APPLICATION NUMBER:
21-132

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS
1.3.5.3 Patent Exclusivity

Allergan, Inc., (the applicant) is requesting that three years of exclusivity be granted for NDA 22-427, Ketorolac tromethamine ophthalmic solution 0.45% based on the provisions set forth in 21 CFR 314.108(b)(4). The results of the following two controlled clinical trials (191578-005 and 191578-006) demonstrate that Ketorolac tromethamine ophthalmic solution 0.45% is safe and efficacious for the treatment of postoperative inflammation and ocular pain following cataract extraction. The 0.45% formulation includes formulation enhancements that reduce the frequency of dosing from QID to BID, while improving the overall bioavailability into the eye and eye comfort. In the applicant's opinion, these studies are essential to the approval of NDA 22-427. This applicant is the sponsor of IND 21,132 under which these clinical studies were conducted.

Clinical Study No. 191578-005:
A Multi Center, Double Masked, Randomized Parallel Group Study Evaluating the Safety and Efficacy of a New Formulation of Ketorolac Tromethamine 0.45% Ophthalmic Solution Compared with Vehicle Administered Preoperatively and Twice-Daily Postoperatively for Two Weeks for the Treatment of Anterior Segment Inflammation, Pain, and Inhibition of Surgically Induced Miosis Following Cataract Extraction with Posterior Chamber Intraocular Lens (IOL) Implantation.

Clinical Study No. 191578-006:
A Multi Center, Double Masked, Randomized Parallel Group Study Evaluating the Safety and Efficacy of a New Formulation of Ketorolac Tromethamine 0.45% Ophthalmic Solution Compared with Vehicle Administered Preoperatively and Twice-Daily Postoperatively for Two Weeks for the Treatment of Anterior Segment Inflammation, Pain, and Inhibition of Surgically Induced Miosis Following Cataract Extraction with Posterior Chamber Intraocular Lens (IOL) Implantation.

Allergan, Inc., hereby certifies that to the best of our knowledge, clinical investigations 191578-005 and 191578-006 meet the definition of "new clinical investigation" as set forth in 21 CFR 314.108(a).

To the best of our knowledge, there are no published studies or publicly available reports of clinical investigations (other than the studies sponsored by the applicant) to support the approval of NDA 22-427 for Ketorolac tromethamine ophthalmic solution 0.45%.

Elizabeth Bancroft, Senior Director
Regulatory Affairs

15 Aug 2008
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/
------------------
Wiley Chambers
7/22/2009 11:47:39 AM
EXCLUSIVITY SUMMARY

NDA # 22-427
SUPPL #
HFD # 520/DAIOP

Trade Name  ACUVAIL

Generic Name  ketorolac tromethamine ophthalmic solution, 0.45%

Applicant Name  Allergan, Inc.

Approval Date, If Known  July 22, 2009

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? 

NO  

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).
NDA#  19-700      Acular
NDA#  21-528      Acular LS
NDA#  20-811      Acular PF

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:

Clinical trial #191578-005
Clinical trial #191578-006

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


Investigation #2


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


Investigation #2


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

\[ \text{Clinical trial \#191578-005} \]
\[ \text{Clinical trial \#191578-006} \]

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"):

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 # 21,132 YES ✗ ! NO ☐ ! Explain:

   Investigation #2
   
   IND # 21,132 YES ✗ ! 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 ☐  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:  Raphael Rodriguez & William Boyd, M.D.
Title:  RPM & TL Medical Officer
Date:

Name of Office/Division Director signing form:  Wiley A. Chambers, M.D.
Title:  Acting Director, DIAOP

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05
PEDiATRIC PAGE
(Complete for all filed original applications and efficacy supplements)

iDA/BLA#: 22-427
Division Name: Division of Anti-Infective and Ophthalmology Products
Proprietary Name: Acuvail
Established/Generic Name: ketorolac tromethamine ophthalmic solution 0.45%
Dosage Form: topical ophthalmic solution
Applicant/Sponsor: Allergan, Inc.

Indication(s) previously approved (please complete this question for supplements and Type 6 NDAs only):
(1) 
(2) 
(3) 
(4) 

Pediatric use for each pediatric subpopulation must be addressed for each indication covered by current application under review. A Pediatric Page must be completed for each indication.

Number of indications for this pending application(s): 1
(Attach a completed Pediatric Page for each indication in current application.)

Indication: Treatment of pain and inflammation following cataract surgery.

