CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

205029Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

1.3.5.2 Patent certification - updated 7 March 2013

In accordance with Section 21 CFR 314.50(i)(1) Belcher Pharmaceuticals, LLC (Belcher) makes the following Patent Certification for [redacted] (b) (4) proposed trade name (epinephrine injection, USP 1:1000 [mg/mL]):

As part of this NDA (205029), Belcher references listed drug data contained in CorePharma, LLC's NDA (20800) pertaining to Twinject, an approved epinephrine (0.3 mg/mL) product for use in the emergency treatment of severe allergic reactions.

There is one method of manufacturing patent that applies to the production of the active pharmaceutical ingredient, i.e., epinephrine. Paragraph (i)(1)(iii)(2) of 21 CFR 314.50 states that "an applicant is not required to make a certification with respect to any patent that claims only a method of manufacturing the drug product for which the applicant is seeking approval." As such, no patent certification for this method of manufacturing patent has been made.

On October 31, 2012, Belcher had certified that there were no relevant patents related to Twinject or Belcher's proposed epinephrine product for use in septic shock.

On February 20, 2013, the Agency sent Belcher an information request for patent certification on two unexpired patents, 7297136 and 7621891, associated with Twinject (NDA 20800), as listed in the Orange Book. Belcher now makes such paragraph IV patent certification per the Agency's request in accordance with 21 CFR 314.50(i)(1)(i)(A)(4).

Belcher's proposed epinephrine drug product will be supplied in ampoules made available for continuous intravenous infusion upon dilution and does not include a delivery device. Both patents 7297136 and 7621891 consist of apparatus claims only for an injector device (i.e., autoinjector) for delivery of one or two doses. Patent 7297136 does not claim delivery of epinephrine. Patent 7621891, which is a continuation-in-part of patent 7297136, does claim delivery of epinephrine by this particular autoinjector. Belcher's proposed drug product does not consist of such a pre-filled injector device intended for self-administration. Therefore, Belcher's proposed epinephrine drug product will not infringe on device patents 7297136 and 7621891.

Paragraph IV Certification

I, Mihir Taneja of Belcher Pharmaceuticals, LLC, certify that Patent No. 7297136 and Patent No. 7621891 will not be infringed by the manufacture, use, or sale of [redacted] (b) (4) (epinephrine injection, USP 1:1000 [mg/mL]) for which this application is submitted.

To this effect, I and Belcher have complied with the requirements under 314.52(a) with respect to providing a notice to each owner of the patent or their representatives and to the holder of the approved application for the drug product which is claimed by the patent or a use of which is claimed by the patent and with the requirements under 314.52(c) with respect to the content of the notice. These notices were sent out on February 27, 2013.

Delivery receipts for each of these notices, sent to the following, are attached:

- Owner of Patents 7,621,891 and 7,297,136:
  Ron Wyrick, President
  Washington Biotech Corporation
  4503 E Red Roan Drive
  Spokane, WA 99217-9734
- Holder of Twinject NDA 20800:
  Amedra Pharmaceuticals LLC
  Christopher Worrell, CEO
  2 Walnut Grove Dr., Suite 190
  Horsham, PA 19044-7707

Sincerely,

Mihir Taneja
Vice President
Belcher Pharmaceuticals, LLC
6911 Bryan Dairy Road
Largo, FL 33777
(727) 471-0850
mihirt@belcherpharma.com

1.3.5.2 Patent certification - updated 4 March 2013

In accordance with Section 21 CFR 314.50(i)(i)(1) Belcher Pharmaceuticals, LLC (Belcher) makes the following Patent Certification for [redacted] (b) (4) proposed trade name (epinephrine injection, USP 1:1000 [mg/mL]):

As part of this NDA (205029), Belcher references listed drug data contained in CorePharma, LLC's NDA (20800) pertaining to Twinject, an approved epinephrine (0.3 mg/mL) product for use in the emergency treatment of severe allergic reactions.

There is one method of manufacturing patent that applies to the production of the active pharmaceutical ingredient, i.e., epinephrine. Paragraph (i)(1)(iii)(2) of 21 CFR 314.50 states that "an applicant is not required to make a certification with respect to any patent that claims only a method of manufacturing the drug product for which the applicant is seeking approval." As such, no patent certification for this method of manufacturing patent has been made.

On October 31, 2012, Belcher had certified that there were no relevant patents related to Twinject or Belcher's proposed epinephrine product for use in septic shock.

