

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22279Orig1s000

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

EXCLUSIVITY SUMMARY

NDA # 22279

SUPPL #

HFD #

Trade Name: Hycufenix

Generic Name: Hydrocodone/Guaifenesin/Pseudoephedrine

Applicant Name: Mikart, Inc.

Approval Date, If Known May 14, 2015

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.

Mikart has submitted this application through 505(b) (2) pathway and is relying on FDA's safety and efficacy findings from Over-The-Counter (OTC) monographs 21 CFR 341.18 (guaifenesin) and 21CFR 341.20 (pseudoephedrine)and NDA 5-213 Hycodan (hydrocodone).

The clinical development program in this application comprised of two pilot and two pivotal relative bioavailability/bioequivalence (BA/BE) studies.

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#05213 NDA#19111 NDA#21282

NDA#22442 NNDA#205474 NDA#21585

NDA#22439 NDA 204307 NDA#21620

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:

Name of person completing form: Laura Musse
Title: Regulatory Health Project Manager
Date: May XX, 2015

OND/DPARP Deputy Director signing form: Lydia Gilbert-McClain, M.D.
Title: Deputy Director

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05; removed hidden data 8/22/12;

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

/s/

LAURA MUSSE
05/14/2015

LYDIA I GILBERT MCCLAIN
05/14/2015

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 22279 BLA #	NDA Supplement # BLA Supplement #	If NDA, Efficacy Supplement Type: <i>(an action package is not required for SE8 or SE9 supplements)</i>
Proprietary Name: Hycofenix Established/Proper Name: Hydrocodone/Guaifenesin/Pseudoephedrine Dosage Form: Oral Solution		Applicant: Mikart, Inc. Agent for Applicant (if applicable):
RPM: Laura Musse		Division: DPARP
NDA Application Type: <input type="checkbox"/> 505(b)(1) <input checked="" type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) BLA Application Type: <input type="checkbox"/> 351(k) <input type="checkbox"/> 351(a) Efficacy Supplement: <input type="checkbox"/> 351(k) <input type="checkbox"/> 351(a)		<p><u>For ALL 505(b)(2) applications, two months prior to EVERY action:</u></p> <ul style="list-style-type: none"> Review the information in the 505(b)(2) Assessment and submit the draft² to CDER OND IO for clearance. Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity) <p><input checked="" type="checkbox"/> No changes <input type="checkbox"/> New patent/exclusivity <i>(notify CDER OND IO)</i> Date of check:</p> <p><i>Note: If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</i></p>
❖ Actions		
<ul style="list-style-type: none"> Proposed action User Fee Goal Date is 		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR
<ul style="list-style-type: none"> Previous actions <i>(specify type and date for each action taken)</i> 		<input checked="" type="checkbox"/> Approved May 14, 2015 CR- January 11, 2012 CR-January 25, 2011 CR-June 22, 2009
❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____		<input type="checkbox"/> Received
❖ Application Characteristics ³		

¹ The **Application Information** Section is (only) a checklist. The **Contents of Action Package** Section (beginning on page 2) lists the documents to be included in the Action Package.

² For resubmissions, 505(b)(2) applications must be cleared before the action, but it is not necessary to resubmit the draft 505(b)(2) Assessment to CDER OND IO unless the Assessment has been substantively revised (e.g., new listed drug, patent certification revised).

³ Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

Review priority: Standard Priority
 Chemical classification (new NDAs only):
(confirm chemical classification at time of approval)

- | | |
|---|---|
| <input type="checkbox"/> Fast Track | <input type="checkbox"/> Rx-to-OTC full switch |
| <input type="checkbox"/> Rolling Review | <input type="checkbox"/> Rx-to-OTC partial switch |
| <input type="checkbox"/> Orphan drug designation | <input type="checkbox"/> Direct-to-OTC |
| <input type="checkbox"/> Breakthrough Therapy designation | |

NDAs: Subpart H

- Accelerated approval (21 CFR 314.510)
- Restricted distribution (21 CFR 314.520)

Subpart I

- Approval based on animal studies

- Submitted in response to a PMR
- Submitted in response to a PMC
- Submitted in response to a Pediatric Written Request

BLAs: Subpart E

- Accelerated approval (21 CFR 601.41)
- Restricted distribution (21 CFR 601.42)

Subpart H

- Approval based on animal studies

- REMS: MedGuide
 Communication Plan
 ETASU
 MedGuide w/o REMS
 REMS not required

Comments:

❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 <i>(approvals only)</i>	<input type="checkbox"/> Yes <input type="checkbox"/> No
❖ Public communications <i>(approvals only)</i>	
<ul style="list-style-type: none"> • Office of Executive Programs (OEP) liaison has been notified of action 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> • Indicate what types (if any) of information were issued 	<input checked="" type="checkbox"/> None <input type="checkbox"/> FDA Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other
❖ Exclusivity	
<ul style="list-style-type: none"> • Is approval of this application blocked by any type of exclusivity (orphan, 5-year NCE, 3-year, pediatric exclusivity)? • If so, specify the type 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
❖ Patent Information (NDAs only)	
<ul style="list-style-type: none"> • Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. 	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
CONTENTS OF ACTION PACKAGE	
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list <i>(approvals only)</i>	<input checked="" type="checkbox"/> Included
Documentation of consent/non-consent by officers/employees	<input checked="" type="checkbox"/> Included

Action Letters	
❖ Copies of all action letters (<i>including approval letter with final labeling</i>)	Action(s) and date(s) Approval May 14, 2015, CR-January,11, 2012, CR-January, 25, 2011, CR- June 22, 2009
Labeling	
❖ Package Insert (<i>write submission/communication date at upper right of first page of PI</i>)	
• Most recent draft labeling (<i>if it is division-proposed labeling, it should be in track-changes format</i>)	<input checked="" type="checkbox"/> Included
• Original applicant-proposed labeling	<input checked="" type="checkbox"/> Included
❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling (<i>write submission/communication date at upper right of first page of each piece</i>)	<input type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input checked="" type="checkbox"/> None
• Most-recent draft labeling (<i>if it is division-proposed labeling, it should be in track-changes format</i>)	<input checked="" type="checkbox"/> Included
• Original applicant-proposed labeling	<input checked="" type="checkbox"/> Included
❖ Labels (full color carton and immediate-container labels) (<i>write submission/communication date on upper right of first page of each submission</i>)	
• Most-recent draft labeling	<input checked="" type="checkbox"/> Included
❖ Proprietary Name	Granted Letter-March 2, 2015 Granted-Review- February 27, 2015, Denied Letter-January 4, 2011, and September 7, 2010 Review December 30, 2010, and August 26, 2010 Withdrawal-March 21, 2011, December 18, 2009
• Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>)	
• Review(s) (<i>indicate date(s)</i>)	
❖ Labeling reviews (<i>indicate dates of reviews</i>)	RPM: <input checked="" type="checkbox"/> July 23, 2009 DMEPA: <input checked="" type="checkbox"/> May 4, and March 16, 2015 DMPP/PLT (DRISK): <input checked="" type="checkbox"/> None OPDP: <input checked="" type="checkbox"/> April 28, 2015 SEALD: <input checked="" type="checkbox"/> None CSS: <input checked="" type="checkbox"/> August 26, 2009 Other: <input checked="" type="checkbox"/> None
Administrative / Regulatory Documents	
❖ RPM Filing Review ⁴ /Memo of Filing Meeting (<i>indicate date of each review</i>)	<input type="checkbox"/>
❖ All NDA 505(b)(2) Actions: Date each action cleared by 505(b)(2) Clearance Committee	<input checked="" type="checkbox"/> March 31, 2015
❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>)	<input checked="" type="checkbox"/> Included
❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	

⁴ Filing reviews for scientific disciplines are NOT required to be included in the action package.

