

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-429

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

1.3 Administration Information
1.3.5.2 Patent Certification

Banner Pharmacaps Inc.
Cetirizine HCl, Capsules 10 mg & 5 mg
505(b)(2) NDA Submission

Paragraph I

Patent Certification

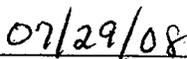
In the opinion and to the best knowledge of Banner Pharmacaps Inc., no patent information has been submitted to FDA for the listed drug referred to in this application.

Exclusivity Statement

According to information published in the Orange Book, the RLD, Zyrtec®, has no unexpired period of marketing exclusivity.



Dana Toops,
Director, Regulatory Affairs



Date

EXCLUSIVITY SUMMARY

NDA # 22-429

SUPPL #

HFD #

Trade Name Cetirizine HCl

Generic Name Cetirizine HCl

Applicant Name Banner Pharmacaps

Approval Date, If Known July 23, 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)(2)

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.

This NDA is submitted under a 505(b)(2) application and relies on the Agency's previous finding of safety and efficacy for cetirizine HCl tablets. There were no efficacy trials conducted for this application except for PK evaluation. Efficacy is based on prior approval for the RLD and supported by the sponsor's PK data from the single-dose relative bioavailability studies assessing the sponsor's cetirizine HCl 10 mg capsule and Zyrtec® 10 mg tablet (RLD). Study 20-219-SA was a single-center, randomized, single-dose, 2-sequence, crossover bioavailability study that compared BPI's cetirizine capsule and Zyrtec® (Pfizer) 10 mg tablets under fasting conditions in healthy adult male and female subjects. Study 20-220-SA was also a single-dose bioavailability study with a study design similar to Study 20-219-SA but was conducted under fed conditions.

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?

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).

NDA#

NDA#

NDA#

2. Combination product.

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

YES NO

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

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 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:

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"):

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

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

Investigation #1
IND # YES ! NO
! Explain:

Investigation #2
IND # 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: ! Explain:

Investigation #2
!
!
YES ! NO
Explain: ! 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: Janice Adams-King
Title: Regulatory Project Manager
Date: July 23, 2009

Name of Office/Division Director signing form: Joel Schiffenbauer
Title: Deputy Director, Division of Nonprescription Clinical Evaluation

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

Linked Applications	Submission Type/Number	Sponsor Name	Drug Name / Subject
NDA 22429	ORIG 1	BANNER PHARMACAPS INC	CETIRIZINE HCL CAPSULES

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

/s/

JANICE Adams
07/31/2009

JOEL SCHIFFENBAUER
07/31/2009

Pediatric Research and Equity Act Waivers

Product name and active ingredient/ dosage form: _____ (cetirizine HCl) _____ capsules **b(4)**

IND/NDA/BLA #: 22-429 Supplement Type: Supplement Number:

HFD- 560 DNCE

Sponsor: **Banner Pharmaceuticals**

Indications(s): (OTC)

- (1) temporarily relieves these symptoms due to hay fever or other respiratory allergies: runny nose, sneezing, itchy, watery eyes, itching of the nose or throat (Allergic rhinitis)
- (2) relief of itching due to hives (Hives relief)

(NOTE: If the drug is approved for or Sponsor is seeking approval for more than one indication, address the following for each indication.)

Allergic Rhinitis (OTC)

1. Pediatric age group(s) to be waived: 0 to <6 years of age
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. See justification.**
 - 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.

Hives Relief (OTC)

1. Pediatric age group(s) to be waived: **0 to <6 years of age**

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)." (See justification).

 - 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.**

 - 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.

Justification

(a) Allergic Rhinitis:

The Division considers that there is no need for further studies in children < 6 y/o as requested in the waiver because:

- The proposed product would not offer any additional meaningful therapeutic benefit over existing therapies for the pediatric population <6 y/o because there are other age appropriate cetirizine formulations approved for the same indications in children as young as 6 months old to treat (perennial) allergic rhinitis.
 - Cetirizine syrup (1 mg/mL) is available for *prescription* use in children 6 months to <2 years old, and for *OTC* use in children ≥ 2 y/o.
 - A cetirizine chewable 5 mg tablet formulation is also available for OTC use in children ≥ 2 y/o.
- It is the Agency's decision not to label cetirizine children < 2 y/o for (seasonal) allergic rhinitis based on the knowledge that children generally need to be exposed to allergens for at least two seasons before they develop a seasonal allergy. In addition, for children < 2 y/o, there is also a concern that parents may not be able to properly diagnose an allergic rhinitis condition in this age group in an OTC environment.
- The proposed product does not provide dosing for the proposed product in *children < 6 years of age*; the label directs a consumer to ask a doctor for this age group. The doctor/healthcare professional is assumed to direct the consumer to a formulation that is more appropriate for this age group, such as the syrup or chewable tablet.

(b) Hives Relief

- Cetirizine is available by prescription use and labeled down to the age of 6 months to treat hives (urticaria). For children <6 y/o, it is the Agency's decision not to label cetirizine for *OTC use* below this age because there is a concern that parents may not be able to properly diagnose hives in this age group in an OTC environment.
- There are other second-generation antihistamines (desloratadine, fexofenadine) available by prescription and labeled down to the age of 6 months to treat hives (urticaria).
- All Currently marketed OTC antihistamines indicated for relief of itching due to hives are labeled for children ages ≥ 6 years.

The efficacy of cetirizine for the treatment of allergic rhinitis and hives relief in this age group is based on extrapolation of the demonstrated efficacy of cetirizine in patients 12 years and older for this condition and the consideration that the disease course, pathophysiology, and the drug's effect is substantially similar in children and adults. Pharmacokinetic studies in children down to 6 months of age were also performed as part of the prescription cetirizine development program. Safety data collected during pediatric safety studies and postmarketing surveillance did not reveal new or unexpected safety signals in pediatric population.

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

PEDIATRIC PAGE
(Complete for all filed original applications and efficacy supplements)

NDA/BLA#: 22-429 Supplement Number: _____ NDA Supplement Type (e.g. SE5): _____

Division Name: DNCE PDUFA Goal Date: 6/01/09 Stamp Date: _____

Proprietary Name: _____

Established/Generic Name: Cetirizine **b(4)**

Dosage Form: softgel capsule

Applicant/Sponsor: Banner

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

- (1) _____
- (2) _____
- (3) _____
- (4) _____

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

If Yes, NDA/BLA#: _____ Supplement #: _____ PMC #: _____

Does the division agree that this is a complete response to the PMC?

- Yes. **Skip to signature block.**
- 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); 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.**

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): 2
(Attach a completed Pediatric Page for each indication in current application.)

Indication: Treatment of allergic rhinitis (OTC)

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 the remaining 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.)

IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL OR AT 301-796-0700.

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

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

- 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.
- Evidence strongly suggests that product would be ineffective or 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 and entered into DFS.

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).

		Reason (see below for further detail):					
		minimum	maximum	Not feasible [#]	Not meaningful therapeutic benefit*	Ineffective or unsafe [†]	Formulation failed ^Δ
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input checked="" type="checkbox"/>	Other	0 yr. __ mo.	<2 yr. __ mo.	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input checked="" type="checkbox"/>	Other	2yr. __ mo.	<6 yr. __ mo.	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

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): _____

For children less than 2 years of age, there is a concern that parents may not be able to properly diagnose allergic rhinitis conditions in this age group in an OTC environment. It is the Agency's decision not to label cetirizine below this age based on the knowledge that children generally need to be exposed to allergens for at least two seasons before they develop a seasonal allergy. Cetirizine and other second-generation antihistamines (clarinex) are available by prescription for those aged 6 months to less than 2 years to treat (perennial) allergic rhinitis.

* Not meaningful therapeutic benefit: Children 2 y/o to < 6 y/o

- 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).

There are other age appropriate cetirizine (Zyrtec) formulations approved for the same indication; these are the cetirizine syrup (1 mg/mL) and cetirizine chewable 5 mg tablets.

† Ineffective or unsafe:

- Evidence strongly suggests that product would be ineffective or unsafe in this/these pediatric population(s) (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)

Δ 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 F and complete the PeRC Pediatric Plan Template); (2) submitted studies that have been completed (if so, proceed to Sections D and F and complete the PeRC Pediatric Assessment form); and/or (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 Sections E and F). Note that more than one of these options may apply for this indication to cover all of the pediatric subpopulations.

Section C: Deferred Studies (for remaining pediatric subpopulations). Complete Section F on Extrapolation.

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

Deferrals (for each or all age groups):			Reason for Deferral			Applicant Certification †	
Population	minimum	maximum	Ready for Approval in Adults	Need Additional Adult Safety or Efficacy Data	Other Appropriate Reason (specify below)*	Yes	No
<input type="checkbox"/> Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> All Pediatric Populations	0 yr. 0 mo.	16 yr. 11 mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
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 the partial waivers and deferrals, proceed to Section F. For those pediatric subpopulations for which studies have been completed, proceed to Sections D and F and complete the PeRC Pediatric Assessment form. For those pediatric subpopulations for which additional studies are not needed because the drug is appropriately labeled in one or more pediatric subpopulations, proceed to Sections E and F.

IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL OR AT 301-796-0700.

Section D: Completed Studies (for some or all pediatric subpopulations). Complete Section F on Extrapolation.

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

Population		minimum	maximum	PeRC Pediatric Assessment form attached?	
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>

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: For those pediatric subpopulations for which additional studies are not needed because the drug is appropriately labeled in one or more pediatric subpopulations, proceed to Sections E and F. If there are no further pediatric subpopulations to cover based on the partial waivers, deferrals and completed studies, go to Section F.

Section E: Drug Appropriately Labeled (for some or all pediatric subpopulations): (Complete section F)

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

Population		minimum	maximum
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.
<input checked="" type="checkbox"/>	Other	2 yr. __ mo.	17 yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	6 yr. 11 mo.

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 studies are not needed because efficacy is being extrapolated from other adult and/or pediatric studies, proceed to Section F. Otherwise, this Pediatric Page is complete and should be signed and entered into DFS.

There are other cetirizine formulations currently marketed OTC and labeled for children aged 2 to 17 years.

Section F: Extrapolation from Other Adult and/or Pediatric Studies (for deferred and 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 target pediatric subpopulation needing studies. 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 pharmacokinetic and safety studies.

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:

Population	minimum	maximum	Extrapolated from:	
			Adult Studies?	Other Pediatric Studies?
<input type="checkbox"/> Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input checked="" type="checkbox"/> Other	2 yr. __ mo.	17 yr. __ mo.	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	<input type="checkbox"/>	<input type="checkbox"/>

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.

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

(Revised: 4/2008)

NOTE: If you have no other indications for this application, you may delete the attachments from this document.

IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL OR AT 301-796-0700.

PEDIATRIC PAGE
(Complete for all filed original applications and efficacy supplements)

NDA/BLA#: 22-429 Supplement Number: _____ NDA Supplement Type (e.g. SE5): _____

Division Name: DNCE PDUFA Goal Date: 6/01/09 Stamp Date: _____

Proprietary Name: _____

Established/Generic Name: Cetirizine **b(4)**

Dosage Form: softgel capsule

Applicant/Sponsor: Banner

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

- (1) _____
- (2) _____
- (3) _____
- (4) _____

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

If Yes, NDA/BLA#: _____ Supplement #: _____ PMC #: _____

Does the division agree that this is a complete response to the PMC?

- Yes. **Skip to signature block.**
- 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); 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.**

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): 2
(Attach a completed Pediatric Page for each indication in current application.)

Indication: Relief of itching due to hives (OTC)

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 the remaining 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.)

IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL OR AT 301-796-0700.

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

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

- 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.
- Evidence strongly suggests that product would be ineffective or 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 and entered into DFS.

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).

		Reason (see below for further detail):					
		minimum	maximum	Not feasible [#]	Not meaningful therapeutic benefit [*]	Ineffective or unsafe [†]	Formulation failed ^Δ
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input checked="" type="checkbox"/>	Other	0 yr. __ mo.	<6yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

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: <6 y/o for OTC use

- Evidence strongly suggests that product would be ineffective or unsafe in this/these pediatric population(s) (Note: if studies are partially waived on this ground, this information must be included in

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the labeling.)

