

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

204767Orig1s000

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**



Fresenius Kabi USA, LLC

Three Corporate Drive
Lake Zurich, Illinois 60047
T 847-550-2300
T 888-391-6300
www.fresenius-kabi.us

11 August 2015

Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

RE: **NDA # 204767**
Acetaminophen Injection
10 mg/mL (Product Code 434050 and 434100)
Manufacturing Site: Ostfold, Norway (Halden)

PATENT AMENDMENT/RESPONSE
(SEQ-0019)

Dear Sir or Madam:

Reference is made to Fresenius Kabi USA, LLC's (FK USA) New Drug Application (NDA) submitted on 28 September 2012 for 10 mg/mL in accordance with Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act to seek marketing clearance for Acetaminophen Injection, 10 mg/mL.

Fresenius Kabi USA, LLC hereby submits this Patent Amendment in response to the *Agency's* comments within the attached **FDA Email-Update Request 05 aug 2015**. The following list of attachments is supplied in this response and should answer all of the questions regarding the patent and litigation status for NDA 204767 adequately:

ORDER OF DISMISSAL OF CASE NO. 13-CV-00139 DMS (MDD)

The litigation is now dismissed, and Fresenius Kabi USA, LLC has a license to launch its product before patent expiration.

This electronic submission contains a file size of approximately 40 MB. This electronic submission is certified as virus-free: scanned using Symantec™ Endpoint Protection with a virus definition current at the time of submission and is being sent through the Electronic Submissions Gateway (ESG).

Should you have any questions regarding this filing, please feel free to contact the undersigned or Andrea Redd, Director, Regulatory Affairs, at (847) 550-5767.

Sincerely,

Michelle Lemaire
Senior Regulatory Specialist
Fresenius Kabi USA, LLC
Phone: (847) 550-2687
Fax: (847) 550-7120
Email: Michelle.Lemaire@fresenius-kabi.com

From: Walker, Diana <Diana.Walker@fda.hhs.gov>
Sent: Wednesday, August 5, 2015 1:39 PM
To: Michelle.Lemaire@fresenius-kabi.com
Subject: NDA 204767 Update Request 05aug15

Dear Michelle,

Can you please update me as to whether there have been any changes in your patent or litigation status for this application? Since this current resubmission is from April 2015, and the latest information submitted as a Patent Amendment/Notice of Litigation is from December 2012 and February of 2013, I just wanted to check with you to confirm that you are in the same status and to see if you can provide an update on the litigation.

Warm regards,
Diana

Diana L. Walker, Ph.D.
Sr. Regulatory Health Project Manager
FDA/CDER/ODE II/DAAAP
Tel: 301-796-4029
Fax: 301-796-9723/9713
Email: Diana.Walker@fda.hhs.gov

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**UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF CALIFORNIA**

CADENCE PHARMACEUTICALS,
INC., SCR PHARMATOP &
MALLINCKRODT IP,

Plaintiffs,

v.

FRESENIUS KABI USA LLC.,
Defendant.

CASE NO. 13-CV-00139 DMS (MDD)

ORDER OF DISMISSAL

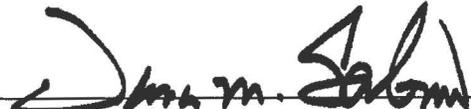
(Doc. No. 328)

AND RELATED COUNTERCLAIMS

1 Pursuant to Rule 41(a)(2) of the FEDERAL RULES OF CIVIL PROCEDURE and
2 the joint motion of Plaintiffs, Cadence Pharmaceuticals, Inc., SCR Pharmatop and
3 Mallinckrodt IP, and Defendant Fresenius Kabi USA, LLC (collectively, “the
4 Parties”), it is hereby ORDERED that all claims, counterclaims, defenses and any
5 pending motions in the above-styled action as between the Parties, are dismissed
6 with prejudice. The Parties shall bear their own fees and costs.

7 **IT IS SO ORDERED.**

8
9 Dated: August 8, 2014


HON. DANA M. SABRAW
U.S. DISTRICT COURT JUDGE

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1.3.5.2 Patent Certification (Acetaminophen Injection, 10 mg/mL, Solution for Infusion)

**1.3.5 Patent Certification and Exclusivity Statement
(Acetaminophen Injection, 10 mg/mL, Solution for
Infusion)**

1.3.5.2 Patent Certification

Fresenius Kabi USA, LLC (FK USA) is submitting a Paragraph IV patent certification with this 505(b)(2) NDA. Based on the *Electronic Orange Book Approved Drug Products with Therapeutic Equivalence Evaluations*, there are unexpired patents and exclusivities for the reference listed drug (Ofirmev™) for which FK USA is the applicant.

The **PATENT AND EXCLUSIVITY CERTIFICATION** from FK USA is attached.

Fresenius Kabi USA, LLC

1501 E. Woodfield Road
Suite 300 East
Schaumburg, Illinois 60173
T 847-969-2700
T 888-391-6300
www.fresenius-kabi.us

PATENT CERTIFICATION AND EXCLUSIVITY STATEMENT

Paragraph IV Certification:

In accordance with Section 505(b)(2)(A)(iv) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 355), 21 C.F.R. § 314.50(i)(1)(A)(4) and based on the patent data in “Approved Drug Products with Therapeutic Equivalence Evaluations” current through September, 2012 (the Orange Book), Fresenius Kabi USA, LLC (FK USA) hereby provides this Paragraph IV Patent Certification for its 505(b)(2) New Drug Application # 204767 for Acetaminophen Injection (10 mg/mL).

Fresenius Kabi USA, LLC (FK USA) hereby certifies that in its opinion and to the best of its knowledge, U.S. Patent No. 6,028,222 is invalid, unenforceable, and/or will not be infringed by the manufacture, use, or sale of Acetaminophen Injection (10 mg/mL), for which this 505(b)(2) New Drug Application # 204767 is submitted. This patent will expire on August 5, 2017.

FK USA also certifies that in its opinion and to the best of its knowledge, U.S. Patent No. 6,992,218 is invalid, unenforceable, and/or will not be infringed by the manufacture, use, or sale of Acetaminophen Injection (10 mg/mL), for which this 505(b)(2) New Drug Application # 204767 is submitted. This patent will expire on June 6, 2021.

In accordance with Section 505(b)(3)(A) and 21 C.F.R. § 314.52(a), FK USA further certifies that upon receipt of acknowledgement from the FDA concerning acceptance for review of this submission, appropriate notice regarding this “Paragraph IV” certification, as required under Section 505(b)(3)(D) and 21 C.F.R. § 314.52(c) with respect to content, will be provided to:

- (I) each owner of the patent that is the subject of the certification, or the representative of such owner designated to receive such notice, and
- (II) the holder (Cadence Pharmaceuticals) of the approved application under section 505(b), specifically New Drug Application # 022450, for the listed drug that is claimed by the patent or a use of which is claimed by the patent or the representative of such holder designated to receive such notice.

