EXCLUSIVITY SUMMARY

NDA # 22-184 SUPPL # HFD # 520

Trade Name  Lumigan, 0.01%

Generic Name  bimatoprost ophthalmic solution

Applicant Name  Allergan, Inc.

Approval Date, If Known  8/31/10

PART I  IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy 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 a 505(b)(1), 505(b)(2) or efficacy supplement?  
      YES ☑️  NO ☐

      If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

      505(b)(1)

   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 ☑️  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 ☒  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 ☒

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

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

YES ☐  NO ☒

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (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).
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 8. (Caution: The questions in part II of the summary should only be answered “NO” for original approvals of new molecular entities.)

IF “YES,” GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs 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 ☒ NO ☐

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

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.

(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 8:

(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:

Study 192024-031

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

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 ☒
Investigation #2                       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:

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 ☒
Investigation #2                       YES ☐   NO ☐
If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

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"):

Study 192024-031

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

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Investigation #2

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<td>! Explain:</td>
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</table>

(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 □  NO □
Explain:

Investigation #2

YES □  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:

Name of person completing form: Michael Puglisi
Title: Regulatory Project Manager
Date: August 20, 2010

Name of Office/Division Director signing form: Wiley A. Chambers, M.D.
Title: Acting Director, Division of Anti-Infective and Ophthalmology Products

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05
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<td>ORIG-1</td>
<td>ALLERGAN INC</td>
<td>Lumigan (bimatoprost ophthalmic solution) 0.01%</td>
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/s/

MICHAEL J PUGLISI
09/02/2010

WILEY A CHAMBERS
09/03/2010
1.3.3 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.

Paul Stone, Ph.D.,
Director,
Global Regulatory Affairs

31 May, 2007
Date
To: Paul Stone  From: Mike Puglisi, Project Manager

Fax: 714-246-4272  Fax: 301-796-9881

Phone:  Phone: 301-796-0791

Pages: 2 (including cover page)  Date: April 14, 2008

Re: CMC Information Request re: NDA 22-184

☐ Urgent  ☐ For Review  ☐ Please Comment  ☐ Please Reply  ☐ Please Recycle

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW. If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination or other action based on the content of the communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us at the above address by mail. Thank you.

● Comments:

Paul,

Attached please find an information request from the CMC reviewer concerning NDA 22-184. Please respond in an amendment to the NDA. Please let me know if you have any questions about this matter. Thanks.

Mike
Reviewer’s Comments:

We acknowledge receiving the stability update via the March 11, 2008 amendment. Please explain the high variability in the testing results observed for the sublots deriving from different bulk batches of the drug product. As an example, the following variable results of the weight loss testing were observed: Please provide a response by April 15, 2008.
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/s/
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Michael Puglisi
4/14/2008 12:38:18 PM
Paul,

Below please find an information request from the Quality Micro reviewer concerning NDA 22-184. Please respond in an amendment to the NDA. Please let me know if you have any questions about this matter. Thanks.

Mike

Reviewer's Comments:

The drug product should have an endotoxin limit and a validated endotoxin test method should be part of the drug product specifications. The suggested limit is [redacted]. Endotoxin testing should also be performed at release and expiry on stability samples.
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/s/
Michael Puglisi
2/14/2008 09:41:43 AM
To: Paul Stone  From: Mike Puglisi, Project Manager

Fax: 714-246-4272  Fax: 301-796-9881

Phone: 301-796-0791

Pages: 2 (including cover page)  Date: February 12, 2008

Re: CMC Information Request re: NDA 22-184

☐ Urgent  ☐ For Review  ☐ Please Comment  ☐ Please Reply  ☐ Please Recycle

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Comments:

Paul,

Attached please find another information request from the CMC reviewer concerning NDA 22-184. Please let me know if you have any questions about this matter. Thanks.

Mike
Please address the following CMC comments for NDA 22-184:

1. Please confirm that the container/closure system (including inks) proposed for the current bimatoprost formulation (0.01%) is the same as the one for the approved NDA 21-275 (please provide the date of approval of the bottles for Lumigan™). Please provide a table comparing all components of the container closure systems (e.g. components, bottle sizes, fill volumes and materials, including inks) for the two products.

