

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

202832Orig1s000

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

EXCLUSIVITY SUMMARY

NDA # 202832

SUPPL #

HFD #

Trade Name N/A

Generic Name sodium chloride injection, USP, 0.9%

Applicant Name Medefil

Approval Date, If Known January 6, 2012

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES NO

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

505(b)(2)

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

YES NO

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

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

d) Did the applicant request exclusivity?

YES NO

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

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

YES NO

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

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

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

YES NO

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

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

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

YES NO

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

NDA# 18803

Sodium chloride 0.9% injection (Hospira)

NDA# 19-217 Sodium Chloride 0.9% in Plastic Container, Injectable Injection.
9MG/ML
NDA# 16-366 Sodium Chloride 0.9% in Plastic Container, Injectable Injection.
900MG/100 ML (see attached page for more examples)

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:

Investigation #2

!

YES

! NO

Explain:

! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES

NO

If yes, explain:

=====

Name of person completing form: Eunice Chung-Davies

Title: Regulatory Project Manager, DPARP

Date: December 20, 2011

Name of Office/Division Director signing form: Lydia Gilbert McClain

Title: Deputy Director, DPARP

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

Continued from Part 2 Number 1

NDA 16-677, Sodium Chloride 0.9% in Plastic Container, Injectable Injection. Multiple Strengths

NDA 17-427, Sodium Chloride 0.9% in Plastic Container, Solutions; Irrigation. 900MG/100ML

NDA 21-569, Sodium Chloride 0.9% in Plastic Container, Injectable Injection. Multiple Strengths

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

/s/

EUNICE H CHUNG-DAVIES
01/06/2012

LYDIA I GILBERT MCCLAIN
01/06/2012
Deputy Division Director

MEDEFIL, INC.



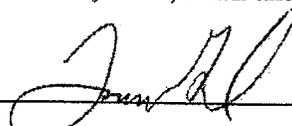
"Continuous improvement today for the
challenges of tomorrow"

Debarment Certification

As required by the Section 306 of the Federal Food, Drug and Cosmetic Act, Medefil, Inc., 250 Windy Point Drive, Glendale Heights, IL. 60139, certifies that the company and its principals have not been debarred, suspended, proposed for debarment, declared ineligible, are not in the process of being debarred.

Medefil Inc. not and will not use in any capacity the services of any person debarred under subsections (a) or (b) [section 306(a) or (b)] of the Act, in connection with Medefil, Inc's application for Sodium Chloride Injection, USP Syringes (Medesal), 1 mL, 2 mL, 2.5 mL, 3 mL, 5 mL and 10 mL.

We are unaware of any convictions of crimes (as specified in section 306 (a) and (b) of the Act) within the previous five years for any Medefil, Inc. employees or affiliated company, or employees of the affiliated companies responsible for the development or submission of this new drug application [505(b)(2)] for Sodium Chloride Injection, USP Syringes (Medesal), 1 mL, 2 mL, 2.5 mL, 3 mL, 5 mL and 10 mL.



Quality Assurance Director
Medefil, Inc.

January 31, 2011

Date

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 202832 BLA #	NDA Supplement # BLA STN #	If NDA, Efficacy Supplement Type:
Proprietary Name: Established/Proper Name: sodium chloride 0.9% injection in plastic syringes Dosage Form: Injection		Applicant: Medefil Agent for Applicant (if applicable):
RPM: Eunice Chung-Davies		Division: Pulmonary, Allergy, and Rheumatology Products
<p>NDA: 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)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the 505(b)(2) Assessment or the Appendix to this Action Package Checklist.)</p>		<p>505(b)(2) Original NDAs and 505(b)(2) NDA supplements: Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s)):</p> <p>Sodium Chloride 0.9% injection in plastic containers (NDA 18803)</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p>The sponsor wishes to market this product in a plastic syringe (a previously 510 k approved product)</p> <p>If no listed drug, explain.</p> <p><input type="checkbox"/> This application relies on literature. <input type="checkbox"/> This application relies on a final OTC monograph. <input type="checkbox"/> Other (explain)</p> <p><u>Two months prior to each action, review the information in the 505(b)(2) Assessment and submit the draft to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.</u></p> <p><u>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</u></p> <p><input checked="" type="checkbox"/> No changes <input type="checkbox"/> Updated Date of check: January 5, 2012</p> <p>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.</p>
❖ Actions		
<ul style="list-style-type: none"> • Proposed action • User Fee Goal Date is <u>January 7, 2012</u> • Previous actions (<i>specify type and date for each action taken</i>) 		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR <input checked="" type="checkbox"/> None

¹ The **Application Information** section is (only) a checklist. The **Contents of Action Package** section (beginning on page 5) lists the documents to be included in the Action Package.

<p>❖ 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 _____</p>	<p><input type="checkbox"/> Received</p>
<p>❖ Application Characteristics²</p>	
<p>Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only): 3S</p> <p><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</p> <p>NDAs: Subpart H BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Accelerated approval (21 CFR 601.41) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) <input type="checkbox"/> Restricted distribution (21 CFR 601.42) Subpart I Subpart H <input type="checkbox"/> Approval based on animal studies <input type="checkbox"/> Approval based on animal studies</p> <p><input type="checkbox"/> Submitted in response to a PMR REMS: <input type="checkbox"/> MedGuide <input type="checkbox"/> Submitted in response to a PMC <input type="checkbox"/> Communication Plan <input type="checkbox"/> Submitted in response to a Pediatric Written Request <input type="checkbox"/> ETASU <input type="checkbox"/> REMS not required</p> <p>Comments:</p>	
<p>❖ BLAs only: Ensure <i>RMS-BLA Product Information Sheet for TBP</i> and <i>RMS-BLA Facility Information Sheet for TBP</i> have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)</p>	<p><input type="checkbox"/> Yes, dates</p>
<p>❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>
<p>❖ Public communications (<i>approvals only</i>)</p>	
<ul style="list-style-type: none"> • Office of Executive Programs (OEP) liaison has been notified of action 	<p><input type="checkbox"/> Yes <input checked="" type="checkbox"/> No</p>
<ul style="list-style-type: none"> • Press Office notified of action (by OEP) 	<p><input type="checkbox"/> Yes <input checked="" type="checkbox"/> No</p>
<ul style="list-style-type: none"> • Indicate what types (if any) of information dissemination are anticipated 	<p><input checked="" type="checkbox"/> None <input type="checkbox"/> HHS Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other</p>

² Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

❖ Exclusivity	
<ul style="list-style-type: none"> Is approval of this application blocked by any type of exclusivity? 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
<ul style="list-style-type: none"> NDA and BLAs: Is there existing orphan drug exclusivity for the “same” drug or biologic for the proposed indication(s)? <i>Refer to 21 CFR 316.3(b)(13) for the definition of “same drug” for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA/BLA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? <i>(Note that, even if the 10-year approval limitation period has not expired, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date 10-year limitation expires: _____
❖ Patent Information (NDAs only)	
<ul style="list-style-type: none"> Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions. 	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
<ul style="list-style-type: none"> Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent. 	21 CFR 314.50(i)(1)(i)(A) <input checked="" type="checkbox"/> Verified 21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii)
<ul style="list-style-type: none"> [505(b)(2) applications] If the application includes a paragraph III certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval). 	<input checked="" type="checkbox"/> No paragraph III certification Date patent will expire _____
<ul style="list-style-type: none"> [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). <i>(If the application does not include any paragraph IV certifications, mark “N/A” and skip to the next section below (Summary Reviews)).</i> 	<input checked="" type="checkbox"/> N/A (no paragraph IV certification) <input type="checkbox"/> Verified

- [505(b)(2) applications] For **each paragraph IV** certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation.

Answer the following questions for **each** paragraph IV certification:

- (1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification?

Yes No

(Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e)).

If "**Yes**," skip to question (4) below. If "**No**," continue with question (2).

- (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)?

Yes No

If "**Yes**," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip the rest of the patent questions.

If "**No**," continue with question (3).

- (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?

Yes No

(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)).

If "**No**," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.

- (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?

Yes No

If "**Yes**," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).

If "**No**," continue with question (5).

<p>(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?</p> <p>(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period).</p> <p><i>If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).</i></p> <p><i>If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.</i></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>
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CONTENTS OF ACTION PACKAGE

❖ Copy of this Action Package Checklist ³	January 6, 2012
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (<i>approvals only</i>)	<input checked="" type="checkbox"/> Included
Documentation of consent/non-consent by officers/employees	<input checked="" type="checkbox"/> Included
Action Letters	
❖ Copies of all action letters (<i>including approval letter with final labeling</i>)	Action(s) and date(s) January 6, 2012
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. If it is division-proposed labeling, it should be in track-changes format. 	January 3, 2012
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	

³ Fill in blanks with dates of reviews, letters, etc.

❖ 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
<ul style="list-style-type: none"> • Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format. 	
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	
❖ 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 	January 3, 2012
❖ 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>) 	July 27, 2011
❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>)	<input checked="" type="checkbox"/> RPM April 22, 2011 <input checked="" type="checkbox"/> DMEPA December 6, 2011 <input type="checkbox"/> DRISK <input checked="" type="checkbox"/> DDMAC October 19, 2011 <input type="checkbox"/> SEALD <input type="checkbox"/> CSS <input type="checkbox"/> Other reviews
Administrative / Regulatory Documents	
❖ Administrative Reviews (<i>e.g., RPM Filing Review⁴/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>)	April 22, 2011
❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte	<input type="checkbox"/> Not a (b)(2) December 20, 2011
❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment (<i>indicate date</i>)	<input type="checkbox"/> Not a (b)(2) January 5, 2012
❖ 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	
<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 _____ If PeRC review not necessary, explain: <u>This product does not trigger PREA because it is a drug-device combination rather than an drug-drug combination</u> • Pediatric Page/Record (<i>approvals only, must be reviewed by PERC before finalized</i>) 	<input type="checkbox"/> Included
❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent (<i>include certification</i>)	<input checked="" type="checkbox"/> Verified, statement is acceptable

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

❖ Outgoing communications (<i>letters (except action letters), emails, faxes, telecons</i>)	12/28/2011;12/20/2011;12/7/2011; 11/23/2011; 11/17/2011; 8/19/2011; 8/15/2011; 5/20/2011;5/2/2011; 3/16/2011; 3/7/2011
❖ Internal memoranda, telecons, etc.	1/4/2012
❖ Minutes of Meetings	
• Regulatory Briefing (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> No mtg
• 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 7/14/2008
• EOP2 meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> No mtg
• Other milestone meetings (e.g., EOP2a, CMC pilots) (<i>indicate dates of mtgs</i>)	
❖ Advisory Committee Meeting(s)	<input checked="" type="checkbox"/> No AC meeting
• Date(s) of Meeting(s)	
• 48-hour alert or minutes, if available (<i>do not include transcript</i>)	
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 1/6/2012
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	<input type="checkbox"/> None 12/22/2011
PMR/PMC Development Templates (<i>indicate total number</i>)	<input checked="" type="checkbox"/> None
Clinical Information⁵	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) (<i>indicate date for each review</i>)	N/A
• Clinical review(s) (<i>indicate date for each review</i>)	12/8/2011; 4/15/2011
• 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>)	See Division Director Summary
❖ 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"/> Not applicable
❖ Risk Management	
• REMS Documents and Supporting Statement (<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
❖ DSI Clinical Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	<input checked="" type="checkbox"/> None requested

⁵ Filing reviews should be filed with the discipline reviews.

Clinical Microbiology <input checked="" type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) <i>(indicate date for each review)</i>	<input type="checkbox"/> None
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"/> None
Statistical Team Leader Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
Statistical Review(s) <i>(indicate date for each review)</i>	<input type="checkbox"/> None 10/4/2011; 4/18/2011
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
Clinical Pharmacology Team Leader Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
Clinical Pharmacology review(s) <i>(indicate date for each review)</i>	<input type="checkbox"/> None 12/8/2011;4/14/2011
❖ DSI Clinical Pharmacology Inspection Review Summary <i>(include copies of DSI letters)</i>	<input checked="" type="checkbox"/> None
Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
• Supervisory Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
• Pharm/tox review(s), including referenced IND reviews <i>(indicate date for each review)</i>	<input type="checkbox"/> None 8/31/2011;5/23/2011;3/31/2011
❖ 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
❖ DSI Nonclinical Inspection Review Summary <i>(include copies of DSI letters)</i>	<input checked="" type="checkbox"/> None requested
Product Quality <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
• Branch Chief/Team Leader Review(s) <i>(indicate date for each review)</i>	<input type="checkbox"/> None See CDTL memo
• Product quality review(s) including ONDQA biopharmaceutics reviews <i>(indicate date for each review)</i>	<input type="checkbox"/> None 12/15/2011;12/9/2011; 4/15/2011
❖ Microbiology Reviews	<input type="checkbox"/> Not needed 10/31/2011
<input checked="" type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) <i>(indicate date of each review)</i>	
<input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (DMPQ/MAPCB/BMT) <i>(indicate date of each review)</i>	
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer <i>(indicate date of each review)</i>	<input type="checkbox"/> None 12/7/2011