Exclusivity Statement:

Fresenius Kabi USA, LLC (FK USA) acknowledges that there is an exclusivity (NP) in effect until November 2, 2013 with respect to the Ofirmev™ drug product which has been referenced by FK USA in this NDA. FK USA certifies that its Acetaminophen Injection (10 mg/mL) drug product will not be marketed until said exclusivity has expired.

Fresenius Kabi USA, LLC

By:  9-17-2012
Dale Carlson, Senior Director Date
Regulatory Affairs



12 December 2012

Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

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Re: NDA # 204767
Acetaminophen Injection
10 mg/mL (Product Codes 434050 and 434100)
Manufacturing Site: Fresenius Kabi Norge AS
Østfold, Norway

**PATENT AMENDMENT
DOCUMENTATION OF NOTIFICATION/RECEIPT NOTICE
(SEQ-0001)**

Dear Sir/Madam:

Reference is made to the Fresenius Kabi USA, LLC (FK USA) New Drug Application (NDA) # 204767 for Acetaminophen Injection submitted 28 September 2012 (SEQ-0000). Additional reference is made to FK USA's "Paragraph IV" patent certification as found in SECTION 1.3.5.2 of SEQ-0000.

FK USA hereby submits this Patent Amendment to NDA # 204767 in accordance with 21 CFR § 314.95(b) to certify that notice regarding the "Paragraph IV" certification has been provided to each person identified under 21 CFR § 314.95(a), namely (1) each owner of the patent or the representative designated by the owner to receive notice; (2) the holder of the approved application under section 505(b) of the Act for the listed drug claimed by the patent and for which the applicant is seeking approval.

Pursuant to the requirements in 21 CFR § 314.95(a), notification has been provided to Cadence Pharmaceuticals (b) (4) via Federal Express (Fed Ex). Refer to the attached EMAIL CORRESPONDENCE from Iain Margand (FDA) where permission to use Fed Ex in lieu of the U.S. Postal Service was given.

Furthermore, FK USA certifies that the Paragraph IV certification notice provided to the patent and NDA holders included all applicable content requirements under 21 CFR § 314.95(c).

In accordance with 21 CFR 314.95(e), enclosed are copies of proof of delivery confirmations to verify the receipt of the aforementioned Paragraph IV certification notices by the patent and NDA holders. The notice was received by CADENCE PHARMACEUTICALS on 6 December 2012 (b) (4).

Patent Amendment – Documentation of Notification/Receipt Notice
NDA # 204767 (SEQ-0001)
Acetaminophen Injection
12 December 2012
Page 2 of 2

This electronic submission contains a file size of approximately 2 MB. This submission is certified as virus-free: Scanned using Symantec Endpoint Protection using virus definition Tuesday, December 11, 2012 r19.

Please NOTE that this original application is being sent through the Electronic Submissions Gateway (ESG).

Should you have any questions or require additional information concerning this application, please do not hesitate to contact the undersigned or Surendera Tyagi, Executive Vice President, IV Drugs and Standard Solutions, Region North America, at (847) 706-2088.

Sincerely,



Aditi Dron
Regulatory Affairs Manager
Fresenius Kabi USA, LLC
847.330.3898 (Phone)
847.413.8570 (Fax)
Aditi.Dron@fresenius-kabi.com

cc: BY

From: Margand, Iain [mailto:Iain.Margand@fda.hhs.gov]
Sent: Wednesday, December 05, 2012 3:09 PM
To: Sklar, Steven
Cc: Shimer, Martin
Subject: RE: NDA No. 204767 (Acetaminophen Injection, 10 mg/mL)

Good Afternoon Mr. Sklar,

It is permissible to use FedEx in lieu of the US Postal Service to send PIV notices to the patent holder(s) and/or assignee(s) in reference to ANDA 204767.

Regards,

Iain

Iain Margand, RPh
Senior Regulatory Management Officer
Regulatory Support Branch
Office of Generic Drugs
FDA/CDER/DLPS
240-276-8676

From: Sklar, Steven [mailto:ssklar@leydig.com]
Sent: Wednesday, December 05, 2012 2:22 PM
To: Margand, Iain
Subject: FW: NDA No. 204767 (Acetaminophen Injection, 10 mg/mL)
Mr. Margand,

I understand that Mr. Shimer is traveling this week. Would it be possible to get your authorization to use FedEx courier as indicated in my e-mail below? Thank you for your prompt attention to this request.

Steve

Steven H. Sklar | **Leydig, Voit & Mayer, Ltd.**
Attorney at Law | Intellectual Property
Two Prudential Plaza, Suite 4900 | Chicago, IL 60601-6731
P: (312) 616-5600 | F: (312) 616-5700
ssklar@leydig.com | www.leydig.com

The information contained in this communication is confidential and may contain information that is privileged and/or exempt from disclosure under applicable law. If you have received this communication in error, please notify me immediately and delete the original and all copies of this communication. Thank you.

From: Sklar, Steven
Sent: Tuesday, December 04, 2012 8:41 AM
To: 'Martin Shimer (shimerm@cdcr.fda.gov)'; 'Shimer, Martin'
Subject: NDA No. 204767 (Acetaminophen Injection, 10 mg/mL)

Mr. Shimer,

On behalf of Fresenius Kabi USA, LLC (FK), the NDA-holder of NDA No. 204767 for acetaminophen injection, 10 mg/mL, we hereby request permission to send FK's notice of Paragraph IV certification,

pursuant to 21 U.S.C. 355(b)(3), to the New Drug Application holder Cadence Pharmaceuticals, Inc. and/or the patent holder [REDACTED] ^{(b) (4)} via FedEx courier in lieu of the U.S. postal system.

We look forward to hearing from you at your earliest convenience as this is a time sensitive request. If you have any questions, you can reach me at the number below. Thank you for your assistance.

Steve Sklar

Steven H. Sklar
Leydig, Voit & Mayer, Ltd.
Two Prudential Plaza, Suite 4900
Chicago, Illinois 60601-6780
Tel: (312) 616-5600
Fax: (312) 616-5700
E-mail: ssklar@leydig.com
Website: www.leydig.com

The information contained in this communication is confidential and may contain information that is privileged and/or exempt from disclosure under applicable law. If you have received this communication in error, please notify me immediately and delete the original and all copies of this communication. Thank you.



FedEx Express
Customer Support Trace
3875 Airways Boulevard
Module H, 4th Floor
Memphis, TN 38116

U.S. Mail: PO Box 727
Memphis, TN 38194-4643
Telephone: 901-369-3600

December 6, 2012

Dear Customer:

The following is the proof-of-delivery for tracking number 794230130018.