2. Please provide information regarding the safety and acceptability of the inks to be used in the marketed container/closure system for the proposed drug product. Confirm that the extractable studies were conducted on the finished container/closure system (i.e. using all the proposed inks) and no extractables were derived from the inks to be used for the commercial containers. Also, confirm that no secondary packaging-related leachables have been detected in the proposed bimatoprost drug product (0.01%).

3. Please note that in your Batch Release Analysis Summary (Table 3.2.P.5.4-2) the acceptance criteria and test results for benzalkonium chloride assay reported for lots 12000, 12001, and 12002 do not correspond to the level of benzalkonium chloride (200 ppm BAK) declared for each of these lots (‘Dosage Strength’, second row of the table). Please clarify.

4. Please provide updated stability data for the drug product. Please include the most updated results of the weight loss. Note that the expiration dating will be based on the available and acceptable stability information including the amount of data generated up to date.
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/s/

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Michael Puglisi
2/12/2008 08:44:01 AM
To: Paul Stone  From: Mike Puglisi, Project Manager
Fax: 714-246-4272  Fax: 301-796-9881
Phone: Phone: 301-796-0791
Pages: 1 (including cover page)  Date: December 10, 2007
Re: CMC Information Request re: NDA 22-184

☐ Urgent  ☐ For Review  ☐ Please Comment  ☐ Please Reply  ☐ Please Recycle

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* Comments: *

Paul,

Below please find an information request from the CMC reviewer concerning NDA 22-184. Please let me know if you have any questions about this matter. Thanks.

Mike

*Reviewer’s Comments:*

*We have been informed that one of the facilities listed in your application as the drug substance tester and the drug product stability tester, i.e., Allergan Pharmaceuticals (Ireland) Ltd., Castle Road, Westport, County Mayo, Ireland (CFN 9610728), is no longer in operation. Please confirm. In addition, please state which facility performs the drug substance release and the drug product stability testing.*
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/s/
---------------------
Michael Puglisi
1/2/2008 11:05:51 AM
Faxed to Sponsor on 12/10/07
**REQUEST FOR CONSULTATION**

**TO**: CDER OSE CONSULTS  
**FROM**: Mike Puglisi  
Phone: 301-796-0791  
Project Manager  
Division of Anti-Infective and Ophthalmology Products

**DATE**: November 9, 2007  
**IND NO.**:  
**NDA NO.**: 22-184  
**TYPE OF DOCUMENT**: Orig. NDA - Trade Name Review  
**DATE OF DOCUMENT**: October 5, 2007  
**NAME OF DRUG**: Lumigan RC (bimatoprost ophthalmic solution) 0.01%  
**PRIORITY CONSIDERATION**: (trade name review)  
**CLASSIFICATION OF DRUG**: Prostaglandin  
**DESIRED COMPLETION DATE**: February 9, 2008

**NAME OF FIRM**: Allergan, Inc.

**REASON FOR REQUEST**

I. GENERAL

- NEW PROTOCOL
- PROGRESS REPORT
- NEW CORRESPONDENCE
- DRUG ADVERTISING
- ADVERSE REACTION REPORT
- MANUFACTURING CHANGE/ADDITION
- MEETING PLANNED BY
- TRADE NAME REVIEW
- CONTROL SUPPLEMENT
- RESPONSE TO DEFICIENCY LETTER
- FINAL PRINTED LABELING
- LABELING REVISION
- ORIGINAL NEW CORRESPONDENCE
- FORMULATIVE REVIEW
- OTHER (SPECIFY BELOW):

II. BIOMETRICS

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<td>CONTROLLED STUDIES</td>
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<td>PROTOCOL REVIEW</td>
<td>OTHER (SPECIFY BELOW):</td>
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III. BIOPHARMACEUTICS

- DISSOLUTION
- BIOAVAILABILITY STUDIES
- PHASE IV STUDIES
- DEFICIENCY LETTER RESPONSE
- PROTOCOL-BIOPHARMACEUTICS
- IN-VIVO WAIVER REQUEST

V. SCIENTIFIC INVESTIGATIONS

- CLINICAL
- PRECLINICAL

**COMMENTS:**

Please provide a trade name review for the name “Lumigan RC” for NDA 22-184. This NDA is for a new lower strength formulation of Allergan’s approved Lumigan product (NDA 21-275). This NDA was submitted as a Gateway electronic submission. It can be accessed in the EDR via the following link: `\\CDSESUB1\EVSPROD\NDA022184\022184.ENX`. The sponsor did not propose a trade name in the original submission dated 7/2/07, but rather in the 10/5/07 amendment. Let me know if you need any additional information.

