

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

207960Orig1s000

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

EXCLUSIVITY SUMMARY

NDA # 207960

SUPPL #

HFD # 130

Trade Name QuilliChew ER

Generic Name methylphenidate hydrochloride

Applicant Name Pfizer Inc.

Approval Date, If Known December 4, 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)

b) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES ☒ NO ☐

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

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

c) Did the applicant request exclusivity?

YES ☒ NO ☐

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

3

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

YES ☒ NO ☐

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

No

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

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

YES ☐ NO ☒

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

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

YES ☒ NO ☐

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

NDA 21514 (Daytrana)
NDA 205831 (Aptensio XR)
NDA 21259 (Metadate CD)
NDA 21284 (Ritalin LA)
NDA 10187 (Ritalin)
NDA 21121 (Concerta)
NDA 21419 (Methylin oral solution)
NDA 18029 (Ritalin SR)
NDA 21475 (Methylin chewable tablets)
NDA 202100 (Quillivant)
NDA 21278 (Focalin)
NDA 21802 (Focalin XR)

2. Combination product.

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

YES ☐ NO ☒

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

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)
IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

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

only if the answer to PART II, Question 1 or 2 was "yes."

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

YES ☒ NO ☐

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

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

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

YES ☒ NO ☐

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

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

YES ☒ NO ☐

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

YES ☐ NO ☒

If yes, explain:

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

YES ☐ NO ☒

If yes, explain:

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

Study B7491005(NWP09-ADHD-300) – A multicenter, dose-optimized, double-blind, randomized, placebo-controlled Phase 3 study to evaluate the efficacy of methylphenidate HCl ERCT in pediatric patients with attention deficit hyperactivity disorder (ADHD) in a laboratory classroom.

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 <input type="checkbox"/>	NO <input checked="" type="checkbox"/>
Investigation #2	YES <input type="checkbox"/>	NO <input type="checkbox"/>

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

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

Study B7491005(NWP09-ADHD-300) – A multicenter, dose-optimized, double-blind, randomized, placebo-controlled Phase 3 study to evaluate the efficacy of methylphenidate HCl ERCT in pediatric patients with attention deficit hyperactivity disorder (ADHD) in a laboratory classroom.

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 # 111020	YES <input checked="" type="checkbox"/> ! NO <input type="checkbox"/>
	! Explain:

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Name of person completing form: Hiren Patel, Pharm.D.
Title: Regulatory Project Manager
Date: 11/29/2015

Name of Office/Division Director signing form: Mitchell Mathis, MD
Title: Division 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/

HIREN PATEL
12/04/2015

MITCHELL V Mathis
12/04/2015

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 207960 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: QuilliChew ER Established/Proper Name: methylphenidate hydrochloride Dosage Form: extended-release chewable tablets		Applicant: Pfizer Inc Agent for Applicant (if applicable):
RPM:		Division:
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)		<u>For ALL 505(b)(2) applications, two months prior to EVERY action:</u> <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) <input checked="" type="checkbox"/> No changes <input type="checkbox"/> New patent/exclusivity (<i>notify CDER OND IO</i>) Date of check:
❖ Actions		
<ul style="list-style-type: none"> Proposed action User Fee Goal Date is <u>December 4, 2015</u> 		<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"/> None
❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____		<input type="checkbox"/> Received
❖ Application Characteristics³		

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.

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 | |

(NOTE: Set the submission property in DARRTS and notify the CDER Breakthrough Therapy Program Manager;
Refer to the "RPM BT Checklist for Considerations after Designation Granted" for other require actions: [CST SharePoint](#))

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 (approvals only)	<input type="checkbox"/> Yes <input type="checkbox"/> No
❖ Public communications (approvals only)	
• Office of Executive Programs (OEP) liaison has been notified of action	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
• 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	
• Is approval of this application blocked by any type of exclusivity (orphan, 5-year NCE, 3-year, pediatric exclusivity)?	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
• If so, specify the type	
❖ Patent Information (NDAs only)	
• 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 (approvals only)	<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 – December 4, 2015
Labeling	
❖ Package Insert <i>(write submission/communication date at upper right of first page of PI)</i>	
<ul style="list-style-type: 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
<ul style="list-style-type: none"> Original applicant-proposed labeling (February 4, 2015) 	<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 checked="" type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input type="checkbox"/> None
<ul style="list-style-type: 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
<ul style="list-style-type: none"> Original applicant-proposed labeling (February 4, 2015) 	<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>	
<ul style="list-style-type: none"> Most-recent draft labeling (November 11, 2015) 	<input checked="" type="checkbox"/> Included
❖ Proprietary Name <ul style="list-style-type: none"> Acceptability/non-acceptability letter(s) <i>(indicate date(s))</i> Review(s) <i>(indicate date(s))</i> 	DMEPA Letter – October 15, 2015; June 11, 2015 DMEPA Review – October 14, 2015; June 10, 2015
❖ Labeling reviews <i>(indicate dates of reviews)</i>	RPM: <input checked="" type="checkbox"/> 04/16/2015None DMEPA: <input checked="" type="checkbox"/> November 13, 2015; November 5, 2015; July 14, 2015None DMPP/PLT (DRISK): <input checked="" type="checkbox"/> November 18, 2015 None OPDP: <input checked="" type="checkbox"/> November 18, 2015 None SEALD: <input type="checkbox"/> None CSS: <input type="checkbox"/> None Product Quality <input type="checkbox"/> None Other: <input checked="" type="checkbox"/> PMHS October 26, 2015; October 16, 2015None
Administrative / Regulatory Documents	

❖ RPM Filing Review ⁴ /Memo of Filing Meeting (<i>indicate date of each review</i>)	RPM Filing Review: April 16, 2015
❖ All NDA 505(b)(2) Actions: Date each action cleared by 505(b)(2) Clearance Committee December 2, 2015	505(b)(2) Assessment: December 4, 2015 <input type="checkbox"/> Not a (b)(2)
❖ 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	
• Applicant is on the AIP	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
• This application is on the AIP	<input type="checkbox"/> Yes <input type="checkbox"/> No
○ 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"/> Not an AP action
❖ Pediatrics (<i>approvals only</i>)	
• Date reviewed by PeRC <u>October 21, 2015</u> If PeRC review not necessary, explain: _____	
❖ Breakthrough Therapy Designation	<input checked="" type="checkbox"/> N/A
• Breakthrough Therapy Designation Letter(s) (granted, denied, an/or rescinded)	
• CDER Medical Policy Council Breakthrough Therapy Designation Determination Review Template(s) (<i>include only the completed template(s) and not the meeting minutes</i>)	
• CDER Medical Policy Council Brief – Evaluating a Breakthrough Therapy Designation for Rescission Template(s) (<i>include only the completed template(s) and not the meeting minutes</i>) (completed CDER MPC templates can be found in DARRTS as clinical reviews or on the MPC SharePoint Site)	
❖ 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, Formal Dispute Resolution Request decisional letters, etc.) (<i>do not include previous action letters, as these are located elsewhere in package</i>)	
❖ 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)	OPQ Memo – 11/24/2015
❖ Minutes of Meetings	
• If not the first review cycle, any end-of-review meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> N/A or no mtg
• Pre-NDA/BLA meeting (<i>indicate date of mtg</i>)	<input type="checkbox"/> No mtg October 30, 2014
• EOP2 meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> No mtg
• Mid-cycle Communication (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> N/A
• Late-cycle Meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> N/A
• Other milestone meetings (e.g., EOP2a, CMC focused milestone meetings)	