❖ Environmental Assessment (check one) (original and supplemental applications)	
<input checked="" type="checkbox"/> Categorical Exclusion (<i>indicate review date</i>)(<i>all original applications and all efficacy supplements that could increase the patient population</i>)	See CMC Review dated 12/9/2011
<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"/> NDAs: Facilities inspections (include EER printout) (<i>date completed must be within 2 years of action date</i>) (<i>only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites⁶</i>)	Date completed: 12/15/2011 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable
<input type="checkbox"/> BLAs: TB-EER (<i>date of most recent TB-EER must be within 30 days of action date</i>) (<i>original and supplemental BLAs</i>)	Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
❖ NDAs: Methods Validation (<i>check box only, do not include documents</i>)	<input type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input checked="" type="checkbox"/> Not needed (per review)

⁶ I.e., a new facility or a change in the facility, or a change in the manufacturing process in a way that impacts the Quality Management Systems of the facility.

Appendix to Action Package Checklist

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

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

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

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

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

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

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

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

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

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/s/

EUNICE H CHUNG-DAVIES
01/06/2012



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

FACSIMILE TRANSMITTAL SHEET

DATE: December 28, 2011

To: Pradeep Aggarwal	From: Eunice Chung-Davies, RPM
Company: Medefil	Division of Pulmonary, Allergy, and Rheumatology Drug Products
Fax number: FAX (630) 681-9100	Fax number: 301-796-9728
Phone number: TEL (630) 682-4600	Phone number: 301-796-4006

Subject: NDA 202832 Labeling Comments

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

Comments: Please provide a response to the request.

Document to be mailed: YES xNO

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We have reviewed your email dated December 22, 2011 and have the following comments:

1.  (b) (4)
While it is acceptable to include CDRH device “labeling” on the back side of the CDER Sodium Chloride USP, 0.9% drug label, because CDER and CDRH labeling/instructions for use are considered as two separate documents which refer to two products (a device and drug) regulated by different entities, the CDRH device labeling information presented must be exactly that which was agreed to between you and CDRH and which is currently supplied with your normal saline flush syringes. Any modification of the instructions or labeling for the flushing indwelling catheters device use must be agreed to with CDRH.
2. We remind you of the comments regarding carton and container labeling which were conveyed to you on December 7, 2011 and December 20, 2011.

Submit revised labeling (word versions and pdf versions of the package insert and carton and container labeling) via email to Eunice.Chung-Davies@fda.hhs.gov by **noon on January 3, 2012**. The revised labeling must also be submitted officially to the NDA by January 4, 2012. If you have any questions, please contact Eunice Chung-Davies, Regulatory Project Manager, at 301-796-4006.

NDA 202832

Drafted by: ADurmowicz/28DEC2011
Initialed by: LJafari/28DEC2011
PPeri/28DEC2011
ADurmowicz/28DEC2011

Finalized by: EChung-Davies/28DEC2011

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/s/

EUNICE H CHUNG-DAVIES
12/28/2011



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

FACSIMILE TRANSMITTAL SHEET

DATE: December 20, 2011

To: Pradeep Aggarwal	From: Eunice Chung-Davies, RPM
Company: Medefil	Division of Pulmonary, Allergy, and Rheumatology Drug Products
Fax number: FAX (630) 681-9100	Fax number: 301-796-9728
Phone number: TEL (630) 682-4600	Phone number: 301-796-4006
Subject: NDA 202832 Comments	

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

Comments: Please provide a response to the request.

Document to be mailed: YES xNO

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Your submission, dated January 31, 2011, to NDA 202832, is currently under review. We have the following comments (these comments are not necessarily all inclusive):

Package Insert:

After further investigation, our opinion remains the same regarding the requirement for the separation of the approved CDRH device labeling (IV catheter flush intended use) from the proposed CDER drug labeling (dilution or dissolving the drugs for intravenous, intramuscular or subcutaneous injections intended use) for your proposed product, sodium chloride injection, USP, 0.9% . With regard to your question during our December 14, 2011, telephone conversation, (b) (4)

 As discussed during the telephone conversation, we also note that the reference product, 0.9% sodium chloride from Hospira (NDA 18803) does not have a “flush IV catheter” indication.

Carton and container labeling:

We recommend that you do not list specific sodium chloride 0.9% indications such as “drug diluent” or “to flush IV catheters” on the carton or syringe labels. This would prevent confusion and the need to produce 2 sets of carton/container product labels.

Submit revised labeling (word versions and pdf versions of the package insert and carton and container labeling) via email to Eunice.Chung-Davies@fda.hhs.gov by December 28, 2011, for your proposed product consistent with that conveyed to you on December 7, 2011. The revised labeling must also be submitted officially to the NDA shortly thereafter. If you have any questions, please contact Eunice Chung-Davies, Regulatory Project Manager, at 301-796-4006.

NDA 202832

Drafted by: ADurmowicz/20DEC2011
Initialed by: LJafari/20DEC2011
ASchroeder/20DEC2011

Finalized by: EChung-Davies/20DEC2011

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/s/

EUNICE H CHUNG-DAVIES
12/20/2011



**Food and Drug Administration
Center for Drug Evaluation and Research**

OFFICE OF DRUG EVALUATION II

FACSIMILE TRANSMITTAL SHEET

DATE: December 7, 2011

To: Pradeep Aggarwal	From: Eunice Chung-Davies
Company: Medefil	Division of Pulmonary, Allergy, and Rheumatology Products
Fax number: (630) 681-9100	Fax number: 301-796-9728
Phone number: (630) 682-4600	Phone number: 301-796-4006

Subject: NDA 202832 Labeling Comments #2. Please confirm receipt.