Delivery Information:

Status:	Delivered	Delivered to:	Receptionist/Front Desk
Signed for by:	[Redacted] (b) (4)		
Service type:	Priority Envelope	Delivery date:	Dec 6, 2012 09:27

[Redacted] (b) (4)

Shipping Information:

Tracking number:	794230130018	Ship date:	Dec 5, 2012
		Weight:	0.5 lbs/0.2 kg

Recipient:
Hazel M. Aker, Senior Vice Pres.
Cadence Pharmaceuticals, Inc.
12481 High Bluff Drive
Suite 200
SAN DIEGO, CA 92130 US
Reference

Shipper:
Steven H. Sklar
Leydig, Voit & Mayer
180 N. Stetson Ave.
Chicago, IL 60601 US

271366

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Signed for by: C.F SIGNATURE

Shipment Dates

Ship date Dec 5, 2012

Delivery date Dec 7, 2012 3:15 PM

Destination

LE CHESNAY FR

Proof of Delivery

Shipment Facts

Service type	Priority Envelope	Delivered to	Receptionist/Front Desk
Weight	1.0 lbs/ 5 kg	Reference	271366

Shipment Travel History

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All shipment travel activity is displayed in local time for the location

Date/Time	Activity	Location	Details
Dec 7, 2012 3:15 PM	Delivered	LE CHESNAY FR	
Dec 7, 2012 1:29 PM	On FedEx vehicle for delivery	TRAPPES FR	
Dec 7, 2012 12:11 PM	Delivery exception	TRAPPES FR	Customer not available or business closed
Dec 7, 2012 11:00 AM	Shipment exception	ROISSY EN FRANCE FR	Delay beyond our control
Dec 7, 2012 9:18 AM	On FedEx vehicle for delivery	TRAPPES FR	
Dec 7, 2012 8:38 PM	International shipment release -	PARIS FR	
Dec 7, 2012 8:38 PM	In transit	PARIS FR	Package available for clearance
Dec 6, 2012 6:36 PM	Arrived at FedEx location	PARIS FR	
Dec 6, 2012 4:34 AM	In transit	INDIANAPOLIS, IN	
Dec 6, 2012 3:15 AM	Departed FedEx location	INDIANAPOLIS, IN	
Dec 6, 2012 1:16 AM	Arrived at FedEx location	INDIANAPOLIS, IN	
Dec 5, 2012 9:45 PM	Left FedEx origin facility	CHICAGO, IL	
Dec 5, 2012 8:31 PM	Picked up	CHICAGO, IL	Tendered at FedEx Office
Dec 5, 2012 4:14 PM	Shipment information sent to FedEx		

EXCLUSIVITY SUMMARY

NDA # 204767

SUPPL #

HFD # 170

Trade Name: n/a

Generic Name: Acetaminophen for Injection, 10 mg/mL

Applicant Name: Fresenius Kabi USA, LLC

Approval Date, If Known: October 28, 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.

No new clinical pharmacology data were submitted in support of this application. The Applicant requested a waiver for in-vivo bioavailability/ bioequivalence studies. The proposed drug product is identical to the referenced drug with the exception of the concentration of the inactive ingredients and the elimination of the buffer from the product under review. The information submitted in support of the request was found adequate and the biowaiver is granted.

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?

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?

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# **022450** **Ofirmev (Cadence Pharmaceuticals), Acetaminophen for Injection**

NDA#

NDA#

2. Combination product.

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

YES NO

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

NDA#

NDA#

NDA#

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

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

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

YES NO

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

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

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

YES NO

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

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

YES NO

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

YES NO

If yes, explain:

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

YES NO

If yes, explain:

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

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

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

b) For each investigation identified as "essential to the approval", does the investigation

duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES NO

Investigation #2 YES NO

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

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

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

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

Investigation #1
IND # YES !
! NO
! Explain:

Investigation #2
IND # YES !
! NO
! Explain:

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/

DIANA L WALKER
10/28/2015

ELLEN W FIELDS
10/28/2015



Fresenius Kabi USA, LLC

1501 E. Woodfield Road
Suite 300 East
Schaumburg, Illinois 60173
T 847-969-2700
T 888-391-6300
www.fresenius-kabi.us

DEBARMENT CERTIFICATION

In compliance with the requirements of the Generic Drug Enforcement Act of 1992, Subsections (a) and (b) of Section 306, Fresenius Kabi USA, LLC hereby certifies that it did not and will not use in any capacity the services of any person debarred under Subsections (a) and (b) of Section 335a of the Federal Food, Drug, and Cosmetic Act in connection with this 505(b)(2) NDA for Acetaminophen Injection.

A handwritten signature in black ink, appearing to be "JC", written over a horizontal line.

James Callanan, Vice President
Human Resources

9/14/12
Date

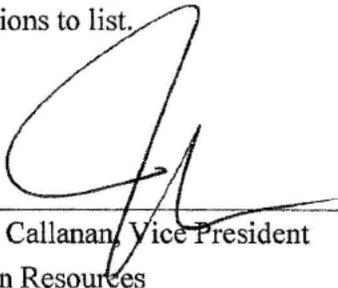


Fresenius Kabi USA, LLC

1501 E. Woodfield Road
Suite 300 East
Schaumburg, Illinois 60173
T 547-969-2700
T 888-391-6300
www.fresenius-kabi.us

CONVICTIONS LISTING CERTIFICATION

Fresenius Kabi USA, LLC hereby certifies that it has not been convicted within the last five years of any crimes described in Subsections (a) and (b) of Section 335a of the Federal Food, Drug, and Cosmetic Act. In compliance with the requirements of the Generic Drug Enforcement Act of 1992, Subsections (a) and (b) of Section 306, Fresenius Kabi USA, LLC hereby certifies that it has not used in any capacity the services of any person who has been convicted within the last five years of any crimes described in Subsections (a) and (b) of Section 335a of the Federal Food, Drug, and Cosmetic Act in connection with this 505 (b) (2) NDA for Acetaminophen Injection. Therefore, Fresenius Kabi USA, LLC has no convictions to list.



James Callanan, Vice President
Human Resources

9/14/12
Date

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 204767 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: N/A Established/Proper Name: Acetaminophen for Injection, 10 mg/mL Dosage Form: Sterile (b) (4) Solution for Infusion		Applicant: Fresenius Kabi USA, LLC Agent for Applicant (if applicable):
RPM: Diana Walker		Division: DAAAP
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 style="text-align: center;"><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 style="margin-left: 20px;"> <input checked="" type="checkbox"/> No changes <input type="checkbox"/> New patent/exclusivity <i>(notify CDER OND IO)</i> Date of check: 10/20/2015 </p> <p style="margin-left: 20px;"><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 October 30, 2015, Action date is October 28, 2015 		<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 type="checkbox"/> None CR – July 25, 2013
❖ 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.