The Sponsor’s proposed labeling does not reflect comment by DAIOP reviewers.

This NDA has a Standard review clock (10-month) with a PDUFA goal date of 5/3/08. The Division is requesting a 90 day (or earlier) turn-around.

Questions? Please let me know. Thanks. Mike

**SIGNATURE OF REQUESTER**  
**METHOD OF DELIVERY (Check one)**  
DFS & email  
**SIGNATURE OF RECEIVER**  
**SIGNATURE OF DELIVERER**
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/s/
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Michael Puglisi
11/9/2007 01:48:58 PM
NDA 22-184

Allergan, Inc.
Attention: Paul Stone, Ph.D.
Director, Regulatory Affairs
2525 Dupont Drive
P.O. Box 19534
Irvine, California  92623-9534

Dear Dr. Stone:

Please refer to your July 2, 2007, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Bimatoprost Ophthalmic Solution, 0.01%.

We also refer to your submission dated August 22, 2007.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application has been filed under section 505(b) of the Act on September 1, 2007, in accordance with 21 CFR 314.101(a).

At this time, we have not identified any potential filing review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review.

If you have any questions, call Michael Puglisi, Project Manager, at (301) 796-0791.

Sincerely,

{See appended electronic signature page}

Maureen P. Dillon-Parker
Chief, Project Management Staff
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
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/s/

Maureen Dillon-Parker
9/13/2007 02:50:22 PM
NDA 22-184 FILING COMMUNICATION
NDA 22-184

Allergan, Inc.
Attention: Paul Stone, Ph.D.
Director, Regulatory Affairs
2525 Dupont Drive
P.O. Box 19534
Irvine, California 92623-9534

Dear Dr. Stone:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: bimatoprost ophthalmic solution, 0.01%

Review Priority Classification: Standard (S)

Date of Application: July 2, 2007

Date of Receipt: July 3, 2007

Our Reference Number: NDA 22-184

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on September 1, 2007, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be May 3, 2008.

Please cite the NDA number listed above at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Anti-Infective and Ophthalmology Products
5901-B Ammendale Road
Beltsville, MD 20705-1266
If you have any questions, call Michael Puglisi, Project Manager, at (301) 796-0791.

Sincerely,

{See appended electronic signature page}

Maureen P. Dillon-Parker  
Chief, Project Management Staff  
Division of Anti-Infective and Ophthalmology Products  
Office of Antimicrobial Products  
Center for Drug Evaluation and Research
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/s/
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Maureen Dillon-Parker
7/31/2007 01:45:47 PM
NDA 22-184; NDA Ack Ltr
**REQUEST FOR CONSULTATION**

**TO (Division/Office):**
Sheila Ryan  
DHHS/FDA/CDER/OMP/DDMAC/HFD-042

**FROM:**
Mike Puglisi /Project Manager  
DHHS/FDA/CDER/OND/ODE4/DAIOP HFD-520

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**NAME OF DRUG:**
bimatoprost ophthalmic solution, 0.01%

**PRIORITY CONSIDERATION:**
CLASSIFICATION OF DRUG: prostaglandin

**DESIRE COMPLETION DATE:**
January 17, 2008

**NAME OF FIRM:**
Allergan, Inc.

**REASON FOR REQUEST**

I. GENERAL

- NEW PROTOCOL
- PROGRESS REPORT
- NEW CORRESPONDENCE
- DRUG ADVERTISING
- ADVERSE REACTION REPORT
- MANUFACTURING CHANGE/ADDITION
- PRE-IND MEETING
- END OF PHASE 2
- RESUBMISSION
- SAFETY/EFFICACY
- ORIGINAL NDA
- CONTROL SUPPLEMENT

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH

- TYPE A OR B NDA REVIEW
- END OF PHASE II MEETING
- CONTROLLED STUDIES
- PROTOCOL REVIEW
- OTHER (SPECIFY BELOW):

STATISTICAL APPLICATION BRANCH

- CHEMISTRY REVIEW
- PHARMACOLOGY
- BIOPHARMACEUTICALS
- OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- DISSOLUTION
- BIOAVAILABILITY STUDIES
- PHASE IV STUDIES
- DEFICIENCY LETTER RESPONSE
- PROTOCOL-BIOPHARMACEUTICS
- IN-VIVO WAIVER REQUEST

V. SCIENTIFIC INVESTIGATIONS

- CLINICAL
- PRECLINICAL

**COMMENTS/SPECIAL INSTRUCTIONS:**
Please provide a consultative review on the sponsor’s proposed labeling for this NDA.

This is an entirely electronic NDA (Gateway). I’ll forward a copy of this consult form via interoffice mail. The NDA can be found in the EDR.