Total no. of pages including cover:

Comments:

Document to be mailed: YES XNO

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We are currently reviewing your November 28, 2011, submission of the package insert and your April 20, 2011, submission of carton and container labels, for NDA 202832 for sodium chloride injection. We have the following comments listed below as well as edits in track change format in the enclosed highlights and package insert. These comments are not all-inclusive, and we may have additional comments and/or requests as we continue our review of your proposal for dual drug/device labeling.

General Comment:

1. We have investigated the regulatory precedent for combining drug and device labels for your product. The separation of the device and drug indications has been deemed necessary.

Highlights and Package Insert:

2. Revise the presentation of the 'How Supplied' section to remove (b) (4) and the (b) (4) statement following each drug product presentation.
3. Use a two column format for the Highlights section in order for the Highlights section to comply with the ½ page requirement. If the Highlights section does not comply with the ½ page requirement, submit a request for a waiver of the ½ page requirement.

Carton and Container Labels:

With regard to your syringe label (1 mL fill in 6 mL; 2 mL fill in 6 mL; 2.5 mL in 6 mL; 3 mL fill in 6 mL; 5 mL fill in 6 mL; 3 mL fill in 12 mL; 5 mL fill in 12 mL; 10 mL fill in 12 mL):

4. Delete the proposed proprietary name, (b) (4)
5. Revise the presentation of the established name to read, 'Sodium Chloride Injection, USP, 0.9%'.
6. Increase the font size and prominence of the Sodium Chloride Injection, USP, 0.9%' statement, to help minimize the risk of wrong product selection.
7. Revise the statement, (b) (4) to read, 'Not made with natural rubber latex'.
8. To decrease clutter and improve readability, please make the following revisions:
 - a. Delete the statement, (b) (4)
 - b. Delete (b) (4) appearing after, 'Syringe'.

- c. Relocate the statement, '0.308 mOSM/mL', to appear following the statement, 'Each mL contains 9 mL Sodium Chloride, USP' and before the statement, '...in Water for Injection'.
- d. Delete the [REDACTED] (b) (4) on the principal display panel.

With regard to your carton labeling (60 count cartons of: 1 mL fill in 6 mL; 2 mL fill in 6 mL; 2.5 mL in 6 mL; 3 mL fill in 6 mL; 5 mL fill in 6 mL; 3 mL fill in 12 mL; 5 mL fill in 12 mL; 10 mL fill in 12 mL):

9. See comments 4 through 8(a-d) above and apply accordingly.
10. Revise the statement, [REDACTED] (b) (4) to read, 'Usual Dose'.
11. Include the concentration statement, '0.308 mOSM/mL', as presented on the syringe label.
12. Delete the statement, [REDACTED] (b) (4) which appears at the top of the principal display panel.

Submit revised labeling incorporating these comments no later than **December 14, 2011**. Submit a clean copy in word version and a track changed version in word version officially to the NDA. If you have any questions, please contact Eunice Chung-Davies, Regulatory Project Manager, at 301-796-4006.

Enclosures:
Highlights
Package Insert (in track change format)
Carton and Container Labels

Drafted by: Echung-Davies/6DEC2011
Initialed by: LJafari/7DEC2011
ASchroeder/7DEC2011

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

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/s/

EUNICE H CHUNG-DAVIES
12/07/2011



Food and Drug Administration
Center for Drug Evaluation and Research
OFFICE OF DRUG EVALUATION II

FACSIMILE TRANSMITTAL SHEET

DATE: November 23,2011

To: Pradeep Aggarwal	From: Eunice Chung-Davies
Company: Medefil	Division of Pulmonary, Allergy, and Rheumatology Products
Fax number: (630) 681-9100	Fax number: 301-796-9728
Phone number: (630) 682-4600	Phone number: 301-796-4006
Subject: NDA 202832 Labeling Comments #1	

Total no. of pages including cover:

Comments:

Document to be mailed: YES XNO

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We are currently reviewing your package insert and carton and container labels, submitted on July 5, 2011 for NDA 202832 for sodium chloride injection. We have the following comments listed below as well as edits in track change format in the enclosed highlights and package insert. These comments are not all-inclusive, and we may have additional comments and/or requests as we continue our review.

General Comment:

1. We are currently investigating the regulatory precedent for combining drug and device labels for their product. Pending the decision, further label revisions including separation of the device and drug indications may be necessary.

Highlights and Package Insert:

2. The established name should be “sodium chloride injection, USP, 0.9%.” When referring to the established name, the name should not include the word (b) (4). Remove all occurrences globally throughout the labeling.
3. The request for the proprietary trade name, (b) (4) was withdrawn. Remove all occurrences of (b) (4) throughout the labeling.

Submit revised labeling incorporating these comments by **November 30, 2011**. Submit a clean copy in word version and a track changed version in word version officially to the NDA. If you have any questions, please contact Eunice Chung-Davies, Regulatory Project Manager, at 301-796-4006.

Enclosures:

Highlights

Package Insert (in track change format)

NDA 202832
Sodium chloride injection
Medefil

Drafted by: Echung-Davies/22NOV2011
Initialed by: LJafari/23NOV2011
ASchroeder/23NOV2011

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

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EUNICE H CHUNG-DAVIES
11/23/2011

Patwardhan, Swati

From: Patwardhan, Swati
Sent: Thursday, November 17, 2011 1:50 PM
To: 'Pradeep Aggarwal'
Subject: RE: Information request for NDA 202832(11-17-2011)

Dear Mr. Aggarwal,

We are reviewing the CMC section of the pending application for NDA 202832 and following information is requested:

1. Indicate the source and grade of [REDACTED] (b) (4) used in the manufacturing of sodium chloride, USP. Provide representative certificate of analysis of these [REDACTED] (b) (4).

2. Indicate the suppliers and specifications of the container/closure systems used for sodium chloride, USP.

Please acknowledge the receipt and provide a response latest by November 23, 2011.

Thank you

Swati Patwardhan
Regulatory Health Project Manager for Quality
Office of New Drug Quality Assessment (ONDQA)
Center of New Drug Evaluation and Research
Phone: 301-796-4085
Fax: 301-796-9748

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/s/

SWATI A PATWARDHAN
11/17/2011



NDA 202832

INFORMATION REQUEST

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Medefil, Inc.
250 Windy Point Drive
Glendale Heights, Illinois 60139

Attention: Pradeep Aggarwal
President and CEO

Dear Mr. Aggarwal:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Sodium Chloride Injection, USP, 9 mg/mL.

