Ophthalmic Solution (Allergan, Inc.);		

This application contains the following items: (Check all that apply)		
<input checked="" type="checkbox"/>	1. Index	
<input checked="" type="checkbox"/>	2. Labeling (check one) <input checked="" type="checkbox"/> Draft Labeling <input type="checkbox"/> Final Printed Labeling	
<input checked="" type="checkbox"/>	3. Summary (21 CFR 314.50 (c))	
<input checked="" type="checkbox"/>	4. Chemistry section	
	A. Chemistry, manufacturing, and controls information (e.g. 21 CFR 314.50 (d) (1), 21 CFR 601.2)	
	B. Samples (21 CFR 314.50 (e) (1), 21 CFR 601.2 (a)) (Submit only upon FDA's request)	
<input checked="" type="checkbox"/>	C. Methods validation package (e.g. 21 CFR 314.50 (e) (2) (i), 21 CFR 601.2)	
<input checked="" type="checkbox"/>	5. Nonclinical pharmacology and toxicology section (e.g. 21 CFR 314.50 (d) (2), 21 CFR 601.2)	
<input checked="" type="checkbox"/>	6. Human pharmacokinetics and bioavailability section (e.g. 21 CFR 314.50 (d) (3), 21 CFR 601.2)	
<input checked="" type="checkbox"/>	7. Clinical Microbiology (e.g. 21 CFR 314.50 (d) (4))	
<input checked="" type="checkbox"/>	8. Clinical data section (e.g. 21 CFR 314.50 (d) (5), 21 CFR 601.2)	
<input checked="" type="checkbox"/>	9. Safety update report (e.g. 21 CFR 314.50 (d) (5) (vi) (b), 21 CFR 601.2)	
<input checked="" type="checkbox"/>	10. Statistical section (e.g. 21 CFR 314.50 (d) (6), 21 CFR 601.2)	
<input checked="" type="checkbox"/>	11. Case report tabulations (e.g. 21 CFR 314.50 (f) (1), 21 CFR 601.2)	
<input checked="" type="checkbox"/>	12. Case report forms (e.g. 21 CFR 314.50 (f) (2), 21 CFR 601.2)	
<input checked="" type="checkbox"/>	13. Patent information on any patent which claims the drug (21 U.S.C. 355 (b) or (c))	
<input checked="" type="checkbox"/>	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b) (2) or (j) (2) (A))	
	15. Establishment description (21 CFR Part 600, if applicable)	
<input checked="" type="checkbox"/>	16. Debarment certification (FD&C Act 306 (k)(1))	
<input checked="" type="checkbox"/>	17. Field copy certification (21 CFR 314.5 (k) (3))	
<input checked="" type="checkbox"/>	18. User Fee Cover Sheet (Form FDA 3397)	
<input checked="" type="checkbox"/>	19. OTHER (Specify) Financial Disclosure	
<p>CERTIFICATION I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:</p> <ol style="list-style-type: none"> 1. Good manufacturing practice regulations in 21 CFR 210 and 211, 608, and/or 620. 2. Biological establishment standards in 21 CFR Part 600. 3. Labeling regulations in 21 CFR 201, 606, 610, 680 and/or 608. 4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR 202. 5. Regulations on making changes in applications in 21 CFR 314.70, 314.71, 314.72, 314.87, 314.88, and 601.12. 6. Regulations on reports in 21 CFR 314.80, 314.81, 600.80 and 600.81. 7. Local, state and Federal environmental impact laws. <p>If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision. The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate. Warning: a willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.</p>		
SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT		DATE
		6/29/00
TYPED NAME AND TITLE		
Lewis Gryziewicz, Director, Regulatory Affairs		
ADDRESS (Street, City, State, and ZIP Code)		Telephone Number
2525 Dupont Drive, P.O. Box 19534, Irvine, CA 92623-9534		(714) 246-6088
<p>Points regarding burden for this collection of information is estimated to average 40 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:</p> <p>OMB Reports Clearance Officer Paperwork Reduction Project (0910-0038) Hubert H. Humphrey Building, Room 531-H 200 Independence Avenue, S.W. Washington, DC 20501 Please DO NOT RETURN this form to the address.</p> <p>An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.</p>		

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION
APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR
AN ANTIBIOTIC DRUG FOR HUMAN USE
(Title 21, Code of Federal Regulations 314 & 601)

Form Approved: OMB No. 0910-0338
 Expiration Date: April 30, 2000
 See OMB Statement on last page.