The sponsor’s proposed labeling does not reflect comment by HFD-520 reviewers.

If you have any questions, please contact me, Mike Puglisi, Project Manager at 301-796-0791. Thanks.
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/s/

Michael Puglisi
7/17/2007 01:29:39 PM
## ACTION PACKAGE CHECKLIST

### APPLICATION INFORMATION

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<td>Established/Proper Name:</td>
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<td>Applicant: Allergan, Inc.</td>
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<td>Agent for Applicant (if applicable):</td>
<td>DAIOP</td>
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<td>RPM:</td>
<td>Michael Puglisi</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### NDAs:

- NDA Application Type: [x] 505(b)(1) [ ] 505(b)(2)
- Efficacy Supplement: [ ] 505(b)(1) [x] 505(b)(2)

(A 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). Consult page 1 of the 505(b)(2) Assessment or the Appendix to this Action Package Checklist.)

- 505(b)(2) Original NDAs and 505(b)(2) NDA supplements:
  - Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s)):

  Provide a brief explanation of how this product is different from the listed drug.

  - If no listed drug, explain.
    - [ ] This application relies on literature.
    - [ ] This application relies on a final OTC monograph.
    - [ ] Other (explain)

  **Two months prior to each action, review the information in the 505(b)(2) Assessment and submit the draft to CDER OND IQ for clearance.** Finalize the 505(b)(2) Assessment at the time of the approval action.

  **On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.**

  - [ ] No changes [ ] Updated Date of check:

  If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.

### Actions

- Proposed action
- User Fee Goal Date is 5/3/08
- Previous actions (specify type and date for each action taken)

![ ] AP [ ] TA [ ] CR

![ ] None

- If accelerated approval or approval based on efficacy studies in animals, were promotional materials received?
  - Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain.

  [ ] Received

---

1 The Application Information section is (only) a checklist. The Contents of Action Package section (beginning on page 5) lists the documents to be included in the Action Package.

Version: 7/8/10
**Application Characteristics**

<table>
<thead>
<tr>
<th>Review priority:</th>
<th>Standard</th>
<th>Priority</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemical classification (new NDAs only):</td>
<td>5-S</td>
<td></td>
</tr>
</tbody>
</table>

| Fast Track | Rx-to-OTC full switch |
| Rolling Review | Rx-to-OTC partial switch |
| Orphan drug designation | Direct-to-OTC |

**NDAs: Subpart H**
- Accelerated approval (21 CFR 314.510)
- Restricted distribution (21 CFR 314.520)
- Approval based on animal studies

**BLAs: Subpart E**
- Accelerated approval (21 CFR 601.41)
- Restricted distribution (21 CFR 601.42)
- Approval based on animal studies

**Submitted in response to a PMR**

**Submitted in response to a PMC**

**Submitted in response to a Pediatric Written Request**

**Comments:**

**BLAs only: Ensure RMS-BLA Product Information Sheet for TBP and RMS-BLA Facility Information Sheet for TBP have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)**

**BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (approvals only)**

**Public communications (approvals only)**
- Office of Executive Programs (OEP) liaison has been notified of action
- Press Office notified of action (by OEP)
- Indicate what types (if any) of information dissemination are anticipated

---

2 Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new RMS-BLA Product Information Sheet for TBP must be completed.