<ul style="list-style-type: none"> Applicant is on the AIP 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> This application is on the AIP <ul style="list-style-type: none"> If yes, Center Director's Exception for Review memo (<i>indicate date</i>) If yes, OC clearance for approval (<i>indicate date of clearance communication</i>) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Not an AP action
<ul style="list-style-type: none"> ❖ Pediatrics (<i>approvals only</i>) <ul style="list-style-type: none"> Date reviewed by PeRC April 29, 2015 If PeRC review not necessary, explain: _____ 	
<ul style="list-style-type: none"> ❖ Outgoing communications: letters, emails, and faxes considered important to include in the action package by the reviewing office/division (e.g., clinical SPA letters, RTF letter, etc.) (<i>do not include previous action letters, as these are located elsewhere in package</i>) 	May 15, 13 6, April 21, March 16, February 5, January 7, 2015, September 29 and 13, and August 4, 2011, September 16, 14, and August 27, January 26, 2010, June 16, April 3, March 19, 2009, December 12, November 3, October 28 and 9, 2008
<ul style="list-style-type: none"> ❖ Internal documents: memoranda, telecons, emails, and other documents considered important to include in the action package by the reviewing office/division (e.g., Regulatory Briefing minutes, Medical Policy Council meeting minutes) 	May 10, 2012, March 21, and January 5, 2011, October 6 and 24, 2008
<ul style="list-style-type: none"> ❖ Minutes of Meetings <ul style="list-style-type: none"> If not the first review cycle, any end-of-review meeting (<i>indicate date of mtg</i>) Pre-NDA/BLA meeting (<i>indicate date of mtg</i>) EOP2 meeting (<i>indicate date of mtg</i>) Mid-cycle Communication (<i>indicate date of mtg</i>) Late-cycle Meeting (<i>indicate date of mtg</i>) Other milestone meetings (e.g., EOP2a, CMC pilots) (<i>indicate dates of mtgs</i>) 	<input checked="" type="checkbox"/> N/A or no mtg <input checked="" type="checkbox"/> No mtg <input checked="" type="checkbox"/> No mtg <input checked="" type="checkbox"/> N/A <input checked="" type="checkbox"/> N/A
<ul style="list-style-type: none"> ❖ Advisory Committee Meeting(s) <ul style="list-style-type: none"> Date(s) of Meeting(s) 	<input checked="" type="checkbox"/> No AC meeting
Decisional and Summary Memos	
<ul style="list-style-type: none"> ❖ Office Director Decisional Memo (<i>indicate date for each review</i>) 	<input checked="" type="checkbox"/> None
Division Director Summary Review (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> May 14, 2015 <input checked="" type="checkbox"/> November 11, 2012 <input checked="" type="checkbox"/> January 25, 2011 <input checked="" type="checkbox"/> June 22, 2009
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> December 20, 2011
PMR/PMC Development Templates (<i>indicate total number</i>) 2	<input checked="" type="checkbox"/> May 11, 2015
Clinical	
<ul style="list-style-type: none"> ❖ Clinical Reviews <ul style="list-style-type: none"> Clinical Team Leader Review(s) (<i>indicate date for each review</i>) Clinical review(s) (<i>indicate date for each review</i>) Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>) 	<input checked="" type="checkbox"/> May 13, 2015 April 29, 2015, November 2, January 6, 2011, April 23, 2009, and October 6, 2008 <input checked="" type="checkbox"/> None

❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here <input type="checkbox"/> and include a review/memo explaining why not (<i>indicate date of review/memo</i>)	January 28, 2015
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> May 22, 2009
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> March 27, 2009
❖ Risk Management <ul style="list-style-type: none"> REMS Documents and REMS Supporting Document (<i>indicate date(s) of submission(s)</i>) REMS Memo(s) and letter(s) (<i>indicate date(s)</i>) Risk management review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>) 	<input checked="" type="checkbox"/> None
❖ OSI Clinical Inspection Review Summary(ies) (<i>include copies of OSI letters to investigators</i>)	<input checked="" type="checkbox"/> December 20, 2, October 18, September 30, August 30, 26, 2, and July 26, 2011
Clinical Microbiology <input checked="" type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No separate review
Clinical Microbiology Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Biostatistics <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No separate review
Statistical Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No separate review
Statistical Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> October 14, 2011 and October 26, 2010
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No separate review
Clinical Pharmacology Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No separate review
Clinical Pharmacology review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> April 24, and February 4, 2015 October 3, and January 21 2011, September 9, and December 28, 2010, May 13, 2009, October 30, 2008
❖ OSI Clinical Pharmacology Inspection Review Summary (<i>include copies of OSI letters</i>)	<input checked="" type="checkbox"/> January 21, 2011

Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No separate review
• Supervisory Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> May 1, 2015, December 20, 2011 and April 30, 2009
• Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> April 23, 2015, November 1, 2011, April, 24, 2009, and October 7, 2008
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input checked="" type="checkbox"/> None
❖ OSI Nonclinical Inspection Review Summary (<i>include copies of OSI letters</i>)	<input checked="" type="checkbox"/> None requested
Product Quality <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No separate review
• Branch Chief/Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> January 7, 2011 (2)
• Product quality review(s) including ONDQA biopharmaceutics reviews (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> May 5, 2015, November 4, January 3, and 31, 2011, December 27, 2010, June 16, April 30, 2009, and October 7, 2008
❖ Microbiology Reviews	<input checked="" type="checkbox"/> February 4, January 16, 2015 January 5, 2012
<input checked="" type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) (<i>indicate date of each review</i>) <input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (OMPQ/MAPCB/BMT) (<i>indicate date of each review</i>)	
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> June 17, 2009
❖ Environmental Assessment (check one) (original and supplemental applications)	
<input checked="" type="checkbox"/> Categorical Exclusion (<i>indicate review date</i>)(<i>all original applications and all efficacy supplements that could increase the patient population</i>)	Page 7, April 30, 2009
<input type="checkbox"/> Review & FONSI (<i>indicate date of review</i>)	
<input type="checkbox"/> Review & Environmental Impact Statement (<i>indicate date of each review</i>)	

❖ Facilities Review/Inspection	
<input type="checkbox"/> NDAs: Facilities inspections (include EER printout or EER Summary Report only; do NOT include EER Detailed Report; date completed must be within 2 years of action date) (<i>only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites⁵</i>)	<input checked="" type="checkbox"/> Acceptable-April 23, 2015 July 22, and January 3, 2011 <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable
<input type="checkbox"/> BLAs: TB-EER (date of most recent TB-EER must be within 30 days of action date) (<i>original and supplemental BLAs</i>)	Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
❖ NDAs: Methods Validation (<i>check box only, do not include documents</i>)	<input checked="" type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input type="checkbox"/> Not needed (per review)

⁵ i.e., a new facility or a change in the facility, or a change in the manufacturing process in a way that impacts the Quality Management Systems of the facility.

Day of Approval Activities	
❖ For all 505(b)(2) applications: <ul style="list-style-type: none"> • Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity) 	<input checked="" type="checkbox"/> No changes <input type="checkbox"/> New patent/exclusivity (<i>Notify CDER OND IO</i>)
<ul style="list-style-type: none"> • Finalize 505(b)(2) assessment 	<input checked="" type="checkbox"/> Done
❖ For Breakthrough Therapy(BT) Designated drugs: <ul style="list-style-type: none"> • Notify the CDER BT Program Manager 	<input type="checkbox"/> Done (<i>Send email to CDER OND IO</i>)
❖ Send a courtesy copy of approval letter and all attachments to applicant by fax or secure email	<input checked="" type="checkbox"/> Done
❖ If an FDA communication will issue, notify Press Office of approval action after confirming that applicant received courtesy copy of approval letter	<input type="checkbox"/> Done
❖ Ensure that proprietary name, if any, and established name are listed in the <i>Application Product Names</i> section of DARRTS, and that the proprietary name is identified as the “preferred” name	<input checked="" type="checkbox"/> Done
❖ Ensure Pediatric Record is accurate	<input checked="" type="checkbox"/> Done
❖ Send approval email within one business day to CDER-APPROVALS	<input checked="" type="checkbox"/> Done

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

/s/

LAURA MUSSE
05/14/2015

PeRC Meeting Minutes
April 29, 2015

PeRC Members Attending:

Lynne Yao (Chair for all products (Non Responsive)
Robert "Skip" Nelson
Wiley Chambers
Rosemary Addy
George Greeley
Frede Crooner
Tom Smith
Karen Davis-Bruno
Daiva Shetty
Andrew Mulberg (Non Responsive
Greg Reaman (Did not review (Non Responsive
Barbara Buch
Adrienne Hornatko-Munoz
Barbara Buch
Andrew Mosholder (Non Responsive
Hari Cheryl Sachs
Julia Pinto
Lily Mulugeta
Olivia Ziolkowski
Kevin Krudys
Rachel Witten
Dianne Murphy
Maura O'Leary
Kristiana Brugger (Did not review (Non Responsive)

Agenda

9:00	NDA	Non Responsive		
9:40	NDA			
9:50	IND			
10:10	IND			
10:30	IND			
10:50	NDA			
11:00	NDA			
11:10	BLA			
11:20	NDA			
11:30	NDA			22279 & 22424
11:40	BLA	Non Responsive		
11:50	IND			
	<i>IND</i>			

4 Page(s) has been Withheld in Full as Non Responsive

Non Responsive

Hycofesin & Hydrocodone and Guifenesin (Partial Waiver/Assessment)

- Proposed Indication: (b) (4)

- The Division is requesting a partial waiver of studies for both products in children less than 6 year of age due to safety since hydrocodone is contraindicated in this age group due to the increased risk for fatal respiratory depression. The Division is requesting a deferral of studies in children 6 years and older because adult studies are complete and ready for approval. The plan for pediatric studies includes an evaluation of PK and safety.
- PeRC Recommendations:
 - The PeRC agreed with the plan for a partial waiver (based on safety) and deferral of pediatric studies.
 - The PeRC also recommends that the sponsor advance the timeline for completion of pediatric studies.