FDA investigators have identified significant violations to the bioavailability and bioequivalence requirements of Title 21, Code of Federal Regulation, Part 320 in bioanalytical studies conducted by Cetero Research in Houston, Texas (Cetero).¹ The pervasiveness and egregious nature of the violative practices by Cetero has led FDA to have significant concerns that the bioanalytical data generated at Cetero from April 1, 2005 to June 15, 2010, as part of studies submitted to FDA in New Drug Applications (NDA) and Supplemental New Drug Applications (sNDA) are unreliable. FDA has reached this conclusion for three reasons: (1) the widespread falsification of dates and times in laboratory records for subject sample extractions, (2) the apparent manipulation of equilibration or “prep” run samples to meet pre-determined acceptance criteria, and (3) lack of documentation regarding equilibration or “prep” runs that prevented Cetero and the Agency from determining the extent and impact of these violations.

Serious questions remain about the validity of any data generated in studies by Cetero Research in Houston, Texas during this time period. In view of these findings, FDA is informing holders of approved and pending NDAs of these issues.

The impact of the data from these studies (which may include bioequivalence, bioavailability, drug-drug interaction, specific population, and others) cannot be assessed without knowing the details regarding the study and how the data in question were considered in the overall development and approval of your drug product. At this time, the Office of New Drugs is

¹ These violations include studies conducted by Bioassay Laboratories and BA Research International specific to the Houston, Texas facility.

searching available documentation to determine which NDAs are impacted by the above findings.

To further expedite this process, we ask that you inform us if you have submitted any studies conducted by Cetero Research in Houston, Texas during the time period of concern (April 1, 2005 to June 15, 2010). Please submit information on each of the studies, including supplement number (if appropriate), study name/protocol number, and date of submission. With respect to those studies, you will need to do one of the following: (a) re-assay samples if available and supported by stability data, (b) repeat the studies, or (c) provide a rationale if you feel that no further action is warranted.

Please respond to this query within 30 days from the date of this letter.

This information should be submitted as correspondence to your NDA. In addition, please provide a desk copy to:

Office of New Drugs
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Room 6300
Silver Spring, MD 20993-0002

If you have any questions, call Christine Chung, Regulatory Project Manager, at (301) 796-3420.

Sincerely,

{See appended electronic signature page}

Sandy Barnes
Chief, Project Management Staff
Division of Pulmonary, Allergy, and Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

SANDRA L BARNES
09/15/2011



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

FACSIMILE TRANSMITTAL SHEET

DATE: August 19, 2011

To: Pradeep Aggarwal	From: Eunice Chung-Davies, RPM
Company: Medefil	Division of Pulmonary, Allergy, and Rheumatology Drug Products
Fax number: FAX (630) 681-9100	Fax number: 301-796-9728
Phone number: TEL (630) 682-4600	Phone number: 301-796-4006
Subject: CMC Information Request	

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

Comments: Please provide a response to the request.

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Your submission, dated January 31, 2011, to NDA 202832, is currently under review. We have the following requests for information:

1. The following comment is pertinent to the manufacturing of the prefilled saline syringes:

Provide a detailed comparison of the terminal sterilization processes in terms of media, temperature, duration, and cycling, for the products described in this NDA and in 510(k) K091583.
2. The following comment is pertinent to the controls of the prefilled saline syringes:

Indicate any differences in the prefilled saline syringe specifications (both release and shelf life) proposed in this NDA and that in K091583.
3. The following comments are pertinent to the controls of the container/closure system:
 - a. Confirm that you will periodically conduct full testing of all components of the container/closure system used for future commercial production to verify information on the vendors' Certificates of Analysis (COAs).
 - b. Conduct a controlled extractable study for the barrel, cap, and stopper plunger, using validated HPLC/GC methods. Determine the level of each extractable, and provide safety evaluations based on the possible maximum daily exposures of those extractables. The possible maximum daily exposures should be based on the worse case scenario, in which the largest total volume of saline may be used daily for dilution/dissolution. Alternatively, the safety evaluation can be conducted based on the detected levels of those compounds as leachables in the drug product during stability study.
4. The following comments are pertinent to the stability and shelf life of the prefilled saline syringes:
 - a. Conduct leachable testing during stability study, based on the results of the controlled extractable study. Provide safety evaluations for all leachables based on the possible maximum daily exposures of those leachables. The possible maximum daily exposures should be based on the worse case scenario, in which the largest total volume of saline may be used daily for dilution/dissolution.
 - b. Conduct an investigation for the causative factors of the observed upward trending for pH during the stability study, especially from samples stored at accelerated and intermediate conditions.
 - c. Given that only very limited testing was conducted at the 18 month time point, provide stability data through 24 month time point per the stability

protocol to support the proposed shelf life of 24 months for the prefilled saline syringes.

5. Comments pertinent to the labeling will be forthcoming.

Please provide a formal submission to the NDA by October 12, 2011. If you have any questions, please contact Eunice Chung-Davies, Regulatory Project Manager, at 301-796-4006.

NDA 202832

Drafted by: EChung-Davies/12AUG2011
Initialed by: SBarnes/19AUG2011
EJao/12AUG2011
ASchroeder/12AUG2011
PPeri/12AUG2011

Finalized by: EChung-Davies/19AUG2011

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/s/

EUNICE H CHUNG-DAVIES
08/19/2011



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

FACSIMILE TRANSMITTAL SHEET

DATE: August 15, 2011

To: Pradeep Aggarwal	From: Eunice Chung-Davies, RPM
Company: Medefil	Division of Pulmonary, Allergy, and Rheumatology Drug Products
Fax number: FAX (630) 681-9100	Fax number: 301-796-9728
Phone number: TEL (630) 682-4600	Phone number: 301-796-4006

Subject: DMEPA Information Request

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

Comments: Please provide a response to the request.

Document to be mailed: YES xNO

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

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

Your submission, dated January 31, 2011, to NDA 202832, is currently under review. We have the following requests for information:

We are aware that your company manufactures heparin prefilled syringes. In order to ensure that your proposed product's carton and container labeling is differentiated from your heparin product line with regard to color and trade dress, provide copies of your heparin labels and heparin carton labeling.