FOR FDA USE ONLY
 APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT Allergan, Inc.		DATE OF SUBMISSION 8/28/2000	
TELEPHONE NO. (Include Area Code) 800/347-4500		FACSIMILE (FAX) Number (Include Area Code) 714/246-4272	
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): 2525 Dupont Drive P.O. Box 19534 Irvine, CA 92623-9534		AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE	

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (if previously issued)		21-262
ESTABLISHED NAME (e.g., Proper name, USP/USAN name) Brimonidine Tartrate (USAN/INN)		PROPRIETARY NAME (trade name) IF ANY
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (if any)	CODE NAME (if any) AGN 190342	
DOSAGE FORM: Topical Ophthalmic	STRENGTHS: 0.15%	ROUTE OF ADMINISTRATION: Topical

(PROPOSED) INDICATION(S) FOR USE: Indicated for the lowering of intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

APPLICATION INFORMATION

APPLICATION TYPE (check one) NEW DRUG APPLICATION (21 CFR 314.50) ABBREVIATED APPLICATION (ANDA, AADA, 21 CFR 314.94) BIOLOGICS LICENSE APPLICATION (21 CFR part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE 505 (b) (1) 505 (b) (2) 507

IF AN ANDA, OR AADA, IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
 Name of Drug: _____ Holder of Approved Application: _____

TYPE OF SUBMISSION

(check one) ORIGINAL APPLICATION AMENDMENT TO A PENDING APPLICATION RESUBMISSION

PRESUBMISSION ANNUAL REPORT ESTABLISHMENT DESCRIPTION SUPPLEMENT SUPAC SUPPLEMENT

EFFICACY SUPPLEMENT LABELING SUPPLEMENT CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT OTHER

REASON FOR SUBMISSION

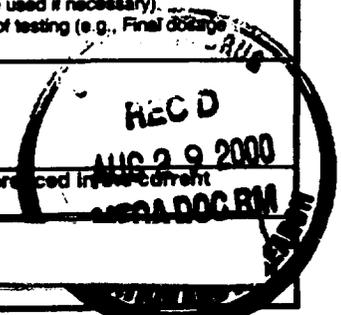
PROPOSED MARKETING STATUS (check one) PRESCRIPTION PRODUCT (Rx) OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED 1 THIS APPLICATION IS PAPER PAPER AND ELECTRONIC ELECTRONIC

ESTABLISHMENT INFORMATION

Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g., Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in this current application)



DEPARTMENT OF HEALTH AND HUMAN SERVICES
 Public Health Service
 Food and Drug Administration

Form Approved: OMB No. 0910-0396
 Expiration Date: 3/31/02

**CERTIFICATION: FINANCIAL INTERESTS AND
 ARRANGEMENTS OF CLINICAL INVESTIGATORS**

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

- (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigator	List Attached	

- (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).
- (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME Eric Brandt	TITLE Corporate Vice President and Chief Financial Officer
FIRM/ORGANIZATION Allergan, Inc.	
SIGNATURE 	DATE 10 APR 00

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
 Food and Drug Administration
 5600 Fishers Lane, Room 14C-03
 Rockville, MD 20857

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

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Please mark the applicable checkbox.

- (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators	List Attached	

- (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

- (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME Eric Brandt	TITLE Corporate Vice President and Chief Financial Officer
FIRM/ORGANIZATION Allergan, Inc.	
SIGNATURE 	DATE 10 APR 00

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Department of Health and Human Services
 Food and Drug Administration
 5600 Fishers Lane, Room 14C-03
 Rockville, MD 20857