Non Responsive

2 Page(s) has been Withheld in Full as Non Responsive

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

/s/

GEORGE E GREELEY
05/14/2015



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

FACSIMILE TRANSMITTAL SHEET

DATE: May13, 2015

To: Jason Waldroup Director, Regulatory Affairs	From: Laura Musse, RN, MS, CRNP Regulatory Health Project Manager
Company: Mikart Inc.	Division of Pulmonary, Allergy, and Rheumatology Products
Fax number: (404) 352-0351	Fax number: (301) 796-9728
Phone number: (404) 351-4510	Phone number: (240) 402-3720
Subject: NDA 22424- Flowtuss, (hydrocodone and guaifenesin)-and NDA 22279-Hycofenix (hydrocodone/guaifenesin/pseudoephedrine -Label information request.	

Total no. of pages including cover: 22

Comments:

Document to be mailed: YES X- 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.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at 240-402-3720. Thank you.

9 Page(s) has been Withheld in Full as b4 (CCI/TS) immediately following this page

NDA 22424
NDA 22279

Your NDA submissions dated, November 18, 2014 to NDA 22424 and December 4, 2014 to NDA 22279 are currently under review. The Division's proposed insertions are underlined; deletions are in strike-outs. These comments are not all-inclusive and we may have additional comments as we continue our review. We have the following comments and requests for information:

1. Review and accept the required changes to the Highlight section for both the Flowtuss and Hycofenix labels and the corrections and edits to section 12.3 which are in Tracked
2. Change format in the Label attachments. The following are your questions from your e-mail correspondence dated May 11, 2015 and our responses:

For item #2, we have several comments/questions:

Mikart intends to use lower case lettering for the established name in accordance with current Agency guidance.

- *Should a similar change be made for the 22-279 product (e.g., Hycofenix (hydrocodone bitartrate, pseudoephedrine hydrochloride and guaifenesin) Oral Solution?*
- *This comment indicates the change is to be made on the package insert, however earlier Agency comment requested deletion of "Oral Solution" from all instances of Flowtuss, except in sections 11 and 16. Is it in these two sections that the Agency is requesting that the established name be added?*

FDA Response:

- Use of lower case is acceptable. This should also be reflected in the Hycofenix label.
- With regard to the inclusion of "oral solution", the IR may have been confusing or incorrect. For the package insert "oral solution" should be included in the Highlight section (see tracked changes), and in the first sentences of sections 11 and 16 only (where they are already correctly placed).

(b) (4)

Respond to these Information Requests by email (Laura.Musse@fda.hhs.gov) or facsimile (301-796-9728), by Thursday, May 14, 2015. Your response must also be submitted formally to the NDA shortly thereafter. If you have any questions, please contact Laura Musse, Regulatory Health Project Manager, at 240-402-3720.

10 Page(s) has been Withheld in Full as b4 (CCI/TS) immediately following this page

Review/History Clearance From

Initiated by:	A Durmowicz	Date:	5/13/15
Drafted by:	LMusse	Date:	5/13/15
Clearance:	SBarnes	Date:	5/13/15
Finalized:	LMusse	Date:	5/13/15
File Name:	Labeling IR Round 4	Date:	5/13/15

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

/s/

LAURA MUSSE
05/13/2015



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

FACSIMILE TRANSMITTAL SHEET

DATE: May 6, 2015

To: Jason Waldroup Director, Regulatory Affairs	From: Laura Musse, RN, MS, CRNP Regulatory Health Project Manager
Company: Mikart Inc.	Division of Pulmonary, Allergy, and Rheumatology Products
Fax number: (404) 352-0351	Fax number: (301) 796-9728
Phone number: (404) 351-4510	Phone number: (240) 402-3720
Subject: NDA 22279-Hycufenix (hydrocodone/guaifenesin/pseudoephedrine) Labeling information request 2.	

Total no. of pages including cover: 12

Comments:

Document to be mailed: YES X- 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.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at 240-402-3720. Thank you.

NDA 22279

Your NDA submission dated, December 4, 2014, to NDA 22279 is currently under review. The enclosed label contains the Division's edits to your draft package insert (PI) and carton and container submitted on April 27, 2015. The Division's proposed insertions are underlined; deletions are in strike-outs. These comments are not all-inclusive and we may have additional comments as we continue our review. We also have the following comments and request for information:

Recently, FDA has begun a formal review of label formatting in an attempt to comply with official labeling format and foster consistency in labeling. As a result, you will note that there are several format and naming alterations that are different from those found in similar products already on the market. These labels will undergo a similar label format review when new label supplements are received.

1. Package Insert

In addition to the edits shown in the attach package insert, to comply with up to date labeling format (see above), incorporate all formatting changes conveyed to you in the information request to NDA 22424 dated May 1, 2015.

2. Carton and Container

- a. The established names should be presented in a manner consistent with 21 CFR 201.10(g)(2) which requires that the established name be at least half the size of the letters comprising the proprietary name and have a prominence consistent with the proprietary name in terms of type, size, color, and font.

(b) (4)

Respond to these Information Requests by email (Laura.Musse@fda.hhs.gov) or facsimile (301-796-9728), by Friday, May 8, 2015. Your response must also be submitted formally to the NDA shortly thereafter. If you have any questions, please contact Laura Musse, Regulatory Health Project Manager, at 240-402-3720.

Review/History Clearance From

(To be used/added as a third page to faxed, electronic, or other correspondence, where applicable)

Initiated by:	ADurmowicz YRen/AShaw	Date: 5/6/15
Drafted by:	LMusse	Date: 5/6/15
Clearance:	SBarnes	Date: 5/6/15
Finalized:	LMusse	Date: 5/6/15
File Name:	Labeling IR Round 2	Date: 5/6/15

11 Page(s) has been Withheld in Full as b4 (CCI/TS) immediately following this page

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

/s/

LAURA MUSSE
05/06/2015



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

FACSIMILE TRANSMITTAL SHEET

DATE: April 21, 2015

To: Jason Waldroup Director, Regulatory Affairs	From: Laura Musse, RN, MS, CRNP Regulatory Health Project Manager
Company: Mikart Inc.	Division of Pulmonary, Allergy, and Rheumatology Products
Fax number: (404) 352-0351	Fax number: (301) 796-9728
Phone number: (404) 351-4510	Phone number: (240) 402-3720
Subject: NDA 22279-Hycufenix (hydrocodone/guaifenesin/pseudoephedrine) Labeling information request.	

Total no. of pages including cover: 15

Comments:

Document to be mailed: YES X- 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.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at 240-402-3720. Thank you.

NDA 22279

Your NDA submission dated December 4, 2014, to NDA 22279, is currently under review. The enclosed labels contain the Division's edits to your propose package insert (PI) and the carton and container. The Division's proposed insertions are underlined; deletions are in strike-outs. These comments are not all-inclusive and we may have additional comments as we continue our review. We also have the following comments:

1. In your drug label, section 12.3 Pharmacokinetics; (b) (4)
[REDACTED]
Please update those values with those obtained from your own studies (i.e., study 110028 and study 11467601).
2. Revise the presentation of the proprietary name from all caps (i.e. HYCOFENIX) to title case (i.e. Hycofenix) to improve readability of the name.
3. (b) (4)
[REDACTED]
Consider revising the container labels to adequately differentiate the products to eliminate selection error as they may have the potential to be near each other on a shelf in a pharmacy.

Respond to these Information Requests by email (Laura.Musse@fda.hhs.gov) or facsimile (301-796-9728), by Friday, April 24, 2015. Your response must also be submitted formally to the NDA shortly thereafter. If you have any questions, please contact Laura Musse, Regulatory Health Project Manager, at 240-402-3720.

Review/History Clearance From

Drafted by:	LMusse	Date: 4/17/15
Clearance:	SBarnes	Date: 4/17/15
	XWang	Date: 4/17/15
	ADurmowicz	Date: 4/17/15
	YRen	Date: 4/17/15
	SDoddapaneni	Date: 4/20/15
Finalized:	LMusse	Date: 4/21/15
File Name:	Labeling IR	Date: 4/21/15

12 Page(s) has been Withheld in Full as b4 (CCI/TS) immediately following this page

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

/s/

LAURA MUSSE
04/21/2015



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

FACSIMILE TRANSMITTAL SHEET

DATE: March 16, 2015

To: Jason Waldroup Director, Regulatory Affairs	From: Laura Musse, RN, MS, CRNP Regulatory Health Project Manager
Company: Mikart Inc.	Division of Pulmonary, Allergy, and Rheumatology Products
Fax number: (404) 352-0351	Fax number: (301) 796-9728
Phone number: (404) 351-4510	Phone number: (240) 402-3720
Subject: NDA 22279-(Hydrocodone/Guaifenesin/Pseudoephedrine) and NDA 22424- (Hydrocodone and Guaifenesin)-Post Marketing Requirements information request.	

Total no. of pages including cover: 3

Comments:

Document to be mailed: **YES** **X- 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.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at 240-402-3720. Thank you.

Your resubmissions dated December 4, 2014, to NDA 22279, and November 18, 2014, to NDA 22424 are currently under review. We have the following comments and requests for information:

Attached are our current general requirements for the pediatric post marketing requirements (PMR) studies for the opioid-containing combination cough and cold products.

We note you have submitted a request for a waiver for patients less than 6 years of age. We request your agreement to conduct the following studies and completion of milestone timelines.