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

<i>(indicate dates of mtgs)</i>	
❖ Advisory Committee Meeting(s)	<input checked="" type="checkbox"/> No AC meeting
• Date(s) of Meeting(s)	
Decisional and Summary Memos	
❖ Office Director Decisional Memo <i>(indicate date for each review)</i>	<input type="checkbox"/> None
Division Director Summary Review <i>(indicate date for each review)</i>	<input type="checkbox"/> None December 4, 2015
Cross-Discipline Team Leader Review <i>(indicate date for each review)</i>	<input type="checkbox"/> None November 24, 2015
PMR/PMC Development Templates <i>(indicate total number)</i>	<input type="checkbox"/> None Three
Clinical	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> No separate review
• Clinical review(s) <i>(indicate date for each review)</i>	November, 6, 2015; March 24, 2015
• Social scientist review(s) (if OTC drug) <i>(indicate date for each review)</i>	<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>	Addressed in November 6, 2015 review
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers <i>(indicate date of each review)</i>	<input checked="" type="checkbox"/> None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation <i>(indicate date of each review)</i>	<input type="checkbox"/> N/A December 4, 2015 (See Labeling Review)
❖ Risk Management	
• 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 type="checkbox"/> None requested November 5, 2015; July 22, 2015; June 11, 2015
Clinical Microbiology <input checked="" type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) <i>(indicate date for each review)</i>	<input type="checkbox"/> No separate review
Clinical Microbiology Review(s) <i>(indicate date for each review)</i>	<input 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 type="checkbox"/> None November 3, 2015; March 23, 2015

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)		<input type="checkbox"/> None October 27, 2015; March 27, 2015
❖ OSI Clinical Pharmacology Inspection Review Summary <i>(include copies of OSI letters)</i>		<input checked="" type="checkbox"/> None requested
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"/> No separate review
• Pharm/tox review(s), including referenced IND reviews <i>(indicate date for each review)</i>		<input type="checkbox"/> None November 4, 2015; March 27, 2015
❖ 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 Included in P/T review, page
❖ 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		
• Tertiary review <i>(indicate date for each review)</i>		<input checked="" type="checkbox"/> None
• Secondary review (e.g., Branch Chief) <i>(indicate date for each review)</i>		<input checked="" type="checkbox"/> None
• Integrated Quality Assessment (contains the Executive Summary and the primary reviews from each product quality review discipline) <i>(indicate date for each review)</i>		<input type="checkbox"/> None October 2, 2015; February 4, 2015
❖ Reviews by other disciplines/divisions/Centers requested by product quality review team <i>(indicate date of each review)</i>		<input checked="" type="checkbox"/> None
❖ Environmental Assessment (check one) (original and supplemental applications)		
<input checked="" type="checkbox"/> Categorical Exclusion <i>(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)</i>		October 2, 2015
<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 checked="" type="checkbox"/> Facilities inspections <i>(action must be taken prior to the re-evaluation date) (only original applications and efficacy supplements that require a manufacturing facility inspection(e.g., new strength, manufacturing process, or manufacturing site change))</i>		<input checked="" type="checkbox"/> Acceptable Re-evaluation date: <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable

Day of Approval Activities	
❖ For all 505(b)(2) applications: • 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>)
• Finalize 505(b)(2) assessment	<input checked="" type="checkbox"/> Done
❖ For Breakthrough Therapy (BT) Designated drugs: • Notify the CDER BT Program Manager	<input checked="" type="checkbox"/> Done (<i>Send email to CDER OND IO</i>)
❖ For products that need to be added to the flush list (generally opioids): Flush List • Notify the Division of Online Communications, Office of Communications	<input checked="" type="checkbox"/> Done
❖ 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 checked="" 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/

HIREN PATEL
12/04/2015



IND 111020

MEETING MINUTES

NextWave Pharmaceuticals, Inc., a subsidiary of Pfizer Inc.
Attention: Greg Carrier
Senior Director, Worldwide Safety and Regulatory
235 E 42nd Street (219/9/2)
New York, NY 10017-5755

Dear Mr. Carrier:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for methylphenidate extended-release chewable tablets.

We also refer to the meeting between representatives of your firm and the FDA on October 2, 2014. The purpose of the meeting was to discuss and reach agreement on the structure, content, format, data presentation and basis for the preliminary draft label for a 505(b)(2) NDA.

A copy of the official minutes of the meeting is enclosed for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, contact Hiren Patel, Regulatory Project Manager at hiren.patel@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Mitchell V. Mathis, M.D.
CAPT, USPHS
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure:
Meeting Minutes



FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

MEMORANDUM OF MEETING MINUTES

Meeting Type: B
Meeting Category: Pre-NDA

Meeting Date and Time: October 2, 2014 from 3:00pm-4:00pm (EST)
Meeting Location: CDER WO Bldg. 22, Room 1311

Application Number: IND 111020
Product Name: Methylphenidate HCl Extended-Release Chewable Tablets
Indication: Attention Deficit Hyperactivity Disorder
Sponsor/Applicant Name: NextWave Pharmaceuticals, Inc., a subsidiary of Pfizer Inc.

Meeting Chair: Dr. Mitchell Mathis
Meeting Recorder: Dr. Hiren Patel

FDA ATTENDEES

Mitchell Mathis, M.D.	Division Director, Division of Psychiatry Products (DPP)
Tiffany Farchione, M.D.	Deputy Division Director (Acting), DPP
Jing Zhang, M.D.	Clinical Team Leader, DPP
Gregory Dubitsky, M.D.	Clinical Reviewer, DPP
Peiling Yang, Ph.D.	Biometrics Team Leader, DPP
Thomas Birkner, Ph.D.	Biometrics Reviewer, DPP
David Claffey, Ph.D.	CMC Lead, Office of New Drug Quality Assessment (ONDQA)
Linda Fossom, Ph.D.	Pharmacology/Toxicology Supervisor, DPP
Ikram Elayan, Ph.D.	Pharmacology/Toxicology Reviewer
Hao Zhu, Ph.D.	Clinical Pharmacology Team Leader, Office of Clinical Pharmacology (OCP)
Andre Jackson, Ph.D.	Clinical Pharmacology Reviewer, OCP
Hiren Patel, PharmD	Regulatory Project Manager, DPP
Loretta Holmes, PharmD	Safety Evaluator, DMEPA
Okpo Eradiri, Ph.D.	Biopharmaceutics Reviewer

SPONSOR ATTENDEES

Phil Chappell, M.D.	Executive Director, Clinical Affairs
Donna Palumbo, Ph.D.	Medical Affairs Team Lead
Richat Abbas, Ph.D.	Director, Clinical Pharmacology Lead
John Orazem, Ph.D.	Senior Director, Global Established Pharma Clinical Statistics
Lisha Cole, MSc, MBA	Director, Cluster Lead Worldwide Safety and Regulatory
Greg Carrier, MBA	Senior Director, Worldwide Safety and Regulatory