For children <6 y/o, it is the Agency's decision not to label cetirizine for OTC use below this age because there is a concern that parents may not be able to properly diagnose hives in this age group in an OTC environment. Age appropriate cetirizine formulations are available by *prescription use* and labeled down to the age of 6 months to treat hives (urticaria).

Δ 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 F and complete the PeRC Pediatric Plan Template); (2) submitted studies that have been completed (if so, proceed to Sections D and F and complete the PeRC Pediatric Assessment form); and/or (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 Sections E and F). Note that more than one of these options may apply for this indication to cover all of the pediatric subpopulations.

Section C: Deferred Studies (for remaining pediatric subpopulations). Complete Section F on Extrapolation.

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

Deferrals (for each or all age groups):				Reason for Deferral			Applicant Certification †	
Population	minimum	maximum	Ready for Approval in Adults	Need Additional Adult Safety or Efficacy Data	Other Appropriate Reason (specify below)*	Yes	No	
<input type="checkbox"/> Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<input type="checkbox"/> All Pediatric Populations	0 yr. 0 mo.	16 yr. 11 mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
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

IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL OR AT 301-796-0700.

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 the partial waivers and deferrals, proceed to Section F. For those pediatric subpopulations for which studies have been completed, proceed to Sections D and F and complete the PeRC Pediatric Assessment form. For those pediatric subpopulations for which additional studies are not needed because the drug is appropriately labeled in one or more pediatric subpopulations, proceed to Sections E and F.

Section D: Completed Studies (for some or all pediatric subpopulations). Complete Section F on Extrapolation.

Pediatric subpopulation(s) in which studies have been completed (check below):					
Population		minimum	maximum	PeRC Pediatric Assessment form attached?	
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>

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: For those pediatric subpopulations for which additional studies are not needed because the drug is appropriately labeled in one or more pediatric subpopulations, proceed to Sections E and F. If there are no further pediatric subpopulations to cover based on the partial waivers, deferrals and completed studies, go to Section F.

Section E: Drug Appropriately Labeled (for some or all pediatric subpopulations): (Complete section F)

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

Population		minimum	maximum
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.
<input checked="" type="checkbox"/>	Other	<u>6</u> yr. __ mo.	<u>17</u> yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	6 yr. 11 mo.

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 studies are not needed because efficacy is being extrapolated from other adult and/or pediatric studies, proceed to Section F. Otherwise, this Pediatric Page is complete and should be signed and entered into DFS.

Section F: Extrapolation from Other Adult and/or Pediatric Studies (for deferred and 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 target pediatric subpopulation needing studies. 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 pharmacokinetic and safety studies.

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:

Population	minimum	maximum	Extrapolated from:	
			Adult Studies?	Other Pediatric Studies?
<input type="checkbox"/> Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input checked="" type="checkbox"/> Other	6 yr. __ mo.	17 yr. __ mo.	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	<input type="checkbox"/>	<input type="checkbox"/>

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.

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

(Revised: 4/2008)

NOTE: If you have no other indications for this application, you may delete the attachments from this document.

IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL OR AT 301-796-0700.

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

/s/

Melissa Furness
6/23/2009 02:41:38 PM
Signing for Janice Adams-King

1.9 Pediatric Administrative Information
1.9.1 Pediatric studies Waiver

Banner Pharmacaps Inc.
Cetirizine HCl Capsules, 10 mg & 5 mg
505(b)(2) NDA Submission

REQUEST FOR PEDIATRIC WAIVER

As provided for in the Pediatric Research Equity Act of 2003 ("PREA"), Sec. 505B (a) (4) (B) (iii), and in accordance with 21 CFR 314.55 (2).

Banner Pharmacaps Inc. (BPI) hereby requests a ~~waiver~~ waiver of the pediatric assessment requirement for our proposed drug product Cetirizine HCl Capsules, 10 mg and 5 mg, the subject of this original 505 (b)(2) application. BPI is submitting herein the age groups by indication for the requested waiver.

b(4)

Product Name:	Cetirizine HCl Capsules, 10 mg & 5 mg	
Applicant:	Banner Pharmacaps Inc.	
Proposed Indications & Usage	ALLERGY	HIVES
Pediatric Age Group Waiver Request	Children: 2 to 5 years	Children: 2 to 5 years
	Infants: 6 to 23 months	Infants: 6 to 23 months
	Neonates: less than 6 months	Neonates: less than 6 months

This waiver is requested on the basis that the proposed over the counter drug product:

- (i) Does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients; and
- (ii) is not likely to be used in a substantial number of pediatric patients.

This pediatric waiver provides for the points

1. Regulatory Approval history of Cetirizine products approved for marketing in the US.
2. Cetirizine HCl offers no meaningful full therapeutic benefits over existing treatments.
3. Pharmacokinetic and clinical efficacy similarities of Cetirizine in adults and children.
4. ZYRTEC® Pediatric Use: Labeling Information.
5. Literature review of Cetirizine HCl use in pediatric Populations

Regulatory Approval History: Cetirizine HCl tablets, 10 & 5 mg, has recently been approved for over-the-counter use in the US by the FDA for various companies including McNeil Consumer/Pfizer, (Zyrtec®, NDA 19-835, Perrigo: ANDA 78-336, Activis Elizabeth: ANDA 78-615, Apotex Inc: ANDA 78-317, Caraco: ANDA 77-499, Contract Pharma: 76-047, Dr. Reddy's Labs: 78-343, Mylan: 76-677, Ranbaxy: 77-498, Sandoz: 77-946 etc.) The reference listed drug (RLD) in this class, Zyrtec® has the following indications listed below (Drug Facts and container labeling can be referenced in section 1.14.1 of this application).

1.9 Pediatric Administrative Information**1.9.1 Pediatric studies Waiver****Banner Pharmacaps Inc.****Cetirizine HCl Capsules, 10 mg & 5 mg****505(b)(2) NDA Submission**

ALLERGY: Temporarily relieves these symptoms due to hay fever or other upper respiratory allergies: runny nose, sneezing, itchy, watery eyes, itching of the nose and throat

HIVES: Relieves itching due to hives (urticaria). This product will not prevent hives or an allergic skin reaction from occurring.

The current over the counter Zyrtec® tablets labeling contains directions for adults and children 6 years and older. BPI seeks to match the RLD's labeling for over the counter marketing of its proposed drug for adults and children 6 years and older. The enclosed application relies on the agency's findings of safety and efficacy for the RLD, Zyrtec®.

CETIRIZINE HCl OFFERS NO MEANINGFUL THERAPEUTIC BENEFITS OVER EXISTING TREATMENTS:

Drugs with antihistamine action are among the most commonly prescribed medicines in pediatrics. According to the International Medical Statistics (IMS), almost two million antihistamine units for pediatric use were sold internationally in 2006 (A del Cuvillo *et al* 2007)⁵.

Cetirizine dihydrochloride available under trademark Zyrtec®; is approved worldwide for both adults and children for the relief of symptoms of seasonal and perennial allergic rhinitis and chronic idiopathic urticaria. The product is marketed under the following names: Zyrtec® in the US, Zirtek® in the United Kingdom, Zyrlex® in many European countries, Reactine® in Canada (all by Pfizer/McNeil Consumer), and Virlix® in Mexico and parts of Europe and a variety of other names in other countries.

In the US alone; second-generation antihistamines include, levocetirizine, fexofenadine, desloratadine and loratadine all have well established and documented safety and clinical efficacy in children and adults (Golightly *et al* 2005)¹¹ and offer adequate therapeutic benefits for similar indications as BPI's Cetirizine HCl, Capsules product. The available pediatric products are widely accessible both by prescription and OTC for the treatment and relief of symptoms associated with allergy and hives for this population.

The US market supports the following products, available and labeled for pediatric use, both by prescription and OTC.

Active Ingredient	Applicant	Application No.	Dosage Form	Pediatric Dosage Recommendation
Cetirizine HCl (Zyrtec®)	McNeil Consumer Pfizer Inc.	020346	Syrup	5 MG/5ML
Cetirizine HCl (Zyrtec®)	McNeil Consumer Pfizer Inc.	021621	Chewable Tablets	5MG
Cetirizine HCl	Taro	090182 076601	Syrup	5 MG/5ML

1.9 Pediatric Administrative Information
1.9.1 Pediatric studies Waiver

Banner Pharmacaps Inc.
Cetirizine HCl Capsules, 10 mg & 5 mg
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Active Ingredient	Applicant/Application No.		Dosage Form	Pediatric Dosing Recommendation
Cetirizine HCl	Ranbaxy	090183 077472	Syrup	5 MG/5ML
Cetirizine HCl	Perrigo Israel	078398	Syrup	5 MG/5ML
Cetirizine HCl	Perrigo	090254	Syrup	5 MG/5ML
Cetirizine HCl	Apotex Inc.	090188 078412	Syrup	5 MG/5ML
Cetirizine HCl	Teva Pharms	077279	Syrup	5 MG/5ML
Levocetirizine Dihydrochloride	UCB	022157	Solution	2.5MG/5ML
Loratadine (Clarinet®)	Schering Plough	020641	Syrup	1MG/ML
Loratadine (Claritin®)	Schering Plough	021891	Chewable Tablet	5 MG
Loratadine	Taro	021734	---	1MG/ML
Loratadine	Ranbaxy	076529	Syrup	1MG/ML
Loratadine	Perrigo	075728	Syrup	1MG/ML
Loratadine	Apotex Inc.	075565	Syrup	1MG/ML
Loratadine	Teva Pharms	075505	Syrup	1MG/ML
Loradatine	Morton Grove	075815	Syrup	1MG/ML
Desloratadine (Clarinet®)	Schering	021300	Syrup	0.5 MG

b(4)

Usual adult and pediatric dosages and suggested recommended daily oral dosage of second-generation antihistamines are summarized in the table below (Golightly et al, 2005).¹¹

Drug	Adults	Children	Elderly
Cetirizine	5-10 mg	6-11 years: 5-10 mg 0.5-5years: 2.5-5 mg	5-10 mg
Desloratadine	5 mg	>12 years: 5 mg	5 mg
Fexofenadine	180 mg	6-11 years: 30 mg twice daily	180 mg
Loratadine	10 mg	>6 years: 10 mg 2-5 years: 5 mg	Not stated in product labeling

As noted above there is a wide variety of second generation antihistamines/ingredients available on the market that have been evaluated and indicated for pediatric use, both by prescription and over the counter use. There is no rationale, nor evidence that an additional pediatric cetirizine formulation would offer meaningful therapeutic benefit over existing options available for pediatrics use. Based on the availability of alternate drug products, the current market acceptance of other pediatric second generation antihistamine products such as levocetirizine, fexofenadine,

desloratadine and loratadine, an additional pediatric Cetirizine product would be unlikely to be used in a substantial number of pediatric patients.

PHARMACOKINETIC AND CLINICAL EFFICACY SIMILARITIES OF CETIRIZINE IN ADULTS AND CHILDREN

Reference is also being made to 21 CFR 314.55 (a) that states: " Where the course of the disease and the effects of the drug are sufficiently similar in adults and pediatric patients, FDA may conclude that pediatric effectiveness can be extrapolated from adequate and well-controlled studies in adults usually supplemented with other information obtained in pediatric patients..."

The following points support the extrapolation from adult's efficacy data and other available information obtained in pediatric patients:

- Zyrtec® Summary basis of approval
- Published Literature Review

For Cetirizine, multiple clinical safety and efficacy studies and pharmacokinetic studies in pediatric patients were conducted by the RLD applicant holder. The approval of RLD's Cetirizine for children less than 12 years of age, and was based on extrapolation of efficacy from adults and adolescent population as well as pharmacokinetic and safety data in pediatric patients. Based on the agency's summary basis for approval of the RLD, it was determined from the clinical studies submitted that pathophysiology, symptomatology, clinical course and treatment of chronic urticaria, seasonal allergic rhinitis and perennial allergic rhinitis are essentially the same in children and adults.

Additional reference is being made to ZYRTEC® syrup subject of NDA 20-346 held by Pfizer Inc./McNeil Consumer.

ZYRTEC® PEDIATRIC USE: LABELING INFORMATION

The information below is being provided directly from the Zyrtec® prescription labeling.

The safety of ZYRTEC® has been demonstrated in pediatric patients aged 6 months to 11 years. The safety of cetirizine has also been demonstrated on patients aged 2 to 5 years in placebo controlled clinical trials.