On February 20, 2013, the Agency sent Belcher an information request for patent certification on two unexpired patents, 7297136 and 7621891, associated with Twinject (NDA 20800), as listed in the Orange Book. Belcher now makes such patent certifications per the Agency's request in accordance with 21 CFR 314.50, paragraph (i)(i)(4).

Belcher's proposed epinephrine drug product will be supplied in ampoules made available for continuous intravenous infusion upon dilution and does not include a delivery device. Both patents 7297136 and 7621891 consist of apparatus claims only for an injector device (i.e., autoinjector) for delivery of one or two doses. Patent 7297136 does not claim delivery of epinephrine. Patent 7621891, which is a continuation-in-part of patent 7297136, does claim delivery of epinephrine by this particular autoinjector. Belcher's proposed drug product does not consist of such a pre-filled injector device intended for self-administration. Therefore, Belcher's proposed epinephrine drug product will not infringe on device patents 7297136 and 7621891.

I, Mihir Taneja of Belcher Pharmaceuticals, LLC, certify that Patent No. 7297136 and Patent No. 7621891 will not be infringed by the manufacture, use, or sale of [redacted] (b) (4) (epinephrine injection, USP 1:1000 [mg/mL]) for which this application is submitted.

To this effect, I and Belcher have complied with the requirements under 314.52(a) with respect to providing a notice to each owner of the patent or their representatives and to the holder of the approved application for the drug product which is claimed by the patent or a use of which is claimed by the patent and with the requirements under 314.52(c) with respect to the content of the notice. These notices were sent out on February 27, 2013.

Delivery receipts for each of these notices, sent to the following, are attached:

- Owner of Patents 7,621,891 and 7,297,136:
  Ron Wyrick, President
  Washington Biotech Corporation
  4503 E Red Roan Drive
  Spokane, WA 99217-9734
- Holder of Twinject NDA 20800:
  Amedra Pharmaceuticals LLC
  Christopher Worrell, CEO
  2 Walnut Grove Dr., Suite 190
  Horsham, PA 19044-7707

Sincerely,

Mihir Taneja
Vice President
Belcher Pharmaceuticals, LLC
6911 Bryan Dairy Road
Largo, FL 33777
(727) 471-0850
mihirt@belcherpharma.com

1.3.5.2 Patent certification

31 October 2012

In accordance with Section 21 CFR 314.50(i)(1)(i)(1) Belcher Pharmaceuticals, LLC (Belcher) makes the following Patent Certification for [redacted] (b) (4) proposed trade name, (epinephrine injection, USP 1:1000 [mg/mL]):

As part of this NDA (205029), Belcher references listed drug data contained in CorePharma, LLC's NDA (N020800) pertaining to Twinject, an approved epinephrine (0.3 mg/mL) product for use in the emergency treatment of severe allergic reactions.

There is one method of manufacturing patent that applies to the production of the active pharmaceutical ingredient, ie, epinephrine. Paragraph (i)(1)(iii)(2) of 21 CFR 314.50 states that "an applicant is not required to make a certification with respect to any patent that claims only a method of manufacturing the drug product for which the applicant is seeking approval." As such, no patent certification for this method of manufacturing patent has been made.

In accordance with 21 CFR 314.50, paragraph (i)(1)(ii), Belcher certifies that to the best of its knowledge as of this date that there are no relevant patents related to Twinject or Belcher's proposed epinephrine drug product, epinephrine injection, USP 1:1000 (1 mg/mL) for use in increasing systemic arterial blood pressure in acute hypotensive states associated with septic shock, and that patent information has not been submitted to the FDA for any patent that claims epinephrine on which investigations or literature references have been relied upon by Belcher for approval of this application.

Sincerely,

Mihir Taneja
Vice President
Belcher Pharmaceuticals, LLC
6911 Bryan Dairy Road
Largo, FL 33777
(727) 471-0850
mihirt@belcherpharma.com

1.3.5.1 Patent information

There are no patents claiming drug, drug product, or method of use for Belcher's epinephrine drug product. Belcher Pharmaceuticals, LLC does not currently have any patents related to its proposed epinephrine drug product (b) (4) epinephrine injection, USP 1:1000 (1 mg/mL) for use in increasing systemic arterial blood pressure in acute hypotensive states associated with septic shock.

There is one method of manufacturing patent that applies to the production of the active pharmaceutical ingredient, ie, epinephrine. The Active Ingredient Manufacturer (AIM) is (b) (4) see corresponding DMF No. (b) (4) authorization letter to Belcher Pharmaceuticals, LLC (Section 1.4.1). (b) (4) is the assignee of US Patent Number 6,218,575 with expiration date 26 July 2020 for the process for preparing adrenaline (epinephrine) by asymmetric hydrogenation.