Review priority: Standard Priority
 Chemical classification (new NDAs only): Type 5 – New Formulation or New Manufacturer
 (*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 (<i>approvals only</i>)	<input type="checkbox"/> Yes <input type="checkbox"/> No
❖ Public communications (<i>approvals only</i>)	
• 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)? • If so, specify the type	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
❖ 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 (<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>	Actions and dates: CR: July 25, 2013 Approval: October 28, 2015
---	---

Labeling

❖ Package Insert <i>(write submission/communication date at upper right of first page of PI)</i>	
--	--

- Most recent draft labeling *(if it is division-proposed labeling, it should be in track-changes format)* Included
- Original applicant-proposed labeling 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 *(if it is division-proposed labeling, it should be in track-changes format)* Included
- Original applicant-proposed labeling 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 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> 	N/A No Proprietary Name review requested.
---	--

❖ Labeling reviews <i>(indicate dates of reviews)</i>	RPM: <input type="checkbox"/> None DMEPA: <input type="checkbox"/> None June 5, 2013 June 11, 2015 July 9, 2015 DMPP/PLT (DRISK): <input checked="" type="checkbox"/> None OPDP: <input type="checkbox"/> None 5/17/2013 10/2/2015 SEALD: <input checked="" type="checkbox"/> None CSS: <input checked="" type="checkbox"/> None Product Quality <input checked="" type="checkbox"/> None Other: <input checked="" type="checkbox"/> None
---	--

Administrative / Regulatory Documents

❖ RPM Filing Review ⁴ /Memo of Filing Meeting <i>(indicate date of each review)</i>	November 23, 2012
❖ All NDA 505(b)(2) Actions: Date each action cleared by 505(b)(2) Clearance Committee	<input type="checkbox"/> Not a (b)(2) Cleared -September 22, 2015 Dated – October 28, 2015

❖ NDAs only: Exclusivity Summary <i>(signed by Division Director)</i>	<input checked="" type="checkbox"/> Included
---	--

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

❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	
<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
❖ Pediatrics (<i>approvals only</i>) <ul style="list-style-type: none"> • Date reviewed by PeRC <i>n/a</i> If PeRC review not necessary, explain: PREA does not apply. 	
❖ Breakthrough Therapy Designation	<input checked="" type="checkbox"/> N/A
<ul style="list-style-type: none"> • Breakthrough Therapy Designation Letter(s) (granted, denied, an/or rescinded) 	
<ul style="list-style-type: none"> • CDER Medical Policy Council Breakthrough Therapy Designation Determination Review Template(s) (<i>include only the completed template(s) and not the meeting minutes</i>) 	
<ul style="list-style-type: none"> • 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>) <p>(<i>completed CDER MPC templates can be found in DARRTS as clinical reviews or on the MPC SharePoint Site</i>)</p>	
❖ 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>)	Included.
❖ 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)	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>) 	<input checked="" type="checkbox"/> N/A or no mtg
<ul style="list-style-type: none"> • Pre-NDA/BLA meeting (<i>indicate date of mtg</i>) 	<input checked="" type="checkbox"/> No mtg
<ul style="list-style-type: none"> • EOP2 meeting (<i>indicate date of mtg</i>) 	<input checked="" type="checkbox"/> No mtg
<ul style="list-style-type: none"> • Mid-cycle Communication (<i>indicate date of mtg</i>) 	<input checked="" type="checkbox"/> N/A
<ul style="list-style-type: none"> • Late-cycle Meeting (<i>indicate date of mtg</i>) 	<input checked="" type="checkbox"/> N/A
<ul style="list-style-type: none"> • Other milestone meetings (e.g., EOP2a, CMC focused milestone meetings) (<i>indicate dates of mtgs</i>) 	N/A

❖ 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 checked="" type="checkbox"/> None
Division Director Summary Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None Cycle #1 - July 25, 2013 Cycle #2 – October 28, 2015
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
PMR/PMC Development Templates (<i>indicate total number</i>)	<input checked="" type="checkbox"/> None
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>)	Filing: November 20, 2012
• 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 checked="" type="checkbox"/> and include a review/memo explaining why not (<i>indicate date of review/memo</i>)	No clinical studies were submitted.
❖ 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 checked="" type="checkbox"/> N/A
❖ 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"/> None requested
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 checked="" type="checkbox"/> None	
❖ Statistical Division Director Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> No separate review
Statistical Team Leader Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> No separate review
Statistical Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None

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 type="checkbox"/> No separate review Final Memo – June 21, 2013
Clinical Pharmacology review(s) <i>(indicate date for each review)</i>	<input type="checkbox"/> None Filing – November 15, 2012
❖ 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 type="checkbox"/> No separate review June 21, 2013
• Pharm/tox review(s), including referenced IND reviews <i>(indicate date for each review)</i>	<input type="checkbox"/> None Filing – November 27, 2012 Review #1 – June 20, 2013 Review #2 – October 13, 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 Filing – November 27, 2012 Review #1 – June 21, 2013 Review #2 – October 26, 2015
❖ Reviews by other disciplines/divisions/Centers requested by product quality review team <i>(indicate date of each review)</i>	<input type="checkbox"/> None Biopharmaceutics Filing – November 27, 2012 Final – June 17, 2013 Microbiology Filing – November 15, 2012 Final – June 7, 2013
❖ 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>	See CMC Review #1, page 62, dated June 21, 2013
<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</i>) (<i>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 (October 22, 2015) Re-evaluation date: <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable

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>)
❖ For products that need to be added to the flush list (generally opioids): Flush List <ul style="list-style-type: none"> • Notify the Division of Online Communications, Office of Communications 	<input 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 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 type="checkbox"/> Done
❖ Ensure Pediatric Record is accurate	<input type="checkbox"/> Done
❖ Send approval email within one business day to CDER-APPROVALS	<input checked="" type="checkbox"/> Done

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/s/

DIANA L WALKER
10/29/2015

From: [Walker, Diana](#)
To: Michelle.Lemaire@fresenius-kabi.com
Subject: NDA 204767 Proposed Label Revisions 20Oct15
Date: Tuesday, October 20, 2015 12:27:58 PM
Attachments: [Working draft-pi-track changes 20Oct15.doc](#)

Dear Michelle,

I am attaching the Package Insert label for NDA 204767. We have made some minor format revisions to the references in the Black Box in both Highlights and the Full Prescribing section. The only other revision would be the issued date, which would change if/when approved.

Please review these proposed revisions, and if you agree, please send me your concurrence via email. There is no need to resubmit revised labeling at this time; email concurrence is adequate. If you do happen to notice any typos, etc., while you are reviewing the label, please let me know so we can make the corrections.

Warm regards,

Diana

Diana L. Walker, Ph.D.
Sr. Regulatory Health Project Manager
FDA/CDER/ODE II/DAAAP
Tel: 301-796-4029
Fax: 301-796-9723/9713
Email: Diana.Walker@fda.hhs.gov

18 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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/s/

DIANA L WALKER
10/23/2015

From: [Walker, Diana](mailto:Walker.Diana)
To: Michelle.Lemaire@fresenius-kabi.com
Cc: Andrea.Redd@fresenius-kabi.com
Subject: NDA 204767 Container Labeling Revision Request 22Jun15
Date: Monday, June 22, 2015 10:49:54 AM

Dear Ms. Lemaire,

I have received comments concerning your labeling. Please respond to this comment with a submission to your NDA 204767 of revised draft container labeling.