LIST OF PRINCIPAL INVESTIGATORS/SUBINVESTIGATORS

Principal Investigators	Subinvestigators
Richard S. Bennion, M.D. (2973) Wenatchee Valley Clinic Research Dept. 820 North Chelan Wenatchee, WA 98801	Brian E. Bowe, M.D. (subinvestigator) Cooky Ogle, CCRC, Exec. Dir. (subinvestigator) Joan Horner, CRC (subinvestigator) Sandi Jones, CCRC (subinvestigator) Jamie Akers, CRC (subinvestigator)
E. Randy Craven, M.D. (2027) Glaucoma Consultants of Colorado 8381 South Park Lane Littleton, CO 80120	
Richard Evans, M.D. (2975) Keystone Research 9150 Huebner, Suite 280 San Antonio, TX 78229	Raymond H. Hernandez III, M.D. (subinvestigator)
Maher Fanous, M.D./ Gary N. Foulks, M.D. (2976) University of Pittsburgh The Eye and Ear Institute 203 Lothrop Street rm. 827 Pittsburgh, PA 15213	Francis S. Mah, M.D. (subinvestigator)
William C. Flynn, M.D. (3047) 999 E. Basse, Ste. 116 San Antonio, TX 78209	Stephen Waller, M.D. (subinvestigator) Monte Dirks, M.D. (subinvestigator) Steven Grimes, M.D. (subinvestigator)
Daniel Foreman, M.D. (2977) Clinical Research, Inc. 6620 Coyle Avenue, Suite 300 Carmichael, CA 95608	Dena Davidson, O.D. (subinvestigator)
Stephen Gee, M.D. (2978) 1210 Ward Ave. Honolulu, Oahu, HI 96814	
Charles S. Ostrov, M.D. (1796) Medical Vision Center Apache Medical Building 4001 Stinson Blvd., N.E., Suite 224 Minneapolis, MN 55421	Bonnie Bongard, M.D. (subinvestigator)
Michael J. Price, M.D., FRCSC (1183) 578 Main St. Malden, MA 02148	Mehmoosh Ashabi, O.D. (subinvestigator)

Edward R. Rashid, M.D. (1819) Keystone Research 5430 Fredericksburg Road, Suite 100 San Antonio, TX 78229	Robert A. Rice, M.D. (subinvestigator)
John Samples, M.D. (0622) Casey Eye Institute Oregon Health Sciences 3375 SW Terwilliger Blvd. Portland, OR 97201-4197	
Howard I. Schenker, M.D. (2429) Rochester Ophthalmological Group, P.C. 2100 South Clinton Avenue Rochester, NY 14618	Alan Gruber, M.D. (subinvestigator) Paul Hartman, M.D. (subinvestigator) Ronald Monacelli, O.D. (subinvestigator)
Gail F. Schwartz, M.D., P.A. (2944) GBMC Physicians Pavilion East 6565 N. Charles Street, Suite 316 Baltimore, MD 21204	Babak Eliassi-Rad, M.D. (subinvestigator) Lisa Abrams, M.D. (subinvestigator)
John D. Sheppard, M.D. (2091) VA Eye Consultants 403 Medical Tower Norfolk, VA 23507-1901	Bruce I. Bodner, M.D. (subinvestigator) April S. Rusch, B.S., COMT, CCRC (subinvestigator) Peter V. Mitrev, M.D. (subinvestigator)
Dong H. Shin, M.D., Ph.D. (0136) Detroit Medical Center University Eye Associates, P.C. Kresge Eye Institute 4717 St. Antoine Detroit, MI 48201-1423	Padmaja Nootheti, M.D. (subinvestigator) Bret A. Hughs, M.D. (subinvestigator) Mark S. Juzych, M.D. (subinvestigator)
Dara Stevenson, M.D. (2366) Stevenson Eye Center 3535 Bienville St., Ste. 325 East New Orleans, LA 70119	
William C. Stewart, M.D. (1783) Atlanta Research Company 2814 Spring Road, Suite 230 Atlanta, GA 30339	Douglas Day, M.D. (subinvestigator)
Lloyd Suter, M.D. (2985) Twin Tiers Eye Care Associates 40 Mitchell Ave. Binghamton, NY 13903	Francis Gilroy, M.D. (subinvestigator)
Thomas R. Walters, M.D. (1634) 1700 South Mopac Austin, TX 78746	James Montgomery, M.D. (subinvestigator)

Robert D. Williams, M.D. (2710) Taustine Eye Center Medical Arts Building 1169 Eastern Parkway, Suite 3334 Louisville, KY 40217	Lloyd R. Taustine, M.D. (subinvestigator) Brian K. Kritchman, M.D. (subinvestigator)
Lisa Wohl, M.D., S.C. (2986) Wohl Eye Center Willowlake Centre, Suite 200 303 E. Army Trail Rd. Bloomington, IL 60108	
Brandon Wool, M.D. (2835) 315 Metairie Road, Ste. 302 Metairie, LA 70005	