Q1: Is this application in response to a PREA PMR? 
Yes ☐ Continue
No ☒ Please proceed to Question 2.

If Yes, iDA/BLA#: ________ Supplement #:______ PMR #:______

Does the division agree that this is a complete response to the PMR?
☐ Yes. Please proceed to Section D.
☐ No. Please proceed to Question 2 and complete the Pediatric Page, as applicable.

Q2: Does this application provide for (If yes, please check all categories that apply and proceed to the next question):
(a) NEW ☐ active ingredient(s) (includes new combination); ☒ indication(s); ☐ dosage form; ☐ dosing regimen; or ☐ route of administration?*

(b) ☐ No. PREA does not apply. Skip to signature block.

* Note for CDER: SE5, SE6, and SE7 submissions may also trigger PREA.

Q3: Does this indication have orphan designation?
☐ Yes. PREA does not apply. Skip to signature block.
☒ No. Please proceed to the next question.

Q4: Is there a full waiver for all pediatric age groups for this indication (check one)?
☒ Yes: (Complete Section A.)
☐ No: Please check all that apply.
☐ Partial Waiver for selected pediatric subpopulations (Complete Sections B)
☐ Deferred for some or all pediatric subpopulations (Complete Sections C)
☐ Completed for some or all pediatric subpopulations (Complete Sections D)
☐ Appropriately Labeled for some or all pediatric subpopulations (Complete Sections E)
☐ Extrapolation in One or More Pediatric Age Groups (Complete Section F)

IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL (cedrpmhs@fda.hhs.gov) OR AT 301-796-0700.
Pediatric Research and Equity Act Waivers

IND/NDA/BLA #: 22-427  Supplement Type:  Supplement Number:

Product name and active ingredient/dosage form: Acuvail (ketorolac tromethamine ophthalmic solution) 0.45%

Sponsor: Allergan, Inc.

Indications(s): Treatment of pain and inflammation following cataract surgery

1. Pediatric age group(s) to be waived.

Full waiver for all pediatric groups.

2. Reason(s) for waiving pediatric assessment requirements (choose all that apply and provide justification):

   a. Studies are impossible or highly impractical (e.g. the number of pediatric patients is so small or is geographically dispersed). If applicable, chose from adult-related conditions in Attachment I

   b. The product would be ineffective or unsafe in one or more of the pediatric group(s) for which a waiver is being requested. Note: If this is the reason the studies are being waived, this information MUST be included in the pediatric use section of labeling. Please provide the draft language you intend to include in the label. Suggested language includes, “FDA has not required pediatric studies in ages ___ to ___ because (state the safety or effectiveness reason).”

   c. The product fails to represent a meaningful therapeutic benefit over existing therapies for pediatric patients and is unlikely to be used in a substantial number of all pediatric age groups or the pediatric age group(s) for which a waiver is being requested.

The product fails to represent a meaningful therapeutic benefit for pediatric patients and is unlikely to be used in a substantial number of all pediatric age groups.

   d. Reasonable attempts to produce a pediatric formulation for one or more of the pediatric age group(s) for which the waiver is being requested have failed. (Provide documentation from Sponsor) Note: Sponsor must provide data to support this claim for review by the Division, and this report submitted by the Sponsor will be publicly posted.
**Attachment I**

**Adult-Related Conditions that do not occur in pediatrics and qualify for a waiver**

These conditions qualify for waiver because studies would be impossible or highly impractical

- Age-related macular degeneration
- Alzheimer’s disease
- Amyotrophic lateral sclerosis
- Atherosclerotic cardiovascular disease
- Benign prostatic hypertrophy
- Chronic Obstructive Pulmonary Disease
- Erectile Dysfunction
- Infertility
- Menopausal and perimenopausal disorders
- Organic amnesic syndrome
- (not caused by alcohol or other psychoactive substances)
- Osteoarthritis
- Parkinson’s disease
- Postmenopausal Osteoporosis
- Vascular dementia/ Vascular cognitive disorder/impairment

Cancer:
- Basal cell
- Bladder
- Breast
- Cervical
- Colorectal
- Endometrial
- Gastric
- Hairy cell leukemia
- Lung (small & non-small cell)
- Multiple myeloma
- Oropharynx (squamous cell)
- Ovarian (non-germ cell)
- Pancreatic
- Prostate
- Renal cell
- Uterine
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

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Wiley Chambers
7/22/2009 11:48:33 AM
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.