A. (b) (4) **LABELING**

Remove the (b) (4) strength presentation “1,000 mg” located to the right of the primary strength presentation from the principal display panel (b) (4)

If you have any questions for the DMEPA review team regarding this request or wish to discuss this requested change, please contact me.

Warm regards,
Diana

Diana L. Walker, Ph.D.
Sr. Regulatory Health Project Manager
FDA/CDER/ODE II/DAAAP
Tel: 301-796-4029
Fax: 301-796-9723/9713
Email: Diana.Walker@fda.hhs.gov

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/s/

DIANA L WALKER
07/08/2015



NDA 204767

**ACKNOWLEDGE –
CLASS 2 RESUBMISSION**

Fresenius Kabi USA, LLC
Three Corporate Drive
Lake Zurich, Illinois 60047

Attention: Michelle Lemaire
Senior Specialist, Regulatory Affairs

Dear Ms. Lemaire:

We acknowledge receipt on April 30, 2015, of your resubmission to your new drug application submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Acetaminophen Injection, 10 mg/mL.

We also refer to your December 12, 2014, resubmission, responding to our July 25, 2013, action letter, and to the Incomplete Response letter sent to you from FDA dated December 23, 2014.

We consider this a complete, class 2 response to our July 25, 2013, action letter. Therefore, the user fee goal date is October 30, 2015.

If you have any questions, call me at (301) 796-4029.

Sincerely,

{See appended electronic signature page}

Diana L. Walker, Ph.D.
Sr. Regulatory Health Project Manager
Division of Anesthesia, Analgesia, and
Addiction Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

DIANA L WALKER
05/08/2015



NDA 204767

ACKNOWLEDGE INCOMPLETE RESPONSE

Fresenius Kabi USA, LLC
Three Corporate Drive
Lake Zurich, Illinois 60047

Attention: Michelle Lemaire
Senior Specialist, Regulatory Affairs

Dear Ms. Lemaire:

We acknowledge receipt on December 12, 2014, of your resubmission to your new drug application for Acetaminophen Injection, 10 mg/mL.

We do not consider this a complete response to our July 25, 2013, action letter. Therefore, we will not start the review clock until we receive a complete response. The following deficiency from our action letter still needs to be addressed:

PRODUCT QUALITY

2. The leachable study data that you have submitted, 6 months at three different storage conditions and 12 months (b) (4)

You have not submitted leachable data at the 18-month and 24 month time points, for several targeted compounds that were previously quantitated in Tables 3.2.P2-17 and 19 of the NDA submission, up to 6 and 12 months. These include (b) (4)

To resolve this deficiency, submit data for the identified leachables as specified above at the 18-month and 24-month time points for all stability batches at long-term storage conditions for the 100 mL fill volume of the freeFlex (b) (4) container closure system.

If you have questions, call Diana Walker, PhD, Senior Regulatory Health Project Manager, at (301) 796-4029.

Sincerely,

{See appended electronic signature page}

Sharon Hertz, MD
Acting Director
Division of Anesthesia, Analgesia, and
Addiction Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

SHARON H HERTZ
12/23/2014

From: [Walker, Diana](#)
To: Aditi.Dron@fresenius-kabi.com
Subject: NDA 204767 Package Insert Label Revisions 27Jun13
Date: Thursday, June 27, 2013 11:08:06 AM
Attachments: [NDA 204767 APAP -Working-draft-pi to Sponsor 27June13 .pdf](#)
[NDA 204767 APAP -Working-draft-pi to Sponsor 27June13 .doc](#)

Dear Ms Dron,

Please find attached the Division's proposed revisions to the package insert label for your pending NDA 204767 for acetaminophen injection, both PDF and Word (in track changes). Please review these revisions. For those revisions with which you agree, please "accept" the change. If you do not agree with a particular revision, please indicate your proposed wording and insert a comment as to your rationale (again, please use track changes). Please return to me a Word document (still in track changes) with your revisions. For formatting changes (such as extra spaces between words, paragraph alignment, etc) you can also accept those changes prior to sending me back the Word document. Please send me your responses as soon as possible.

Note that some of the revisions we are sending you, such as the Box Warning, are to align your label with the listed drug, Ofirmev.

Please let me know if you have any questions and I will be happy to assist you.

Warm regards,

Diana

Diana L. Walker, Ph.D.
Sr. Regulatory Health Project Manager
FDA/CDER/ODE II/DAAAP
Tel: 301-796-4029
Fax: 301-796-9723/9713
Email: Diana.Walker@fda.hhs.gov

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/s/

DIANA L WALKER
06/27/2013

From: [Walker, Diana](#)
To: Aditi.Dron@fresenius-kabi.com
Subject: NDA 204767 Acetaminophen Injection Carton and Container Information Request 26jun13
Date: Wednesday, June 26, 2013 2:17:23 PM
Importance: High

Dear Ms. Dron,

Our CMC review team has sent me an additional request for information regarding your NDA 204767 container (b) (4) labeling. Please respond to the following request/comment via email, followed by an official submission to your NDA. Mock-ups are acceptable. You can (and should, if possible), combine this response with our previous request concerning your container and pouch labeling sent to you on June 10, 2013.

Container Label (b) (4)

Delete the following statement:

“(b) (4)”

If you have any questions about this request, please feel free to contact me.

Warm regards,

Diana

Diana L. Walker, Ph.D.
Regulatory Health Project Manager
FDA/CDER/ODE II/DAAAP
Tel: 301-796-4029
Fax: 301-796-9723/9713
Email: Diana.Walker@fda.hhs.gov

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/s/

DIANA L WALKER
06/26/2013



NDA 204767

DISCIPLINE REVIEW LETTER

Fresenius Kabi USA, LLC
Three Corporate Drive
Lake Zurich, IL 60047

Attention: Aditi Dron
Manager, Regulatory Affairs

Dear Ms. Dron:

Please refer to your September 28, 2012, New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Acetaminophen Injection, 10 mg/mL.

We also refer to your amendments dated December 27, 2012, and February 4 and 22, March 13 and 29, and April 17, 2013.

Our reviews of the Nonclinical and the Chemistry, Manufacturing, and Controls (CMC) sections of your submission are complete, and we have identified the following deficiencies:

1. [REDACTED] (b) (4)
Therefore, provide additional leachable data at 18-month and 24-month time points for all stability batches at long-term storage condition for the 100 mL fill volume of the freeflex [REDACTED] (b) (4) container closure system.
2. You have not provided adequate safety justification for the levels of [REDACTED] (b) (4) leachables from the container closure system. To resolve this deficiency:
 - a. Submit the results of the proposed 4-week IV toxicology study of [REDACTED] (b) (4) and a revised toxicological risk assessment.
 - b. Conduct and submit the results of a 4-week IV toxicology study of [REDACTED] (b) (4) and a revised toxicological risk assessment for this compound. Alternatively, you may be able to provide adequate data to support your conclusion that [REDACTED] (b) (4) is virtually instantaneous in vivo such that exposure to the parent compound, when the product is used as directed, would not occur and your risk assessment based on the major metabolites alone is adequate to address the safety of the parent compound.