"The effectiveness of ZYRTEC® for the treatment of allergic rhinitis and chronic idiopathic urticaria in pediatric patients aged 6 months to 11 years is based on an extrapolation of the demonstrated efficacy of ZYRTEC® in adults with these conditions and the likelihood that the disease course, pathophysiology and the drug's effect are substantially similar between these two populations. Efficacy is extrapolated down to 6 months of age for perennial allergic rhinitis and down to 2 years of age for seasonal allergic rhinitis because these diseases are thought to occur down to these ages in children. The recommended doses for the pediatric population are based on

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1.9.1 Pediatric studies Waiver

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cross-study comparisons of the pharmacokinetics and pharmacodynamics of Cetirizine in adult and pediatric subjects and on the safety profile of cetirizine in both adults and pediatric patients at doses equal to or higher than the recommended doses”.

As noted above, the RLD has already performed the necessary studies to support extrapolation of safety and efficacy from adults/adolescents to pediatrics. BPI intends to rely on the agency’s findings for Zyrtec® to support this waiver. BPI believes there is no medical need necessitating additional pediatric investigation.

LITERATURE REVIEW OF CETIRIZINE HCl USE IN PEDIATRIC POPULATIONS

Published literature provided herein further provides adequate substantiation that Cetirizine is safe and effective anti-histamine in the pediatric population. The pediatric use of Cetirizine hydrochloride is further supported by the availability of adequate and well controlled adult studies, the comparability of the conditions being treated and the therapeutic effects of the drug, which are sufficiently similar in the adult and pediatric populations to permit extrapolation.

According to Eick Ten and his colleagues in one study, the elimination half-life of Cetirizine may vary with age. However, the elimination half-life of approximately 7.0 hours in children 8 to 10 years of age appears to be similar to that reported in healthy adults approximately 7.4 to 8.6 hours Eick Ten et al, 2001.⁸

A review of medical literature indicates that cetirizine has been specifically studied in adult and pediatric populations (ages: infant to adolescent) for the treatment of chronic urticaria, seasonal allergic rhinitis and perennial allergic rhinitis. A literature search further reveals an extremely positive efficacy profile of cetirizine for use in children. Furthermore, the efficacy of cetirizine in children is analogous to the benefits seen in adolescents and adults. Therefore, based on the studies described in the table below, there is sufficient evidence to conclude that cetirizine is effective for the treatment of chronic urticaria, seasonal allergic rhinitis and perennial allergic rhinitis in children 6 months to 12 years.

Author (Year)	Design	Sample Size	Age	Comparator	Findings
Baena-Cagnani et al, 2004	Review	1980-2003	<12 yrs	None	For children <12 years of age, the newer three oral antihistamines cetirizine, loratadine and fexofenadine based on proven efficacy and good safety profile suggests that they are also safe for use in children.
Blic J, et al 2005	A double blind, placebo controlled, randomized study	177	6-12 yrs	Levocetirizine	Levocetirizine is safe and efficacious in reducing the symptoms of SAR.
Ciprandi et al, 2003	Double –blind, randomized, and placebo controlled	20 children	3-10 years	Placebo	All of the 20 patients completed the study. Cetirizine administered daily for prolonged periods (ie. 3 years) may decrease the development of new sensations showing a potential effect of prevention of allergy.

1.9 Pediatric Administrative Information Banner Pharmacaps Inc.
1.9.1 Pediatric studies Waiver Cetirizine HCl Capsules, 10 mg & 5 mg
505(b)(2) NDA Submission

Author (Year)	Design	Sample Size	Age	Comparator	Findings
Cranswick et al, 2005	Pilot Study	15 toddlers	13-25 months	None	Levocetirizine was well tolerated in children aged 12-24 months and demonstrated good safety profile when given twice a day.
Cuvillo A del, et al, 2007	Review of antihistamines in pediatrics	second generation antihistamines summary clinical studies >200	Children	None	The non-cardio toxic second-generation antihistamines cetirizine, loratadine and fexofenadine are the drugs of choice for the recommended treatment of SAR, PAR and urticaria indications, for patients of all ages
Diepgen TL, et al, 2002.	A prospective, multi-country, double-blind, randomized, placebo-controlled trial over 18 months	817 infants	12-24 months	Placebo	This study establishes the safety of Cetirizine use in the treatment of infants and children with atopic dermatitis.
Dubuske, et al, 2007.	Randomized, double blind, placebo controlled studies summarized	>700	Adults Children 6 months to 11 years	Placebo	Desloratadine was safe and well tolerated in clinical trials of patients with CIU. The adverse effect profiles in adults, as well as children aged from 6 months to 11 years were comparable to placebo.
Eick Ten et al, 2001	A review article: Safety of Antihistamines In children.	-	Cetirizine Review included infants and adults	None	The availability of newer generation antihistamine compounds such as loratadine, fexofenadine, mizolastine, ebastine, azelastine and cetirizine in place of terfenadine and astemizole have been shown to be efficacious with few side effects.
Galant S. et al, 2001.	A review article: Allergic Rhinitis medication in the preschool and young school age child.	-	Cetirizine review included children 2-12 years	None	Cetirizine has been evaluated in doses ranging from 2.5 mg to 10 mg in double-blind controlled studies in children as young as 2 years of age with SAR and PAR, and found to be effective and well tolerated.
Gillman et al, 2002	Open label	544 children	6-11 years	No comparator	The results suggest that the symptomatic relief and tolerability profile of Cetirizine HCl syrup daily into improvements in the HRQL (health-related quality of life) of children with SAR.
Golightly et al, 2005	A review	>1000 patients	Wide range of children and adults 3 years – 75 years	None	This review article substantiates the clinical evidence supporting the usefulness of second generation antihistamines for treatment of allergic rhinitis, chronic urticaria and possibly other allergic disorders. Both clinical studies and widespread use attest to the safety of available antihistamines with only rarely occurring side effects.

1.9 Pediatric Administrative Information
1.9.1 Pediatric studies Waiver

Banner Pharmacaps Inc.
Cetirizine HCl Capsules, 10 mg & 5 mg
505(b)(2) NDA Submission

Author (Year)	Design	Sample Size	Age	Comparator	Findings
Horak et al 2000.	Investigator – blinded crossover study	39 subjects	Adults	Fexofenadine	This study demonstrated that both Cetirizine and fexofenadine are safe, well tolerated and significantly better than placebo in subjects suffering from seasonal allergic rhinitis when exposed to grass pollen under the strictly controlled conditions of allergen exposure found in the Vienna Challenge Chamber. Cetirizine appeared to have a longer duration of action than fexofenadine.
Hussien Z. et al, 2005.	Retrospective population study	343 young children	12-24 months	Levocetirizine	The model suggests administration of levocetirizine 0.125 mg twice daily in children 12-48 months of age weighing 8-20 kg yields the same exposure as adults taking the recommended dose of 5 mg once daily.
Mario La Rosa, et al 2001	Double Blind Study Multi-center study	31 children	2 to 6 years	Oxatomide	The results of the present study suggest that Cetirizine may represent an effective and safe pharmacologic therapy for chronic urticaria in preschool children. There was no evidence for changes in hematochemical and urinary values, demonstrating the safety and the tolerability of the two histamines, even when given to young children.
Pariente-Khayat et al, 1995	Open label	8 children	2-6 years	None	No influence of age on the Cetirizine parameters was evidenced. These results suggest that a higher dosage bid (frequency) is required in children when compared with results of (once a day) in adults.
Pitsiu M. et al 2004.	Retrospective Population	112 children	6 months to 12 years	None	Population analysis predicts a linear increase in Cetirizine apparent clearance CL/F and apparent volume distribution V/F with age, volume distribution V/F increased more rapidly with age than CL/F, a non-linear half life was seen, from <4 hrs in infants to near the adult values at 12 years of age. The current recommended dosing regimens that younger children should receive lower but more frequent doses of Cetirizine was confirmed by this analysis.

1.9 Pediatric Administrative Information
1.9.1 Pediatric studies Waiver

Banner Pharmacaps Inc.
Cetirizine HCl Capsules, 10 mg & 5 mg
505(b)(2) NDA Submission

Author (Year)	Design	Sample Size	Age	Comparator	Findings
Segal et al, 2003.	Randomized, multi-center, double blind, placebo controlled study	172 children	6 -11 years	Placebo	This study builds on previous reported data describing the safety and efficacy of Cetirizine in infants as young as 6 months, and indicates that Cetirizine is safe, tolerable, and effective for controlling the symptoms of seasonal allergic rhinitis in children aged 6-11 years, including those with concomitant, intermittent asthma.
Simmons FER et al, 2003.	Randomized, double blind Cross over Single dose study	15 children	6- 11 years	Fexofenadine	In children 6-11 yrs, Cetirizine 10 mg has a rapid onset activity, a 24 hr duration of action and greater H ₁ activity than fexofendine 30 mg.
Simmons F. Estelle et al, 2003.	A randomized parallel group, double blind, placebo-controlled study	85 children	6 months to 11 months	Placebo	This study provides documented safety of Cetirizine in children 6-11 months of age.
Simmons F. Estelle et al, 2001.	A randomized double-blind, placebo controlled study	817 children	12-24 months	Placebo	This ETAC study establishes evidence that regular treatment with Cetirizine effectively reduces acute episodes of urticaria in young children with atopic dermatitis.

CONCLUSIONS

The aforementioned studies provide adequate substantiation that cetirizine is both safe, well tolerated and an effective antihistamine for the treatment of chronic urticaria, seasonal allergic rhinitis and perennial allergic rhinitis in children 6 months to 12 years. Even at relatively high cetirizine doses, approximately twice that recommended worldwide for use in children age 2 to 6 years, there were no statistically significant or clinically relevant differences between the cetirizine and placebo treatment groups with regard to safety outcomes (Simmons et al, 2001).²⁰

Therefore, BPI's proposed product, does not offer meaningful therapeutic benefit over existing prescription dosage forms for children under age 6, and it would have limited use in this population due to lack of dosing flexibility (capsules).

BPI asserts that based on the preceding information, further pediatric studies for BPI's proposed Cetirizine HCl Capsules, 10 mg and 5 mg, constitute unnecessary medical research in this special population due to the availability of other prescription formulations. Accordingly under the section 505B(a)(4)(A)(iii) of the Act, BPI respectfully requests a ~~waiver~~ waiver for its Cetirizine HCl Capsules, 10 mg and 5 mg drug product. **b(4)**

REFERNECES

1. Baena-Cagnani Carolos E., Safety and Tolerability of Treatments for Allergic Rhinitis in Children Drug Safety 2004; 27(12) 883-898.
2. Blic D. J, Wahn U, Billard E, Alt R, Pujazon MC. Levocetirizine in children: evidenced efficacy and safety in a 6-week randomized seasonal allergic rhinitis trial. Pediatric Allergy Immunology 2005;16:267-275.
3. Ciprandi M.D, Frati.F M.D, Marcucci M.D, Sensi M.D, Milanese M, Tosca M.D, Long-term Cetirizine Treatment may reduce New Sensitisations in Allergic Children: Pilot Study; European Annals of Allergy and Clinical Immunology, volume 35, number 6, 2003:208-211.
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6. Diepgen TL on behalf of the ETAC™ study Group. Long-term treatment with Cetirizine of infants with atopic dermatitis: A multi-country, double-blind, randomized, placebo-controlled trial (the ETAC™ trial) over 18 months. Pediatric Immunology 2002;13:278-286.
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1.3 Administration Information
1.3.3 Debarment Certification

Banner Pharmacaps Inc.
Cetirizine HCl Capsules, 10 mg & 5 mg
505(b)(2) NDA Submission

Provided in this section is the list of Debarment Certificates provided in this application.

	TESTING FACILITY
1.	Banner Pharmacaps Inc. Debarment Certification
2.	_____ Debarment Certification
3.	_____ Debarment Certification
4.	_____ Debarment Certification
5.	_____ Debarment Certification
6.	_____ Debarment Certification

b(4)

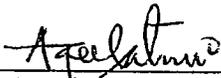
b(4)

Debarment Certification Statement

Banner Pharmacaps 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 NDA.

Conviction Statement

There have been no convictions of crimes (as specified in section 306(a) and (b) of the Act) within the previous five years of any Banner Pharmacaps employees or affiliated companies, or employees of the affiliated companies responsible for the development or submission of this NDA.