EXCLUSIVITY SUMMARY

NDA # 205029 SUPPL # HFD # 110

Trade Name N/A

Generic Name epinephrine injection 1 mg/mL

Applicant Name Belcher Pharmaceuticals

Approval Date, If Known 7/25/14

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).

See attached list

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 ☒

(This is a literature-based application.)
IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

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

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

YES ☐ NO ☐

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

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

YES ☐ NO ☐

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

YES ☐ NO ☐

If yes, explain:

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

YES ☐ NO ☐

If yes, explain:

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical

investigations submitted in the application that are essential to the approval:

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

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

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

Investigation #1 YES ☐ NO ☐

Investigation #2 YES ☐ NO ☐

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

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES ☐ NO ☐

Investigation #2 YES ☐ NO ☐

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

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

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

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

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

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

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

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

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

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

YES ☐ NO ☐

If yes, explain:

==========

Name of person completing form: Russell Fortney
Title: RHPM
Date: 7/22/14

Name of Office/Division Director signing form: Norman Stockbridge
Title: Director, Division of Cardiovascular and Renal Products

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/

RUSSELL FORTNEY
07/28/2014

NORMAN L STOCKBRIDGE
07/28/2014

1.3.3 DEBARMENT CERTIFICATION

Belcher Pharmaceuticals, LLC hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application.

March 6, 2013

Mihir Taneja
Vice President
Belcher Pharmaceuticals, LLC
6911 Bryan Dairy Road
Largo, FL 33777

Date

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION[1]

NDA # 205029 BLA #	NDA Supplement # BLA Supplement #	If NDA, Efficacy Supplement Type: *(an action package is not required for SE8 or SE9 supplements)*
Proprietary Name: **N/A** Established/Proper Name: **epinephrine** Dosage Form: **injection**		Applicant: **Belcher Pharmaceuticals** Agent for Applicant (if applicable): **N/A**
RPM:		Division:

NDA Application Type: ☐ 505(b)(1) ☒ 505(b)(2)
Efficacy Supplement: ☐ 505(b)(1) ☐ 505(b)(2)

BLA Application Type: ☐ 351(k) ☐ 351(a)
Efficacy Supplement: ☐ 351(k) ☐ 351(a)

For ALL 505(b)(2) applications, two months prior to EVERY action:

- **Review the information in the 505(b)(2) Assessment and submit the draft[2] to CDER OND IO for clearance.**
- **Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity)**

☒ No changes
☐ New patent/exclusivity *(notify CDER OND IO)*
Date of check: **7/22/14**

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.

› Actions	
• Proposed action • User Fee Goal Date is **7/27/14**	☒ AP ☐ TA ☐ CR
• Previous actions *(specify type and date for each action taken)*	☒ **CR, 10/4/13**
❖ 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 _____	☐ Received
❖ Application Characteristics[3]	

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

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

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

Review priority: ☒ Standard ☐ Priority
Chemical classification (new NDAs only): **5**
(confirm chemical classification at time of approval)

☐ Fast Track
☐ Rolling Review
☐ Orphan drug designation
☐ Breakthrough Therapy designation
☐ Rx-to-OTC full switch
☐ Rx-to-OTC partial switch
☐ Direct-to-OTC

NDAs: Subpart H
☐ Accelerated approval (21 CFR 314.510)
☐ Restricted distribution (21 CFR 314.520)
Subpart I
☐ Approval based on animal studies

BLAs: Subpart E
☐ Accelerated approval (21 CFR 601.41)
☐ Restricted distribution (21 CFR 601.42)
Subpart H
☐ 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

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

Comments:

❖ BLAs only: Ensure *RMS-BLA Product Information Sheet for TBP* and *RMS-BLA Facility Information Sheet for TBP* have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)	☐ Yes, dates
❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 *(approvals only)*	☐ Yes ☐ No
❖ Public communications *(approvals only)*	
• Office of Executive Programs (OEP) liaison has been notified of action	☐ Yes ☒ No
• Indicate what types (if any) of information were issued	☒ None ☐ FDA Press Release ☐ FDA Talk Paper ☐ CDER Q&As ☐ 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	☒ No ☐ 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.	☒ Verified ☐ Not applicable because drug is an old antibiotic.