Elizabeth Bancroft
Senior Director
Regulatory Affairs

15 August 2008
# ACTION PACKAGE CHECKLIST

## APPLICATION INFORMATION

<table>
<thead>
<tr>
<th>NDA #</th>
<th>22427</th>
</tr>
</thead>
<tbody>
<tr>
<td>BLA #</td>
<td></td>
</tr>
<tr>
<td>NDA Supplement #</td>
<td>N/A</td>
</tr>
<tr>
<td>BLA STN #</td>
<td></td>
</tr>
<tr>
<td>If NDA, Efficacy Supplement Type</td>
<td>N/A</td>
</tr>
</tbody>
</table>

### Proprietary Name: ACUVAIL
Established/Proper Name: ketorolac tromethamine ophthalmic solution, 0.45%
Dosage Form: 

RPM: Raphael Rodriguez

### Division: Anti-Infective & Ophthalmology Products

### NDA(s):
- NDA Application Type: □ 505(b)(1) □ 505(b)(2)
- Efficacy Supplement: □ 505(b)(1) □ 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 NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)

505(b)(2) Original NDAs and 505(b)(2) NDA supplements:
Listed drug(s) referred to in 505(b)(2) application (include NDA/ANDA #(s) and drug name(s)):

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

☐ If no listed drug, check here and explain:

Prior to approval, review and confirm the information previously provided in Appendix B to the Regulatory Filing Review by re-checking the Orange Book for any new patents and pediatric exclusivity. If there are any changes in patents or exclusivity, notify the OND ADRA immediately and complete a new Appendix B of the Regulatory Filing Review.

☐ 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.

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

- User Fee Goal Date
  Action Goal Date (if different)  07-31-09
- Actions
  - Proposed action
    ☒ AP ☐ TA ☐ AE
    ☐ NA ☐ CR
  - Previous actions (specify type and date for each action taken)
    ○ None
- Promotional Materials (accelerated approvals only)
  Note: If accelerated approval (21 CFR 314.510/601.41), promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see guidance www.fda.gov/cder/guidance/2197dft.pdf). If not submitted, explain
  ☐ Received

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: 9/23/08
Application Characteristics

- Review priority: [X] Standard  [ ] Priority
- Chemical classification (new NDAs only): 3S
- [ ] Fast Track
- [ ] Rolling Review
- [ ] Orphan drug designation
- [ ] Rx-to-OTC full switch
- [ ] Rx-to-OTC partial switch
- [ ] 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

**Comments:**

1. Date reviewed by PeRC (required for approvals only)
   If PeRC review not necessary, explain:  
   - 05-06-09

2. BLAs only: *RMS-BLA Product Information Sheet for TBP* has been completed and forwarded to OBPS/DRM (approvals only)
   - [ ] Yes, date

3. BLAs only: is the product subject to official FDA lot release per 21 CFR 610.2 (approvals only)
   - [ ] Yes  [ ] No

4. Public communications (approvals only)
   - [ ] Yes  [ ] No
   - [ ] No
   - [ ] HHS Press Release
   - [ ] FDA Talk Paper
   - [ ] CDER Q&As
   - [ ] Other

---

2 All questions in all sections pertain 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.
<table>
<thead>
<tr>
<th>Exclusivity</th>
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</table>
| • Is approval of this application blocked by any type of exclusivity?  
  | ☒ No ☐ Yes |
| • 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.  
  | ☒ No ☐ Yes |
| • (b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? (Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval)  
  | ☐ No ☐ Yes |
| • (b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? (Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval)  
  | ☐ No ☐ Yes |
| • (b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? (Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval)  
  | ☐ No ☐ Yes |
| • NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? (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)  
  | ☒ No ☐ Yes |

<table>
<thead>
<tr>
<th>Patent Information (NDAs only)</th>
</tr>
</thead>
</table>
| • 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.  
  | ☒ Verified ☐ Not applicable because drug is an old antibiotic. |
| • Patent Certification [505(b)(2) applications]: 
  Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent.  
  | 21 CFR 314.50(i)(1)(A) ☒ Verified |
| • [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).  
  | ☐ No paragraph III certification Date patent will expire |
| • [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). (If the application does not include any paragraph IV certifications, mark “N/A” and skip to the next section below (Summary Reviews)).  
  | ☐ N/A (no paragraph IV certification) ☒ Verified |

Version: 9/5/08
• [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.