Aqeel A. Fatmi, Ph.D.
Global Vice President,
Research & Development



Date

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

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

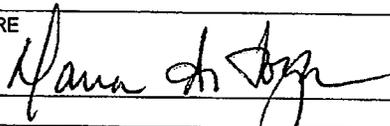
Please mark the applicable checkbox.

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

Clinical Investigators	_____	

b(6)

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

NAME Dana Toops	TITLE Director, Regulatory Affairs
FIRM / ORGANIZATION Banner Pharmacaps Inc.	
SIGNATURE 	DATE 07/29/08

Paperwork Reduction Act Statement

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

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

6 Page(s) Withheld

§ 552(b)(4) Trade Secret / Confidential

§ 552(b)(4) Draft Labeling

§ 552(b)(5) Deliberative Process



Food and Drug Administration
 Center for Drug Evaluation and Research
 Office of Drug Evaluation ONP

FACSIMILE TRANSMITTAL SHEET

DATE: May 14, 2009

To: Dana S. Toops and Vandana Garikipati	From: Janice Adams-King
Company: Banner Pharmacaps	Division of Nonprescription Clinical Evaluation
Fax number: (336) 812-9091	Fax number: 301-796-9899
Phone number: (336) 812-8700 x23312	Phone number: 301-796-3713
Subject: Discipline Review Completed for NDA 22-429 Labeling for cetirizine HCl capsules, 5 mg and 10 mg	

Total no. of pages including cover: 2

Comments:

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

Document to be mailed: YES NO

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.

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APPLICATION: NDA 22-429
DRUG: cetirizine, 5 mg and 10 mg, capsules
SPONSOR: Banner Pharmacaps, Inc.

I. The following comment is in response to your April 14, 2009 submission of revised labeling for cetirizine HCl capsules, 5mg and 10 mg.

- 7

b(4)

II. The following comment is in response to your May 22, 2009 submission of proposed proprietary name _____

b(4)

- The proposed proprietary name, _____ is acceptable for this product provided that the active ingredients (cetirizine) and strength (5 mg and 10 mg) remain unchanged. If any of the proposed product characteristics are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

b(4)

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

/s/

Janice Adams-King
6/26/2009 12:40:40 PM

Adams-King, Janice

From: VGarikipati@banpharm.com
Sent: Wednesday, April 15, 2009 2:00 PM
To: Adams-King, Janice
Cc: DSToops@banpharm.com; MUOparaugo@banpharm.com
Subject: RE: NDA 22-429

Hi Janice,

The trade name for NDA 22-429 is _____

b(4)

Thanks
Vandana

Vandana Garikipati, MS, RAC
Manager, Regulatory Affairs
Banner Pharmacaps Inc
4125 Premier Drive
High Point 27265
Phone: 336-812-8700, Ext 23988
Fax: 336-812-9091

"Adams-King, Janice" <Janice.Adams-King@fda.hhs.gov>

To VGarikipati@banpharm.com

cc DSToops@banpharm.com, MUOparaugo@banpharm.com

04/15/2009 01:51 PM

Subject RE: NDA 22-429

Vandana, Can you clarify the trade name of the drug product for NDA 22-429? Is the trade name _____ Thank you, Janice

b(4)

CDR Janice Adams-King, RN, BSN, MS (USPHS)
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products, CDER/FDA
10903 New Hampshire Avenue, Bldg. 22, Room 5483
Silver Spring, MD 20993
Phone: 301-796-3713 Fax: 301-796-9899
Janice.Adams-King@fda.hhs.gov

6/23/2009

From: VGarikipati@banpharm.com [mailto:VGarikipati@banpharm.com]
Sent: Tuesday, April 14, 2009 6:43 PM
To: Adams-King, Janice
Cc: DSToops@banpharm.com; MUOparaugo@banpharm.com
Subject: RE: NDA 22-429

Hi Janice,

Please find attached the cover letter of the Labeling Amendment sent to the document control room today. In addition, as requested 4 desk copies (including a CD with labeling) are being forwarded to your attention. Kindly acknowledge the receipt of this mail. Thanks.

Best regards
Vandana

Vandana Garikipati, MS; RAC
Manager, Regulatory Affairs
Banner Pharmacaps Inc
4125 Premier Drive
High Point 27265
Phone: 336-812-8700, Ext 23988
Fax: 336-812-9091

"Adams-King, Janice" <Janice.Adams-King@fda.hhs.gov>

03/31/2009 09:56 AM

To: DSToops@banpharm.com
Cc: VGarikipati@banpharm.com, MUOparaugo@banpharm.com
Subject: RE: NDA 22-429

Good Morning Dana, You may submit labeling for both; however, please identify which (tradename or generic) will be your primary label. The labeling will be reviewed for your use and not ~~use~~ use -- Thank you, Janice

CDR Janice Adams-King, RN, BSN, MS (USPHS)
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products, CDER/FDA
10903 New Hampshire Avenue, Bldg. 22, Room 5483
Silver Spring, MD 20993
Phone: 301-796-3713 Fax: 301-796-9899
Janice.Adams-King@fda.hhs.gov

6/23/2009

b(4)

From: DSToops@banpharm.com [mailto:DSToops@banpharm.com]
Sent: Tuesday, March 24, 2009 10:50 PM
To: Adams-King, Janice
Cc: VGarikipati@banpharm.com; MUOparaugo@banpharm.com
Subject: Re: NDA 22-429

Dear Janice,

Do we have the option to submit both the tradename and generic? We also will submit labeling (desk copies and to document room) to you by April 15th as requested.

Best Regards,

Dana

Dana S. Toops
Executive Director
US R&D
Banner
336-812-8700 ext. 23312
"Adams-King, Janice" <Janice.Adams-King@fda.hhs.gov>

03/23/2009 10:02 AM

To DSToops@banpharm.com
cc
Subject NDA 22-429

Hi Dana -- Which labeling is Banner planning to submit for review, i.e., tradename or generic name? We need to have the labeling to us no later than April 15, 2009. In addition to submitting the revised labeling to the document room, please send four desk copies to my attention by this date -- Thank you, Janice

CDR Janice Adams-King, RN, BSN, MS (USPHS)
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products, CDER/FDA
10903 New Hampshire Avenue, Bldg. 22, Room 5483
Silver Spring, MD 20993
Phone: 301-796-3713 Fax: 301-796-9899
Janice.Adams-King@fda.hhs.gov

6/23/2009

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Adams-King, Janice

From: DSToops@banpharm.com
Sent: Tuesday, March 10, 2009 5:01 PM
To: Adams-King, Janice
Cc: VGarikipati@banpharm.com; MUOparaugo@banpharm.com
Subject: Re: NDA 22-429: Information Request

Janice, Thanks for your email request. We will address the information as requested no later than March 25, 09 concerning the Module 5 review. We will also respond to the other items as well. Regards, Dana

Dana S. Toops
Executive Director
US R&D
Banner
336-812-8700 ext. 23312

"Adams-King, Janice" <Janice.Adams-King@fda.hhs.gov>

To DSToops@banpharm.com
cc

03/09/2009 02:40 PM

Subject NDA 22-429: Information Request

Dana,

We are reviewing the Clinical section of your submission and have the following information request. We request a prompt written response (by March 25, 2009) in order to continue our evaluation of your NDA.

Please provide the following information:

1) AERS Data section 3.1 of your Integrated Safety Summary (ISS):

- For the 240 cases reported for cetirizine, provide the total number of adverse events associated with the cases. In addition, for the most frequently reported AEs (preferred term) that you identified during the reporting period, provide the number and percentage for each of the AE.
- For all the tables, provide a grand total across each column and row. If there is a discrepancy in the total number of events (or cases) and the breakdown, provide an explanation in narrative.

2) AAPCC Data section 3.4 of your Integrated Safety Summary (ISS):

- For the 254 cases exposed to cetirizine in this database, provide the total number of

6/23/2009

clinical effects associated with these cases, and provide the most frequently reported clinical effects with cetirizine exposure.

- Provide a table of Medical Outcomes (similar in format to your Table 3.4.2, ISS p.64 of 85) . The age breakdown of medical outcomes should be grouped as follows: 0 to 5 y/o, 6 to 12 y/o, 13 to 18 y/o, 19 to 64 y/o and > 65 y/o. Totals for each age group and medical outcome should be included in the table. If there is a discrepancy in the total number of events (or cases) and the breakdown, provide an explanation in narrative.

3) As previously requested via email on --(Janice, pls. put date), you need to:

- Specify the dictionary used to describe all AEs during the clinical trials (if none, you state so).
- In both fasting and fed studies, the Table of Events lists ECG as one the procedures performed during screening but was no discussion on ECG findings was included in the study report. You need to include a summary of ECG findings in the study report if performed; including a descriptive summary of relevant ECG findings. If not performed, then this should be stated also.

With respect to the Agency's labeling information request dated February 9, 2009 and your recent proprietary name review request, please submit respective labeling for which Banner is seeking approval. Hence, if the labeling is reflective of the proprietary name under review, please submit that respective labeling. The labeling must be submitted for all SKUs that is covered by your stability program and provided in the container/closure information in the CMC section of your application. The labeling must be received by the Agency no later than April 1, 2009.

In addition to your official response to this request, please send 3 desk copies to my attention by April 1, 2009. Thank you, Janice

CDR Janice Adams-King, RN, BSN, MS (USPHS)
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products, CDER/FDA
10903 New Hampshire Avenue, Bldg. 22, Room 5483
Silver Spring, MD 20993
Phone: 301-796-3713 Fax: 301-796-9899
Janice.Adams-King@fda.hhs.gov

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6/23/2009

Adams-King, Janice

From: DSToops@banpharm.com
Sent: Monday, February 09, 2009 1:43 PM
To: Adams-King, Janice
Cc: VGarikipati@banpharm.com; MUOparaugo@banpharm.com
Subject: RE: NDA 22-429: Ceterizine HCl Capsules

Thanks Janice, This is to confirm receipt of the request and let you know we will be working on this diligently.
Best Regards, Dana

Dana S. Toops
Executive Director
US R&D
Banner
336-812-8700 ext. 23312

"Adams-King, Janice" <Janice.Adams-King@fda.hhs.gov>

To DSToops@banpharm.com
cc

02/09/2009 11:00 AM

Subject RE: NDA 22-429: Ceterizine HCl Capsules

Good Morning Dana, We remain in the process of reviewing the above-referenced NDA application -- Please see the information requests below and respond accordingly. Please provide 3 desk copies of the modified labeling. Feel free to contact me should you have questions or need clarification.

Clinical:

1. What kind of dictionary was used to describe all AEs during the clinical trials?
2. In both fasting and fed studies, the Table of Events lists ECG as one the procedures performed during screening but no discussion on ECG findings was included in the study report. The sponsor should include a summary of ECG findings in the study report if performed; these should include a descriptive summary of relevant ECG findings. If not performed, then this should be stated, and provide an updated table.

Labeling:

1. Draft carton label for principal display panel for Hives Relief: 5 mg (20- and 200-count) and 10 mg (20 and 200-count).
 - a. Remove subheading " _____", located under "Hives Relief". **b(4)**
2. Draft carton label for 10 mg Hives Relief 20-count
 - a. Label format information missing, please submit font specifications

6/23/2009

3. Draft carton label for 200-count carton labels for 5 and 10 mg Allergy and Hives Relief
 - a. Recertification is needed because the font size for the label text seems smaller than indicated.
4. Draft drug facts on carton label, subheading "Questions or comments"
 - a. A telephone number of a source to answer questions about these products is not provided. A telephone number must be provided to be in accordance with 21 CFR 201.66 (c) (9).
5. Draft immediate container labels for 5 mg and 10 mg (20-count Allergy bottle labels); 5 mg and 10 mg (200-count Hives Relief bottle labels).
 - a. If you use the title ~~_____~~ the label, content, format, and graphical specifications must contain the information to be in accordance with 21 CFR 201.66. **b(4)**

Thank you, Janice

CDR Janice Adams-King, RN, BSN, MS (USPHS)
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products, CDER/FDA
10903 New Hampshire Avenue, Bldg. 22, Room 5483
Silver Spring, MD 20993
Phone: 301-796-3713 Fax: 301-796-9899
Janice.Adams-King@fda.hhs.gov

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6/23/2009

Adams-King, Janice

From: DSToops@banpharm.com
Sent: Wednesday, February 04, 2009 1:38 PM
To: Adams-King, Janice
Cc: VGarikipati@banpharm.com; MUOparaugo@banpharm.com
Subject: Re: NDA 22-429: Cetirizine HCl

Janice, Thanks for the phone call and this email. We will provide you the information requested during the next 2-3 business days. Best Regards, Dana

"Adams-King, Janice" <Janice.Adams-King@fda.hhs.gov>

To DSToops@banpharm.com

cc

Subject NDA 22-429: Cetirizine HCl

02/04/2009 01:09 PM

Dana,

I am in the process of conducting a regulatory review of your NDA package and have identified items that Banner Pharmacaps should address.