3. Your application referenced the Master File (MF) 26696. This MF was found inadequate to support your submission and a deficiency letter was sent to the MF holder on June 24, 2013.

In addition, although not required for NDA approval, we have the following comments:

1. Once you have evaluated the levels of leachables in the drug product over the course of the entire intended shelf-life, you must submit revised risk assessments based on the worst-case exposures. Final determination of the adequacy of your leachables safety assessment can only be provided upon review of the definitive stability data.
2. You have proposed to complete in vitro bacterial reverse mutation studies (Ames tests) for both [REDACTED] (b)(4). The final reports for these studies are not required for approval. However, when the studies have been completed, the results should be submitted to the NDA.

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 or 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 Diana L. Walker, PhD, Sr. Regulatory Health Project Manager, at (301) 796-4029.

Sincerely,

{See appended electronic signature page}

Parinda Jani
Chief, Project Management Staff
Division of Anesthesia, Analgesia, and
Addiction Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

PARINDA JANI
06/26/2013

Walker, Diana

From: Walker, Diana
Sent: Monday, June 10, 2013 4:00 PM
To: Aditi.Dron@fresenius-kabi.com
Subject: NDA 204767 Acetaminophen Injection DMEPA Information Request 10jun13

Importance: High

Dear Ms. Dron,

Our Division of Medication Error Prevention and Analysis (DMEPA) review team has sent me a request for information regarding your NDA 204767 container (b) (4) labeling. Please respond to the following requests/comments via email, followed by an official submission to your NDA. Mock-ups are acceptable.

Container Label and Outer pouch Labeling

- 1. Delete the following statements to minimize clutter and to improve the overall readability of the label:** (b) (4)
- 2. Delete the extraneous numbers from the container label. These numbers clutter the label and are not useful to the user:** (b) (4)
(all located at bottom of container label). If the numbers cannot be deleted, then attempt to decrease their prominence, and relocate the number directly to the right of the NDC to the lower portion of the label.
- 3. Relocate the inactive ingredient list to appear directly following the “Single Use Only, Discard Unused Portion” statements on the principal display panel.**
- 4. Relocate the statements which begin with “Single Use Only, Discard Unused Portion” to appear just below the boxed statement “For Intravenous Use Only”.**
- 5. Delete the** (b) (4)
- 6. Add the following statement on the 1000 mg per 100 mL label “Doses less than 1000 mg require aseptic transfer to a separate container prior to dispensing”. Locate this after the Usual Dosage statement.**
- 7. Revise the statement “Injection” to the same font style as the active ingredient, Acetaminophen. The italics give unnecessary prominence to this dosage form.**
- 8. Revise the strength presentation to appear in a stacked format as follows:**

1000 mg/100 mL
(10 mg/mL)

If you have any questions about this request, please feel free to contact me.

Warm regards,

Diana

Diana L. Walker, Ph.D.
Regulatory Health Project Manager
FDA/CDER/ODE II/DAAAP
Tel: 301-796-4029
Fax: 301-796-9723/9713
Email: Diana.Walker@fda.hhs.gov

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/s/

DIANA L WALKER
06/10/2013

From: [Walker, Diana](#)
To: Aditi.Dron@fresenius-kabi.com
Subject: NDA 204767 Acetaminophen Injection Information Request 10Jun13
Date: Monday, June 10, 2013 10:22:09 AM
Importance: High

Dear Ms. Dron,

Our review team has sent me a request for information regarding your NDA 204767. Please respond to the following request no later than June 12, 2013, via email, followed by an official submission to your NDA.

Submit the chemical structure and CAS number for (b) (4).

If you have any questions about this request, please feel free to contact me.

Warm regards,

Diana

Diana L. Walker, Ph.D.
Regulatory Health Project Manager
FDA/CDER/ODE II/DAAAP
Tel: 301-796-4029
Fax: 301-796-9723/9713
Email: Diana.Walker@fda.hhs.gov

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/s/

DIANA L WALKER
06/10/2013



NDA (b) (4)/NDA 010417
NDA 016297/NDA 204767

**ACKNOWLEDGE CORPORATE
ADDRESS CHANGE**

Fresenius Kabi USA, LLC
Three Corporate Drive
Lake Zurich, IL 60047

Attention: Dale Carlson
Senior Director, Regulatory Affairs

Dear Mr. Carlson:

We acknowledge receipt on of your April 26, 2013, correspondence notifying the Food and Drug Administration (FDA) that the corporate address has been changed from

Fresenius Kabi USA, LLC
1501 East Woodfield Road
Suite 300E
Schaumburg, IL 60173

to

Fresenius Kabi USA, LLC
Three Corporate Drive
Lake Zurich, IL 60047

for the following new drug applications (NDAs):

NDA #	Indication and Dosage Form
(b) (4)	(b) (4)
NDA 010417	Xylocaine Topical
NDA 016297	Xylocaine in 7.5% Dextrose Injection
NDA 204767	Acetaminophen Injection

We have revised our records to reflect this change.

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 Anesthesia, Analgesia, and Addiction Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you have any questions, call me at (301) 796-4029.

Sincerely,

{See appended electronic signature page}

Diana L. Walker, Ph.D.
Regulatory Health Project Manager
Division of Anesthesia, Analgesia, and
Addiction Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

DIANA L WALKER
05/20/2013



NDA 204767

INFORMATION REQUEST

Fresenius Kabi USA, LLC
Attention: Aditi Dron
Manager Regulatory Affairs
Three Corporate Drive
Lake Zurich, Illinois 60047

Dear Ms. Dron:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Acetaminophen Injection, 10mg/mL, sterile (b) (4) solution.

We also refer to your May 7, 2013, submission, containing the environment impact analysis.

We have reviewed the environment impact analysis of your submission and have the following comments and information requests. We request a written response by **Friday, May 17, 2013** in order to continue our evaluation of your NDA.

You provided the incorrect CFR citation for your claim of categorical exclusion. The correct CFR citation is 21CFR 25.31(b). You also need to provide the following statement per 21CFR25.15(d), unless "extraordinary circumstances" as defined at 21CFR25.21, exist:

To the applicant's knowledge, no extraordinary circumstances exist.

Revise the section with the correct CFR citation and statement. Submit the revised section to the NDA.

If you have any questions, call LCDR Luz E Rivera, Regulatory Project Manager, at (301) 796-4013.

Sincerely,

{See appended electronic signature page}

Prasad Peri, Ph.D.
Branch Chief, Branch VIII
Division of New Drug Quality Assessment III
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

PRASAD PERI
05/13/2013



NDA 204767

INFORMATION REQUEST

Fresenius Kabi USA, LLC
Attention: Aditi Dron
Manager Regulatory Affairs
Three Corporate Drive
Lake Zurich, Illinois 60047

Dear Ms. Dron:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Acetaminophen Injection, 10mg/mL, sterile (b) (4) solution.