<table>
<thead>
<tr>
<th>CONTENTS OF ACTION PACKAGE</th>
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<tbody>
<tr>
<td>Copy of this Action Package Checklist enclosed</td>
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</tbody>
</table>

**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 division-proposed labeling (only if generated after latest applicant submission of labeling) 7/15/09
  - Most recent submitted by applicant labeling (only if subsequent division labeling does not show applicant version) 7/17/09
  - Original applicant-proposed labeling 9/28/09
  - Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable

- Medication Guide/Patient Package Insert/Instructions for Use (write submission/communication date at upper right of first page of each piece) Medication Guide, Patient Package Insert, Instructions for Use, None

3 Fill in blanks with dates of reviews, letters, etc.
Version: 9/5/08
- Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling)
- Most recent submitted by applicant labeling (only if subsequent division labeling does not show applicant version)
- Original applicant-proposed labeling
- Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable

* Labels (full color carton and immediate-container labels) *(write submission/communication date at upper right of first page of each submission)*
  - Most-recent division proposal for (only if generated after latest applicant submission)
  - Most recent applicant-proposed labeling

<table>
<thead>
<tr>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>7/15/09</td>
</tr>
<tr>
<td>7/17/09</td>
</tr>
</tbody>
</table>

* Labeling reviews *(indicate dates of reviews and meetings)*

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

### Administrative / Regulatory Documents

- Administrative Reviews *(e.g., RPM Filing Review/Memo of Filing Meeting) (indicate date of each review)*  Included
- NDAs only: Exclusivity Summary *(signed by Division Director)*  Included
- Application Integrity Policy (AIP) Status and Related Documents  www.fda.gov/ora/compliance_ref/aip_page.html
  - Applicant in on the AIP
  - This application is on the AIP
    - If yes, Center Director’s Exception for Review memo *(indicate date)*
    - If yes, OC clearance for approval *(indicate date of clearance communication)*
  - Pediatric Page *(approvals only, must be reviewed by PERC before finalized)*  Included
- 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)*  Verified, statement is acceptable
- Postmarketing Requirement (PMR) Studies  None
  - Outgoing communications *(if located elsewhere in package, state where located)*
  - Incoming submissions/communications
- Postmarketing Commitment (PMC) Studies  None
  - Outgoing Agency request for postmarketing commitments *(if located elsewhere in package, state where located)*

---

4 Filing reviews for other disciplines should be filed behind the discipline tab.

Version: 9/5/08
<table>
<thead>
<tr>
<th>Incoming submission documenting commitment</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Outgoing communications (letters except previous action letters, emails, faxes, telecons)</td>
<td></td>
</tr>
<tr>
<td>❖ Internal memoranda, telecons, etc.</td>
<td></td>
</tr>
<tr>
<td>❖ Minutes of Meetings</td>
<td></td>
</tr>
<tr>
<td>• PeRC (indicate date; approvals only)</td>
<td>☑ Not applicable</td>
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<tr>
<td>• Pre-Approval Safety Conference (indicate date; approvals only)</td>
<td>☑ Not applicable</td>
</tr>
<tr>
<td>• Regulatory Briefing (indicate date)</td>
<td>☑ No mtg</td>
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<tr>
<td>• Pre-NDA/BLA meeting (indicate date)</td>
<td>☑ No mtg</td>
</tr>
<tr>
<td>• EOP2 meeting (indicate date)</td>
<td>☑ No mtg</td>
</tr>
<tr>
<td>• Other (e.g., EOP2a, CMC pilot programs)</td>
<td></td>
</tr>
<tr>
<td>❖ Advisory Committee Meeting(s)</td>
<td>☑ No AC meeting</td>
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<tr>
<td>• Date(s) of Meeting(s)</td>
<td></td>
</tr>
<tr>
<td>• 48-hour alert or minutes, if available</td>
<td></td>
</tr>
<tr>
<td>Decisional and Summary Memos</td>
<td></td>
</tr>
<tr>
<td>❖ Office Director Decisional Memo (indicate date for each review)</td>
<td>☑ None</td>
</tr>
<tr>
<td>Division Director Summary Review (indicate date for each review)</td>
<td>☑ None 7/22/09</td>
</tr>
<tr>
<td>Cross-Discipline Team Leader Review (indicate date for each review)</td>
<td>☑ None 7/22/09</td>
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<tr>
<td>Clinical Information ¹</td>
<td></td>
</tr>
<tr>
<td>Clinical Reviews</td>
<td></td>
</tr>
<tr>
<td>• Clinical Team Leader Review(s) (indicate date for each review)</td>
<td>see CDTL review</td>
</tr>
<tr>
<td>• Clinical review(s) (indicate date for each review)</td>
<td>07-16-09</td>
</tr>
<tr>
<td>• Social scientist review(s) (if OTC drug) (indicate date for each review)</td>
<td>☑ None</td>
</tr>
<tr>
<td>❖ Safety update review(s) (indicate location/date if incorporated into another review)</td>
<td>Included in the clinical review</td>
</tr>
<tr>
<td>❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, review/memo explaining why not</td>
<td>Included in the clinical review; CDTL review: Form 3455 included.</td>
</tr>
<tr>
<td>❖ Clinical reviews from other clinical areas/divisions/Centers (indicate date of each review)</td>
<td>☑ None</td>
</tr>
<tr>
<td>❖ Controlled Substance Staff review(s) and Scheduling Recommendation (indicate date of each review)</td>
<td>☑ Not needed</td>
</tr>
<tr>
<td>❖ Risk Management</td>
<td></td>
</tr>
<tr>
<td>• Review(s) and recommendations (including those by OSE and CSS) (indicate date of each review and indicate location/date if incorporated into another review)</td>
<td>☑ None</td>
</tr>
<tr>
<td>• REMS Memo (indicate date)</td>
<td></td>
</tr>
<tr>
<td>• REMS Document and Supporting Statement (indicate date(s) of submission(s))</td>
<td></td>
</tr>
<tr>
<td>❖ DSI Clinical Inspection Review Summary(ies) (include copies of DSI letters to investigators)</td>
<td>☑ enclosed 04-17-09</td>
</tr>
</tbody>
</table>