PREA Post Marketing Requirement (PMR)

1. A single-dose pharmacokinetic study whose primary objective is to identify the dose(s) of INSERT PRODUCT that result in exposures of INSERT DRUG COMPONENTS in children (aged 6 to 11) and adolescents (aged 12 to 17 years) that are similar to the exposures seen in adults at the recommended dose. The population eligible for enrollment should be otherwise healthy children and adolescents with cough/cold symptoms for whom a combination product that includes an opioid antitussive would be an appropriate symptomatic treatment.

PMR Scheduled Milestones:

Final Protocol Submission:

Trial Completion:

Final Report Submission:

2. An open-label multi-dose safety and tolerability study at the dose(s) that result in drug exposures in children (aged 6 to 11) and adolescents (aged 12 to 17 years) that are similar to the exposures seen in adults at the recommended dose. The population eligible for the study would be children and adolescents with cough/cold symptoms for whom a combination product that includes an opioid antitussive would be an appropriate symptomatic treatment. The study will enroll a total of approximately 400 children aged 6 to 17 inclusive in two cohorts (6-11 years, 12 to 17 years).

PMR Scheduled Milestones:

Final Protocol Submission:

Trial Completion:

Final Report Submission:

Respond to these Information Requests by email (Laura.Musse@fda.hhs.gov) or facsimile (301-796-9728), by Friday, March 20, 2015. Your response must also be submitted formally to the NDA shortly thereafter. If you have any questions, please contact Laura Musse, Regulatory Health Project Manager, at 240-402-3720.

Attachment

General Cough and Cold Combination Product PREA Requirements

Below are our current general requirements for pediatric PMR studies for opioid-containing combination cough and cold products. The requirements could change in the future based on changes in regulatory policy.

Waivers and Deferrals

- a. Waiver for pediatric patients less than 6 years of age based on evidence the product would be unsafe or ineffective
- b. Deferral for pediatric patients 6-17 years of age until drug product is approved for the adult population.

Pediatric Studies

- A single-dose pharmacokinetic study whose primary objective is to identify the dose(s) of INSERT PRODUCT that result in exposures of INSERT DRUG COMPONENTS in children (aged 6 to 11) and adolescents (aged 12 to 17 years) that are similar to the exposures seen in adults at the recommended dose. The population eligible for enrollment should be otherwise healthy children and adolescents with cough/cold symptoms for whom a combination product that includes an opioid antitussive would be an appropriate symptomatic treatment.
- An open-label multi-dose safety and tolerability study at the dose(s) that result in drug exposures in children (aged 6 to 11) and adolescents (aged 12 to 17 years) that are similar to the exposures seen in adults at the recommended dose. The population eligible for the study would be children and adolescents with cough/cold symptoms for whom a combination product that includes an opioid antitussive would be an appropriate symptomatic treatment. The study will enroll a total of approximately 400 children aged 6 to 17 inclusive in two cohorts (6-11 years, 12 to 17 years).

Timelines

In general, the submission of the single-dose PK study report should take no longer than 2-3 years from the start. The submission of the safety study report should take no longer than about 3-4 years from the start.

Review/History Clearance From

Initiated by:	ADurmowicz	Date: 3/12/15
Drafted by:	LMusse	Date: 3/16/15
Clearance:	SBarnes	Date: 3/16/15
Finalized:	LMusse	Date: 3/16/15
File Name:	PREA PMR IR	

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

/s/

LAURA MUSSE
03/16/2015



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 022279

**PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE**

Mikart, Inc.
1750 Chattahoochee Avenue, NW
Atlanta, GA 30318

ATTENTION: Jason Waldroup
Director, Regulatory Affairs

Dear Mr. Waldroup:

Please refer to your New Drug Application (NDA) dated December 2, 2014, received December 4, 2014, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Hydrocodone Bitartrate, Pseudoephedrine Hydrochloride and Guaifenesin Oral Solution, 2.5 mg/30 mg/200 mg per 5mL.

We also refer to your December 2, 2014, correspondence, and received December 4, 2014, requesting review of your proposed proprietary name, Hycofenix. We have completed our review of the proposed proprietary name, Hycofenix and have concluded that it is acceptable.

If any of the proposed product characteristics as stated in your December 2, 2014, 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, contact Nichelle Rashid, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-3904. For any other information regarding this application, contact Laura Musse, Regulatory Project Manager in the Office of New Drugs, at (240) 402-3720.

Sincerely,

{See appended electronic signature page}

Todd Bridges, RPh
Deputy Director
Division of Medication Error Prevention and Analysis
Office of Medication Error Prevention and Risk Management
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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

/s/

TODD D BRIDGES
03/02/2015



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

FACSIMILE TRANSMITTAL SHEET

DATE: February 5, 2015

To: Jason Waldroup Director, Regulatory Affairs	From: Laura Musse, RN, MS, CRNP Regulatory Health Project Manager
Company: Mikart Inc.	Division of Pulmonary, Allergy, and Rheumatology Products
Fax number: (404) 352-0351	Fax number: (301) 796-9728
Phone number: (404) 351-4510	Phone number: (240) 402-3720
Subject: NDA 022279-(Hydrocodone/Guaifenesin/Pseudoephedrine) and NDA 022424- (Hydrocodone and Guaifenesin) Information Request	

Total no. of pages including cover: 3

Comments:

Document to be mailed: **YES** **X- 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.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at 240-402-3720. Thank you.

Your resubmissions dated December 4, 2014, to NDA 022279, and November 18, 2014, to NDA 022424 is currently under review. We have the following requests for information:

1. Submit revised labeling assuring that the labeling structure format and language conforms to the Physician Labeling Rule (PLR) Requirements for Prescribing Information including format labeling tools and checklist, available at: <http://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/lawsactsandrules/ucm084159.htm>
2. Refer to the labels of recently approved combination cough and cold medications for guidance.

Respond to these Information Requests by email (Laura.Musse@fda.hhs.gov) or facsimile (301-796-9728), by Friday, February 20, 2015. Your response must also be submitted formally to the NDA shortly thereafter. If you have any questions, please contact Laura Musse, Regulatory Health Project Manager, at 240-402-3720.

Review/History Clearance From

Initiated by:	XWang	Date:	2/5/15
Drafted by:	LMusse	Date:	2/5/15
Clearance:	SBarnes	Date:	2/5/15
Finalized:	LMusse	Date:	2/5/15
File Name:	Label PLR format Request		

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

/s/

LAURA MUSSE
02/05/2015



NDA 22279

**ACKNOWLEDGE –
CLASS 2 RESUBMISSION**

Mikart, Inc.
1750 Chattahoochee Avenue, NW.
Atlanta, GA 30318

Attention: Jason Waldroup
Director, Regulatory Affairs

Dear Mr. Waldroup:

We acknowledge receipt on December 4, 2014 of your December 2, 2014, resubmission to your supplemental new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for hydrocodone/pseudoephedrine /guaifenesin oral solution, 2.5 mg/30mg/200 mg per 5 milliliters.

We consider this a complete, class 2 response to our September 28, 2011 action letter. Therefore, the user fee goal date is June 4, 2015.

If you have any questions, call me, at (240) 402-3720.

Sincerely,

{See appended electronic signature page}

Laura Musse, R.N., M.S., C.R.N.P.
Regulatory Health Project Manager
Division of Pulmonary, Allergy, and Rheumatology
Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

/s/

LAURA MUSSE
01/07/2015



NDA 22279

DISCIPLINE REVIEW LETTER

[Redacted] (b) (4)

Attention: [Redacted] (b) (4)

Dear [Redacted] (b) (4)

Please refer to your August 22, 2008, New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for hydrocodone, pseudoephedrine, and guaifenesin oral solution

We acknowledge receipt of your complete response submission dated July 18, 2011.

The clinical pharmacology section of your submission is under review, and we have identified the following potential review issues:

The clinical pharmacology studies submitted to support this application (studies S11-028 a single-dose bioavailability study and S11-0029 a single-dose crossover food effect study) have been reviewed under NDA 22-424 and show that the guaifenesin component of your oral solution product is not bioequivalent to the reference guaifenesin product [Redacted] (b) (4)

[Redacted] (b) (4) As such, the acceptability of the studies to support the approval of your proposed hydrocodone, pseudoephedrine, and guaifenesin product is in question and will be a review issue.

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.

If you have any questions, call Philantha Bowen, Regulatory Project Manager, at (301) 796-2466

Sincerely,

{See appended electronic signature page}

Lydia Gilbert-McClain, M.D., FCCP
Deputy Director
Division of Pulmonary, Allergy, and Rheumatology
Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

/s/

LYDIA I GILBERT MCCLAIN
09/29/2011

3 Page(s) have been Withheld in Full as b4 (CCI/TS)
immediately following this page



NDA 22279

**ACKNOWLEDGE –
CLASS 2 RESPONSE**

[Redacted] (b) (4)

Attention: [Redacted] (b) (4)

Dear [Redacted] (b) (4)

We acknowledge receipt on July 19, 2011, of your July 18, 2011, resubmission of your new drug application submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for hydrocodone, pseudoephedrine, and guaifenesin oral solution.