1) The following items are missing from your **Form FDA 356h**:

- Under **Product Description**, the established/chemical name and the proposed indication are blank (Refer to CFR 314.50(a)(1))
- Under **Establishment Information**, please indicate on the form where in the body of the application this information is located
- Under **Cross References**, please list all referenced applications (Refer to 314.50(a)(1))

2) The following items are missing from your **Comprehensive Index Summary**:

- **Marketing history outside the United States** (Refer to CFR 314.50©(2)(ii))
- **Concluding discussion** is needed to include risk/benefit as well as postmarketing studies/surveillance (Refer to CFR 314.50©(2)(ix))

3) We are unable to locate **referenced information authorized and signed** (Refer to 314.50(g)(1))

4) We are unable to locate **right of reference or use signed by owner of the data** (Refer to 314.50(g)(3))

Please contact me should you have questions or need additional information — Thank you, Janice

CDR Janice Adams-King, RN, BSN, MS (USPHS)
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation

6/23/2009

Office of Nonprescription Products, CDER/FDA
10903 New Hampshire Avenue, Bldg. 22, Room 5483
Silver Spring, MD 20993
Phone: 301-796-3713 Fax: 301-796-9899
Janice.Adams-King@fda.hhs.gov

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6/23/2009

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/s/

Janice Adams-King
6/23/2009 01:59:43 PM
CSO

505(b)(2) ASSESSMENT

Application Information		
NDA # 22-429	NDA Supplement #:S-	Efficacy Supplement Type SE-
Proprietary Name: Established/Proper Name: Cetirizine HCl Dosage Form: capsule Strengths: 5 mg/10 mg		
Applicant: Banner Pharmacaps.		
Date of Receipt: 08-01-2008		
PDUFA Goal Date: 09-01-2009		Action Goal Date (if different):
Proposed Indication(s): 1) temporarily relieves the symptoms due to hay fever or other respiratory allergies: runny nose, sneezing, itchy, watery eyes, itching of nose or throat and 2) itching due to hives (urticaria)		

GENERAL INFORMATION

1. Is this application for a drug that is an "old" antibiotic as described in the Guidance to Industry, Repeal of Section 507 of the Federal Food, Drug and Cosmetic Act? (Certain antibiotics are not entitled to Hatch-Waxman patent listing and exclusivity benefits.)

YES NO

If "YES," proceed to question #3.

2. Is this application for a recombinant or biologically-derived product and/or protein or peptide product?

YES NO

If "YES "contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.



**INFORMATION PROVIDED VIA RELIANCE
(LISTED DRUG OR LITERATURE)**

3. List the information essential to the approval of the proposed drug that is provided by reliance on our previous finding of safety and efficacy for a listed drug or by reliance on published literature. *(If not clearly identified by the applicant, this information can usually be derived from annotated labeling.)*

Source of information (e.g., published literature, name of referenced product)	Information provided (e.g., pharmacokinetic data, or specific sections of labeling)
NDA 19-835, Zyrtec®, 5 mg and 10 mg, tablets	Pharmacokinetic data

4. Reliance on information regarding another product (whether a previously approved product or from published literature) must be scientifically appropriate. An applicant needs to provide a scientific “bridge” to demonstrate the relationship of the referenced and proposed products. Describe how the applicant bridged the proposed product to the referenced product(s). (Example: BA/BE studies)

Pharmacokinetic studies to bridge proposed cetirizine capsule to Zyrtec® that is approved for OTC use (referenced drug)

RELIANCE ON PUBLISHED LITERATURE

5. (a) Does the application rely on published literature to support the approval of the proposed drug product (i.e., the application *cannot* be approved without the published literature)?

YES NO

If “NO,” proceed to question #6.

(b) Does any of the published literature necessary to support approval identify a specific (e.g., brand name) *listed* drug product?

YES NO

*If “NO”, proceed to question #6
If “YES”, list the listed drug(s) identified by name and answer question #5(c).*

(c) Are the drug product(s) listed in (b) identified by the applicant as the listed drug(s)?

YES NO



RELIANCE ON LISTED DRUG(S)

Reliance on published literature which identifies a specific approved (listed) drug constitutes reliance on that listed drug. Please answer questions #6-10 accordingly.

6. Regardless of whether the applicant has explicitly referenced the listed drug(s), does the application rely on the finding of safety and effectiveness for one or more listed drugs (approved drugs) to support the approval of the proposed drug product (i.e., the application cannot be approved without this reliance)?
- YES NO

If "NO," proceed to question #11.

7. Name of listed drug(s) relied upon, and the NDA/ANDA #(s). Please indicate if the applicant explicitly identified the product as being relied upon (see note below):

Name of Drug	NDA/ANDA #	Did applicant specify reliance on the product? (Y/N)
Zyrtec®, 5 mg and 10 mg, tablets	19-835	Y

Applicants should specify reliance on the 356h, in the cover letter, and/or with their patent certification/statement. If you believe there is reliance on a listed product that has not been explicitly identified as such by the applicant, please contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.

8. If this is a supplement, does the supplement rely upon the same listed drug(s) as the original (b)(2) application?
- YES NO

If "NO", please contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.

9. Were any of the listed drug(s) relied upon for this application:
- a. Approved in a 505(b)(2) application? YES NO

If "YES", please list which drug(s).

Name of drug(s) approved in a 505(b)(2) application:

- b. Approved by the DESI process? YES NO

If "YES", please list which drug(s).

Name of drug(s) approved via the DESI process:

- c. Described in a monograph? YES NO

If "YES", please list which drug(s).

Name of drug(s) described in a monograph:

d. Discontinued from marketing?

YES NO

If "YES", please list which drug(s) and answer question d.1.

If "NO", proceed to question #10.

Name of drug(s) discontinued from marketing:

1. Were the products discontinued for reasons related to safety or effectiveness?

YES NO

(Information regarding whether a drug has been discontinued from marketing for reasons of safety or effectiveness may be available in the Orange Book. Refer to section 1.11 for an explanation, and section 6.1 for the list of discontinued drugs. If a determination of the reason for discontinuation has not been published in the Federal Register (and noted in the Orange Book), you will need to research the archive file and/or consult with the review team. Do not rely solely on any statements made by the sponsor.)

10. Describe the change from the listed drug(s) relied upon to support this (b)(2) application (for example, "This application provides for a new indication, otitis media" or "This application provides for a change in dosage form, from capsule to solution").

The change from the listed drug: this application provides for a change in dosage form, from tablet to capsule.

The purpose of the following two questions is to determine if there is an approved drug product that is equivalent or very similar to the product proposed for approval that should be referenced as a listed drug in the pending application.

11. (a) Is there a pharmaceutical equivalent(s) to the product proposed in the 505(b)(2) application that is already approved (via an NDA or ANDA)?

(Pharmaceutical equivalents are drug products in identical dosage forms that: (1) contain identical amounts of the identical active drug ingredient, i.e., the same salt or ester of the same therapeutic moiety, or, in the case of modified release dosage forms that require a reservoir or overage or such forms as prefilled syringes where residual volume may vary, that deliver identical amounts of the active drug ingredient over the identical dosing period; (2) do not necessarily contain the same inactive ingredients; and (3) meet the identical compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates. (21 CFR 320.1(c))

Note that for proposed combinations of one or more previously approved drugs, a pharmaceutical equivalent must also be a combination of the same drugs.

YES NO

If "NO," to (a) proceed to question #12.

(b) Is the pharmaceutical equivalent approved for the same indication for which the 505(b)(2) application is seeking approval?

YES NO

(c) Is the listed drug(s) referenced by the application a pharmaceutical equivalent? YES NO

If "YES" and there are no additional pharmaceutical equivalents listed, proceed to question #13.

If "NO" or if there are additional pharmaceutical equivalents that are not referenced by the application, list the NDA pharmaceutical equivalent(s); you do not have to individually list all of the products approved as ANDAs, but please note that there are approved generics listed in the Orange Book. Please contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.

12. (a) Is there a pharmaceutical alternative(s) already approved (via an NDA or ANDA)?

(Pharmaceutical alternatives are drug products that contain the identical therapeutic moiety, or its precursor, but not necessarily in the same amount or dosage form or as the same salt or ester. Each such drug product individually meets either the identical or its own respective compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times and/or dissolution rates. (21 CFR 320.1(d)) Different dosage forms and strengths within a product line by a single manufacturer are thus pharmaceutical alternatives, as are extended-release products when compared with immediate- or standard-release formulations of the same active ingredient.)

Note that for proposed combinations of one or more previously approved drugs, a pharmaceutical alternative must also be a combination of the same drugs.

YES NO

If "NO", proceed to question #13.

(b) Is the pharmaceutical alternative approved for the same indication for which the 505(b)(2) application is seeking approval?

YES NO

(c) Is the approved pharmaceutical alternative(s) referenced as the listed drug(s)?

YES NO

If "YES" and there are no additional pharmaceutical alternatives listed, proceed to question #13.

If "NO" or if there are additional pharmaceutical alternatives that are not referenced by the application, list the NDA pharmaceutical alternative(s); you do not have to individually list all of the products approved as ANDAs, but please note that there are approved generics listed in the Orange Book. Contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.

Pharmaceutical alternative(s): NDAs 21-621, 78-692 cetirizine HCl, 5 mg and 10 mg, chewable oral tablet; NDAs 78-615, 78-317 cetirizine HCl, 5 mg and 10 mg, oral tablets; NDA 90-378, cetirizine HCl, 5mg/5mL, oral syrup

PATENT CERTIFICATION/STATEMENTS

13. List the patent numbers of all patents listed in the Orange Book for the listed drug(s) for which our finding of safety and effectiveness is relied upon to support approval of the (b)(2) product.

Listed drug/Patent number(s): There are no patents for the reference listed drug relied upon for this application.

14. Did the applicant address (with an appropriate certification or statement) all of the patents listed in the Orange Book for the listed drug(s)?

YES NO

If "NO", list which patents (and which listed drugs) were not addressed by the applicant.

Listed drug/Patent number(s):

15. Which of the following patent certifications does the application contain? *(Check all that apply and identify the patents to which each type of certification was made, as appropriate.)*

- No patent certifications are required (e.g., because application solely based on published literature that does not cite a specific innovator product or for an "old antibiotic" (see question 1.))
- 21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA. (Paragraph I certification)
- 21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired. (Paragraph II certification)
- Patent number(s):
- 21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire. (Paragraph III certification)
- Patent number(s):
- 21 CFR 314.50(i)(1)(i)(A)(4): The patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the application is submitted. (Paragraph IV certification)

Patent number(s):

If the application has been filed, did the applicant submit a signed certification stating that the NDA holder and patent owner(s) were notified the NDA was filed [21 CFR 314.52(b)]?

YES NO

Did the applicant submit documentation showing that the NDA holder and patent owner(s) received the notification [21 CFR 314.52(e)]? This is generally provided in the form of a registered mail receipt.

YES NO

Date Received:

Has the applicant been sued for patent infringement (within 45-days of receipt of the notification listed above)? Note: you may need to call the applicant to verify this information.

YES NO

- 21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the patent owner (must also submit certification under 21 CFR 314.50(i)(1)(i)(A)(4) above).

Patent number(s):

If the application has been filed, did the applicant submit a signed certification stating that the NDA holder and patent owner(s) were notified the NDA was filed [21 CFR 314.52(b)]?

YES NO

Did the applicant submit documentation showing that the NDA holder and patent owner(s) received the notification [21 CFR 314.52(e)]? This is generally provided in the form of a registered mail receipt.