Version: 78/10
<table>
<thead>
<tr>
<th><strong>Exclusivity</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Is approval of this application blocked by any type of exclusivity?</td>
</tr>
<tr>
<td>• NDAs and BLAs: Is there existing orphan drug exclusivity for the “same” drug or biologic for the proposed indication(s)? Refer to 21 CFR 316.3(b)(13) for the definition of “same drug” for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.</td>
</tr>
<tr>
<td>If yes, NDA/BLA # and date exclusivity expires:</td>
</tr>
<tr>
<td>• (b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? <em>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</em></td>
</tr>
<tr>
<td>If yes, NDA # and date exclusivity expires:</td>
</tr>
<tr>
<td>• (b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? <em>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</em></td>
</tr>
<tr>
<td>If yes, NDA # and date exclusivity expires:</td>
</tr>
<tr>
<td>• (b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? <em>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</em></td>
</tr>
<tr>
<td>If yes, NDA # and date exclusivity expires:</td>
</tr>
<tr>
<td>• NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? <em>(Note that, even if the 10-year approval limitation period has not expired, the application may be tentatively approved if it is otherwise ready for approval.)</em></td>
</tr>
<tr>
<td>If yes, NDA # and date 10-year limitation expires:</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Patent Information (NDAs only)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions.</td>
</tr>
<tr>
<td>21 CFR 314.50(i)(1)(i)(A)</td>
</tr>
<tr>
<td>☐ Verified</td>
</tr>
<tr>
<td>21 CFR 314.50(i)(1)</td>
</tr>
<tr>
<td>☐ (ii) ☐ (iii)</td>
</tr>
<tr>
<td>• [505(b)(2) applications] If the application includes a paragraph III certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval).</td>
</tr>
<tr>
<td>Date patent will expire</td>
</tr>
<tr>
<td>• [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). <em>(If the application does not include any paragraph IV certifications, mark “N/A” and skip to the next section below (Summary Reviews)).</em></td>
</tr>
</tbody>
</table>
• [505(b)(2) applications] For each paragraph IV certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation.

Answer the following questions for each paragraph IV certification:

(1) Have 45 days passed since the patent owner’s receipt of the applicant’s notice of certification?

(Note: The date that the patent owner received the applicant’s notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e)).

If “Yes,” skip to question (4) below. If “No,” continue with question (2).

(2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant’s notice of certification, as provided for by 21 CFR 314.107(f)(3)?

If “Yes,” there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip the rest of the patent questions.

If “No,” continue with question (3).

(3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?

(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2))).

If “No,” the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.

(4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?

If “Yes,” there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).

If “No,” continue with question (5).
(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner’s receipt of the applicant’s notice of certification?

(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period).

If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).

If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.

---

CONTENTS OF ACTION PACKAGE

- Copy of this Action Package Checklist
  - In Package

  Officer/Employee List

  - List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (approvals only)  - Included

  Documentation of consent/non-consent by officers/employees  - Included

  Action Letters

  - Copies of all action letters (including approval letter with final labeling)  - Action(s) and date(s)

  Labeling

  - Package Insert (write submission/communication date at upper right of first page of PI)
    - Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.  - Submitted 3/9/10
    - Original applicant-proposed labeling  - Submitted 7/2/07 - In Package
    - Example of class labeling, if applicable

---

3 Fill in blanks with dates of reviews, letters, etc.
Version: 7/8/10
Medication Guide/Patient Package Insert/Instructions for Use (write submission/communication date at upper right of first page of each piece)

- Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.
- Original applicant-proposed labeling
- Example of class labeling, if applicable

Labels (full color carton and immediate-container labels) (write submission/communication date on upper right of first page of each submission)

- Most-recent draft labeling

Proprietary Name
- Acceptability/non-acceptability letter(s) (indicate date(s))
- Review(s) (indicate date(s))

Labeling reviews (indicate dates of reviews and meetings)