Suzanne Mouton, M.D.	Safety Risk Lead
Sally Berry, M.D., Ph.D.	Chief Medical Officer, Tris Pharma (collaborative partner)
Bharat Damle, Ph.D.	Senior Director, Clinical Pharmacology Team Lead, Global Established Pharmaceuticals
Rich Rolke, MSc, MBA	Director, Global CMC
Christine Seymour, Ph.D.	Director, Global CMC
Yu-Hsing Tu, Ph.D.	Vice President, Product Development, Tris Pharma (collaborative partner)

1.0 BACKGROUND

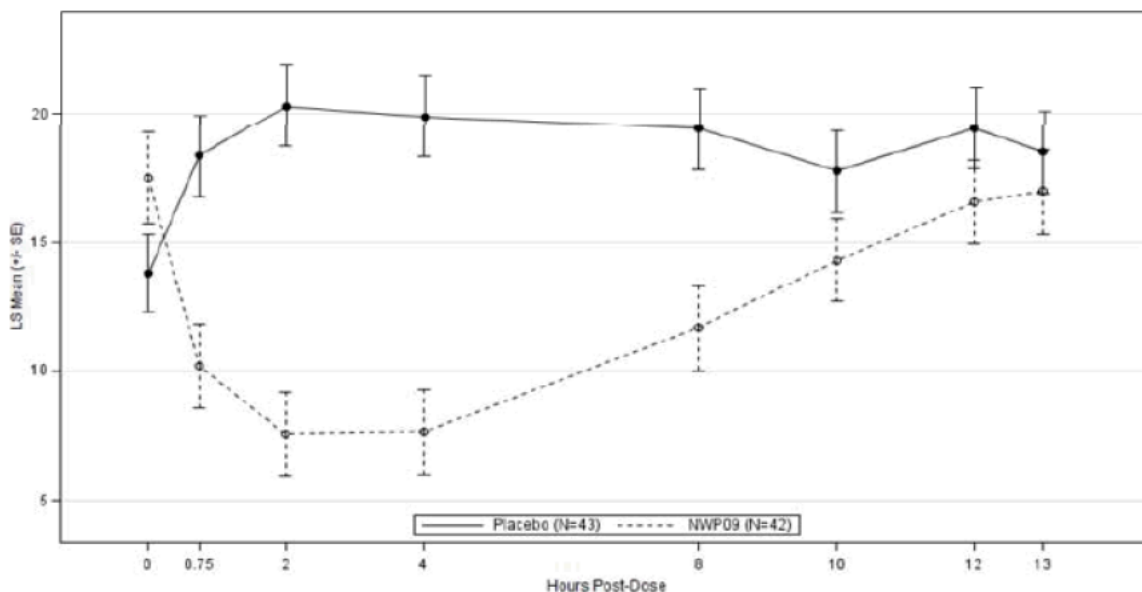
NextWave Pharmaceuticals (now Pfizer) has developed an extended-release chewable tablet (ERCT) formulation of methylphenidate (MPH), also known as NWP09, for the treatment of Attention Deficit Hyperactivity Disorder (ADHD). A 505(b)(2) NDA based on Methylin Chewable Tablets (NDA 21-475) as the Reference Listed Drug (RLD) is planned (pre-assigned NDA #207-960). The difference between the ERCT product and the RLD is that the former is an extended release formulation, whereas the latter is an immediate release product; both are chewable formulations. NWP09 (b) (4) the MPH extended release powder for oral suspension, Quillivant XR.

The development program is comprised of two clinical trials: a Phase 1 relative bioavailability trial in healthy adults to establish a bridge to the RLD (Study 1004), and a Phase 3 laboratory classroom study in ADHD patients, ages 6 to 12 years, to demonstrate the safety and efficacy of this new formulation (Study 1005). Additional data are provided from two pilot studies (Studies 1002 and 1003) that used prototype formulations to support the ERCT product development.

Study 1004 was a randomized, three-way crossover, single dose, relative bioavailability study comparing MPH ERCT 40mg under fed and fasted conditions and Methylin IR (2 doses of 20mg 6 hours apart) under fasted conditions in 33 healthy, non-smoking, males and females (ages 18-55). The analysis of PK data included partial AUCs up to 4 hours post-dose.

Study 1005 enrolled 90 children (ages 6-12) with ADHD into the 6-week open-label dose optimization period using doses of 20 to 60 mg/day. From these, 86 subjects were then randomized to one week of double-blind treatment with ERCT or placebo, which ended with an all-day assessment in a laboratory classroom. The intent-to-treat (ITT) population consisted of 85 subjects. The primary efficacy endpoint was the average of all post-dose SKAMP-combined scores collected during the double-blind laboratory classroom day (0.75, 2, 4, 8, 10, 12, and 13 hours after dosing), which showed a 7.0 point improvement on the SKAMP-Combined score favoring drug over placebo ($p < 0.001$). Key secondary variables were the onset and duration of effect. Significant differences, after adjusting for multiplicity, favoring drug were found at 2, 4, and 8 hours post-dose but not at 0.75, 10, 12, or 13 hours (see the Figure 1 below, excerpted from the sponsor's meeting package). Thus, the onset is considered to be at 2 hours, with demonstrated efficacy for 6 hours after onset.

Figure 1: SKAMP-Combined Scores Over Time (LS Mean \pm SE) by Treatment Group during the Double-blind Laboratory Classroom Day



The sponsor intends to request a waiver of PREA requirements for children ages 0 to (b) (4) years, citing the following reasons: 1) studies in this age group are highly impractical because diagnostic criteria and efficacy measures are not well-defined and (b) (4)

(b) (4) The sponsor further states that behavioral approaches are generally recommended as first-line therapy in this age range and, when drug therapy is chosen in this age group, there are non-MPH products with an approved indication for use. Thus, the sponsor asserts that this product would not represent a meaningful therapeutic benefit.

The sponsor contends that no PK study conducted in pediatric subjects using the ERCT formulation is necessary to support their application. The PK profile of the ERCT in pediatric subjects would be expected to be similar to that seen in adults and in pediatric subjects who take Quillivant XR for the following reasons: 1) the formulation composition of Quillivant XR and methylphenidate HCl ERCT are similar, (b) (4) 2) Quillivant XR and the ERCT have similar in-vitro dissolution profiles; 3) comparable exposures (C_{max} and AUC) were observed between the oral suspension and prototype chewable tablets, and between Quillivant XR and methylphenidate ERCT, and 4) similar PK properties were observed between children, adolescents and adults after administration of Quillivant XR.¹

This product will be marketed in 20, 30, and 40mg strengths, and is intended to be taken once daily in the morning with or without food. The recommended starting dose for patients age 6 years and older is 20mg. The dose may be titrated weekly in increments of 10 to 20mg. Daily doses above 60mg have not been studied and are not recommended.

¹ Quillivant XR is labeled for use in patients age 6 years and older. PK studies were conducted in children, adolescents, and adults but clinical trials were performed only in children ages 6-12 years.