**APPEARS THIS WAY
ON ORIGINAL**

LIST OF PRINCIPAL INVESTIGATORS/SUBINVESTIGATORS

Principal Investigators	Subinvestigators
Mark Abelson, M.D. (1584)	Terry L.N. Chin, O.D. (subinvestigator) Jack V. Greiner, O.D., D.O., Ph.D. (subinvestigator) Kathleen Krenzer, O.D., Ph.D. (subinvestigator) Charles Leahy, O.D. (subinvestigator) H. Jerome Cramton, M.D. (subinvestigator) Gerald Spindel, M.D. (subinvestigator) Bernard Heersink, M.D. (subinvestigator) Diane Risco, O.D. (subinvestigator) Nabeel Jarudi, M.D. (subinvestigator) John Pietriantonio, O.D. (subinvestigator) Timothy Jordan, O.D. (subinvestigator) Douglas J. Blair, O.D. (subinvestigator) James R. Lenhart, O.D. (subinvestigator)
Edward Andersen, M.D. (2972)	Thomas P. Lang, M.D. (subinvestigator)
Jon Dietlein, M.D. (2974)	James Montgomery, M.D. (subinvestigator)
Harvey DuBiner, M.D. (2450)	
L. Jay Katz, M.D. (1960)	George L. Spaeth, M.D. (subinvestigator) Jonathan S. Myers, M.D. (subinvestigator) Richard P. Wilson, M.D. (subinvestigator) Marlene R. Moster, M.D. (subinvestigator) Court M. Schmidt, M.D. (subinvestigator) Richard Dwight Ten Hulzen, M.D. (subinvestigator) Asher Weiner, M.D. (subinvestigator) Helen Vistoria Danesh-Meyer, M.D. (subinvestigator) Jeff Henderer, (subinvestigator) Karl Siebert, M.D. (subinvestigator) Erkan Mutlukan, M.D. (subinvestigator)
Alex Kent, M.D. (2980)	Lisa Langdale, R.N. (subinvestigator)

Jeff Lozier, M.D. (2981)	Belinda Dure-Smith, M.D. (subinvestigator) Margaret Drehobl, M.D. (subinvestigator) Linda Skific, RNP(subinvestigator)
Jeffrey Morris, M.D. (2122)	Larry Rice, M.D. (subinvestigator) Janie Bodman, OD (subinvestigator) Chantelle Clarizio, OD (subinvestigator)
Thomas Mundorf, M.D. (1485)	
Matthew Parsons, M.D. (2983)	David Edwin Brodstein, M.D. (subinvestigator) Bradley W. Richards, M.D. (subinvestigator) Scott C. Richards, M.D. (subinvestigator)
Jay Perlman, M.D., Ph.D. (2987)	Geoffrey Emerick, M.D. (subinvestigator) Anuradha Khanna, M.D. (subinvestigator)
Arnold Prywes, M.D. (2893)	Craig Marcus, M.D. (subinvestigator)
Patrick Riedel, M.D. (2984)	Patricia Buehler, M.D. (subinvestigator) Robert C. Mathews, M.D. (subinvestigator) Nancy M. Bonetto, OD (subinvestigator) Janet Wilkerson, CCRC, Mgr. (subinvestigator)
Thomas Samuelson, M.D. (2161)	Elizabeth Davis, M.D. (subinvestigator) Eric Linebarger, M.D. (subinvestigator) Liz Davies (subinvestigator)
Steven Simmons, M.D. (1655)	Martin Kaback, M.D. (subinvestigator) Michael Moore, M.D (subinvestigator)
Richard T. Sturm, M.D. (1587)	Ronald M. Caronia, M.D. (subinvestigator) Stanley J. Berke, M.D. (subinvestigator) Barbara J. Burger, RN (subinvestigator)