We consider this a complete, class 2 response to our January 25, 2011, action letter. Therefore, the user fee goal date is January 19, 2012.

If you have any questions, call me at (301) 796-2466.

Sincerely,

{See appended electronic signature page}

Philantha Montgomery Bowen, M.P.H., RN
Sr. Regulatory Project Management Officer
Division of Pulmonary, Allergy, and Rheumatology
Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

/s/

PHILANTHA M BOWEN
08/04/2011



NDA 022279

**PROPRIETARY NAME REQUEST
WITHDRAWN**

(b) (4)

ATTENTION: (b) (4)

Dear (b) (4)

Please refer to your New Drug Application (NDA) dated August 22, 2008, received August 22, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Hydrocodone Bitartrate, Pseudoephedrine Hydrochloride, and Guaifenesin Oral Solution, 2.5 mg/30 mg/200 mg per 5 mL.

We acknowledge receipt of your February 1, 2011, correspondence, on February 2, 2011, notifying us that you are withdrawing your request for review of the proposed proprietary names (b) (4). These proposed proprietary name requests are considered withdrawn as of February 1, 2011.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, call Nichelle Rashid, Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-3904. For any other information regarding this application, contact the Office of New Drugs (OND) Regulatory Project Manager, Philantha Bowen, at (301) 796-2466.

Sincerely,

{See appended electronic signature page}

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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

/s/

CAROL A HOLQUIST
03/21/2011

MEMORANDUM

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

DATE: January 5, 2011

TO: NDA 22279 File

FROM: Philantha Montgomery Bowen, MPH, RN
Sr. Regulatory Project Management Officer

SUBJECT: **GRMP -Communication of NDA Review Issues**

APPLICATION/DRUG: NDA 22279 (hydrocodone/guaifenesin/PSE)

In accordance with GRMP, the Clinical Pharmacology and Clinical Review Team for the application held a teleconference meeting on September 27, 2010, to discuss the review issues outlined in the Discipline Review Letter dated September 16, 2010. Reviewers in attendance: Yun Xu, Ph.D., Acting Clinical Pharmacology Team Leader, Arun Agrawal, Ph.D., Clinical Pharmacology Reviewer, Anthony Durmowicz, M.D., Clinical Team Leader, and Xu Wang, M.D., Clinical Reviewer

Following the October 21, 2010, Mid-Cycle Review meeting, a subsequent teleconference was held between [REDACTED]^{(b) (4)} on November 4, 2010. During this meeting Anthony Durmowicz, M.D., Clinical Team Leader, discussed the review status of the application, to include communicating that the deficiencies identified in September still remain a review issue.

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

/s/

PHILANTHA M BOWEN
01/05/2011



NDA 022279

**PROPRIETARY NAME REQUEST
UNACCEPTABLE**

(b) (4)

ATTENTION: (b) (4)

Dear (b) (4)

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Hydrocodone Bitartrate, Pseudoephedrine Hydrochloride, and Guaifenesin Oral Solution, 2.5 mg/30 mg/200 mg per 5 mL.

We also refer to your October 14, 2010, correspondence, received October 15, 2010, requesting review of your proposed proprietary name, (b) (4). We have completed our review of this proposed proprietary name and have concluded that this name is unacceptable for the following reasons.

(b) (4)

support its use, we consider it ambiguous and vulnerable to confusion.

(b) (4)

Thus, if you intend to have a proprietary name for this product, we recommend that you submit a new request for a proposed proprietary name review. (See the Guidance for Industry, Complete Submission for the Evaluation of Proprietary Names, <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm075068.pdf> and “PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2008 through 2012”).

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, call Nichelle Rashid, Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-3904. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager.

Sincerely,

{See appended electronic signature page}

Denise P. Toyer, PharmD.

Deputy Director

Division of Medication Error Prevention and Analysis

Office of Surveillance and Epidemiology

Center for Drug Evaluation and Research

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

/s/

DENISE P TOYER
01/04/2011



NDA 22279

DISCIPLINE REVIEW LETTER

(b) (4)

Attention: (b) (4)

Dear (b) (4)

Please refer to your July 22, 2010, New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for hydrocodone, pseudoephedrine, and guaifenesin oral solution.

The Clinical Pharmacology section of your submission is under review, and we have identified the following deficiencies:

1. The lower 90% CI for C_{max} is not within the acceptance range of 80-125% for guaifenesin of the proposed product when dosed following an overnight fast. In addition, the exposure to guaifenesin of the proposed product does not meet the acceptance criteria (80-125%) under fed versus fasted conditions, indicating a food effect on guaifenesin of the proposed product. Whether these findings are acceptable will be a review issue.
2. The protocol S09-0009 submitted on January 16, 2009, indicated that Hycodan (Endo Pharma) will be used as the reference drug. However, in the resubmission Hycodan was not used in the study. Provide an explanation stating why Hycodan was not used.

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.

NDA 22279

Page 2

If you have any questions, call Philantha Montgomery Bowen, Regulatory Project Manager, at (301) 796-2466.

Sincerely,

{See appended electronic signature page}

Yun Xu, Ph.D.

Acting Team Leader

Division of Clinical Pharmacology II

Office of Clinical Pharmacology

Center for Drug Evaluation and Research

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22279

ORIG-1

 (b) (4)

HYDROCODONE
HCL/GUAIFENESIN/PSEUDOEP
HEDR

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

/s/

YUN XU
09/16/2010



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

FACSIMILE TRANSMITTAL SHEET

DATE: September 14, 2010

To: Jason Waldroup, Director, Regulatory Affairs of Mikart, Inc.	From: Philantha Bowen, MPH, RN Sr. Regulatory Management Officer
Company: (b) (4)	Division of Pulmonary, Allergy, and Rheumatology Drug Products
Fax number: (b) (4)	Fax number: 301-796-9728
Phone number: (b) (4)	Phone number: 301-796-2466

Subject: NDA 22279 – CMC Information Request

Total no. of pages including cover: 3

Comments: Confirm Receipt

Document to be mailed: YES X 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.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 796-2300. Thank you.

NDA 22279

Hydrocodone/Pseudoephedrine/Guaifenesin Oral Solution

(b) (4)

Your submission dated July 22, 2010, to NDA 22-279 is currently under review. We acknowledge receipt of your submission dated August 23, 2010. Submit the following CMC information regarding the comparator products:

1. The components and composition.
2. The specifications used for accepting these comparator products.
3. Stability data showing that the comparator products remain within specifications during the test period of the BE studies.
4. Identification of the manufacturer of the pseudoephedrine HCl solution. Include the address and FEI or CFN number.

Formally submit the requested information in triplicate to the NDA by September 20, 2010.

If you have any questions, contact Philantha Montgomery Bowen, Sr. Regulatory Project Management Officer, at 301-796-2466.

Drafted by: Bowen/September 13, 2010

Initialed by: Raggio/September 13, 2010
Shaw/September 13, 2010
Peri/September 13, 2010

Finalized by: Bowen/September 14, 2010

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22279

ORIG-1



HYDROCODONE
HCL/GUAIFENESIN/PSEUDOEP
HEDR

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

/s/

PHILANTHA M BOWEN
09/14/2010



NDA 022279

**PROPRIETARY NAME REQUEST
UNACCEPTABLE**

(b) (4)

ATTENTION: (b) (4)

Dear (b) (4)

Please refer to your New Drug Application (NDA) dated July 22, 2010, received July 26, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Hydrocodone Bitartrate, Pseudoephedrine Hydrochloride, and Guaifenesin Oral Solution, 2.5 mg/30 mg/200 mg per 5 mL.

We also refer to your August 2, 2010, correspondence, received August 3, 2010, requesting review of your proposed proprietary name, (b) (4). We have completed our review of this proposed proprietary name and have concluded that this name is unacceptable for the following promotional reasons.

The proposed proprietary name, (b) (4). The proposed proprietary name, (b) (4)

The proposed indication for this drug product is the symptomatic relief of cough and nasal congestion. Therefore, the proposed proprietary name

(b) (4) (b) (4)
In the absence of (b) (4)

(b) (4)

(b) (4)

We note that you have not proposed an alternate proprietary name for review. If you intend to have a proprietary name for this product, we recommend that you submit a new request for a proposed proprietary name review. (See the Guidance for Industry, *Contents of a Complete Submission for the Evaluation of Proprietary Names*, <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM075068.pdf> and “PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2008 through 2012”.)

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Carolyn Volpe, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-5204. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Philantha Bowen at 301-796-2466.

Sincerely,

{See appended electronic signature page}

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22279

ORIG-1

 (b) (4)

HYDROCODONE
HCL/GUAIFENESIN/PSEUDOEP
HEDR

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

/s/

CAROL A HOLQUIST
09/07/2010



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

FACSIMILE TRANSMITTAL SHEET

DATE: August 27, 2010

To: Jason Waldroup, Director, Regulatory Affairs of Mikart, Inc.	From: Philantha Bowen, MPH, RN Sr. Regulatory Management Officer
Company: (b) (4)	Division of Pulmonary, Allergy, and Rheumatology Drug Products
Fax number: (b) (4)	Fax number: 301-796-9728
Phone number: (b) (4)	Phone number: 301-796-2466

Subject: NDA 22279 – Information Request

**Total no. of pages including
cover:** 3

Comments: Confirm Receipt

Document to be mailed: YES X 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.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 796-2300. Thank you.