Pre-IND meetings between the Agency and the sponsor took place on April 1, 2011, and April 4, 2012. The 2011 meeting included a discussion of 1) whether a 505(b)(2) NDA could be filed for NWP09 based on MPH extended-release powder for oral suspension as the reference drug and 2) the design of a pivotal bioequivalence trial to support the NDA. The decision regarding the 505(b)(2) pathway was deferred at the meeting until Agency regulatory staff could be consulted. In a letter dated April 15, 2011, we advised the sponsor that the 505(b)(2) pathway was acceptable using MPH extended-release powder for oral suspension as the reference if that product was approved at the time of the application and if it was scientifically valid to do so. We also provided the conditions under which the proposed bioequivalence study could be conducted without an IND. The 2012 meeting entailed several topics including, but not limited to, the following: 1) a change of the reference drug in the bioequivalence study to Methylin Chewable Tablets, 2) discussion of a Phase 3 laboratory classroom trial to support the 505(b)(2) application because the PK of the ERCT product (taken once daily) and Methylin (taken BID) were different, and 3) the need for an alcohol effect study on all strengths of the product. There was considerable discussion regarding the efficacy endpoint structure for the Phase 3 trial. The Agency advised the sponsor that use of the mean SKAMP-Combined scores over the course of the laboratory day as the primary variable was not objectionable but the Agency review of the study results would examine the score at each time point to insure that efficacy was not driven by robust findings at only one or two time points. Also, the Agency stated that this variable alone would not support an onset or duration claim, and advice on the data needed to support such claims was conveyed to the sponsor (i.e., sequential testing at multiple time points in a pre-specified order). In addition, further advice pertaining to the 505(b)(2) pathway was given to the sponsor.

An IND application for the MPH ERCT formulation was submitted on May 2, 2012, and a May Proceed letter was issued on June 11, 2012. Several comments were included in this letter from the Office of Clinical Pharmacology and the Office of Biometrics, including advice that the Agency considered the duration of efficacy to be defined by the difference between the time of onset and the last consecutive time point at which the treatment group difference is statistically significant (as opposed to simply the last consecutive time point at which the treatment group difference is statistically significant).

The sponsor has requested this meeting to discuss and reach agreement on the structure, content, format, and data presentation for the NDA and the basis for the preliminary draft labeling. More specifically, they seek FDA concurrence regarding the adequacy of the studies proposed for inclusion in the application, and assurance that any outstanding FDA comments have been fully addressed.

2. DISCUSSION

2.1. Clinical Basis for Approval

Question 1: The Sponsor proposes that the following key confirmatory methylphenidate HCl ERCT clinical studies, along with reliance on the substantial body of pre-existing safety and efficacy data for methylphenidate, will be the primary basis for the approval of methylphenidate HCl ERCT for use in the treatment of ADHD in patients 6 years and older:

- Phase 1 Bioavailability (BA) study in adults (PMRI Study Number: 2012-2950/B7491004)
- Phase 3 study in 6-12 year olds (NWP09-ADHD-300/B7491005)

Does the Food and Drug Administration (FDA) concur that the above will be sufficient to support review?

FDA Response to Question 1: *Yes.*

Pfizer pre-meeting response to Question 1: No further discussion necessary

Discussion: *No further discussion.*


Question 2: A waiver request for children under age 6 is planned. Does the FDA agree?

FDA Response to Question 2: *A waiver for ages 0-4 years is reasonable. A deferral will likely be granted for ages 4-5 years in view of the fact that many patients in this age range require pharmacotherapy when non-drug interventions fail.*

Pfizer pre-meeting response to Question 2: Pfizer would like to discuss Question 2 to gain further understanding regarding the Agency's view on potential proposed study design elements for such a study, anticipated expected timing for completion of the PSP and for providing data in ages 4-5 years. Pfizer would also like confirmation that the Agency considers the extended release chewable tablet as a new dosage form as a trigger for requiring PREA studies in the pediatric population.

Discussion: *There was considerable discussion between the sponsor and the Agency regarding the deferred requirement for ADHD studies in the 4 to 5 year age range. The sponsor proposed to submit the initial Pediatric Study Plan (iPSP) for this age range with the NDA submission, which is planned for February 2015. The Agency replied that the iPSP should be submitted sooner but the Project Manager stated that he will consult with the Pediatric Review Committee (PeRC) to ascertain whether submission with the NDA was acceptable. The Project Manager also cautioned that lack of an agreed upon iPSP at the time of NDA filing would be a filing issue. The Agency explained that the specific requirements for a study in 4 to 5 year olds have not yet been finalized because this is a novel age range for ADHD drug trials.*

(b) (4)



(b) (4)

Post-Meeting Note: *The Agency will permit the PSP to be submitted with the NDA.*

2.2. Labeling

Question 3: Labeling content for the proposed methylphenidate HCl ERCT would be based upon the most recently approved USPI for the reference drug used as basis for this 505(b)(2) filing, NDA 21-475 (Methylin™ Chewable Tablets), including a Medication Guide. The proposed labeling for the methylphenidate HCl ERCT will be provided in Physician's Labeling Rule (PLR) format, with information specific to the proposed drug product replacing that specific to the reference drug product. Does the FDA agree?

- a. Primary efficacy data from the Phase 3 pivotal study NWP09-ADHD-300/B7491005 will be presented in the CLINICAL STUDIES section and safety data from the Phase 3 study will be reported in the adverse events section. No discussion of the secondary endpoints is planned. Does the FDA agree?

FDA Response to Question 3: *No. Labeling must inform prescribers about the onset and duration of efficacy so that they can determine if the ERCT formulation is appropriate for a given patient. Thus, onset and duration data will be described in labeling, probably including a plot of SKAMP data throughout the laboratory day as in Section 14 of Quillivant XR labeling. Otherwise, the acceptability of the labeling will be a review issue.*

Pfizer pre-meeting response to Question 3: Pfizer does not intend to discuss this question further at the meeting.

Discussion: *No further discussion.*

Question 4: The Sponsor currently holds an NDA for a methylphenidate extended release oral suspension formulation that is marketed under the trade name Quillivant XR® and is considering use of a trade name other than 'Quillivant' for the proposed methylphenidate HCl ERCT. Does the FDA concur with the Sponsor that use of a different trade name may be considered?

FDA Response to Question 4: *The acceptability of another proprietary name will be a review issue. At the time of proprietary name review request submission, please provide your justification, including any compelling safety reasons that you believe supports the need for a different proprietary name for this product.*

Pfizer pre-meeting response to Question 4: Pfizer does not intend to discuss this question further at the meeting.

Discussion: *No further discussion.*

2.3. Clinical Summaries for the NDA

Question 5: NDA will include a pivotal Phase 3 study and a pivotal Phase 1 BA study. It is proposed to provide a Summary of Clinical Safety (SCS), Summary of Clinical Efficacy (SCE) and a Clinical Overview (CO) for these pivotal studies with no Integrated Summary of Safety (ISS) or Integrated Summary of Efficacy (ISE). Does the FDA agree that an ISS and an ISE are not required?

FDA Response to Question 5: *Yes.*

Pfizer pre-meeting response to Question 5: No further discussion of Question 5 is anticipated.