**APPEARS THIS WAY
ON ORIGINAL**

Stuart A. Terry, M.D. (1512)	Sheldon Braverman, M.D. (subinvestigator) Thomas Oei, M.D. (subinvestigator)
Christopher M. Tortora, M.D. (2026)	Bruce Ballon, M.D. (subinvestigator) Douglas Chu, M.D. (subinvestigator)
Mark Weiss, M.D. (0642)	
Sidney Weiss, M.D. (0565)	William E. Berger, M.D., MBA (subinvestigator) Luis A. Channes, M.D. (subinvestigator) Mark S. Sugar, M.D. (subinvestigator) J. Ellen Schonfeld, RN, MN, CNP (subinvestigator) Janis K. Davidson, RN, MSN, CPNP (subinvestigator)
Eugene Barry Wolchok, M.D. (2988)	Anil Mahajan, M.D. (subinvestigator) Michael J. Koren, M.D. (subinvestigator)

**APPEARS THIS WAY
ON ORIGINAL**

DEPARTMENT OF HEALTH AND HUMAN SERVICES
 Public Health Service
 Food and Drug Administration

Form Approved: OMB No. 0910-0366
 Expiration Date: 3/31/02

**DISCLOSURE: FINANCIAL INTERESTS AND
 ARRANGEMENTS OF CLINICAL INVESTIGATORS**

TO BE COMPLETED BY APPLICANT

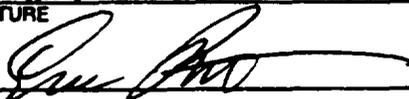
The following information concerning Dong H. Shin, who participated as a clinical investigator in the submitted study 190342-007

Brimonidine Purite™ Ophthalmic Solution, is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable checkboxes.

- any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;
- any significant payments of other sorts made on or after February 2, 1999 from the sponsor of the covered study such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;
- any proprietary interest in the product tested in the covered study held by the clinical investigator;
- any significant equity interest as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME		TITLE	
Eric Brandt		Corporate Vice President and Chief Financial Officer	
FIRM/ORGANIZATION			
Allergan, Inc.			
SIGNATURE		DATE	
		10 APR 00	

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 4 hours per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to:

Department of Health and Human Services
 Food and Drug Administration
 3600 Fishers Lane, Room 14C-03
 Rockville, MD 20857

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

The following information concerning Dong H. Shin, who participated as a clinical investigator in the submitted study 190342-007

Brimonidine Purite[®] Ophthalmic Solution, is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable checkboxes.

- any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;
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- any significant equity interest as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

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FIRM/ORGANIZATION	
Allergan, Inc.	
SIGNATURE	DATE
	10 APR 00

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Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

Financial Disclosure by Clinical Investigators

Investigator or Subinvestigator Name (Last, First, Middle Initial)	Date	Study Number
Shin, Dong H.	3/9/99	190342-007

Study Phase

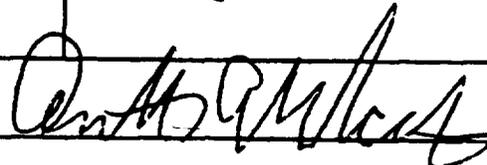
- Prestudy
- On-going monitoring (Only to be done for investigators/subinvestigators from whom information has not been previously collected for this study)
- Site close-out
- One year after close-out

Method of Information Collection

- Telephone contact
- Site visit

Question	Response	Comments If yes, describe briefly; If investigator does not provide information, state reason for refusal
1. Have you, your spouse or your dependent children entered into a financial arrangement with Allergan whereby the value of the compensation could be influenced by the outcome of the study?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
2. Have you, your spouse or your dependent children received any significant payments of other sorts (see definitions for clarification, if necessary) totaling more than \$25,000 (US) made on or after February 2, 1999 from Allergan? (Payment of other sorts would include a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, honoraria, etc.)	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
3. Do you, your spouse or your dependent children have any proprietary interest in the product being tested?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
4. Do you, your spouse or your dependent children have any equity interest (i.e., Allergan stock) greater than \$50,000 (US)?	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	maybe with \approx \$50,000 stock

Allergan Representative Obtaining Information:



Version date: February 1999

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

Form Approved: OMB No. 0910-0396
Expiration Date: 3/31/02

**DISCLOSURE: FINANCIAL INTERESTS AND
ARRANGEMENTS OF CLINICAL INVESTIGATORS**

TO BE COMPLETED BY APPLICANT

The following information concerning Dara Stevenson, who participated as a clinical investigator in the submitted study 190342-007, is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable checkboxes.