NDA 22279

Hydrocodone/Pseudoephedrine/Guaifenesin Oral Solution

(b) (4)

Your submission dated July 22, 2010, to NDA 22-279 is currently under review. We have the following Clinical Pharmacology, CMC, and Labeling comments and/or requests for information:

Clinical Pharmacology

Submit the following dataset/information in electronic form:

1. Dataset of blood sampling time (target and actual) and corresponding plasma concentration for each individual in study S09-0009 and study S09-0010.
2. Dataset of PK parameters for each individual in study S09-0009 and study S09-0010.
3. Dataset and SAS code used to calculate the 90% CI for each PK parameters in study S09-0009 and study S09-0010.

CMC

4. In your August 23, 2010, CMC response to the Agency, you indicated that the hydrocodone bitartrate/homatropine methylbromide solution used in study S09-0009 was manufactured by Morton Grove Pharmaceutical, Inc. Submit information to clarify under which NDA or ANDA this product was approved.

Labeling

5. Submit carton and container labeling in electronic format for the drug product.
6. Submit the content of labeling [21 CFR 314.50(1)] in structured product labeling (SPL) format, as described in the *Guidance to Industry: Providing Regulatory Submissions in Electronic Format – Content of Labeling*.

Formally submit the requested information in triplicate to the NDA.

If you have any questions, contact Philantha Montgomery Bowen, Sr. Regulatory Project Management Officer, at 301-796-2466.

Drafted by: Bowen/August 25, 2010

Initialed by: Raggio/August 26, 2010
Xu/August 26, 2010
Schroeder/August 26, 2010

Finalized by: Bowen/August 27, 2010

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22279

ORIG-1

 (b) (4)

HYDROCODONE
HCL/GUAIFENESIN/PSEUDOEP
HEDR

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

/s/

PHILANTHA M BOWEN
08/27/2010



**Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II
Division of Pulmonary and Allergy Products**

Memorandum of Facsimile Correspondence

Date: January 26, 2010

To: [REDACTED] (b) (4)

Company: [REDACTED] (b) (4)

Fax: [REDACTED] (b) (4)

Phone: [REDACTED] (b) (4)

From: Carol Hill, MS
Regulatory Health Project Manager
Division of Pulmonary and Allergy Products

Subject: Acknowledgement of Incomplete Response

re: NDA 22-279

of Pages: 3

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If you are not the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you received this document in error, please immediately notify us by telephone at (301) 796-2300 and return it to us at FDA, 10903 New Hampshire Ave, Building 22, DPAP, Silver Spring, MD 20993.

Thank you. Please acknowledge receipt.
carol.hill@fda.hhs.gov



NDA 22279

ACKNOWLEDGE INCOMPLETE RESPONSE

[Redacted] (b) (4)

Attention: [Redacted] (b) (4)

Dear [Redacted] (b) (4)

We acknowledge receipt on December , 2009 of your December 22, 2009 submission to your new drug application (NDA) Hydrocodone, Pseudoephedrine and Guaifenesin Oral Solution.

We do not consider this a complete response to our action letter. Therefore, the review clock will not start until we receive a complete response. To be considered a complete response, all of the deficiencies in our June 22, 2009, action letter should be addressed. Please refer to the June 22, 2009 action letter for the list of deficiencies and our recommendations for resolution. We also recommend that you contact us for instructions regarding how to submit your document.

If you have any questions, call Carol Hill, Regulatory Health Project Manager, at (301) 796-1226.

Sincerely,

{See appended electronic signature page}

Sandy Barnes
CPMS
Division of Pulmonary and Allergy Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22279	ORIG-1	(b) (4)	HYDROCODONE HCL/GUAIFENESIN/PSEUDOEP HEDR
NDA-22279	GI-1		HYDROCODONE HCL/GUAIFENESIN/PSEUDOEP HEDR

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

/s/

CAROL F HILL
01/26/2010
Signed for Sandy Barnes



NDA 022279

**PROPRIETARY NAME REQUEST
WITHDRAWN**

(b) (4)

ATTENTION: (b) (4)

Dear (b) (4)

Please refer to your New Drug Application (NDA) dated August 22, 2008, received August 22, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Hydrocodone Bitartrate, Pseudoephedrine Hydrochloride, and Guaifenesin Oral Solution, 2.5 mg/30 mg/200 mg per 5 ml.

We acknowledge receipt of your December 4, 2009, correspondence, on December 7, 2009, notifying us that you are withdrawing your November 16, 2009 request for a review of the proposed proprietary name (b) (4). This proposed proprietary name request is considered withdrawn as of December 7, 2009.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Carolyn Volpe, Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-5204. For any other information regarding this application, contact the Office of New Drugs (OND) Regulatory Project Manager, Carol Hill at 301-796-1226.

Sincerely,

{See appended electronic signature page}

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22279

ORIG-1

 (b) (4)

HYDROCODONE
HCL/GUAIFENESIN/PSEUDOEP
HEDR

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

/s/

CAROL A HOLQUIST
12/18/2009



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-279

(b) (4)

Attention: (b) (4)

Dear (b) (4)

We acknowledge receipt on April 22, 2009, of your April 21, 2009, correspondence notifying the Food and Drug Administration of the change of ownership of the following new drug application (NDA):

Name of Drug Product: Hydrocodone Bitartrate/Pseudoephedrine Hydrochloride/Guaifenesin,
Oral Solution (2.5 mg, 30 mg and 200 mg/5 mL)

NDA Number: 22-279

Name of New Applicant: (b) (4)

Name of Previous Applicant: (b) (4)

Your correspondence provided the information necessary to effect this change, and we have revised our records to indicate (b) (4) as the applicant of record for this application

All changes in the NDA from those described by the original owner, such as manufacturing facilities and controls, must be reported to us prior to implementation except that changes in the drug product's label or labeling to change the product's brand or the name of its manufacturer, packer, or distributor may be reported in the next annual report. Refer to the *Guidance for Industry: Changes to an Approved NDA or ANDA* for information on reporting requirements. We request that you notify your suppliers and contractors who have DMFs referenced by your application of the change in ownership so that they can submit a new letter of authorization (LOA) to their Drug Master File(s).

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81. In addition, you are responsible for any correspondence outstanding as of the effective date of the transfer.

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

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Pulmonary and Allergy Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you have any question, call Carol Hill, Regulatory Health Project Manager, at (301) 796-1226.

Sincerely,

{See appended electronic signature page}

Carol Hill, M.S.
Regulatory Health Project Manager
Division of Pulmonary and Allergy Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc:



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

/s/

Carol F. Hill
6/16/2009 06:58:06 PM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-279

[REDACTED] (b) (4)

Attention: [REDACTED] (b) (4)

Dear [REDACTED] (b) (4)

Please refer to your new drug application (NDA) submitted pursuant to section 505(b)(2) for the Federal Food, Drug, and Cosmetic Act (FDCA) for Hydrocodone Bitartrate/Pseudoephedrine Hydrochloride/Guaifenesin Oral Solution. This correspondence is in reference to our telephone conversation on April 2, 2009 regarding the requirements for the transfer of ownership of an NDA.

Under 21 CFR 314.72, the following information is required to complete the change of ownership procedure:

1. The date the new ownership became effective.
2. A new Form FDA 356h signed by an authorized agent or official of the company.
3. Evidence of the new ownership of the NDA. This may be in the form of a letter or other documentation from the former applicant to show that all rights have been assigned or transferred to you. Patent or copyright ownership is not acceptable evidence of ownership of the NDA.
4. A commitment to all agreements, promises, and conditions made by the former owner and contained in the application.
5. Assurance that you were provided a complete copy of the previous owner's NDA.

All changes in the NDA from those described by the original owner, such as manufacturing facilities and controls, must be reported to us prior to implementation except that changes in the drug product's label or labeling to change the product's brand or the name of its manufacturer, packer, or distributor may be reported in the next annual report. Refer to the *Guidance for Industry: Changes to an Approved NDA or ANDA* for information on reporting requirements.

We request that you notify your suppliers and contractors who have DMFs referenced by your application(s) of the change in ownership so that they can submit a new letter of authorization (LOA) to their Drug Master File(s).

The new owner must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81. In addition, they are responsible for any correspondence outstanding as of the effective date of the transfer.

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

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Pulmonary and Allergy Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you have any question, call Carol Hill, Regulatory Health Project Manager, at (301) 796-1226.

Sincerely,

{See appended electronic signature page}

Sandy Barnes
Supervisory CPMS
Division of Pulmonary and Allergy Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

/s/

Carol F. Hill
4/3/2009 03:45:59 PM



NDA 22-279

INFORMATION REQUEST LETTER

(b) (4)

Attention: (b) (4)

Dear (b) (4)

Please refer to your August 22, 2008, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for hydrocodone, pseudoephedrine, and guaifenesin oral solution.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission. We request a prompt written response in order to continue our evaluation of your NDA.