¹ Filing reviews should be filed with the discipline reviews.

Version: 9/5/08
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<thead>
<tr>
<th><strong>Biostatistics</strong></th>
<th>None</th>
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<tr>
<td>Statistical Division Director Review(s) (<em>indicate date for each review</em>)</td>
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<td>Statistical Team Leader Review(s) (<em>indicate date for each review</em>)</td>
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</tr>
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<td>Statistical Review(s) (<em>indicate date for each review</em>)</td>
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<td>Clinical Pharmacology Team Leader Review(s) (<em>indicate date for each review</em>)</td>
<td>None</td>
</tr>
<tr>
<td>Clinical Pharmacology review(s) (<em>indicate date for each review</em>)</td>
<td>None 05-08-09</td>
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<tr>
<td><strong>DSI Clinical Pharmacology Inspection Review Summary (include copies of DSI letters)</strong></td>
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<table>
<thead>
<tr>
<th><strong>Nonclinical</strong></th>
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<tbody>
<tr>
<td>Pharmacology/Toxicology Discipline Reviews</td>
<td></td>
</tr>
<tr>
<td>• ADP/T Review(s) (<em>indicate date for each review</em>)</td>
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</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 05-18-09</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>None 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><strong>DSI Nonclinical Inspection Review Summary (include copies of DSI letters)</strong></td>
<td>None requested</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>CMC/Quality</strong></th>
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</thead>
<tbody>
<tr>
<td>CMC/Quality Discipline Reviews</td>
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</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>• CMC/product quality review(s) (<em>indicate date for each review</em>)</td>
<td>None 4-30 and 07-15-09</td>
</tr>
<tr>
<td>• BLAs only: Facility information review(s) (<em>indicate dates</em>)</td>
<td>None</td>
</tr>
<tr>
<td>Microbiology Reviews</td>
<td>07-08-09 Not needed</td>
</tr>
<tr>
<td>• NDAs: Microbiology reviews (sterility &amp; pyrogenicity) (<em>indicate date of each review</em>)</td>
<td></td>
</tr>
<tr>
<td>• BLAs: Sterility assurance, product quality microbiology (<em>indicate date of each review</em>)</td>
<td></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>
<tr>
<td>Environmental Assessment (check one) (original and supplemental applications)</td>
<td>04-30-09</td>
</tr>
<tr>
<td>• Categorical Exclusion (<em>indicate review date</em>)(all original applications and all efficacy supplements that could increase the patient population)</td>
<td></td>
</tr>
<tr>
<td>• Review &amp; FONSI (<em>indicate date of review</em>)</td>
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Version: 9/5/08
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<thead>
<tr>
<th>Review &amp; Environmental Impact Statement <em>(indicate date of each review)</em></th>
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<tbody>
<tr>
<td>☐ Complete</td>
</tr>
<tr>
<td>☐ Requested</td>
</tr>
<tr>
<td>☐ Not yet requested</td>
</tr>
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<td>☐ Not needed</td>
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<table>
<thead>
<tr>
<th>NDAs: Methods Validation</th>
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<tbody>
<tr>
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<tr>
<td>☐ Requested</td>
</tr>
<tr>
<td>☐ Not yet requested</td>
</tr>
<tr>
<td>☐ Not needed</td>
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</table>