YES NO

Date Received:

Has the applicant been sued for patent infringement (within 45-days of receipt of the notification listed above)? Note: you may need to call the applicant to verify this information.

YES NO

- Written statement from patent owner that it consents to an immediate effective date of approval (applicant must also submit paragraph IV certification under 21 CFR 314.50(i)(1)(i)(A)(4) above).

Patent number(s):

- 21 CFR 314.50(i)(1)(ii): No relevant patents.
- 21 CFR 314.50(i)(1)(iii): The patent on the listed drug is a method of use patent and the labeling for the drug product for which the applicant is seeking approval does not include any indications that are covered by the use patent as described in the corresponding use code in the Orange Book. Applicant must provide a statement that the method of use patent does not claim any of the proposed indications. (Section viii statement)

Patent number(s):

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/s/

Janice Adams-King
6/2/2009 03:53:56 PM
CSO



Food and Drug Administration
 Center for Drug Evaluation and Research
 Office of Drug Evaluation ONP

FACSIMILE TRANSMITTAL SHEET

DATE: May 14, 2009

To: Dana S. Toops and Vandana Garikipati	From: Janice Adams-King
Company: Banner Pharmacaps	Division of Nonprescription Clinical Evaluation
Fax number: (336) 812-9091	Fax number: 301-796-9899
Phone number: (336) 812-8700 x23312	Phone number: 301-796-3713
Subject: Discipline Review Completed for NDA 22-429 Labeling for cetirizine HCl capsules, 5 mg and 10 mg	

Total no. of pages including cover: 3

Comments:

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

Document to be mailed: YES NO

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- I. The following comments are in response to your April 14, 2009 submission of revised labeling for cetirizine HCl capsules, 5mg and 10 mg submitted in response to the Agency's information request dated February 9, 2009. These comments are preliminary in nature and should not be considered a complete evaluation of your proposed labeling.

Principal Display Panel (PDP)

1. For consistency in labeling, the phrase "Hives Relief" should be either all upper cases or using upper case for the first word in all packaging sizes. (i.e. "HIVES RELIEF" versus "Hives Relief").
2. The potency (i.e., 5 mg and 10 mg) for different strengths must be distinct from each other. We encourage to use a larger font (i.e., at least 5 size larger) and different color schemes to distinguish the two different strengths.

Drug Facts Panel

1. For the cetirizine 5 mg and 10 mg (Allergy) 20-count carton labels. The bullets in the "Drug Facts" label under the heading, "Other Information" must be left aligned in accordance to 21 CFR 201.66(d)(4).
2. For all carton labels - under the subheading, "Questions or comments?"; it is recommended that the days of the week and times of the day when a person is available to respond to questions should stated as in 21 CFR 201.66(c)(9).

II. ↵

b(4)

b(4)

Principal Display Panel

1. Statement of Identity

The trade name request for this product is “_____” The sponsor must revised the trade name from “_____” to “_____” i.e., the dosage form must adjacent to _____

b(4)

2. Promotional Statements

Graphic Liquid Filled Capsule: the actual capsule that the consumer will use must be identical to the graphic displayed on the carton label. The current graphic depicts a _____, which is not the _____ capsule as being requested for approval. This could lead to consumer confusion.

b(4)

Drug Facts

1. For the 5 mg and 10 mg, 20-count Allergy carton labels under the subheading “Other Information” the bullets in this section must be left aligned in accordance to 21 CFR 201.66(d)(4).
2. For all carton labels; under the heading, “Questions or comments?”, it is recommended that the days of the week and times of the day when a person is available to respond to questions should be stated as in accordance with 21 CFR 201.66(c)(9).

Other comment

1. The “New” flag should be removed from the carton label 180 days following approval.

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/s/

Melissa Furness
5/19/2009 03:10:44 PM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 22-429

**PROPRIETARY NAME REQUEST
- CONDITIONALLY ACCEPTABLE**

Banner Pharmacaps, Inc.
ATTENTION: Vandana Garikipati, MS, RAC
Manager, Regulatory Affairs
4125 Premier Drive
High Point, North Carolina 27265

Dear Ms. Garikipati:

Please refer to your New Drug Application (NDA) dated July 31, 2008, received August 1, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cetirizine HCl Capsules, 10 mg and 5 mg.

We also refer to your February 19, 2009, correspondence, received February 20, 2009, requesting review of your proposed proprietary name. _____, Please note that we do not normally review _____

b(4)

_____ However, we reviewed the proposed proprietary name for the _____, as you requested. We have completed our review of the proposed proprietary name _____, and have concluded that it is acceptable.

b(4)

If any of the proposed product characteristics as stated in your February 19, 2009, submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, call Darrell Jenkins, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0558. For any other information regarding this application contact Janice Adams-King, Regulatory Project Manager in the Division of Nonprescription Products, at 301-796-3713.

Sincerely,

{See appended electronic signature page}

Joel Schiffenbauer, M.D.
Deputy Director
Division of Nonprescription Products
Office of Nonprescription Products
Center for Drug Evaluation and Research

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/s/

Joel Schiffenbauer
5/19/2009 11:47:58 AM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-429
Banner Pharmacaps
Attention: Dana S. Toops
Director, Regulatory Affairs
4125 Premier Drive
High Point, NC 27265

Dear Mr. Toops:

Please refer to your July 31, 2008 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for cetirizine HCl capsules, 5 mg and 10 mg.

We also refer to and acknowledge your April 3, 2009 submission to withdraw your proposal to add _____ as an _____ in your March 13, 2009 amendment.

b(4)

As described in our March 31, 2009 letter, your March 13, 2009 submission constituted a major amendment to your application and the review clock was extended accordingly. The new PDUFA goal date for your application is September 1, 2009. While your April 3, 2009 submission withdrew a portion of your March 13, 2009 amendment, we cannot reclassify the amendment to your application as a minor amendment and change the goal date back to the original June 1, 2009 date at this time in the review cycle.

Based on your March 13, 2009 amendment, the internal review timelines were also adjusted accordingly. However, we will endeavor to take action on your application as close to the original June 1, 2009 goal date as possible.

If you have any questions, call Janice Adams, Regulatory Project Manager, at 301-796-3713.

Sincerely,

{See appended electronic signature page}

Joel Schiffenbauer, M.D.
Deputy Director
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research

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/s/

Joel Schiffenbauer
5/5/2009 11:41:26 AM

Adams-King, Janice

From: Durmowicz, Anthony
Sent: Thursday, April 23, 2009 2:26 PM
To: Adams-King, Janice
Cc: Chowdhury, Badrul A; Furness, Melissa; Barnes, Sandy L (CDER); Gilbert McClain, Lydia I
Subject: RE: NDA 22-429: Cetirizine 5 mg and 10 mg

Dear Janice:

A DPAP review will not be placed in DFS for this NDA. DPAP's role through this review process was to act as a resource to ONP with the primary review activities to be handled by ONP. Let me know if you have any questions. Thanks.

Tony

Anthony G. Durmowicz, M.D.
Division of Pulmonary and Allergy Products
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave, Building 22, Room 3375
Silver Spring, MD 20993-0002
durmowicza@fda.hhs.gov

From: Adams-King, Janice
Sent: Thursday, April 23, 2009 11:10 AM
To: Durmowicz, Anthony
Cc: Chowdhury, Badrul A; Furness, Melissa; Barnes, Sandy L (CDER)
Subject: NDA 22-429: Cetirizine 5 mg and 10 mg

Good Morning Tony -- I just checked DFS and did not see the DPAP review for this NDA. Please let me know when you may expect to have the DPAP review for this NDA in DFS. The Action Date of this NDA is June 1. Thanks and take care, Janice

CDR Janice Adams-King, RN, BSN, MS (USPHS)
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products, CDER/FDA
10903 New Hampshire Avenue, Bldg. 22, Room 5483
Silver Spring, MD 20993
Phone: 301-796-3713 Fax: 301-796-9899
Janice.Adams-King@fda.hhs.gov



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-429

INFORMATION REQUEST LETTER

Banner Pharmacaps Inc.
Attention: Dana Toops, Executive Director
U.S. Research and Development
4125 Premier Drive
High Point, NC 27265

Dear Mr. Toops:

Please refer to your July 31, 2008 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cetirizine HCl Capsules, 10 mg & 5 mg.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following comments and information requests. Your response is requested within 3-5 business days of receipt of this letter:

1. You claim categorical exclusion from making an environmental assessment of the impact of marketing the drug product on the basis that marketing the proposed product will not increase the release of cetirizine to the environment. Please justify your assertion with an assurance that the total use of cetirizine HCl does not increase as a result of the marketing of your product. Otherwise, you must show, as described in 21 CFR 25.31(b), that the marketing of your product will not increase the total estimated concentration of cetirizine at the entry point in the aquatic environment above 1 part per billion. If you choose this option, please be reminded that the use of all Zyrtec® products will have to be included in your calculations.
2. You have listed mannitol as an ingredient in the inactive ingredients section of the "Drug Facts" labeled submitted in your original submission. However, mannitol is not listed in the formulation. Please rectify this discrepancy, and re-submit all revised labels and labeling.

To facilitate prompt review of your response, a courtesy copy (electronic or fax) of your official submission would be kindly appreciated. Please send this to Jeannie David, Regulatory Project Manager in the Office of New Drug Quality Assessment (jeannie.david@fda.hhs.gov; fax 301-796-9877), and Janice Adams-King, Regulatory Project Manager the Office of New Drugs (janice.adams-king@fda.hhs.gov; fax 301-796-9899).

If you have any questions, call Jeannie David, Regulatory Project Manager, at 301-796-4247.

Sincerely,

{See appended electronic signature page}

Moo-Jhong Rhee, Ph.D.
Chief, Branch III
Division Pre-Marketing Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

Moo-Jhong Rhee
4/8/2009 02:14:57 PM
Chief, Branch III



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-429

Banner Pharmacaps
Attention: Dana S. Toops
Director, Regulatory Affairs
4125 Premier Drive
High Point, NC 27265

Dear Mr. Toops:

Please refer to your July 31, 2008 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for cetirizine HCl capsules, 5 mg and 10 mg.

On March 16, 2009, we received your March 13, 2009 major amendment to this application. The receipt date is within 3 months of the user fee goal date. Therefore, we are extending the goal date by three months to provide time for a full review of the submission. The extended user fee goal date is September 1, 2009.

If you have any questions, call Janice Adams-King, Regulatory Project Manager, at 301-796-3713.

Sincerely,

{See appended electronic signature page}

Melissa Furness
Chief, Project Management Staff
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research

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/s/

Melissa Furness
3/31/2009 07:46:45 AM

Adams-King, Janice

From: Greeley, George
Sent: Tuesday, March 31, 2009 9:09 AM
To: Adams-King, Janice
Cc: Mathis, Lisa
Subject: NDA 22-429

b(4)

Importance: High

Hi Janice,

The partial waiver/drug appropriately labeled application was reviewed by the PeRC PREA Subcommittee on March 25, 2009. The Division recommended a partial waiver from 0>6 years because evidence strongly suggests that product would be ineffective or unsafe in this/these pediatric population/s. The PeRC agreed with the Division to grant a partial waiver and that this product is appropriately labeled for pediatric use from 6-16 years.

b(4)

Thank you.