Discussion: *No further discussion.*

Question 6: In the SCS, it is proposed that no pooling of adverse event data be included, as the primary studies contributing safety data (the Phase 3 study in children ages 6-12 years with ADHD and the BA study in healthy adults) are in different subject populations. Is this acceptable to the Agency?

FDA Response to Question 6: *No pooling is acceptable from a clinical point of view. The Agency assumes that the analysis data was generated from the SDTM data. If the SDTM data is not the raw data traceable to CRFs, please also submit the raw data. Note that creation of analysis datasets from SDTM data will require traceability seen in SAS programs. As such, we suggest submission of SAS programs used to generate analysis datasets.*

Pfizer pre-meeting response to Question 6: Pfizer confirms the Agency assumption that the analysis data was generated from SDTM data. Pfizer also confirms that the SDTM is traceable to the CRFs. SAS programs used to generate analysis datasets can be submitted.

Discussion: *No further discussion.*

2.4. Clinical Safety Datasets

Question 7: Clinical datasets for the following studies will be provided in SAS transport files which will include analysis datasets and Study Data Tabulation Model (SDTM) files and no SAS code. Is this acceptable to the Agency?

- Phase 3 study NWP09-ADHD-300/B7491005: “A Multicenter, Dose-Optimized, Double-Blind, Randomized, Placebo-Controlled Study to Evaluate the Efficacy of NWP09 in Pediatric Patients with Attention Deficit Hyperactivity Disorder (ADHD) in a Laboratory Classroom”

- Phase 1 study PMRI Study Number: 2012-2950/B7491004: “A Three-Way Crossover Relative Bioavailability Study Comparing Methylphenidate HCl Extended-Release Chewable Tablets and Methylin[™] Chewable Tablets under Fasting Conditions and Determining the Effect of Food on 40 mg Methylphenidate ER Chewable Tablets”

FDA Response to Question 7: *From a clinical perspective, this is acceptable.*

From a statistical perspective, please include the following items for the phase 3 study in your NDA submission:

- (a) all raw and derived variables; if clinical data were not originally collected in SDTM format, you would need to submit raw data in the legacy format, as well as the detailed descriptions of mappings from the legacy to the SDTM format together with a document of variables definition;*
- (b) the SAS programs that produced all efficacy results (intended for labeling description);*
- (c) the SAS programs by which the derived variables were produced from the raw variables;*
- (d) a list of IND number with serial numbers and submission dates of the protocols, SAPs, amendments, and any relevant meetings.*

Pfizer pre-meeting response to Question 7:

- a) Pfizer confirms that the data was originally collected in SDTM format. There was no legacy mapping to SDTM format.
- b) The SAS programs that produced all efficacy results intended for labeling description can be provided.
- c) The analysis dataset SAS programs can be provided.
- d) The requested list will be included in the NDA

Discussion: *No further discussion.*

Question 8: The NDA submission will also include Clinical Study Reports (CSRs) for the two Phase 1 pilot studies listed below. Datasets for these pilot studies are not planned to be provided. Is this acceptable to the Agency?

- C11-0082/B7491002: “A Three-Way Pilot Relative Bioavailability Study Comparing Methylphenidate 40mg ER Chewable Tablets (Chewed and Swallowed Whole) Versus 25mg/5mL ER Suspension Under Fasted Conditions”
- C11-1200/S11-0154/B7491003: “A Relative Bioavailability Study of Two Formulations of Methylphenidate 40 mg ER Chewable Tablets Versus Methylphenidate 25 mg/5 mL ER Oral Suspension Under Fasted Conditions”

FDA Response to Question 8: *From a clinical perspective, this is acceptable.*

Pfizer pre-meeting response to Question 8: Is it also acceptable from the perspective of other FDA disciplines, such as Clinical Pharmacology and Biopharmaceutics that may refer to the information provided in these study reports?

Discussion: *No further discussion.*

2.5. In-vitro Studies

Question 9: An in-vitro assessment of the effect of alcohol has been conducted based on the request in the FDA [Study May Proceed letter dated June 11, 2012](#). Does the Agency agree that no further studies are necessary?

FDA Response to Question 9: *Yes.*

Pfizer pre-meeting response to Question 9: No further discussion of question 9 is necessary.

Discussion: *No further discussion.*

Question 10: Can the Agency comment as to whether it is sufficient to provide the alcohol study report through the Tris Pharma Drug Master File (DMF; 025909), with a complementary summary in the NDA?

FDA Response to Question 10: *Please submit the report on the alcohol dose-dumping studies in the NDA. Include in the report the justification for not conducting an additional in-vivo pharmacokinetic study upon observation of different degrees of dose dumping at the 20% and 40% alcohol concentrations.*

Pfizer pre-meeting response to Question 10: We would like to propose that the in vitro study on the effect of alcohol be provided in the DMF due to the partnership relationship between Pfizer and Tris Pharma. In addition, we would like to discuss the justification for not conducting an additional in-vivo pharmacokinetic study and confirm that our proposal will meet FDA's expectations.

Discussion:

Biopharmaceutics

It was agreed at the meeting that the sponsor may provide the report on in-vitro alcohol dose dumping studies in the DMF.

Office of Clinical Pharmacology

The sponsor indicated that they plan to describe the in vitro alcohol dose dumping study results under clinical pharmacology section and recommend in the label that the chewable tablet not be used with alcohol. The proposal is acceptable to the Agency.

2.6. Non-Clinical Studies

Question 11: The Sponsor has not conducted non-clinical studies with the drug substance methylphenidate HCl. Please confirm that the Division does not require any non-clinical studies in support of a 505(b)(2) NDA submission and filing acceptance for methylphenidate HCl ERCT.

FDA Response to Question 11: *On face, we agree. However, we remind you that any new impurities, inactive ingredients, excipients, or degradants might require qualification.*

Pfizer pre-meeting response to Question 11: We do not anticipate further discussion on this question. There are no new impurities, inactive ingredients, excipients or degradants that might require qualification.

Discussion: *No further discussion.*

2.7. Clinical Pharmacology

Question 12: The Sponsor notes the request for partial AUC data (i.e., “optimal partial AUC metric for bioequivalence (BE) by determining, via simulations using typical BE-type study designs”) in the Agency’s letter dated June 11, 2012. The Sponsor also notes that the requested information is not required for registration. In response, the Sponsor proposes to submit the following:

- a. Study 2012-2950/B7491004: “A Three-Way Crossover Relative Bioavailability Study Comparing Methylphenidate HCl Extended-Release Chewable Tablets and MethylinTM Chewable Tablets under Fasting Conditions and Determining the Effect of Food on 40 mg Methylphenidate ER Chewable Tablets”, which will be submitted in the NDA, includes the following partial AUC data: AUC_{0-0.5}, AUC₀₋₂, AUC₀₋₃, and AUC₀₋₄. Are these data sufficient to satisfy the request for partial AUC data (i.e., “optimal partial AUC metric for BE by determining, via simulations using typical BE-type study designs”) or will additional data still be requested?
- b. If additional specific partial AUC data are requested, it is proposed that it be submitted post-NDA submission as an informational document to the Agency. Is this acceptable to the Agency?
- c. Can the FDA clarify how the data will be used?