- any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;
- any significant payments of other sorts made on or after February 2, 1999 from the sponsor of the covered study such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;
- any proprietary interest in the product tested in the covered study held by the clinical investigator;
- any significant equity interest as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME Eric Brandt	TITLE Corporate Vice President and Chief Financial Officer
FIRM/ORGANIZATION Allergan, Inc.	
SIGNATURE 	DATE 10 APR 00

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Rockville, MD 20857

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

The following information concerning Dara Stevenson, who participated as a clinical investigator in the submitted study 190342-007

Brimonide Purite[®] Ophthalmic Solution, is submitted in accordance with 21 CFR part

54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable checkboxes.

- any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;
- any significant payments of other sorts made on or after February 2, 1999 from the sponsor of the covered study such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;
- any proprietary interest in the product tested in the covered study held by the clinical investigator;
- any significant equity interest as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME	TITLE
Eric Brandt	Corporate Vice President and Chief Financial Officer
FIRM/ORGANIZATION	
Allergan, Inc.	
SIGNATURE	DATE
	10 APR 00

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Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

1 233

Financial Disclosure by Clinical Investigators

Investigator or Subinvestigator Name (Last, First, Middle Initial)	Date	Study Number
<i>Hewson, Dara</i>	<i>04 Mar 1999</i>	<i>190342-007</i>

Study Phase

- Prestudy
- On-going monitoring (Only to be done for investigators/subinvestigators from whom information has not been previously collected for this study)
- Site close-out
- One year after close-out

Method of Information Collection

- Telephone contact
- Site visit

Question	Response	Comments If yes, describe briefly; If investigator does not provide information, state reason for refusal
1. Have you, your spouse or your dependent children entered into a financial arrangement with Allergan whereby the value of the compensation could be influenced by the outcome of the study?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
2. Have you, your spouse or your dependent children received any significant payments of other sorts (see definitions for clarification, if necessary) totaling more than \$25,000 (US) made on or after February 2, 1999 from Allergan? (Payment of other sorts would include a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, honoraria, etc.)	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
3. Do you, your spouse or your dependent children have any proprietary interest in the product being tested?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
4. Do you, your spouse or your dependent children have any equity interest (i.e., Allergan stock) greater than \$50,000 (US)?	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	<i>Purchased several years ago. Valued at ~ \$76,000.</i>

Allergan Representative Obtaining Information: _____

Version date: February 1999

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

FINAL EVALUATION OF CLINICAL INVESTIGATOR INSPECTIONS.

DATE: January 25, 2001

NDA 21-262
HFD-550

SPONSOR: Allergan
Product: brimonidine tartrate 0.15% topical ophthalmic solution
Chemical

Type: 3
Potential: S

Indications: For the lowering of intraocular pressure in patients with chronic open angle glaucoma or ocular hypertension.

Project
Manager: Lori Gorski

Medical
Officer: Jennifer Harris

I. Background:

These routine inspections were part of FDA's Bioresearch Monitoring Program, which includes inspections designed to validate clinical studies on which NDA 21-262 approval may be based and to assure that the rights and welfare of the human subjects of those studies were protected. These inspections were conducted in accordance with CP 7348.811, Clinical Investigators, in addition to concentrate in comparing source documents, case report forms (CRFs), and data listings in regard to primary endpoints, adverse drug events reporting and discontinued subjects in these protocols. Sites selected in corroboration between HFD-550 Division medical officer, Dr. Harris and DSI reviewer, Dr. Jose Carreras.

Name	City	Protocol	CL
O. Dara Stevenson, M.D.	New Orleans, Louisiana	#190342-007	NAI
Howard I. Schenker, M.D.	Rochester, New York	#190342-007	NAI
Alexander R. Kent, M.D.	Charleston, South Carolina	#190342-008	NAI
Jeffrey Morris, M.D.	Encinitas, CA	#190342-008	NAI

Key to Classifications

NAI = No deviation from regulations

VAI = Minor Deviation(s) from regulations

VERALL ASSESSMENT OF FINDINGS AND GENERAL RECOMMENDATIONS:

No objectionable conditions were found in the above sites, which would preclude the use of the data submitted in support of pending NDA.

Jose A. Carreras, M.D.

cc:
NDA 21-262
Division File
HFD-47/Currier