Submitted 7/2/07

<table>
<thead>
<tr>
<th>Administrative / Regulatory Documents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Administrative Reviews (e.g., RPM Filing Review/Memo of Filing Meeting) (indicate date of each review)</td>
</tr>
<tr>
<td>All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte</td>
</tr>
<tr>
<td>NDA (b)(2) Approvals Only: 505(b)(2) Assessment (indicate date)</td>
</tr>
<tr>
<td>NDAs only: Exclusivity Summary (signed by Division Director)</td>
</tr>
<tr>
<td>Application Integrity Policy (AIP) Status and Related Documents <a href="http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm">http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm</a></td>
</tr>
<tr>
<td>Applicant is on the AIP</td>
</tr>
<tr>
<td>This application is on the AIP</td>
</tr>
<tr>
<td>o If yes, Center Director's Exception for Review memo (indicate date)</td>
</tr>
<tr>
<td>o If yes, OC clearance for approval (indicate date of clearance communication)</td>
</tr>
<tr>
<td>Pediatrics (approvals only)</td>
</tr>
<tr>
<td>o Date reviewed by PeRC</td>
</tr>
<tr>
<td>If PeRC review not necessary, explain: PREA is N/A</td>
</tr>
<tr>
<td>o Pediatric Page (approvals only, must be reviewed by PERC before finalized)</td>
</tr>
<tr>
<td>Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent (include certification)</td>
</tr>
<tr>
<td>Outgoing communications (letters (except action letters), emails, faxes, telecons)</td>
</tr>
<tr>
<td>Internal memoranda, telecons, etc.</td>
</tr>
</tbody>
</table>

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4 Filing reviews for scientific disciplines should be filed behind the respective discipline tab.
Version: 7/8/10
## Minutes of Meetings

- Regulatory Briefing *(indicate date of mtg)*
  - No mtg

- If not the first review cycle, any end-of-review meeting *(indicate date of mtg)*
  - N/A or no mtg

- Pre-NDA/BLA meeting *(indicate date of mtg)*
  - No mtg

- EOP2 meeting *(indicate date of mtg)*
  - No mtg 8/18/05

- Other milestone meetings (e.g., EOP2a, CMC pilots) *(indicate dates of mtgs)*

## Advisory Committee Meeting(s)

- Date(s) of Meeting(s)
  - No AC meeting

- 48-hour alert or minutes, if available *(do not include transcript)*

### Decisional and Summary Memos

- Office Director Decisional Memo *(indicate date for each review)*
  - None

- Division Director Summary Review *(indicate date for each review)*
  - None

- Cross-Discipline Team Leader Review *(indicate date for each review)*
  - None 5/1/08

- PMR/PMC Development Templates *(indicate total number)*
  - None

### Clinical Information

- Clinical Reviews
  - Clinical Team Leader Review(s) *(indicate date for each review)*
    - 4/15/08, 5/1/08
  - Clinical review(s) *(indicate date for each review)*
  - Social scientist review(s) (if OTC drug) *(indicate date for each review)*
    - None N/A

- Financial Disclosure reviews(s) or location/date if addressed in another review
  - In 4/15/08, Clinical Review

  OR
  - If no financial disclosure information was required, check here and include a review/memo explaining why not *(indicate date of review/memo)*

- Clinical reviews from immunology and other clinical areas/divisions/Centers *(indicate date of each review)*
  - None

- Controlled Substance Staff review(s) and Scheduling Recommendation *(indicate date of each review)*
  - Not applicable

- Risk Management
  - REMS Documents and Supporting Statement *(indicate date(s) of submission(s))*
  - None
  - REMS Memo(s) and letter(s) *(indicate date(s))*
  - None
  - Risk management review(s) and recommendations (including those by OSE and CSS) *(indicate date of each review and indicate location/date if incorporated into another review)*
    - None

- DSI Clinical Inspection Review Summary(ies) *(include copies of DSI letters to investigators)*
  - None requested In Package