George Greeley
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Pediatric and Maternal Health Staff
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NDA/BLA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

Application Information		
NDA # 22-429 BLA#	NDA Supplement #:S- BLA STN #	Efficacy Supplement Type SE-
Proprietary Name: cetirizine HCl Established/Proper Name: cetirizine HCl Dosage Form: capsule Strengths: 5 mg and 10mg		
Applicant: Banner Pharmacaps Agent for Applicant (if applicable): N/A		
Date of Application: 07-31-2008 Date of Receipt: 08-01-08 Date clock started after UN: N/A		
PDUFA Goal Date: 06-01-09	Action Goal Date (if different):	
Filing Date: 09-30-08 Date of Filing Meeting: 09-10-08		
Chemical Classification: (1,2,3 etc.) (original NDAs only)		
Proposed Indication(s): 1) temporarily relieves these symptoms due to have fever or other respiratory allergies: runny nose, sneezing, itchy, watery eyes, itching of nose or throat, and 2) itching due to hives (urticaria)		
Type of Original NDA: AND (if applicable) Type of NDA Supplement:		<input type="checkbox"/> 505(b)(1) <input checked="" type="checkbox"/> 505(b)(2) <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)
<i>Refer to Appendix A for further information.</i>		
Review Classification: <i>If the application includes a complete response to pediatric WR, review classification is Priority.</i> <i>If a tropical disease Priority review voucher was submitted, review classification defaults to Priority.</i>		<input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority <input type="checkbox"/> Tropical disease Priority review voucher submitted
Resubmission after withdrawal? <input type="checkbox"/>		
Resubmission after refuse to file? <input type="checkbox"/>		
Part 3 Combination Product? <input type="checkbox"/>	<input type="checkbox"/> Drug/Biologic <input type="checkbox"/> Drug/Device <input type="checkbox"/> Biologic/Device	
<input type="checkbox"/> Fast Track <input type="checkbox"/> Rolling Review <input type="checkbox"/> Orphan Designation <input type="checkbox"/> Rx-to-OTC switch, Full <input type="checkbox"/> Rx-to-OTC switch, Partial <input type="checkbox"/> Direct-to-OTC	<input type="checkbox"/> PMC response <input type="checkbox"/> PMR response: <input type="checkbox"/> FDAAA [505(o)] <input type="checkbox"/> PREA deferred pediatric studies [21 CFR 314.55(b)/21 CFR 601.27(b)] <input type="checkbox"/> Accelerated approval confirmatory studies (21 CFR 314.510/21 CFR 601.41) <input type="checkbox"/> Animal rule postmarketing studies to verify	

Other:	clinical benefit and safety (21 CFR 314.610/21 CFR 601.42)
Collaborative Review Division (if OTC product): Division of Pulmonary and Allergy Products	
List referenced IND Number(s): No IND referenced, however sponsor has IND 74,232 for this drug.	
PDUFA and Action Goal dates correct in tracking system? <i>If not, ask the document room staff to correct them immediately. These are the dates used for calculating inspection dates.</i>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
Are the proprietary, established/proper, and applicant names correct in tracking system? <i>If not, ask the document room staff to make the corrections. Also, ask the document room staff to add the established name to the supporting IND(s) if not already entered into tracking system.</i>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
Are all classification codes/flags (e.g. orphan, OTC drug, pediatric data) entered into tracking system? <i>If not, ask the document room staff to make the appropriate entries.</i>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
Application Integrity Policy	
Is the application affected by the Application Integrity Policy (AIP)? Check the AIP list at: http://www.fda.gov/ora/compliance_ref/aip.html If yes, explain: If yes, has OC/DMPQ been notified of the submission? Comments:	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO
User Fees	
Form 3397 (User Fee Cover Sheet) submitted	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
User Fee Status Comments:	<input checked="" type="checkbox"/> Paid <input type="checkbox"/> Exempt (orphan, government) <input type="checkbox"/> Waived (e.g., small business, public health) <input type="checkbox"/> Not required
<i>Note: 505(b)(2) applications are no longer exempt from user fees pursuant to the passage of FDAAA. It is expected that all 505(b) applications, whether 505(b)(1) or 505(b)(2), will require user fees unless otherwise waived or exempted (e.g., business waiver, orphan exemption).</i>	
Exclusivity	

<p>Does another product have orphan exclusivity for the same indication? <i>Check the Electronic Orange Book at: http://www.fda.gov/cder/ob/default.htm</i></p> <p>If yes, is the product considered to be the same product according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]?</p> <p><i>If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007)</i></p> <p>Comments:</p>	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO
<p>Has the applicant requested 5-year or 3-year Waxman-Hatch exclusivity? (<i>NDAs/NDA efficacy supplements only</i>)</p> <p><i>Note: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.</i></p> <p>Comments:</p>	<input type="checkbox"/> YES # years requested: <input checked="" type="checkbox"/> NO
<p>If the proposed product is a single enantiomer of a racemic drug previously approved for a different therapeutic use (<i>NDAs only</i>):</p> <p>Did the applicant (a) elect to have the single enantiomer (contained as an active ingredient) not be considered the same active ingredient as that contained in an already approved racemic drug, and/or (b) request exclusivity pursuant to section 505(u) of the Act (per FDAAA Section 1113)?</p> <p><i>If yes, contact Mary Ann Holovac, Director of Drug Information, OGD/DLPS/LRB.</i></p>	<input checked="" type="checkbox"/> Not applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
505(b)(2) (NDAs/NDA Efficacy Supplements only)	
<p>1. Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA?</p> <p>2. Is the application for a duplicate of a listed drug whose only difference is that the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action less than that of the reference listed drug (RLD)? (see 21 CFR 314.54(b)(1)).</p> <p>3. Is the application for a duplicate of a listed drug whose only difference is that the rate at which the proposed product's active ingredient(s) is absorbed or made available to the site of action is unintentionally less than that of the listed drug (see 21 CFR 314.54(b)(2))?</p>	<input type="checkbox"/> Not applicable <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO

<p><i>Note: If you answered yes to any of the above questions, the application may be refused for filing under 21 CFR 314.101(d)(9).</i></p>		
<p>4. Is there unexpired exclusivity on the active moiety (e.g., 5-year, 3-year, orphan or pediatric exclusivity)? Check the Electronic Orange Book at: http://www.fda.gov/cder/ob/default.htm</p>		<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
<p>If yes, please list below:</p>		
Application No.	Drug Name	Exclusivity Code
<p><i>If there is unexpired, 5-year exclusivity remaining on the active moiety for the proposed drug product, a 505(b)(2) application cannot be submitted until the period of exclusivity expires (unless the applicant provides paragraph IV patent certification; then an application can be submitted four years after the date of approval.) Pediatric exclusivity will extend both of the timeframes in this provision by 6 months. 21 CFR 108(b)(2). Unexpired, 3-year exclusivity will only block the approval, not the submission of a 505(b)(2) application.</i></p>		
<p>Format and Content</p>		
<p><i>Do not check mixed submission if the only electronic component is the content of labeling (COL).</i></p> <p>Comments:</p>		<input type="checkbox"/> All paper (except for COL) <input type="checkbox"/> All electronic <input checked="" type="checkbox"/> Mixed (paper/electronic) <input type="checkbox"/> CTD <input type="checkbox"/> Non-CTD <input type="checkbox"/> Mixed (CTD/non-CTD)
<p>If mixed (paper/electronic) submission, which parts of the application are submitted in electronic format?</p>		Labeling, Quality
<p>If electronic submission: <u>paper</u> forms and certifications signed (non-CTD) or <u>electronic</u> forms and certifications signed (scanned or digital signature)(CTD)?</p> <p><i>Forms include: 356h, patent information (3542a), financial disclosure (3454/3455), user fee cover sheet (3542a), and clinical trials (3674); Certifications include: debarment certification, patent certification(s), field copy certification, and pediatric certification.</i></p> <p>Comments: Form 356h, as well as the labeling and quality sections are in paper submission as well as electronic submission.</p>		<input type="checkbox"/> YES <input type="checkbox"/> NO
<p>If electronic submission, does it follow the eCTD guidance? (http://www.fda.gov/cder/guidance/7087rev.pdf)</p> <p>If not, explain (e.g., waiver granted):</p>		<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO

<p>Form 356h: Is a signed form 356h included?</p> <p><i>If foreign applicant, both the applicant and the U.S. agent must sign the form.</i></p> <p>Are all establishments and their registration numbers listed on the form?</p> <p>Comments: Establishments and their registration numbers are provided as an Attachment to FDA form 356h.</p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<p>Index: Does the submission contain an accurate comprehensive index?</p> <p>Comments: Comprehensive index submitted as an application amendment 05-05-08</p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<p>Is the submission complete as required under 21 CFR 314.50 (NDAs/NDA efficacy supplements) or under 21 CFR 601.2 (BLAs/BLA efficacy supplements) including:</p> <p><input type="checkbox"/> legible <input type="checkbox"/> English (or translated into English) <input type="checkbox"/> pagination <input type="checkbox"/> navigable hyperlinks (electronic submissions only)</p> <p>If no, explain:</p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<p>Controlled substance/Product with abuse potential:</p> <p>Abuse Liability Assessment, including a proposal for scheduling, submitted?</p> <p>Consult sent to the Controlled Substance Staff?</p> <p>Comments:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO
<p>BLAs/BLA efficacy supplements only:</p> <p>Companion application received if a shared or divided manufacturing arrangement?</p> <p>If yes, BLA #</p>	<input type="checkbox"/> YES <input type="checkbox"/> NO
Patent Information (NDAs/NDA efficacy supplements only)	
<p>Patent information submitted on form FDA 3542a?</p> <p>Comments:</p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
Debarment Certification	
<p>Correctly worded Debarment Certification with authorized signature?</p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO

<p><i>If foreign applicant, both the applicant and the U.S. Agent must sign the certification.</i></p> <p><i>Note: Debarment Certification should use wording in FD&C Act section 306(k)(1) i.e., "[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application." Applicant may not use wording such as, "To the best of my knowledge..."</i></p> <p>Comments:</p>	
Field Copy Certification (NDAs/NDA efficacy supplements only)	
<p>Field Copy Certification: that it is a true copy of the CMC technical section (<i>applies to paper submissions only</i>)</p> <p><i>If maroon field copy jackets from foreign applicants are received, return them to CDR for delivery to the appropriate field office.</i></p>	<p><input type="checkbox"/> Not Applicable (<i>electronic submission or no CMC technical section</i>)</p> <p><input checked="" type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>
Financial Disclosure	
<p>Financial Disclosure forms included with authorized signature?</p> <p><i>Forms 3454 and/or 3455 must be included and must be signed by the APPLICANT, not an Agent.</i></p> <p><i>Note: Financial disclosure is required for bioequivalence studies that are the basis for approval.</i></p> <p>Comments:</p>	<p><input checked="" type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>
Pediatrics	
PREA	
<p><i>Note: NDAs/BLAs/efficacy supplements for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration trigger PREA. All waiver & deferral requests, pediatric plans, and pediatric assessment studies must be reviewed by PeRC prior to approval of the application/supplement.</i></p>	
<p>Are the required pediatric assessment studies or a full waiver of pediatric studies included?</p>	<p><input type="checkbox"/> Not Applicable</p> <p><input type="checkbox"/> YES</p> <p><input checked="" type="checkbox"/> NO</p>
<p>If no, is a request for full waiver of pediatric studies OR a request for partial waiver/deferral and a pediatric plan included?</p> <ul style="list-style-type: none"> • <i>If no, request in 74-day letter.</i> • If yes, does the application contain the certification(s) required under 21 CFR 314.55(b)(1), (c)(2), (c)(3)/21 CFR 601.27(b)(1), (c)(2), (c)(3) 	<p><input checked="" type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p> <p><input checked="" type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>

Comments:	
BPCA (NDAs/NDA efficacy supplements only):	
Is this submission a complete response to a pediatric Written Request? <i>If yes, contact PMHS (pediatric exclusivity determination by the Pediatric Exclusivity Board is needed).</i>	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
Comments:	
Prescription Labeling	
Check all types of labeling submitted. Comments:	<input checked="" type="checkbox"/> Not applicable <input type="checkbox"/> Package Insert (PI) <input type="checkbox"/> Patient Package Insert (PPI) <input type="checkbox"/> Instructions for Use <input type="checkbox"/> MedGuide <input type="checkbox"/> Carton labels <input type="checkbox"/> Immediate container labels <input type="checkbox"/> Diluent <input type="checkbox"/> Other (specify)
Is electronic Content of Labeling submitted in SPL format? <i>If no, request in 74-day letter.</i>	<input type="checkbox"/> YES <input type="checkbox"/> NO
Comments:	
Package insert (PI) submitted in PLR format? If no, was a waiver or deferral requested before the application was received or in the submission? If before, what is the status of the request? <i>If no, request in 74-day letter.</i>	<input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO
Comments:	
All labeling (PI, PPI, MedGuide, carton and immediate container labels) consulted to DDMAC?	<input type="checkbox"/> YES <input type="checkbox"/> NO
Comments:	
MedGuide or PPI (plus PI) consulted to OSE/DRISK? (<i>send WORD version if available</i>)	<input type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
Comments:	
REMS consulted to OSE/DRISK?	<input type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
Comments:	
Carton and immediate container labels, PI, PPI, and proprietary name (if any) sent to OSE/DMEDP?	<input type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO

Comments:	
OTC Labeling	
Check all types of labeling submitted. Comments:	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> Outer carton label <input checked="" type="checkbox"/> Immediate container label <input type="checkbox"/> Blister card <input type="checkbox"/> Blister backing label <input checked="" type="checkbox"/> Consumer Information Leaflet (CIL) <input type="checkbox"/> Physician sample <input type="checkbox"/> Consumer sample <input type="checkbox"/> Other (specify)
Is electronic content of labeling submitted? <i>If no, request in 74-day letter.</i> Comments:	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
Are annotated specifications submitted for all stock keeping units (SKUs)? <i>If no, request in 74-day letter.</i> Comments:	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
If representative labeling is submitted, are all represented SKUs defined? <i>If no, request in 74-day letter.</i> Comments:	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
Proprietary name, all labeling/packaging, and current approved Rx PI (if switch) sent to OSE/DMEDP? Comments:	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
Meeting Minutes/SPA Agreements	
End-of Phase 2 meeting(s)? <i>If yes, distribute minutes before filing meeting.</i> Comments:	<input type="checkbox"/> YES Date(s): <input checked="" type="checkbox"/> NO
Pre-NDA/Pre-BLA/Pre-Supplement meeting(s)? <i>If yes, distribute minutes before filing meeting.</i> Comments:	<input type="checkbox"/> YES Date(s): <input checked="" type="checkbox"/> NO
Any Special Protocol Assessment (SPA) agreements? <i>If yes, distribute letter and/or relevant minutes before filing meeting.</i> Comments:	<input type="checkbox"/> YES Date(s): <input checked="" type="checkbox"/> NO

ATTACHMENT

MEMO OF FILING MEETING

DATE: March 20, 2009

NDA/BLA #: NDA 422-429

PROPRIETARY/ESTABLISHED NAMES: Cetirizine HCl, 5 mg and 10 mg, capsules.

APPLICANT: Banner Pharmacaps

BACKGROUND: Application is 505(b)(2) using NDA 19-835, Zyrtec® as the reference listed drug. The proposed drug product, cetirizine HCl, 5 mg and 10 mg, capsules differs from the reference listed drug in dosage form (capsule vs. tablet), and is otherwise similar with respect to route of administration, strength and indications.

REVIEW TEAM:

Discipline/Organization	Names		Present at filing meeting? (Y or N)
Regulatory Project Management	RPM:	Elaine Abraham	Y
	CPMS/TL:	Leah Christl	Y
Cross-Discipline Team Leader (CDTL)	N/A		
Clinical	Reviewer:	Lolita Lopez Anythony Dermowicz (DPAP)	Y Y
	TL:	Daiva Shetty	Y Y
Social Scientist Review (for OTC products)	Reviewer:	N/A	
	TL:	N/A	
Labeling Review (for OTC products)	Reviewer:	Ayana Rowley	Y
	TL:	Marina Chang	Y
OSE	Reviewer:	N/A	
	TL:	N/A	
Clinical Microbiology (for antimicrobial products)	Reviewer:	N/A	

Clinical Pharmacology	Reviewer:	Yun Xu	Y
	TL:	Wei Qiu	N
Biostatistics	Reviewer:	N/A	
	TL:	N/A	Y
Nonclinical (Pharmacology/Toxicology)	Reviewer:	Wafa Harrouk	Y
	TL:	N/A	
Statistics, carcinogenicity	Reviewer:	N/A	
	TL:		
Product Quality (CMC)	Reviewer:	Christopher Hough	Y
	TL:	Shulin Ding	Y
Facility (for BLAs/BLA supplements)	Reviewer:	N/A	
	TL:		
Microbiology, sterility (for NDAs/NDA efficacy supplements)	Reviewer:	N/A	
	TL:		
Bioresearch Monitoring (DSI)	Reviewer:	Hyojong Kwon	
	TL:	CT Viswanathan	
Other reviewers	N/A		

OTHER ATTENDEES: Andrea Leonard-Segal, Director, DNCE; Joel Schiffenbauer, Deputy Director, DNCE; Janice Adams-King, Regulatory Project Manager.

505(b)(2) filing issues?	<input type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
If yes, list issues:	
Per reviewers, are all parts in English or English translation?	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
If no, explain:	

<p>Electronic Submission comments</p> <p>List comments:</p>	<input type="checkbox"/> Not Applicable
<p>CLINICAL</p> <p>Comments: Application did not contain integrated safety assessment.</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input checked="" type="checkbox"/> Review issues for 74-day letter
<ul style="list-style-type: none"> Clinical study site(s) inspections(s) needed? <p>If no, explain: No clinical studies for this NDA</p>	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
<ul style="list-style-type: none"> Advisory Committee Meeting needed? <p>Comments:</p> <p><i>If no, for an original NME or BLA application, include the reason. For example:</i></p> <ul style="list-style-type: none"> <i>this drug/biologic is not the first in its class</i> <i>the clinical study design was acceptable</i> <i>the application did not raise significant safety or efficacy issues</i> <i>the application did not raise significant public health questions on the role of the drug/biologic in the diagnosis, cure, mitigation, treatment or prevention of a disease</i> 	<input type="checkbox"/> YES Date if known: <input checked="" type="checkbox"/> NO <input type="checkbox"/> To be determined Reason:
<ul style="list-style-type: none"> If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance? <p>Comments:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
<p>CLINICAL MICROBIOLOGY</p> <p>Comments:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<p>CLINICAL PHARMACOLOGY</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE

Comments:	<input type="checkbox"/> Review issues for 74-day letter
<ul style="list-style-type: none"> Clinical pharmacology study site(s) inspections(s) needed? 	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
BIOSTATISTICS	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
Comments:	
NONCLINICAL (PHARMACOLOGY/TOXICOLOGY)	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
Comments:	
PRODUCT QUALITY (CMC)	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input checked="" type="checkbox"/> Review issues for 74-day letter
Comments: The application did not contain comparative in-vitro dissolution data to support biowaiver; and the application did not contain a letter of authorization for DMF	
<ul style="list-style-type: none"> Categorical exclusion for environmental assessment (EA) requested? <p>If no, was a complete EA submitted?</p> <p>If EA submitted, consulted to EA officer (OPS)?</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO
Comments:	
<ul style="list-style-type: none"> Establishment(s) ready for inspection? 	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> Establishment Evaluation Request (EER/TBP-EER) submitted to DMPQ? 	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
Comments:	

b(4)

<ul style="list-style-type: none"> • Sterile product? 	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
<p>If yes, was Microbiology Team consulted for validation of sterilization? (NDAs/NDA supplements only)</p>	<input type="checkbox"/> YES <input type="checkbox"/> NO
<p>FACILITY (BLAs only)</p>	<input type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE
<p>Comments:</p>	<input type="checkbox"/> Review issues for 74-day letter
REGULATORY PROJECT MANAGEMENT	
<p>Signatory Authority: Director, DNCE</p>	
<p>GRMP Timeline Milestones: Filing Date: 10-14-08; Day 74: 10-14-08; Review Completion Goal Date: 04-10-08; PDUFA Goal Date: 06-01-09</p>	
<p>Comments:</p>	
REGULATORY CONCLUSIONS/DEFICIENCIES	
<input type="checkbox"/>	<p>The application is unsuitable for filing. Explain why:</p>
<input checked="" type="checkbox"/>	<p>The application, on its face, appears to be suitable for filing.</p> <p><input type="checkbox"/> No review issues have been identified for the 74-day letter.</p> <p><input checked="" type="checkbox"/> Review issues have been identified for the 74-day letter. List (optional):</p> <p><input checked="" type="checkbox"/> Standard Review</p> <p><input type="checkbox"/> Priority Review</p>
ACTIONS ITEMS	
<input type="checkbox"/>	<p>Ensure that the review and chemical classification codes, as well as any other pertinent classification codes (e.g., orphan, OTC) are correctly entered into tracking system.</p>
<input type="checkbox"/>	<p>If RTF action, notify everybody who already received a consult request, OSE PM., and Product Quality PM. Cancel EER/TBP-EER.</p>
<input type="checkbox"/>	<p>If filed and the application is under AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.</p>
<input type="checkbox"/>	<p>If BLA or priority review NDA, send 60-day letter.</p>
<input checked="" type="checkbox"/>	<p>Send review issues/no review issues by day 74</p>

<input type="checkbox"/>	Other

Appendix A (NDA and NDA Supplements only)

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

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

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

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

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

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

- (1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies),
- (2) No additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application, and.
- (3) All other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely

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

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

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2),
- (2) The applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement, or
- (3) The applicant is relying upon any data they do not own or to which they do not have right of reference.

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

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

/s/

Janice Adams-King
3/27/2009 10:27:20 AM
CSO



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-429

INFORMATION REQUEST LETTER

Banner Pharmacaps Inc.
Attention: Dana Toops, Executive Director
US Research and Development
4125 Premier Drive
High Point, NC 27265

Dear Ms. Toops:

Please refer to your July 31, 2008 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cetirizine HCl Capsules, 10 mg & 5 mg.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following comments and information requests. Your response is requested within 5-7 business days of receipt of this letter:

1. Regarding the drug substance: the residual solvent specification of the drug substance is unacceptable. The specification should include _____
The proposed limits for _____ should comply with ICH Q3C guidelines. **b(4)**
2. Regarding the drug product: your proposed expiration dating period is unacceptable. Based on the stability data presented in the application, the Agency will set _____ as the expiration dating period. **b(4)**

To facilitate prompt review of your response, a courtesy copy (electronic or fax) of your official submission would be kindly appreciated. Please send this to Jeannie David, Regulatory Project Manager in the Office of New Drug Quality Assessment (jeannie.david@fda.hhs.gov; fax 301-796-9877), and Janice Adams-King, Regulatory Project Manager the Office of New Drugs (janice.adams-king@fda.hhs.gov; fax 301-796-9899).

If you have any questions, call Jeannie David, Regulatory Project Manager, at 301-796-4247.

Sincerely,

{See appended electronic signature page}

Moo-Jhong Rhee, Ph.D.
Chief, Branch III
Division Pre-Marketing Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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this page is the manifestation of the electronic signature.**

/s/

Moo-Jhong Rhee
2/9/2009 11:58:53 AM
Chief, Branch III

Abraham, Elaine G

From: MUOparaugo@banpharm.com
Sent: Thursday, August 28, 2008 5:21 PM
To: Abraham, Elaine G
Cc: DSToops@banpharm.com
Subject: Cetirizine NDA 22-429
Attachments: Cetirizine Cover Letter.pdf

Good Afternoon Elaine,

Per your telephone conversation with Dana: This email is to confirm the shipment of the following to you:

1. (2) additional desk copies of our 505 (b)(2) New Drug Application for Cetirizine HCl Capsules, 10 mg & 5 mg.
2. (4) additional desk copies of Volume 1: Module 1 & 2

Provided below is a response to the pending requested information:

- Application missing (SKU) labeling information: **BPI's Response:** Refer to module 1 section: 1.14.1 for the draft labeling text of BPI's proposed carton/container labeling.

-(a) Narrative Description and analysis of adverse events from your PK studies:

BPI's Response: Please refer to the following sections for all AE related information in the study reports

Study 20-219-SA:

Refer to page 22 of 1545 for a narrative description of AEs for this study
Refer to page 23 of 1545 for a summary analysis of AEs for this study
Refer to page 26-35 of 1545 for the clinical listings of AEs for this study

Study 20-220-SA:

Refer to page 21 of 1590 for a narrative description of AEs for this study
Refer to page 23 of 1590 for a summary analysis of AEs for this study
Refer to page 25-34 of 1590 for the clinical listings of AEs for this study

(b) Postmarketing safety surveillance information for the OTC marketing of Cetirizine from the following

- databases:
- Adverse Event Reporting System (AERS)
 - World Health Organization (WHO) International Drug Monitoring Program
 - Toxic Exposure Surveillance System (TESS) database maintained by the American Association of Poison Control Centers (AAPCC)
 - Drug Abuse Warning Network (DAWN) database
 - Medical literature

(c) integrated summary of safety (ISS).

BPI's Response for (b) and (c): Reference is made to 21 CFR 314.54(a)(3) the safety assessment of

11/14/2008