We have the following comments and information requests:

A. Regarding the Drug Substances:

1. Modify the table of specifications for hydrocodone bitartrate to include the test and acceptance criteria for residual solvents (Section 3.2.S.4.1 Specifications Page 1).
2. Clarify which methods are used for receipt of the drug substances: USP or the in house methods described in the Methods Validation report.

In Sections S.4.2: Analytical Procedure[hydrocodone bitartrate], S.4.2: Analytical Procedure[guaifenesin], and S.4.2: Analytical Procedure[pseudoephedrine hydrochloride] USP methods are specified as being used.

However, Sections S.4.3: Validation of Analytical Procedure [hydrocodone bitartrate], S.4.3: Validation of Analytical Procedure [guaifenesin], and S.4.3: Validation of Analytical Procedure [pseudoephedrine hydrochloride] refers to validation reports found in Module 3 Section 3.2.R.3 Method Validation Package (MVP). The test methods in the MVP are (b) (4) and not USP methods.

3. A deficiency letter was sent to [REDACTED] (b) (4) agent regarding DMF [REDACTED] (b) (4) for pseudoephedrine hydrochloride on December 18, 2008. No response has been received.
4. Information has been requested from [REDACTED] (b) (4) regarding DMF [REDACTED] (b) (4) for hydrocodone bitartrate on March 9, 2009, and March 13, 2009.

B. Regarding the Drug Product:

1. For the manufacturing procedure, explain the discrepancy between the proposed commercial sizes in different sections of the application.

Section	Page	Proposed Commercial Size
3.2.P.2	10	[REDACTED] (b) (4)
3.2.P.3.2	1	[REDACTED] (b) (4)

2. Regarding the specifications for the colors
 - a. Submit copies of methods [REDACTED] (b) (4) and explain why two different UV test methods are used to identify the different colors upon receipt.
 - b. Submit the test methods for the tests for the colors, as specified in the tables in Section 3.2.P.4.2 (unpaginated) e.g. testing for organic impurities and metals content. You state that you will test the colors against the specifications listed in those tables.
3. Regarding the specifications for the flavor: Provide a description of test method [REDACTED] (b) (4). The acceptance testing for a flavor should include a test for the taste.
4. Regarding the analytical procedures
 - a. Regarding the Assay, Identification, Related Substances for Hydrocodone bitartrate in [REDACTED] (b) (4) by HPLC [REDACTED] (b) (4): Specify the solution and the peak being assessed in the assessment of the Tailing Factor in the System Suitability test.

b. Regarding the Assay, Identification, Related Substances for Hydrocodone bitartrate in (b) (4) by HPLC (b) (4), Assay, Identification, Related Substances for Guaifenesin in (b) (4) by HPLC (b) (4), Assay, Identification, Related Substances for Pseudoephedrine HCl in (b) (4) by HPLC (b) (4), and Assay and Identification of Methylparaben and Propylparaben in (b) (4) by HPLC (b) (4): Include directions to prepare a second working standard solution under “Sample Preparation.”

5. Regarding the Methods Validation Reports:

a. Specify the diluent used in the preparation of the solutions used for accuracy determinations in Table 8.1b in the Methods Validation Report for hydrocodone Bitartrate.

b. Explain why the directions for the preparation of the Assay Level Simulated Sample in Section 4.2 state that the concentration of the pseudoephedrine HCl is (b) (4) mg/mL when the concentration is actually (b) (4) mg/mL.

c. Regarding all the Methods Validation Reports:

i. Provide the details of the (b) (4)

ii. Specify the solvents used for the (b) (4)

iii. Provide the signal to noise ratio obtained for the LOQ samples.

6. Regarding the Reference Standards: Provide the source and qualification for the (b) (4)

C. Regarding the labeling:

1. Correct the spelling of hydrocodone in the Package insert Highlights

2. Correct the spelling of guaifenesin in the “Description” section

E. Regarding the bottle and carton labeling: Provide copies of the bottle and carton labeling.

F. The Following comments pertain to the Drug Listing Data Elements:

1. Correct the spelling of “pseudoephdrin”
2. Capitalize “fd&c”
3. Change the name of the flavor to “(b) (4) black raspberry flavor.”
4. Change the name (b) (4)

If you have any questions, call Carol Hill, Regulatory Health Project Manager, at 301-796-1226.

Sincerely,

Ali Al-Hakim, Ph.D.
Chief
Office of New Drug Quality Assessment
Division of Pre-Marketing Assessment I, Branch II
Center for Drug Evaluation and Research

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

/s/

Christine Moore
3/19/2009 09:41:56 AM



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

FACSIMILE TRANSMITTAL SHEET

DATE: December 12, 2008

To: (b) (4)	From: Carol Hill, M.S. Regulatory Health Project Manager
Company: (b) (4)	Division of Pulmonary and Allergy Products
Fax number: (b) (4)	Fax number: 301-796-9728
Phone number: (b) (4)	Phone number: 301-796-1226

Subject: NDA 22-279 – Response to 25Nov08 Request for Comment

Total no. of pages including cover: 4

Comments: Please acknowledge receipt.

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.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 796-2300. Thank you.

NDA 22-279

(b) (4)

hydrocodone, pseudoephedrine, guaifenesin

In response to your November 25, 2008 fax regarding New Drug Application (NDA) 22-279 and 22-424 (not yet submitted), we have the following comments. We have placed the contents of your fax below including the questions submitted. Immediately following each question you will find the Agency's response.

During our Pre-IND meeting, held on March 26, 2007, we were informed by the FDA attendees that the study for the 3 ingredient product (hydrocodone, guaifenesin and pseudoephedrine oral solution) would also cover our 2 ingredient product (hydrocodone and guaifenesin oral solution). The only difference between both formulations is the presence of pseudoephedrine in the 3 ingredient formulation, which is not in the 2 ingredient. Every other ingredient is exactly in the same concentration, both active and inactive.

(b) (4)

Question 1:

Is the formulation provided to us on the Study during the Pre-IND meeting still applicable?

FDA Response:

Yes.

Question 2:

The study performed with the 3 ingredient product will also be valid for the 2 ingredient product?

FDA Response:

The study performed with the 3 ingredient product may be valid for the 2 ingredient product if the only difference between both formulations is the presence of pseudoephedrine in the three-ingredient formulation

(b) (4)

and if there is no drug-drug interaction (DDI) among the 3 components. However, in the presence of a DDI in the 3-ingredient combination product, declaration of bioequivalence between the proposed 2 combination product and the references may not hold true. This uncertainty can be answered by modifying the FDA study design #2 proposed in the 74-day letter, dated October 31, 2008 for NDA 22-279 as follows:

Proposed PK study design #2 modification

ARM	BE Study
(b) (4)	√
Hycodan	√
Hycodan+GUA*+PSE*	√
PSE*	√
GUA*	√
Number of groups in crossover	5

*OTC products not containing sorbitol

- You need to apply the appropriate statistical analysis to the proposed 5 way-crossover study design.
- As shown in the table above, the recommended reference products are guaifenesin and pseudoephedrine OTC oral solution products not containing sorbitol and Hycodan. You may choose to use your own simple solutions for guaifenesin and pseudoephedrine following USP and monograph standards.

If you have any questions, contact Carol Hill, Regulatory Health Project Manager, at 301-796-1226.

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

/s/

Carol F. Hill
12/12/2008 01:03:36 PM
CSO



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 22-279

(b) (4)

Attention: (b) (4)

Dear (b) (4)

Please refer to your new drug application (NDA) dated August 22, 2008, received August 22, 2008, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for hydrocodone bitartrate 2.5/mg, pseudoephedrine hydrochloride 30 mg, guaifenesin 200 mg Oral Solution in 5 mL.

We also refer to your submissions dated September 17 and October 9, 2008.

We have completed an initial review of your application to determine its acceptability for filing and have determined that your application is sufficiently complete to permit a substantive review. Under 21 CFR 601.2(a), we filed your application on October 21, 2008. The review classification for this application is Standard.

During our filing review of your application, we identified the following potential review issues.

1. We notice that your product contains sorbitol. Sorbitol has been found to affect the bioavailability (BA) of some compounds with low permeability in a dose-proportional manner.
2. We also notice that your program does not address the potential for formulation effect. It states in 21 CFR 320.25(g) that the purpose of an in vivo BA study involving a combination drug product is to determine if the rate and extent of absorption of each active ingredient in the combination product is equivalent to the rate and extend of absorption of each active drug ingredient administered concurrently in separate single ingredient preparations.
3. The literature provided may not be sufficient information to support the claim of lack of drug-drug interaction effect (DDI).

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application.

We also have the following comments and requests for information, some of which were discussed with you during our teleconferences on October 27 and 31, 2008.

4. We recommend that you conduct an in vivo study in which bioequivalence (BE) is established with respect to each active component of your product. You may choose to follow the designs proposed in Table 1 or Table 2. The design in Table 1 is recommended assuming that there is a lack of drug-drug interaction (DDI) between the active ingredients. The proposed design in Table 2 addresses the potential of DDI and formulation effect.