---

5 Filing reviews should be filed with the discipline reviews.

Version: 7/8/10
<table>
<thead>
<tr>
<th>Clinical Microbiology</th>
<th>☑️ None</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Microbiology Team Leader Review(s) <em>(indicate date for each review)</em></td>
<td>☑️ None</td>
</tr>
<tr>
<td>Clinical Microbiology Review(s) <em>(indicate date for each review)</em></td>
<td>☑️ None</td>
</tr>
<tr>
<td>Biostatistics</td>
<td>☑️ None</td>
</tr>
<tr>
<td>Statistical Division Director Review(s) <em>(indicate date for each review)</em></td>
<td>☑️ None</td>
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<tr>
<td>Statistical Team Leader Review(s) <em>(indicate date for each review)</em></td>
<td>☑️ None</td>
</tr>
<tr>
<td>Statistical Review(s) <em>(indicate date for each review)</em></td>
<td>☑️ None 4/21/08</td>
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<tr>
<td>Clinical Pharmacology</td>
<td>☑️ None</td>
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<tr>
<td>Clinical Pharmacology Division Director Review(s) <em>(indicate date for each review)</em></td>
<td>☑️ None</td>
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<tr>
<td>Clinical Pharmacology Team Leader Review(s) <em>(indicate date for each review)</em></td>
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<td>Clinical Pharmacology review(s) <em>(indicate date for each review)</em></td>
<td>☑️ None 1/24/08</td>
</tr>
<tr>
<td>DSI Clinical Pharmacology Inspection Review Summary <em>(include copies of DSI letters)</em></td>
<td>☑️ None</td>
</tr>
<tr>
<td>Nonclinical</td>
<td>☑️ None</td>
</tr>
<tr>
<td>Pharmacology/Toxicology Discipline Reviews</td>
<td>☑️ None</td>
</tr>
<tr>
<td>ADP/T Review(s) <em>(indicate date for each review)</em></td>
<td>☑️ None</td>
</tr>
<tr>
<td>Supervisory Review(s) <em>(indicate date for each review)</em></td>
<td>☑️ None</td>
</tr>
<tr>
<td>Pharm/tox review(s), including referenced IND reviews <em>(indicate date for each review)</em></td>
<td>☑️ None 3/26/08</td>
</tr>
<tr>
<td>Review(s) by other disciplines/divisions/Centers requested by P/T reviewer <em>(indicate date for each review)</em></td>
<td>☑️ None</td>
</tr>
<tr>
<td>Statistical review(s) of carcinogenicity studies <em>(indicate date for each review)</em></td>
<td>☑️ No carc</td>
</tr>
<tr>
<td>ECAC/CAC report/memo of meeting</td>
<td>☑️ None Included in P/T review, page</td>
</tr>
<tr>
<td>DSI Nonclinical Inspection Review Summary <em>(include copies of DSI letters)</em></td>
<td>☑️ None requested</td>
</tr>
<tr>
<td>Product Quality</td>
<td>☑️ None</td>
</tr>
<tr>
<td>Product Quality Discipline Reviews</td>
<td>☑️ None</td>
</tr>
<tr>
<td>ONDQA/OBP Division Director Review(s) <em>(indicate date for each review)</em></td>
<td>☑️ None</td>
</tr>
<tr>
<td>Branch Chief/Team Leader Review(s) <em>(indicate date for each review)</em></td>
<td>☑️ None</td>
</tr>
<tr>
<td>Product quality review(s) including ONDQA biopharmaceutics reviews <em>(indicate date for each review)</em></td>
<td>☑️ None 3/14/08, 4/18/08, 5/1/08, 4/21/10</td>
</tr>
<tr>
<td>Microbiology Reviews</td>
<td>☑️ Not needed</td>
</tr>
<tr>
<td>NDAs: Microbiology reviews *(sterility &amp; pyrogenicity) (OPS/NDMS) <em>(indicate date of each review)</em></td>
<td>☑️ Not needed 2/4/08, 4/17/08, 6/8/09</td>
</tr>
<tr>
<td>BLAs: Sterility assurance, microbiology, facilities reviews *(DMPQ/MAPCB/BMT) <em>(indicate date of each review)</em></td>
<td>☑️ None</td>
</tr>
<tr>
<td>Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer <em>(indicate date of each review)</em></td>
<td>☑️ None</td>
</tr>
</tbody>
</table>
## Environmental Assessment (check one) (original and supplemental applications)

- **Categorical Exclusion (indicate review date)** (all original applications and all efficacy supplements that could increase the patient population)
  - In 3/14/08 Product Quality Review

- **Review & FONSI (indicate date of review)**
- **Review & Environmental Impact Statement (indicate date of each review)**

## Facilities Review/Inspection

- **NDAs**: Facilities inspections (include EER printout) *(date completed must be within 2 years of action date)* (only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites)
  - Date completed: 4/16/10
  - Acceptable
  - Withhold recommendation
  - Not applicable

- **BLAs**: TB-EER *(date of most recent TB-EER must be within 30 days of action date)* (original and supplemental BLAs)
  - Date completed:
  - Acceptable
  - Withhold recommendation

## NDAs: Methods Validation *(check box only, do not include documents)*

- Completed
- Requested
- Not yet requested
- Not needed (per review)

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* I.e., a new facility or a change in the facility, or a change in the manufacturing process in a way that impacts the Quality Management Systems of the facility.

Version: 7/8/10