FDA Response to Question 12: *a) The data should be sufficient.*

b) If additional specific partial AUC data are requested, they can be submitted post-NDA filing.

c) These data will be used to compare the bioequivalence of the original product to that resulting from any process/formula changes done to the product in the future.

Pfizer pre-meeting response to Question 12: Pfizer does not anticipate discussion of Question 12.

Discussion: *No further discussion.*

Question 13: In the Study May Proceed Letter dated June 11, 2012 the FDA noted additional Phase 1 studies may be required depending on the results of the bioavailability study (PMRI Study Number: 2012-2950/B7491004). Specifically, it was noted that “if the BA of the ER chewable tablet is significantly different from the dose corrected immediate-release (IR), then buccal absorption of the ER product may have to be further investigated.” Results of the BA Study 2012-2950/B7491004 showed that systemic exposure was similar between the methylphenidate HCl ERCT versus Methylin™ IR at equivalent daily doses. Therefore we consider that the buccal absorption study is not required. Does the FDA concur?

FDA Response to Question 13: *If the review of study Number: 2012-2950/B7491004 indeed shows that systemic exposure is similar between the methylphenidate HCl ERCT versus Methylin™ IR at equivalent daily doses, then the buccal absorption study will not be required.*

Pfizer pre-meeting response to Question 13: Pfizer does not anticipate discussion of Question 13.

Discussion: *No further discussion.*

Question 14: In the same Study May Proceed Letter (June 11, 2012), the FDA also noted that depending upon the results of the BA study, a single dose pharmacokinetic (PK) study with the ER product may be required in the target pediatric population. The Sponsor plans to reference results of the pediatric pharmacokinetic study conducted using the Quillivant XR® powder for oral suspension formulation (NDA 202100), which is a methylphenidate HCl product that utilizes similar ER formulation technology to that present in the ERCT and the result of the BA Study 2012-2950/B7491004.

Does the FDA concur that the single dose PK study in the pediatric population (6-17 years) using the ERCT is not required for this submission (please see justification see Question 14 section 8.7.3)?

FDA Response to Question 14: *The acceptability of the results of comparative in vitro dissolution profiles of the chewable tablets and the suspension, which are graphically depicted in the Briefing Document, is a review issue. In addition, note that the dissolution data will be deemed meaningful only after the dissolution method has been assessed and found to be robust, properly validated and shown to be discriminating. Please submit all individual vessel dissolution data for the final clinical formulation and the suspension as part of the dissolution method development report within the NDA. Refer to the Additional*

Biopharmaceutics Comments following Question #21 for details on the dissolution data and information to be included in your NDA.

Pfizer pre-meeting response to Question 14: Pfizer would like to discuss this topic. We propose that the dissolution method development and validation be submitted prior to the NDA submission and would like to request that the dissolution method development and validation be reviewed early, if possible. We would like to confirm that no pediatric PK studies with ERCT are required assuming that the dissolution data and method are deemed acceptable.

Discussion:

Biopharmaceutics

The Agency clarified that validation of the dissolution method is critical since comparative dissolution data will be used to support a waiver for a bioavailability study in the pediatric population. The sponsor stated that the dissolution method development report will be submitted approximately 2 months before NDA filing. The Agency recommended that the report should be submitted to both the IND and the NDA; review of the dissolution data package will continue in the NDA if review within the IND is not completed prior to NDA filing.

Office of Clinical Pharmacology

The sponsor plans to use in vitro dissolution data in combination with a relative BA study using a pilot formulation to justify that the chewable tablet can be administered (b) (4) after chewing. The Agency indicated that, in general, the instructions for administration in the label should be consistent with the clinical trials, which, in this program, is after chewing. A pharmacokinetic study is typically required if the sponsor plans to allow alternative ways for dosing. If the sponsor believes that they can make a case based on the existing information to justify alternative route for administration, it is advised that all relevant information be submitted under NDA.

Question 15: The FDA Study May Proceed Letter dated June 11, 2012 mentions the conduct of a study to examine the impact of swallowing the tablet intact with water versus being chewed. The following data are available that indicate that the tablet can be taken either chewed or swallowed: 1) PK comparison of chewed vs swallowed from the pilot study C11-0082/B7491002 and 2) in-vitro studies on the effects of hardness and grinding on drug release (data provided in Sequence 002, DMF 025909, (b) (4) Study Report). Would these data be acceptable to allow the label to indicate that the tablet can be taken either chewed or swallowed?

FDA Response to Question 15: *The acceptability of the results of the in vivo and in vitro investigations regarding the mode of administration is a review issue. Please provide in the NDA, if available, the validation data for (b) (4) which were investigated in the in vitro experiments.*

Pfizer pre-meeting response to Question 15: If time allows, we would like to discuss Question 15. Pfizer would like to clarify that the anticipated location of the data will be in the DMF with summary in NDA, given the nature of the collaborative agreement between Pfizer and Tris Pharma. If these results are deemed acceptable (b) (4) ?

Discussion: *The Agency agreed that results of the in vitro and in vivo studies may be included in the DMF. The Agency also recommended that validation of the (b) (4) process should be considered and reported in the NDA.*

2.8. Clinical Safety

Question 16: Does the Agency agree that the safety data of the four studies mentioned in this briefing document (i.e., the Phase 1 BA study, the 2 pilot PK studies, and the pivotal Phase 3 study), which the Sponsor proposes for inclusion in the NDA appear sufficient to support review of the NDA?

FDA Response to Question 16: *Yes.*

Pfizer pre-meeting response to Question 16: Pfizer does not anticipate any further discussion of this topic.

Discussion: *No further discussion.*

2.9. Abuse Liability

Question 17: The safety profile of methylphenidate HCl is a well-characterized Schedule II controlled substance. The Sponsor plans to use labeling, including a Medication Guide, to mitigate abuse and dependence. As with all of the Sponsor's products, the Sponsor will conduct routine pharmacovigilance to monitor the methylphenidate HCl ERCT product. Does the FDA have any comments or recommendations regarding this proposal?

FDA Response to Question 17: *We have no comments or recommendations at this time.*

Pfizer pre-meeting response to Question 17: Pfizer does not anticipate any further discussion of this topic.

Discussion: *No further discussion.*

2.10. Regulatory

Question 18: A tabular listing of the overall proposed electronic table of contents of the NDA is included. Does this appear acceptable and complete to the Agency?

FDA Response to Question 18: *From a technical standpoint (not content-related) yes, the proposed format for the planned NDA is acceptable however, please see additional comments below:*

- 1.6.3 Correspondence regarding meetings – a single PDF file can be provided (instead of separate PDF files for each document) with proper bookmarks of all correspondence, table of contents and hyperlinks*
- The tabular listing in module 5.2 and synopsis of individual studies in m2.7.6 (tabular format), should be linked to the referenced studies in m5.*
- To submit the descriptive portion (only) of a post marketing report in eCTD format, it should be provided as a single PDF file with bookmarks, table of contents and hyperlinks in eCTD section, m5.3.6. Please ensure that the leaf title of the report includes the reporting period, since each report is for a specific time period.*

Sponsors options of cross referencing information submitted to another application would be to either place a cross reference document under module m1.4.4 (cross reference to other applications), or use cross application links.