We are reviewing the Chemistry, Manufacturing and Control section of your submission and have the following comments and information requests. We request a written response by **Tuesday, May 7, 2013** in order to continue our evaluation of your NDA.

- You claimed a categorical exclusion from the requirement of an environmental impact analysis. However, you did not provide any estimate of highest yearly quantity of acetaminophen to be marketed in the US. Per FDA “Guidance for Industry: Environmental Assessment of Human Drug and Biologics Applications (July 1998)”, you need to provide a calculation for the highest yearly quantity of acetaminophen in the five coming years to be marketed in the US.

If you have any questions, call LCDR Luz E Rivera, Regulatory Project Manager, at (301) 796-4013.

Sincerely,

{See appended electronic signature page}

Prasad Peri, Ph.D.
Branch Chief, Branch VIII
Division of New Drug Quality Assessment III
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

PRASAD PERI
04/29/2013



NDA 204767

INFORMATION REQUEST

Fresenius Kabi USA, LLC
Attention: Aditi Dron
Manager Regulatory Affairs
1501 East Woodfield Road, Suite 300E
Schaumburg, Illinois 60173

Dear Ms. Dron:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Acetaminophen Injection, 10mg/mL, sterile (b) (4) solution.

We are reviewing the Chemistry, Manufacturing and Control section of your submission and have the following comments and information requests. We request a written response by **Friday, March 22, 2013** in order to continue our evaluation of your NDA.

1. Clarify if the test method for absorbance is a Ph. Eur. Compendia method (list method number) or an internal test method. Provide method description and validation results if it is an internal method. Revise the drug product specification accordingly.
2. In your light sensitivity study for the drug product, assay and impurities were not tested for one of the study batches (batch PP1121029C – Table 3.2.P.2-11). Provide test results for this batch or provide justifications as why these quality attributes were not tested for this specific batch.

If you have any questions, call LCDR Luz E Rivera, Regulatory Project Manager, at (301) 796-4013.

Sincerely,

{See appended electronic signature page}

Prasad Peri, Ph.D.
Branch Chief, Branch VIII
Division of New Drug Quality Assessment III
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

PRASAD PERI
03/14/2013

From: [Walker, Diana](mailto:Walker.Diana)
To: Aditi.Dron@fresenius-kabi.com
Subject: NDA 204767 - (b) (4) Samples - Follow-up Information Request 30Jan13
Date: Wednesday, January 30, 2013 4:09:06 PM
Attachments: [fk-draft \(b\) \(4\).pdf](#)
Importance: High

Dear Ms. Dron,

I have received the following comment and request for further information from our DMEPA (Division of Medication Error Prevention and Analysis) reviewers.

The sample (b) (4) provided do not have sufficient information on them for us to review. Attached is the container label that was submitted September 28, 2012. The sample (b) (4) should represent the product to be introduced in the marketplace in EVERY WAY and should include (at the least) the information on the container label as submitted by the Applicant.

Since the risk of confusion and medication errors depends upon the user's interaction with the product and their interpretation of the information (b) (4) we need to review the same package of Acetaminophen Injection as that which would be used by a healthcare practitioner. Additionally, we would like to review this sample (b) (4) prior to its mass production.

Please submit 6 to 8 sample (b) (4) that represent in EVERY WAY the product that the Applicant proposes to introduce into the marketplace.

You can send the sample (b) (4) directly to me, as you sent the previous samples. The review team would like to receive these samples as soon as possible, as the Mid-Cycle meeting for this application will take place at the end of February, and the DMEPA review group would like to see the (b) (4) provide comments as close to the Mid-Cycle meeting as possible.

Please feel free to contact me if you have any questions about this request.

Warm regards,

Diana

Diana L. Walker, Ph.D.
Regulatory Health Project Manager
FDA/CDER/ODE II/DAAAP
Tel: 301-796-4029
Fax: 301-796-9723/9713
Email: Diana.Walker@fda.hhs.gov

From: Aditi.Dron@fresenius-kabi.com [<mailto:Aditi.Dron@fresenius-kabi.com>]
Sent: Monday, January 28, 2013 4:48 PM
To: Walker, Diana
Subject: Acetaminophen NDA 204767 - (b) (4) Samples

Dear Ms. Walker:

Per the Agency's request received on December 17, 2012, Fresenius Kabi USA, LLC has sent total

six(6) Freeflex (b) (4) samples in support of our NDA 204767 for Acetaminophen Injection via FedEx today.

Please note the following details regarding the samples provided:

- 3 freeflex (b) (4)
- 3 freeflex (b) (4)

(b) (4)

The tracking number of the FedEx package is 7946 1830 1944. It is expected to be delivered to your office tomorrow (1/29/13).

Should you have any questions or require additional samples, please do not hesitate to contact me.

Sincerely,

Aditi Dron

Manager, Regulatory Affairs

Fresenius Kabi USA, LLC
1501 East Woodfield Road, Suite 300 East
Schaumburg, Illinois 60173
T: +1 (847) 330-3898
F: +1 (847) 413-8570
www.fresenius-kabi.us

THIS TRANSMISSION CONTAINS INFORMATION INTENDED FOR THE EXCLUSIVE USE OF THE INDIVIDUAL OR ENTITY TO WHOM IT IS ADDRESSED, AND MAY CONTAIN INFORMATION THAT IS PROPRIETARY, PRIVILEGED, CONFIDENTIAL, AND/OR OTHERWISE EXEMPT FROM DISCLOSURE UNDER APPLICABLE LAW. If you are not the intended recipient (or agent responsible for delivering this transmission to the intended recipient), you are hereby notified that any review, printing, copying, disclosure, distribution, transmission or use of this information (including any attachments) is strictly prohibited and may be subject to legal sanction. If you have received this transmission in error, please permanently delete it, and notify us immediately. Thank you.

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/s/

DIANA L WALKER
03/05/2013

From: [Walker, Diana](#)
To: Aditi.Dron@fresenius-kabi.com
Subject: NDA 204767 Acetaminophen Injection CMC Information Request 28Feb13
Date: Thursday, February 28, 2013 4:25:27 PM
Importance: High

Dear Ms. Dron,

Our CMC/Microbiology review team has sent me a request for information regarding your NDA 204767. Please respond to the following request no later than March 29, 2013, with an official submission to your NDA.

(b) (4) validation study S 11 01.00R used the 100 mL freeflex® (b) (4) filled with (b) (4) the acetaminophen drug product. Provide a rationale that the use of (b) (4) acetaminophen is valid.

If you have any questions about this request, please feel free to contact me.