<table>
<thead>
<tr>
<th>Facilities Review/Inspection</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Completed</td>
</tr>
<tr>
<td>☐ Requested</td>
</tr>
<tr>
<td>☐ Not yet requested</td>
</tr>
<tr>
<td>☐ Not needed</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NDAs: Facilities inspections (include EER printout) <em>(date completed must be within 2 years of action date)</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>✗ Acceptable</td>
</tr>
<tr>
<td>☐ Withhold recommendation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>BLAs:</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ TBP-EER</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Compliance Status Check (approvals only, both original and all supplemental applications except CBEs) <em>(date completed must be within 60 days prior to AP)</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Requested</td>
</tr>
<tr>
<td>☐ Accepted</td>
</tr>
<tr>
<td>☐ Hold</td>
</tr>
</tbody>
</table>

Date completed: 07-15-09
Appendix A to Action Package Checklist

An NDA or NDA supplemental application is likely to be a 505(b)(2) application if:

1. It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.

2. Or it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.

3. Or it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean any reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

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

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

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

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

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

3. And all other “criteria” are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

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

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

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

3. Or the applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE's ADRA.
Q4: Is there a full waiver for all pediatric age groups for this indication (check one)?

☐ Yes: (Complete Section A.)

☐ No: Please check all that apply:
  □ Partial Waiver for selected pediatric subpopulations (Complete Sections B)
  □ Deferred for some or all pediatric subpopulations (Complete Sections C)
  □ Completed for some or all pediatric subpopulations (Complete Sections D)
  □ Appropriately Labeled for some or all pediatric subpopulations (Complete Sections E)
  □ Extrapolation in One or More Pediatric Age Groups (Complete Section F)

(Please note that Section F may be used alone or in addition to Sections C, D, and/or E.)

Section A: Fully Waived Studies (for all pediatric age groups)

Reason(s) for full waiver: (check, and attach a brief justification for the reason(s) selected)

☐ Necessary studies would be impossible or highly impracticable because:
  □ Disease/condition does not exist in children
  □ Too few children with disease/condition to study
  □ Other (e.g., patients geographically dispersed): 

☐ Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients AND is not likely to be used in a substantial number of pediatric patients.

Pediatric cataracts most often result from abnormal lens development during gestation. Lens malformations that occur in conjunction with other findings are often the result of a genetic or metabolic abnormality.

In patients less than 6 months of age, the cataract is most often removed under anesthesia. The preferred procedure is lensectomy with vitrectomy, with or without IOL placement. Postoperative inflammation in the absence of IOL implantation is generally mild, and medical management usually includes topical mydriatic, anti-infective, and steroid medications.

Allergan previously submitted a Pediatric Study Report to the Agency on 18 June 2001 for NDA 19-700 and NDA 20-811 which was done with the same active ingredient, ketorolac tromethamine, formulated at 0.5% in pediatric patients between 3 and 12 years of age. This pediatric study was subsequently accepted by the Agency on 8 February 2002 and pediatric exclusivity was granted to the abovementioned NDAs. The current application for ketorolac tromethamine ophthalmic solution 0.45% uses the same active ingredient, at a lower concentration and lower dosing frequency (BID compared to QID) as that of the 0.5% formulation for which a pediatric clinical trial has been completed.

☐ Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (Note: if studies are fully waived on this ground, this information must be included in the labeling.)

☐ Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (Note: if studies are fully waived on this ground, this information must be included in the labeling.)

☐ Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (Note: if studies are fully waived on this ground, this information must be included in the labeling.)

☐ Justification attached.

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please complete another Pediatric Page for each indication. Otherwise, this Pediatric Page is complete and should be signed.

IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL (cderpms@fda.hhs.gov) OR AT 301-796-0700.
Section B: Partially Waived Studies (for selected pediatric subpopulations)

Check subpopulation(s) and reason for which studies are being partially waived (fill in applicable criteria below):

*Note: If Neonate includes premature infants, list minimum and maximum age in "gestational age" (in weeks).