Please provide a response by August 19, 2011 via email to Eunice.chung-davies@fda.hhs.gov. The response must be formally submitted to the NDA shortly thereafter. If you have any questions, please contact Eunice Chung-Davies, Regulatory Project Manager, at 301-796-4006.

NDA 202832

Drafted by: EChung-Davies/12AUG2011
Initialed by: SBarnes/15AUG2011

Finalized by: EChung-Davies/15AUG2011

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/s/

EUNICE H CHUNG-DAVIES
08/15/2011



NDA 202832

**PROPRIETARY NAME REQUEST
WITHDRAWN**

Medefil, Inc.
250 Windy Point Drive
Glendale Heights, Illinois 60139

ATTENTION: Pradeep Aggarwal
President

Dear Mr. Aggarwal:

Please refer to your New Drug Application (NDA) dated January 31, 2011, received February 01, 2011, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Sodium Chloride Injection, USP, 9 mg/mL.

We acknowledge receipt of your July 11, 2011, correspondence, on July 12, 2011, notifying us that you are withdrawing your request for a review of the proposed proprietary name (b) (4). This proposed proprietary name request is considered withdrawn as of July 12, 2011.

We note that you have not proposed an alternate proprietary name for review. If you intend to have a proprietary name for this product, a new request for a proposed proprietary name review should be submitted.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Nichelle Rashid, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-3904. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Eunice Chung-Davies at (301) 796-4006.

Sincerely,

{See appended electronic signature page}

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Medication Error Prevention and Risk Management
Office of Surveillance and Epidemiology

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/s/

CAROL A HOLQUIST
07/26/2011



NDA 202832

FILING COMMUNICATION

Medefil, Inc.
250 Windy Point Drive
Glendale Heights, IL 60139

Attention: Pradeep Aggarwal
President and CEO

Dear Mr. Aggarwal:

Please refer to your New Drug Application (NDA) dated January 31, 2011, received and accepted for filing on March 7, 2011, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for (b) (4) (0.9% sodium chloride injection, USP in plastic syringes).

We also refer to your submissions, dated March 31 and April 19, 2011.

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 January 7, 2011.

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, midcycle, 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 December 7, 2011.

At this time, we are notifying you that, we have not identified any potential review issues. Please note that our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review.

We also request that you submit the following information:

Chemistry, Manufacturing and Controls:

1. Specify which tests you will perform on receipt of the drug substance, and confirm that you periodically perform all tests for which results are accepted on a Certificate of Analysis.
2. Clarify whether the (b) (4) component of the container closure system of the drug substance conforms to USP physicochemical tests and specify its food additive status.
3. Provide the most recent stability results for the drug substance and confirm that stability testing by (b) (4) is still in place. Provide assurance that the data will be provided to you, and that you will submit the data to this application.
4. Provide data pertaining to the extractables of the drug product container closure system and the leachables that may appear in the drug product over its shelf life. Conduct toxicological (safety) evaluations of the leachables and extractables.
5. Identify the approved vendors that manufacture the individual components of the syringe device, and indicate the compositions of the components if any additives are used by the manufacturers of the components.
6. With regard to the attachments to section 3.2.P.5.1, entitled “Material Specifications: Normal Saline I.V. Flush Syringes...”, clarify whether these apply completely to the proposed sodium chloride injection product. This clarification request also applies to all other documents in the NDA, which refer to: Normal Saline I.V. Flush Syringe.
7. Modify your drug product specifications to include USP monograph tests for the identification of sodium and of chloride.

The following comments pertain to the drug product container closure system.

8. Provide a Certificate of Analysis for the (b) (4) used on the plunger stoppers and syringe barrel, and provide information on the impurity profile of the (b) (4)
9. Provide specifications for the amounts of (b) (4) (maximum and minimum) used on the plunger stoppers and syringe barrels.
10. Clarify whether any constituents of the secondary container/closure components may migrate into the drug product formulation through the primary packaging by submitting the appropriate data.

Clinical:

11. Submit a summary and update of safety information of the proposed product per regulation 21 CFR 314.50 (d)(5)(vi). The safety information should include available data from clinical studies, published literatures, and post-marketing adverse event reports.

During our preliminary review of your submitted labeling, we have identified the following labeling format issues which were communicated to you previously in an information request:

Highlights Section:

12. The Contraindications section must be included in this section and cannot be omitted. If there are no known contraindications, state “none.”
13. A Warnings and Precautions section is required in this section.
14. The Patient Counseling Information Statement is missing. The Patient Counseling Information statement must appear in Highlights and must read
See 17 for PATIENT COUNSELING INFORMATION. [See 21 CFR 201.57(a)(14)]
15. The highlights limitation statement appears twice. It needs to be stated only once.
16. The revision date at the end of the highlights replaces the “revision” or “issued” date at the end of the full prescribing information and should not appear in both places.

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

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 Eunice Chung-Davies, Regulatory Project Manager, at (301) 796-4006.

Sincerely,

{See appended electronic signature page}

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

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/s/

BADRUL A CHOWDHURY
05/20/2011



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

FACSIMILE TRANSMITTAL SHEET

DATE: May 2, 2011

To: Pradeep Aggarwal	From: Eunice Chung-Davies, RPM
Company: Medefil	Division of Pulmonary, Allergy and Rheumatology Drug Products
Fax number: (630) 681-9100	Fax number: 301-796-9728
Phone number: (630) 682-4600	Phone number: 301-796-4006

Subject: Labeling Comments

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

Comments: Please provide a response to the request

Document to be mailed: YES xNO

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

Your submission dated January 31, 2011, to NDA 202832, is currently under review. Address the following labeling comments with regard to format and re-submit by May 10, 2011. This updated version of the labeling will be used for further labeling discussions.

Highlights

1. The Contraindications section must be included in this section and cannot be omitted. If there are no known contraindications, state “none.”
2. A Warnings and Precautions section is required in this section.
3. The Patient Counseling Information Statement is missing. The Patient Counseling Information statement must appear in Highlights and must read
See 17 for PATIENT COUNSELING INFORMATION. [See 21 CFR 201.57(a)(14)]
4. The highlights limitation statement appears twice. It needs to be stated only once.
5. The revision date at the end of the highlights replaces the “revision” or “issued” date at the end of the full prescribing information and should not appear in both places.