Warm regards,

Diana

Diana L. Walker, Ph.D.
Regulatory Health Project Manager
FDA/CDER/ODE II/DAAAP
Tel: 301-796-4029
Fax: 301-796-9723/9713
Email: Diana.Walker@fda.hhs.gov

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/s/

DIANA L WALKER
03/05/2013



NDA 204767

INFORMATION REQUEST

Fresenius Kabi USA, LLC
Attention: Aditi Dron
Manager, Regulatory Affairs
1501 East Woodfield Road, Suite 300 E
Schaumburg, Illinois 60173

Dear Mr. Dron:

Please refer to your New Drug Application (NDA) dated September 28, 2012 submitted under section 505(b) (2) of the Federal Food, Drug, and Cosmetic Act for Acetaminophen Injection 10 mg/ mL, sterile (b) (4) solution.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following comments and information requests. We request a response by **Friday, February 22, 2013** in order to continue our evaluation of your NDA.

- The 6 month leachable study results you provided in the NDA are not sufficient to support your proposed 24 month shelf-life for the drug product. Provide updated leachable study results to this NDA.

If you have any questions, call LCDR Luz E Rivera, Regulatory Project Manager, at (301) 796 4013.

Sincerely,

{See appended electronic signature page}

Prasad Peri, PhD
Branch Chief, Branch VIII
Division of New Drug Quality Assessment III
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

PRASAD PERI
02/13/2013

From: [Walker, Diana](#)
To: Aditi.Dron@fresenius-kabi.com
Subject: NDA 204767 Acetaminophen Injection Information Request 17Dec12
Date: Monday, December 17, 2012 10:48:03 AM

Dear Ms. Dron,

Our review team has asked that I request sample flexfree (b) (4) for review of your NDA 204767. Would you please send me 4 to 6 sample (b) (4) for our review?

You can send these to me at the following address:

Diana Walker, Regulatory Health Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
White Oak Building 22, Room: 3209
10903 New Hampshire Avenue
Silver Spring, Maryland

*Use zip code **20903** if shipping via United States Postal Service (USPS).*

*Use zip code **20993** if sending via any carrier other than USPS (e.g., UPS, DHL, FedEx).*

If you have any questions about this request, please feel free to contact me.

Warm regards,

Diana

Diana L. Walker, Ph.D.
Regulatory Health Project Manager
FDA/CDER/ODE II/DAAAP
Tel: 301-796-4029
Fax: 301-796-9723/9713
Email: Diana.Walker@fda.hhs.gov

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/s/

DIANA L WALKER
12/17/2012



NDA 204767

FILING COMMUNICATION

Fresenius Kabi USA, LLC
1501 East Woodfield Road
Suite 300E
Schaumburg, Illinois 60173

Attention: Aditi Dron
Manager, Regulatory Affairs

Dear Ms. Dron:

Please refer to your New Drug Application (NDA) dated and received September 28, 2012, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Acetaminophen Injection, 10 mg/mL.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Standard**. Therefore, the user fee goal date is July 28, 2013.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, mid-cycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by June 30, 2013.

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

1. Provide osmolalities of your proposed product and the referenced drug to ensure that the change in mannitol composition in the proposed product formulation with respect to the referenced drug has no significant impact on relative bioavailability. If the solution is not isotonic, provide justification for why any differences in osmolality between your drug product and the referenced drug product do not represent a safety concern.

2. The degradant (b) (4) which is also called (b) (4) in the drug product specification should be reduced to as low as technically feasible based on manufacturing capability.
3. Based on preliminary review of the NDA, it appears as though there are inadequate safety justifications for the systemic levels of all leachables from the container closure system for the intravenous route of administration. Specifically, there does not appear to be adequate safety justification for the following three identified leachables: (b) (4). Unless adequately justified otherwise, the IV safety of these three identified leachables from the container closure system should be qualified via an IV toxicology study that provides an adequate safety margin for the levels of these identified leachables that a person would be exposed to when treated with up to 4 grams of acetaminophen per day via this drug product formulation. The duration of such a toxicology study should be comparable to the predicted maximum duration proposed in your drug product labeling (i.e., up to 14 days duration).

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. If you respond to these issues during this review cycle, we may not consider your response before we take an action on your application.

As discussed in the teleconference between Fresenius Kabi USA, LLC representatives and the Agency on November 16, 2012, we anticipate the submission to CDER of a DMF for the *Freeflex*® (b) (4). Include in the DMF the Letter of Authorization, a complete description of the (b) (4) components, and any Letters of Authorization to additional supporting DMFs for packaging sub-components, if applicable.

PROMOTIONAL MATERIAL

You may request advisory comments on proposed introductory advertising and promotional labeling. Please submit, in triplicate, a detailed cover letter requesting advisory comments (list each proposed promotional piece in the cover letter along with the material type and material identification code, if applicable), the proposed promotional materials in draft or mock-up form with annotated references, and the proposed package insert (PI). Submit consumer-directed, professional-directed, and television advertisement materials separately and send each submission to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

Do not submit launch materials until you have received our proposed revisions to the package insert (PI), and you believe the labeling is close to the final version.

For more information regarding OPDP submissions, please see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>. If you have any questions, call OPDP at 301-796-1200.

REQUIRED PEDIATRIC ASSESSMENTS

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.

Because none of these criteria apply to your application, you are exempt from this requirement.

If you have any questions, call Diana L. Walker, PhD, Sr. Regulatory Health Project Manager, at (301) 796-4029.

Sincerely,

{See appended electronic signature page}

Bob A. Rappaport, M.D.
Director
Division of Anesthesia, Analgesia, and
Addiction Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

BOB A RAPPAPORT
12/04/2012



NDA 204767

NDA ACKNOWLEDGMENT

Fresenius Kabi USA, LLC
1501 East Woodfield Road
Suite 300E
Schaumburg, Illinois 60173

Attention: Aditi Dron
Manager, Regulatory Affairs

Dear Mr. Dron:

We have received your New Drug Application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: Acetaminophen Injection, 10 mg/mL

Date of Application: September 28, 2012

Date of Receipt: September 28, 2012

Our Reference Number: NDA 204767

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on November 27, 2012, in accordance with 21 CFR 314.101(a).

If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Failure to submit the content of labeling in SPL format may result in a refusal-to-file action under 21 CFR 314.101(d)(3). The content of labeling must conform to the content and format requirements of revised 21 CFR 201.56-57.

You are also responsible for complying with the applicable provisions of sections 402(i) and 402(j) of the Public Health Service Act (PHS Act) [42 USC §§ 282 (i) and (j)], which was amended by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No, 110-85, 121 Stat. 904).

The NDA number provided above should be cited 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 Anesthesia, Analgesia, and Addiction Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm>.

Secure email between CDER and applicants is useful for informal communications when confidential information may be included in the message (for example, trade secrets or patient information). If you have not already established secure email with the FDA and would like to set it up, send an email request to SecureEmail@fda.hhs.gov. Please note that secure email may not be used for formal regulatory submissions to applications.

If you have any questions, call me at (301) 796-4029.

Sincerely,

{See appended electronic signature page}

Diana L. Walker, Ph.D.
Sr. Regulatory Health Project Manager
Division of Anesthesia, Analgesia, and
Addiction Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

DIANA L WALKER
10/11/2012