<table>
<thead>
<tr>
<th>Reason (see below for further detail):</th>
</tr>
</thead>
<tbody>
<tr>
<td>minimum</td>
</tr>
<tr>
<td>----------</td>
</tr>
<tr>
<td>☐ Neonate _ wk. _ mo. _ wk. _ mo.</td>
</tr>
<tr>
<td>☐ Other _ yr. _ mo. _ yr. _ mo.</td>
</tr>
<tr>
<td>☐ Other _ yr. _ mo. _ yr. _ mo.</td>
</tr>
<tr>
<td>☐ Other _ yr. _ mo. _ yr. _ mo.</td>
</tr>
<tr>
<td>☐ Other _ yr. _ mo. _ yr. _ mo.</td>
</tr>
</tbody>
</table>

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.
Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

Reason(s) for partial waiver (check reason corresponding to the category checked above, and attach a brief justification):

# Not feasible:
☐ Necessary studies would be impossible or highly impracticable because:
  ☐ Disease/condition does not exist in children
  ☐ Too few children with disease/condition to study
  ☐ Other (e.g., patients geographically dispersed): ___

* Not meaningful therapeutic benefit:
☐ Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this/these pediatric subpopulation(s) AND is not likely to be used in a substantial number of pediatric patients in this/these pediatric subpopulation(s).

† Ineffective or unsafe:
☐ Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)
☐ Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)
☐ Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)

△ Formulation failed:
☐ Applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for this/these pediatric subpopulation(s) have failed. (Note: A partial waiver on this ground may only cover the pediatric subpopulation(s) requiring that formulation. An applicant seeking a partial waiver on this ground must submit documentation detailing why a pediatric formulation cannot be developed. This submission will be posted on FDA’s website if waiver is granted.)

☐ Justification attached.

For those pediatric subpopulations for which studies have not been waived, there must be (1) corresponding study plans that have been deferred (if so, proceed to Sections C and complete the PeRC Pediatric Plan Template); (2) submitted studies that have been completed (if so, proceed to Section D and complete the eRC Pediatric Assessment form); (3) additional studies in other age groups that are not needed because the drug is appropriately labeled in one or more pediatric subpopulations (if so, proceed to Section E); and/or (4) additional studies in other age groups that are not needed because efficacy is being extrapolated (if so, proceed to Section F). Note that more than one of these options may apply for this indication to cover all of the

IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL (cedermhs@fda.hhs.gov) OR AT 301-796-0700.
pediatric subpopulations.

**Section C: Deferred Studies (for selected pediatric subpopulations).**

Check pediatric subpopulation(s) for which pediatric studies are being deferred (and fill in applicable reason below):

<table>
<thead>
<tr>
<th>Deferrals (for each or all age groups):</th>
<th>Reason for Deferral</th>
<th>Applicant Certification †</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>Ready for Approval in Adults</td>
<td>Need Additional Adult Safety or Efficacy Data</td>
</tr>
<tr>
<td>Neonate</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Other</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>All Pediatric Populations</td>
<td>□</td>
<td>□</td>
</tr>
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</table>

Date studies are due (mm/dd/yy): ___

Are the indicated age ranges (above) based on weight (kg)?  □ No; □ Yes.

Are the indicated age ranges (above) based on Tanner Stage?  □ No; □ Yes.

* Other Reason: ___

† Note: Studies may only be deferred if an applicant submits a certification of grounds for deferring the studies, a description of the planned or ongoing studies, evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time, and a timeline for the completion of the studies. If studies are deferred, on an annual basis applicant must submit information detailing the progress made in conducting the studies or, if no progress has been made, evidence and documentation that such studies will be conducted with due diligence and at the earliest possible time. This requirement should be communicated to the applicant in an appropriate manner (e.g., in an approval letter that specifies a required study as a post-marketing commitment.)

If all of the pediatric subpopulations have been covered through partial waivers and deferrals, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.
**Section D: Completed Studies (for some or all pediatric subpopulations)**

Pediatric subpopulation(s) in which studies have been completed (check below):

<table>
<thead>
<tr>
<th>Population</th>
<th>minimum</th>
<th>maximum</th>
<th>PeRC Pediatric Assessment form attached?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonate</td>
<td>_ wk. _ mo.</td>
<td>_ wk. _ mo.</td>
<td>Yes □</td>
</tr>
<tr>
<td>Other</td>
<td>_ yr. _ mo.</td>
<td>_ yr. _ mo.</td>
<td>Yes □</td>
</tr>
<tr>
<td>Other</td>
<td>_ yr. _ mo.</td>
<td>_ yr. _ mo.</td>
<td>Yes □</td>
</tr>
<tr>
<td>Other</td>
<td>_ yr. _ mo.</td>
<td>_ yr. _ mo.</td>
<td>Yes □</td>
</tr>
<tr>
<td>Other</td>
<td>_ yr. _ mo.</td>
<td>_ yr. _ mo.</td>
<td>Yes □</td>
</tr>
<tr>
<td>All Pediatric Subpopulations</td>
<td>0 yr. 0 mo.</td>
<td>16 yr. 11 mo.</td>
<td>Yes □</td>
</tr>
</tbody>
</table>

Are the indicated age ranges (above) based on weight (kg)? □ No; □ Yes.