If you have any questions, please contact Eunice Chung-Davies, Regulatory Project Manager, at 301-796-4006.

NDA #202832

Drafted by: EChung-Davies/28APR2011

Initialed by: SBarnes/28APR2011

Finalized by: EChung-Davies/2MAY2011

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/s/

EUNICE H CHUNG-DAVIES
05/02/2011

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR DDMAC LABELING REVIEW CONSULTATION **Please send immediately following the Filing/Planning meeting**	
TO: CDER-DDMAC-RPM		FROM: (Name/Title, Office/Division/Phone number of requestor) Eunice Chung-Davies, RPM, DPARP, 301-796-4006	
REQUEST DATE March 23, 2011	IND NO.	NDA/BLA NO. 202832	TYPE OF DOCUMENTS (PLEASE CHECK OFF BELOW)
NAME OF DRUG (b) (4) (sodium chloride 0.9% injection) in plastic syringes	PRIORITY CONSIDERATION Standard	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE (Generally 1 week before the wrap-up meeting) November 23, 2011
NAME OF FIRM: Medefil		PDUFA Date: January 7, 2011	
TYPE OF LABEL TO REVIEW			
TYPE OF LABELING: (Check all that apply) <input checked="" type="checkbox"/> PACKAGE INSERT (PI) <input type="checkbox"/> PATIENT PACKAGE INSERT (PPI) <input checked="" type="checkbox"/> CARTON/CONTAINER LABELING <input type="checkbox"/> MEDICATION GUIDE <input type="checkbox"/> INSTRUCTIONS FOR USE (IFU)		TYPE OF APPLICATION/SUBMISSION <input checked="" type="checkbox"/> ORIGINAL NDA/BLA <input type="checkbox"/> IND <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> SAFETY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> PLR CONVERSION	
		REASON FOR LABELING CONSULT <input checked="" type="checkbox"/> INITIAL PROPOSED LABELING <input type="checkbox"/> LABELING REVISION	
EDR link to submission: This submission contains a Package Insert (link below) and carton and container labels (available on paper only): \fdswa150\NONECTD\N202832\M_000\2011-01-31			
Please Note: There is no need to send labeling at this time. DDMAC reviews substantially complete labeling, which has already been marked up by the CDER Review Team. After the disciplines have completed their sections of the labeling, a full review team labeling meeting can be held to go over all of the revisions. Within a week after this meeting, "substantially complete" labeling should be sent to DDMAC. Once the substantially complete labeling is received, DDMAC will complete its review within 14 calendar days.			
COMMENTS/SPECIAL INSTRUCTIONS: The following are the scheduled meetings related to this NDA. Filing/Planning Meeting: April 15, 2011 MCR: August 10, 2011 Full Labeling Meeting: November 7, 2011 Wrap Up: December 5, 2011 Label Tecon with Sponsor: December 7, 2011 Please let me know once a reviewer/team leader has been assigned. Thank you.			
SIGNATURE OF REQUESTER Eunice Chung-Davies			
SIGNATURE OF RECEIVER		METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> eMAIL/DAARTS <input type="checkbox"/> HAND	

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EUNICE H CHUNG-DAVIES
03/23/2011

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/s/

EUNICE H CHUNG-DAVIES
03/23/2011



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 202832

Medefil, Inc.
250 Windy Point Drive
Glendale Heights, IL 60139

Attention: Pradeep Aggarwal
President and CEO

Dear Mr. Aggarwal:

We have received your new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: 0.9% Sodium Chloride Injection, USP in plastic syringes

NDA Number: 202832

Date of Application: January 31, 2011

Date of Receipt: March 7, 2011

Please note that the application submitted on January 31, 2011, and received on February 1, 2011, was incomplete and was not accepted for filing since the appropriate user fee was not received at the time of the submission. The user fee for this application was waived on March 7, 2011, therefore, the application has been accepted as of March 7, 2011.

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 May 6, 2011 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).

Title VIII of FDAAA amended the PHS Act by adding new section 402(j) [42 USC § 282(j)], which expanded the current database known as ClinicalTrials.gov to include mandatory registration and reporting of results for applicable clinical trials of human drugs (including biological products) and devices.

In addition to the registration and reporting requirements described above, FDAAA requires that, at the time of submission of an application under section 505 of the FDCA, the application must be accompanied by a certification that all applicable requirements of 42 USC § 282(j) have been met. Where available, the certification must include the appropriate National Clinical Trial (NCT) numbers [42 USC § 282(j)(5)(B)].

You did not include such certification when you submitted this application. You may use Form FDA 3674, "Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank," [42 U.S.C. § 282(j)] to comply with the certification requirement. The form may be found at <http://www.fda.gov/opacom/morechoices/fdaforms/default.html>.

In completing Form FDA 3674, you should review 42 USC § 282(j) to determine whether the requirements of FDAAA apply to any clinical trial(s) referenced in this application. Please note that FDA published a guidance in January 2009, "Certifications To Accompany Drug, Biological Product, and Device Applications/Submissions: Compliance with Section 402(j) of The Public Health Service Act, Added By Title VIII of the Food and Drug Administration Amendments Act of 2007," that describes the Agency's current thinking regarding the types of applications and submissions that sponsors, industry, researchers, and investigators submit to the Agency and accompanying certifications. Additional information regarding the certification form is available at:

<http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCA/ct/SignificantAmendmentstotheFDCAAct/FoodandDrugAdministrationAmendmentsActof2007/ucm095442.htm>. Additional information regarding Title VIII of FDAAA is available at: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-014.html>. Additional information for registering your clinical trials is available at the Protocol Registration System website <http://prsinfo.clinicaltrials.gov/>.

When submitting the certification for this application, **do not** include the certification with other submissions to the application. Submit the certification within 30 days of the date of this letter. In the cover letter of the certification submission clearly identify that it pertains to **NDA 202832** submitted on January 31, 2011, and that it contains the FDA Form 3674 that was to accompany that application.

If you have already submitted the certification for this application, please disregard the above.

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 Pulmonary, Allergy, and Rheumatology 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>.

If you have any questions, call Eunice Chung-Davies, Senior Regulatory Management Officer, at (301) 796-4006.