Table 1. Proposed PK study design

ARM	BE Study
(b) (4)	√
Hycodan+GUA**+PSE*	√
Number of groups in crossover	2

*OTC products not containing sorbitol

Table 2. Proposed PK study design

ARM	BE Study
(b) (4)	√
Hycodan	√
Hycodan+GUA**+PSE*	√
PSE**+ GUA*	√
Number of groups in crossover	4

*OTC products not containing sorbitol

5. Apply the appropriate statistical analysis to the proposed 4-way crossover study design.
6. Conduct an in vivo study to determine the effect of food on the bioavailability of the active ingredients in your oral solution (see comment 2). We recommend you refer to “Guidance for Industry: Food-effect Bioavailability and Fed Bioequivalence Studies” for

the conduct and data analysis of this study. The food effect may be assessed as part of the above mentioned studies.

7. As shown in Tables 1 and 2, the recommended reference products are guaifenesin and pseudoephedrine OTC oral solution products not containing sorbitol and Hycodan. You may choose to use your own simple solutions for guaifenesin and pseudoephedrine following USP and monograph standards.
8. Submit a foreign marketing and regulatory history for your product.
9. Your safety summary includes only safety information from the AERS database covering the period 1/1/2003 to 12/31/2007. Submit additional safety information from other sources such as, a summary of the clinical safety from the literature, the World Health Organization (WHO) adverse event database, and international regulatory actions. Present the safety data by gender, age, and racial subgroups as available.
10. We remind you to submit a 120-day safety update as per 21 CFR 314.50.
11. All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We acknowledge receipt of your request for a waiver of pediatric studies for this application; clarify the age group indicated for this waiver request.
12. We note that you have not provided us with an assessment of leachables in the drug product. Provide us results of your evaluation of extractables and leachables from the container closure system and how have you concluded that they do not exist and are not necessary for routine monitoring.
13. We note that the proposed shelf life is 24 months even though you provided only 6 months of real time data. As per the ICHQ1A, a maximum of 12 months shelf life may be granted provided the stability data are robust.
14. Pursuant to 21 CFR 25.31(a) or (b), provide a request for a claim of categorical exclusion.
15. Provide a quantitative and qualitative chemical composition of the (b) (4) Black Raspberry Flavor (b) (4). Alternately this information may be provided in a authorized Drug Master File (DMF).
16. Clarify if your drug product is packaged with (b) (4). Provide the differences if both are used in the packaging.
17. Provide draft mock ups (100% size) of the proposed container labels.

18. In a letter dated, October 22, 2008, drug master file, DMF (b) (4) has been requested to gather information regarding pseudoephedrine hydrochloride.

We have the following labeling comments regarding conformance of your proposed labeling with the Physician Labeling Rule (PLR) format requirements. Submit revised labeling incorporating the following comments

General Comments

19. For specific requirements on the content and format of labeling for human prescription drug and biologic products refer to 21 CFR 201.57. Also see Draft Guidance for Industry: Labeling for Human Prescription Drug and Biological Products – Implementing the New Content and Format Requirements (Implementation Guidance).
20. Refer to <http://www.fda.gov/cder/regulatory/physLabel/default.htm> for fictitious examples of labeling format.

Highlights

21. (b) (4) This applies only to the Boxed Warning; Indications and Usage; Dosage and Administration; Contraindications; and Warnings and Precautions sections.

Indications and Usage

22. Placed a colon after the words “indicated for”.

Dosage Forms and Strengths

23. (b) (4) This section should contain a concise summary of the dosage forms and strengths.

Full Prescribing Information Contents

24. Remove all periods after the numbers for the section and subsection headings.

Full Prescribing Information

25. Any required section, subsection or specific information that is clearly inapplicable may be omitted from the FPI. However, the numbering does not change. Number the subsection Pharmacokinetics as 12.3 (b) (4)

Please respond only to the above requests for additional information. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

If you have any questions, call Carol Hill, Regulatory Health Project Manager, at (301) 796-1226.

Sincerely,

{See appended electronic signature page}

Badrul A. Chowdhury, M.D., Ph.D.
Director
Division of Pulmonary and Allergy Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

/s/

Badrul Chowdhury
11/3/2008 08:27:44 AM



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

FACSIMILE TRANSMITTAL SHEET

DATE: October 28, 2008

To: (b) (4)	From: Carol Hill, M.S. Regulatory Project Manager
Company: (b) (4)	Division of Pulmonary and Allergy Products
Fax number: (b) (4)	Fax number: 301-796-9728
Phone number: (b) (4)	Phone number: 301-796-1226

Subject: NDA 22-279 – CMC Request for Information

Total no. of pages including cover: 4

Comments: Please acknowledge receipt.

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.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 796-2300. Thank you.

NDA 22-279

(b) (4)

Hydrocodone Bitartrate/Pseudoephedrine Hydrochloride/Guaifenesin

We are in the process of reviewing your application dated, August 22, 2008 received, August 22, 2008. We have the following request for information.

1. Provide a Methods Validation Report for the drug product. Your submission provides only the raw data to support the Methods Validation Package. The report should contain the following sections.
 - A. Accuracy
 - B. Precision
 - a. Repeatability
 - b. Intermediate Precision
 - C. Specificity
 - D. Detection Limit
 - E. Quantitation Limit
 - F. Linearity
 - G. Range
2. Provide a data summary to support the System Suitability testing.
3. You state in your submission that Validation Reports for the raw materials are in the Methods Validation Package. Provide the exact location of this information in the NDA submission.
4. In your fax dated, October 22, 2008, you stated that the 9 month room temperature stability data for the clinical and other batches was complete. In the fax, you asked the following, "Does the Agency require this information to be submitted immediately and in which format would you prefer?"

Agency's Response:

Submit the stability data in the SAS transport format.

Your response to our requests should be forwarded as soon as possible to the Division by fax (301-796-9728) and submitted in the form of an amendment in triplicate to the NDA. In your cover letter, indicate in bold that the submission is a response to FDA request for information. Forward the submission to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Pulmonary and Allergy Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you have any questions, call Carol Hill, Regulatory Health Project Manager at 301-796-1226.

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

/s/

Carol F. Hill
10/28/2008 05:17:07 PM
CSO

MEMORANDUM

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

DATE: October 24, 2008

TO: NDA 22279
Hydrocodone Bitartrate/Pseudoephedrine
Hydrochloride/Guaifenesin Oral Solution

FROM: Carol Hill, MS
Regulatory Health Project Manager
Division of Pulmonary and Allergy Products

SUBJECT: **October 22, 2008 – Applicant Facsimiles**

See attached documents.

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

/s/

Carol F. Hill
10/24/2008 10:50:22 AM
CSO



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

FACSIMILE TRANSMITTAL SHEET

DATE: October 9, 2008

To: [REDACTED] (b) (4)	From: Carol Hill, M.S. Regulatory Project Manager
Company: [REDACTED] (b) (4)	Division of Pulmonary and Allergy Products
Fax number: [REDACTED] (b) (4)	Fax number: 301-796-9728
Phone number: [REDACTED] (b) (4)	Phone number: 301-796-1226

Subject: NDA 22-279 – Request for Information

Total no. of pages including cover: 3

Comments: Please acknowledge receipt.

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.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 796-2300. Thank you.

NDA 22-279

(b) (4)

Hydrocodone Bitartrate/Pseudoephedrine Hydrochloride/Guaifenesin

We are in the process of reviewing your application dated, August 22, 2008 received, August 22, 2008. We have the following request for information.

1. Provide a statement to confirm that all sites are ready for inspection not just the (b) (4) site in (b) (4).
2. Provide a statement that materials used in the manufacture of the plastic bottles are suitable for food contact as per 21 CFR 177.
3. Please confirm your availability to participate in a 30 minute teleconference scheduled for October 27, 2008 at 11 am.
4. Your fax dated, October 6, 2006 must be submitted formally to the NDA.

Your response to our requests should be forwarded as soon as possible to the Division by fax (301-796-9728) and submitted in the form of an amendment in triplicate to the NDA. In your cover letter, indicate in bold that the submission is a response to FDA request for information. Forward the submission to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Pulmonary and Allergy Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you have any questions, call Carol Hill, Regulatory Health Project Manager at 301-796-1226.

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

/s/

Carol F. Hill
10/9/2008 11:26:51 AM
CSO

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH
DIVISION OF PULMONARY AND ALLERGY PRODUCTS

DATE: October 6, 2008
TO: NDA 22-279
FROM: Carol Hill, RPM
SUBJECT: **CMC Request for Information**

Email and phone correspondences received from (b)(4) on October 6, 2008 requested of (b)(4) holder of NDA 22-279 the following information.

1. Provide name, phone number, fax number, email address for each drug substance and drug product manufacturing site listed in the NDA including all contractor testing sites.
2. Clarify what testing is being performed by the following Contract Testing Facilities:
(b)(4)

The request was phoned to (b)(4) on October 6, 2008. The Agency was informed by (b)(4) that the information requested would be forwarded by fax as soon as possible.

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

/s/

Carol F. Hill
10/6/2008 12:08:21 PM
CSO