- 1. To use the first option (placing a cross reference document in m1.4.4), a table formatted document can be submitted in section m1.4.4 of the eCTD, detailing previously submitted information (eCTD and/or non- eCTD) that is being referenced by the current application. The information in the document should include (1) the application number, (2) the date of submission (e.g., letter date), (3) the file name, (4) the page number (if necessary), (5) the eCTD sequence number, (6) the eCTD heading location (e.g., m1.14.1.1– Specifications), (7) the document leaf title and (8) the submission identification (e.g., submission serial number, volume number, electronic folder, file name, etc.) of the referenced document along with a hypertext link to the location of the information, when possible.*
- 2. To use the second option (cross application links), both applications would need to be in eCTD format and reside on the same server. The applications need to include the appropriate prefix in the href links (e.g. nda, ind.). Also, when cross application links are used, it's strongly recommended that a cross reference document be placed in m1.4.4, in case any of the links don't work. In the leaf titles of the documents, it is recommended that the leaf title indicate the words “cross reference to” and also include the application number (e.g. Cross Ref to/from NDA123456). That way, reviewers would know that the document resides in another application which is being referenced in the leaf title. Prior to using cross application linking in an application, it is recommended that sponsor submits an "eCTD cross application links" sample, to ensure successful use of cross application linking.*

To submit an eCTD cross application links sample, sponsor would need to request two sample application numbers from the ESub team - esub@fda.hhs.gov.

For more information on eCTD sample, please refer to the Sample Process web page which is located at

<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm174459.htm>

Pfizer pre-meeting response to Question 18: With regards to bullet 3 ‘post-marketing report’ we do not anticipate including this section within the MPH ERCT NDA as this formulation is not approved or marketed anywhere in the world. Therefore we would not include section m5.3.6 in the proposed NDA.

Pfizer will use the first option (placing a cross reference document in m1.4.4).

Discussion: *No further discussion.*

Question 19: Under Prescription Drug User Fee Act (PDUFA) V, New Molecular Entities (NMEs) have a 2 month evaluation period for acceptability, followed by a 10 month user fee period. Since PDUFA indicates these evaluations for acceptability apply only to NMEs, does this mean that the methylphenidate HCl ERCT will simply have the standard non-NME NDA 10 month review period (ie, no 2 month acceptability evaluation)?

FDA Response to Question 19: *Yes.*

Pfizer pre-meeting response to Question 19: Pfizer does not anticipate any further discussion of this topic.

Discussion: *No further discussion.*

2.11. General

Question 20: The Sponsor believes that it has addressed all outstanding Agency questions and feedback regarding this submission. Does the FDA concur?

FDA Response to Question 20: *From a clinical perspective, yes.*

Pfizer pre-meeting response to Question 20: Are there any outstanding Agency questions or feedback from the perspective of other FDA disciplines with the exception of those outlined with regards to other questions herein?

Discussion: *No further discussion.*

Question 21: Does the Agency have any additional feedback or recommendations on the Sponsor’s proposed methylphenidate HCl ERCT NDA submission for the indication described?

FDA Response to Question 21: *No.*

Pfizer pre-meeting response to Question 21: The above comments are clear, and no further detailed discussion of dissolution is anticipated at the meeting, however, as noted in Question

14, Pfizer would like to outline the proposal for early review of the dissolution data and methodology.

Discussion: *No further discussion.*

Additional Biopharmaceutics Comments:

The presentation of dissolution data for your proposed drug product in the Briefing Document is acknowledged. Since your dissolution method development report was not evaluated in the IND stage, please take the following general guidelines into consideration for the dissolution data and information to be provided in the NDA:

- A. Dissolution Test:*** *Include the dissolution method development report supporting the selection of the proposed dissolution test. The dissolution report should include the following information:*
- i. Solubility data for the drug substance over the physiologic pH range;*
 - ii. Detailed description of the dissolution test being proposed for the evaluation of your product and the developmental parameters (i.e., selection of the equipment/apparatus, in vitro dissolution/release media, agitation/rotation speed, pH, assay, sink conditions, etc.) used to select the proposed dissolution method as the optimal test for your product. If a surfactant was used, include the data supporting the selection of the type and amount of surfactant. The testing conditions used for each test should be clearly specified. The dissolution profile should be complete and cover at least 85% of drug release of the label amount or whenever a plateau (i.e., no increase over three consecutive time-points) is reached. We recommend use of at least twelve samples per testing variable;*
 - iii. Provide the complete dissolution profile data (individual, mean, SD, profiles) for your product. The dissolution data should be reported as the cumulative percentage of drug dissolved with time (the percentage is based on the product's label claim)*
 - iv. Data to support the discriminating ability of the selected method. In general, the testing conducted to demonstrate the discriminating ability of the selected dissolution method should compare the dissolution profiles of the reference (target) product vs. the test products that are intentionally manufactured with meaningful variations for the most relevant critical manufacturing variables (i.e., ± 10 -20% change to the specification-ranges of these variables). In addition, if available, submit data showing that the selected dissolution method is able to reject batches that are not bioequivalent; and*
 - v. Include the supportive validation data for the dissolution method (i.e., method robustness, etc.) and analytical method (precision, accuracy, linearity, stability, etc.).*
- B. Dissolution Acceptance Criteria:*** *For the selection of the dissolution acceptance criteria of your product, the following points should be considered:*
- i) The dissolution profile data from the pivotal clinical batches and primary (registration) stability batches should be used for the setting of the dissolution*

acceptance criteria of your product (i.e., specification-sampling time point and specification value).

- ii) The acceptance criteria should be established based on average in vitro dissolution data for each lot under study, equivalent to USP Stage 2 testing (n=12).*
- iii) A minimum of three time points is recommended to set the specifications. These time points should cover the early, middle, and late stages of the release profile. The last time point should be the time point where at least 80% of drug is released. If the maximum amount released is less than 80%, the last time point should be the time when the plateau of the release profile has been reached.*
- iv) In general, the selection of the dissolution acceptance criteria ranges is based on mean target value $\pm 10\%$ and $\geq 80\%$ for the last specification time-point. Wider specification ranges may be acceptable if they are supported by an approved IVIVC model.*

3.0 PREA REQUIREMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Please be advised that under the Food and Drug Administration Safety and Innovation Act (FDASIA), you must submit an Initial Pediatric Study Plan (PSP) within 60 days of an End of Phase (EOP2) meeting. In the absence of an End-of-Phase 2 meeting, refer to the draft guidance below. The PSP must contain an outline of the pediatric study or studies that you plan to conduct (including, to the extent practicable study objectives and design, age groups, relevant endpoints, and statistical approach); any request for a deferral, partial waiver, or waiver, if applicable, along with any supporting documentation, and any previously negotiated pediatric plans with other regulatory authorities. The PSP should be submitted in PDF and Word format.

For additional guidance on the timing, content, and submission of the PSP, including a PSP Template, please refer to the draft guidance for industry, *Pediatric Study Plans: Content of and Process for Submitting Initial Pediatric Study Plans and Amended Pediatric Study Plans* at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM360507.pdf>. In addition, you may contact the Pediatric and Maternal Health Staff at 301-796-2200 or email pdit@fda.hhs.gov. For further guidance on pediatric product development, please refer to: <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm049867.htm>.