Sincerely,

{See appended electronic signature page}

Sandy Barnes
Chief, Project Management Staff
Division of Pulmonary, Allergy, and Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

SANDRA L BARNES
03/17/2011



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 202832

Medefil, Inc.
250 Windy Point Drive
Glendale Heights, IL 60139

Attention: Pradeep Aggarwal
President and CEO

Dear Mr. Aggarwal:

We have received your new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: 0.9% Sodium Chloride Injection, USP in plastic syringes

NDA Number: 202832

Date of Application: January 31, 2011

Date of Receipt: March 7, 2011

Please note that the application submitted on January 31, 2011, and received on February 1, 2011, was incomplete and was not accepted for filing since the appropriate user fee was not received at the time of the submission. The user fee for this application was waived on March 7, 2011, therefore, the application has been accepted as of March 7, 2011.

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 May 6, 2011 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.

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<http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCA/ct/SignificantAmendmentstotheFDCAAct/FoodandDrugAdministrationAmendmentsActof2007/ucm095442.htm>. Additional information regarding Title VIII of FDAAA is available at: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-014.html>. Additional information for registering your clinical trials is available at the Protocol Registration System website <http://prsinfo.clinicaltrials.gov/>.

When submitting the certification for this application, **do not** include the certification with other submissions to the application. Submit the certification within 30 days of the date of this letter. In the cover letter of the certification submission clearly identify that it pertains to **NDA 202832** submitted on January 31, 2011, and that it contains the FDA Form 3674 that was to accompany that application.

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Food and Drug Administration
Center for Drug Evaluation and Research

Division of Pulmonary, Allergy, and Rheumatology Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

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<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm>.

If you have any questions, call Eunice Chung-Davies, Senior Regulatory Management Officer, at (301) 796-4006.

Sincerely,

{See appended electronic signature page}

Sandy Barnes
Chief, Project Management Staff
Division of Pulmonary, Allergy, and Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

SANDRA L BARNES
03/16/2011



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

PIND (b) (4)

(b) (4)

Dear (b) (4):

Please refer to your Pre-Investigational New Drug Application (PIND) file for Sodium Chloride Injection, USP, 0.9%.

We also refer to your July 10, 2008, email communication requesting cancellation of the meeting we scheduled in response to your May 14, 2008, meeting request because our draft responses were adequate to address all questions. The July 14, 2008, meeting has been cancelled.

If you have any questions, call me at (301) 796-1007.

Sincerely,

{See appended electronic signature page}

Cristi L. Stark, MS
Regulatory Health Project Manager
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

IND (b) (4)

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Draft Responses for Medefil, Inc/ (b) (4) pre-NDA meeting

IND (b) (4)

Drug: Sodium Chloride Injection, USP,

Meeting Date: Monday, July 14, 2008

Time: 4:00-5:00pm EDT

Location: CDER WO Bldg 22, Rm 1309

This material consists of our preliminary responses to your questions and any additional comments in preparation for the discussion at the meeting scheduled for July 14, 2008, between Medefil (b) (4) and the Division of Gastroenterology Products. This material is shared to promote a collaborative and successful discussion at the meeting. The minutes of the meeting will reflect agreements, key issues, and any action items discussed during the formal meeting and may not be identical to these preliminary comments. If these answers and comments are clear to you and you determine that further discussion is not required, you have the option of canceling the meeting (contact the Regulatory Project Manager). If you determine that discussion is needed for only some of the original questions, you have the option of reducing the agenda. It is important to remember that some meetings, particularly milestone meetings, are valuable even if the pre-meeting communications are considered sufficient to answer the questions. Please note that if there are any major changes to the questions (based on our responses herein), we may not be prepared to discuss or reach agreement on such changes at the meeting. If any modifications to the meeting agenda or additional questions for which you would like FDA feedback arise prior to the meeting, contact the Regulatory Project Manager to discuss the possibility of including these for discussion at the meeting.

Sponsor Posed Questions and FDA Response:

CMC:

1. Does the summary CMC data provided by Medefil appear to be acceptable to the Division?

FDA Response:

The information that you plan to submit in the NDA appears generally acceptable, but you will also need to submit data to demonstrate that the syringes conform to USP <661> for plastic containers and a more detailed description of the manufacturing process, describing any in-process testing that will be done, as well as sterile process validation data. In addition, when you submit your batch analysis and stability data, please report actual test results; do not report your results as "conforms".

Please refer to the FDA *Guidance for Industry for the Submission Documentation for Sterilization Process Validation in Applications for Human and Veterinary Drug Products* (<http://www.fda.gov/cder/guidance/cmc2.pdf>) for specific information to be included in the NDA submission.

It is strongly recommended that you explore terminal sterilization for the product as a sterilization process which provides a greater sterility assurance level.

Non-Clinical:

2. No non-clinical studies are planned for the proposed Sodium Chloride Injection, USP, 0.9% in Plastic Syringes. Does the Division concur with this conclusion?

FDA Response:

Yes, the Division concurs.

Clinical Pharmacology:

3. Since the proposed Sodium Chloride Injection, USP, 0.9%, in Plastic Syringes for diluting or dissolving drugs for injection does not raise pharmacokinetic issues, Medefil intends to request a waiver of *in vivo* bioavailability requirements under 21 CFR 320.22. Does the Division concur with this conclusion?

FDA Response:

Yes, we concur.

Clinical:

4. No clinical studies are planned for the proposed Sodium Chloride Injection, USP, 0.9% in Plastic Syringes. Does the Division concur with this conclusion?

FDA Response:

Yes, we concur.

Regulatory:

5. Since there is no FDA approved reference listed Sodium Chloride Injection, USP, 0.9% product in plastic syringes to the best of our knowledge and understanding, such a product, as packaged in plastic syringes is deemed to be a new drug under 21 CFR 310.509. As such, Medefil intends to submit an NDA under section 505(b)(2) of the FD&C Act for the proposed product, Sodium Chloride Injection, USP, 0.9% in Plastic Syringes. Does the Division concur with this regulatory approach?

FDA Response:

Yes, we concur.

Linked Applications

Sponsor Name

Drug Name

IND (b) (4)

SODIUM CHLORIDE INJECTION 0.9% IN
PLASTIC SYRINGES 1,2,2.5,3,5, AND
10ML FILLS

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

/s/

CRISTI L STARK
07/11/2008