Are the indicated age ranges (above) based on Tanner Stage? □ No; □ Yes.

*Note: If there are no further pediatric subpopulations to cover based on partial waivers, deferrals and/or completed studies, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.*

**Section E: Drug Appropriately Labeled (for some or all pediatric subpopulations):**

Additional pediatric studies are not necessary in the following pediatric subpopulation(s) because product is appropriately labeled for the indication being reviewed:

<table>
<thead>
<tr>
<th>Population</th>
<th>minimum</th>
<th>maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonate</td>
<td>_ wk. _ mo.</td>
<td>_ wk. _ mo.</td>
</tr>
<tr>
<td>Other</td>
<td>_ yr. _ mo.</td>
<td>_ yr. _ mo.</td>
</tr>
<tr>
<td>Other</td>
<td>_ yr. _ mo.</td>
<td>_ yr. _ mo.</td>
</tr>
<tr>
<td>Other</td>
<td>_ yr. _ mo.</td>
<td>_ yr. _ mo.</td>
</tr>
<tr>
<td>Other</td>
<td>_ yr. _ mo.</td>
<td>_ yr. _ mo.</td>
</tr>
<tr>
<td>All Pediatric Subpopulations</td>
<td>0 yr. 0 mo.</td>
<td>16 yr. 11 mo.</td>
</tr>
</tbody>
</table>

Are the indicated age ranges (above) based on weight (kg)? □ No; □ Yes.

Are the indicated age ranges (above) based on Tanner Stage? □ No; □ Yes.

*If all pediatric subpopulations have been covered based on partial waivers, deferrals, completed studies, and/or existing appropriate labeling, this Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.*

**Section F: Extrapolation from Other Adult and/or Pediatric Studies (for deferred and/or completed studies)**

*Note: Pediatric efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations if (and only if) (1) the course of the disease/condition AND (2) the effects of the product are sufficiently similar between the reference population and the pediatric subpopulation for which information will be extrapolated. Extrapolation of efficacy from studies in adults and/or other children usually requires supplementation with other information obtained from the target pediatric subpopulation, such as*

*IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL (cederpmhss@fda.hhs.gov) OR AT 301-796-0700.*
Pharmacokinetic and safety studies. Under the statute, safety cannot be extrapolated.

Pediatric studies are not necessary in the following pediatric subpopulation(s) because efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations:

<table>
<thead>
<tr>
<th>Population</th>
<th>minimum</th>
<th>maximum</th>
<th>Extrapolated from:</th>
<th>Adult Studies?</th>
<th>Other Pediatric Studies?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonate</td>
<td>__ wk. __ mo.</td>
<td>__ wk. __ mo.</td>
<td></td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Other</td>
<td>__ yr. __ mo.</td>
<td>__ yr. __ mo.</td>
<td></td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Other</td>
<td>__ yr. __ mo.</td>
<td>__ yr. __ mo.</td>
<td></td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Other</td>
<td>__ yr. __ mo.</td>
<td>__ yr. __ mo.</td>
<td></td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Other</td>
<td>__ yr. __ mo.</td>
<td>__ yr. __ mo.</td>
<td></td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>All Pediatric Subpopulations</td>
<td>0 yr. 0 mo.</td>
<td>16 yr. 11 mo.</td>
<td></td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

Are the indicated age ranges (above) based on weight (kg)?  ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage?  ☐ No; ☐ Yes.

Note: If extrapolating data from either adult or pediatric studies, a description of the scientific data supporting the extrapolation must be included in any pertinent reviews for the application.

If there are additional indications, please complete the attachment for each one of those indications. Otherwise, this Pediatric Page is complete and should be signed and entered into DFS or DARRTS as appropriate after clearance by PeRC.

This page was completed by:

(See appended electronic signature page)

Regulatory Project Manager

(Revised: 6/2008)

NOTE: If you have no other indications for this application, you may delete the attachments from this document.
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Wiley Chambers
7/22/2009 11:47:39 AM