4.0 **PRESCRIBING INFORMATION**

In your application, you must submit proposed prescribing information (PI) that conforms to the content and format regulations found at 21 [CFR 201.56\(a\) and \(d\)](#) and [201.57](#). As you develop your proposed PI, we encourage you to review the labeling review resources on the [PLR Requirements for Prescribing Information](#) website including:

- The Final Rule (Physician Labeling Rule) on the content and format of the PI for human drug and biological products
- Regulations and related guidance documents
- A sample tool illustrating the format for Highlights and Contents, and
- The Selected Requirements for Prescribing Information (SRPI) – a checklist of 42 important format items from labeling regulations and guidances.

Prior to submission of your proposed PI, use the SRPI checklist to ensure conformance with the format items in regulations and guidances.

5.0 **MANUFACTURING FACILITIES**

To facilitate our inspectional process, we request that you clearly identify *in a single location*, either on the Form FDA 356h, or an attachment to the form, all manufacturing facilities associated with your application. Include the full corporate name of the facility and address where the manufacturing function is performed, with the FEI number, and specific manufacturing responsibilities for each facility.

Also provide the name and title of an onsite contact person, including their phone number, fax number, and email address. Provide a brief description of the manufacturing operation conducted at each facility, including the type of testing and DMF number (if applicable). Each facility should be ready for GMP inspection at the time of submission.

Consider using a table similar to the one below as an attachment to Form FDA 356h. Indicate under Establishment Information on page 1 of Form FDA 356h that the information is provided in the attachment titled, “Product name, NDA/BLA 012345, Establishment Information for Form 356h.”

Site Name	Site Address	Federal Establishment Indicator (FEI) or Registration Number (CFN)	Drug Master File Number (if applicable)	Manufacturing Step(s) or Type of Testing [Establishment function]
1.				
2.				

Corresponding names and titles of onsite contact:

Site Name	Site Address	Onsite Contact (Person, Title)	Phone and Fax number	Email address
1.				
2.				

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/s/

MITCHELL V Mathis
10/30/2014



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 207960

**PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE**

Pfizer Inc
235 East 42nd Street
New York, NY 10017-5755

ATTENTION: Lisha Cole, MSc, MBA
Director, US Regulatory Cluster Lead
Worldwide Safety and Regulatory

Dear Ms. Cole:

Please refer to your New Drug Application (NDA) dated and received February 04, 2015, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Methylphenidate Hydrochloride, Extended-release Chewable Tablets 20 mg, 30 mg, and 40 mg.

We also refer to:

- Your correspondence dated and received July 17, 2015, requesting review of your proposed proprietary name, (b) (4)
- Your amendment, dated and received July 30, 2015, submitting the proprietary name safety summary report
- Your amendment, dated and received September 09, 2015, providing updated container labeling reflecting the recommended text regarding distribution of medication guides
- Our October 07, 2015, teleconference requesting that you submit an amendment to your proposed proprietary name (b) (4)
- Your amendment, dated and received October 09, 2015, requesting review of your proposed proprietary name, QuilliChew ER

We have completed our review of the proposed proprietary name, QuilliChew ER and have concluded that it is conditionally acceptable.

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

If you require information on submitting requests for proprietary name review or PDUFA performance goals associated with proprietary name reviews, we refer you to the following:

- Guidance for Industry Contents of a Complete Submission for the Evaluation of Proprietary Names
(<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM075068.pdf>)
- PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2013 through 2017,
(<http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM270412.pdf>)

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Vasantha Ayalasomayajula, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at 240-402-5035. For any other information regarding this application, contact Hiren Patel, Regulatory Project Manager in the Office of New Drugs, at 301-796-2087.

Sincerely,

{See appended electronic signature page}

Todd Bridges, RPh
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

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/s/

TODD D BRIDGES
10/15/2015

Patel, Hiren

From: Patel, Hiren
Sent: Monday, September 14, 2015 3:58 PM
To: Cole, Lisha (Lisha.Cole@pfizer.com)
Subject: NDA 207960

Importance: High

Dear Lisha,

We note that the proposed drug product does not meet the USP <1151> definition of a 'chewable tablet' as the tablets can be either chewed or swallowed whole whereas USP defines a chewable tablet as one that must be chewed. Therefore the dosage form designation in the established name should be "extended release tablets" rather than "extended release chewable tablets". With regards to the "[DRUG]" portion of the established name, it would be misleading if the product was called "methylphenidate hydrochloride extended release tablets" as the USP monograph definition of such a product requires that it "contain NLT 90.0% and NMT 110.0% of the labeled amount of methylphenidate hydrochloride" - the proposed product contains 15% methylphenidate hydrochloride. An appropriate alternative would be to use the established name "methylphenidate extended release tablets". Note that in order to be in accordance with the Agency guidance "Naming of Drug Products Containing Salt Drug Substances" the primary labeled strength would need to be in terms of methylphenidate free base, rather than the hydrochloride salt. In addition, the name and amount of each of the components (as well as an equivalency statement for the methylphenidate hydrochloride component) will need to appear elsewhere on the label and in the labeling.

Therefore we recommend that the drug product's established name be "methylphenidate extended release tablets" with the dosage strength in terms of methylphenidate free base.

Regards,

Hiren

*Hiren D. Patel, Pharm.D., M.S., RAC
LCDR USPHS
Senior Regulatory Health Project Manager
Division of Psychiatry Products
Center For Drug Evaluation and Research, FDA
Office of Drug Evaluation I
Ph: (301) 796-2087
Email: hiren.patel@fda.hhs.gov*

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/s/

HIREN PATEL
09/15/2015



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 207960

**PROPRIETARY NAME REQUEST
UNACCEPTABLE**

Pfizer Inc
235 East 42nd Street
New York, NY 10017-5755

ATTENTION: Lisha Cole, MSc, MBA
Director, US Regulatory Cluster Lead
Worldwide Safety and Regulatory

Dear Ms. Cole:

Please refer to your New Drug Application (NDA) dated and received February 04, 2015, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Methylphenidate HCl, Extended-release Chewable Tablets 20 mg, 30 mg, and 40 mg.

We also refer to:

- Your correspondence dated and received March 13, 2015, requesting review of your proposed proprietary name, (b) (4)
- Our email, dated March 30, 2015, requesting clarification of the strengths
- Your amendment, dated and received March 31, 2015, clarifying the strengths

We have completed our review of the proposed proprietary name, (b) (4), and have concluded that this name is unacceptable for the following reasons:

(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.

If you require additional information on developing proprietary names for drugs, proposing alternative proprietary names for consideration, or requesting reconsideration of our decision, we refer you to the following:

- Draft Guidance for Industry Best Practices in Developing Proprietary Names for Drugs, (<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM398997.pdf>)
- Guidance for Industry Contents of a Complete Submission for the Evaluation of Proprietary Names (<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM075068.pdf>)
- PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2013 through 2017, (<http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM270412.pdf>)

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Vasantha Ayalasomayajula, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (240) 402-5035. For any other information regarding this application, contact Hiren Patel, Regulatory Project Manager in the Office of New Drugs, at (301) 796-2087.

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

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/s/

TODD D BRIDGES
06/11/2015