CONTENTS OF ACTION PACKAGE

Officer/Employee List

❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list *(approvals only)*	☒ Included
Documentation of consent/non-consent by officers/employees	☒ Included

Action Letters	
✦ Copies of all action letters *(including approval letter with final labeling)*	**Included**
Labeling	
❖ Package Insert *(write submission/communication date at upper right of first page of PI)*	
• 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 *(write submission/communication date at upper right of first page of each piece)*	☐ Medication Guide ☐ Patient Package Insert ☐ Instructions for Use ☐ Device Labeling ☒ 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) *(write submission/communication date on upper right of first page of each submission)*	
• Most-recent draft labeling	☒ Included
❖ Proprietary Name • Acceptability/non-acceptability letter(s) *(indicate date(s))* • Review(s) *(indicate date(s)*	**Unacceptable letter, 4/3/13** **Review, 4/2/13**
❖ Labeling reviews *(indicate dates of reviews)*	RPM: ☒ None DMEPA: ☒ **8/7/13, 1/29/14, 7/16/14** DMPP/PLT (DRISK): ☒ None OPDP: ☒ None SEALD: ☒ None CSS: ☒ None Other: ☐ None
Administrative / Regulatory Documents	
❖ RPM Filing Review[4]/Memo of Filing Meeting *(indicate date of each review)* ❖ All NDA 505(b)(2) Actions: Date each action cleared by 505(b)(2) Clearance Committee	**3/12/13** ☐ Not a (b)(2) **6/10/14**
❖ NDAs only: Exclusivity Summary *(signed by Division Director)*	☒ Included
❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	
• Applicant is on the AIP	☐ Yes ☒ No

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

• This application is on the AIP o If yes, Center Director's Exception for Review memo *(indicate date)* o If yes, OC clearance for approval *(indicate date of clearance communication)*	☐ Yes ☒ No ☐ Not an AP action
❖ Pediatrics *(approvals only)* • Date reviewed by PeRC **9/4/13** If PeRC review not necessary, explain: _____	
❖ Outgoing communications: letters, emails, and faxes considered important to include in the action package by the reviewing office/division (e.g., clinical SPA letters, RTF letter, etc.) *(do not include previous action letters, as these are located elsewhere in package)*	**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)	**N/A**
❖ Minutes of Meetings	
• If not the first review cycle, any end-of-review meeting *(indicate date of mtg)*	☒ N/A or no mtg
• Pre-NDA/BLA meeting *(indicate date of mtg)*	☒ No mtg
• EOP2 meeting *(indicate date of mtg)*	☒ No mtg
• Mid-cycle Communication *(indicate date of mtg)*	☒ N/A
• Late-cycle Meeting *(indicate date of mtg)*	☒ N/A
• Other milestone meetings (e.g., EOP2a, CMC pilots) *(indicate dates of mtgs)*	**N/A**
❖ Advisory Committee Meeting(s)	☐ No AC meeting
• Date(s) of Meeting(s)	
Decisional and Summary Memos	
❖ Office Director Decisional Memo *(indicate date for each review)*	☒ None
Division Director Summary Review *(indicate date for each review)*	**9/28/13, 7/25/14**
Cross-Discipline Team Leader Review *(indicate date for each review)*	**7/17/14**
PMR/PMC Development Templates *(indicate total number)*	☒ None
Clinical	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) *(indicate date for each review)*	☒ No separate review
• Clinical review(s) *(indicate date for each review)*	**9/19/13, 1/24/13**
• Social scientist review(s) (if OTC drug) *(indicate date for each review)*	☒ None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here ☒ and include a review/memo explaining why not *(indicate date of review/memo)*	**Clinical review, page 9**
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers *(indicate date of each review)*	☒ None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation *(indicate date of each review)*	☒ N/A

❖ Risk Management • REMS Documents and REMS Supporting Document *(indicate date(s) of submission(s))* • REMS Memo(s) and letter(s) *(indicate date(s))* • Risk management review(s) and recommendations (including those by OSE and CSS) *(indicate date of each review and indicate location/date if incorporated into another review)*	**N/A** **N/A** ☒ None
❖ OSI Clinical Inspection Review Summary(ies) *(include copies of OSI letters to investigators)*	☒ None requested
Clinical Microbiology ☐ None	
❖ Clinical Microbiology Team Leader Review(s) *(indicate date for each review)*	☒ No separate review
Clinical Microbiology Review(s) *(indicate date for each review)*	☒ None
Biostatistics ☐ None	
❖ Statistical Division Director Review(s) *(indicate date for each review)*	☒ No separate review
Statistical Team Leader Review(s) *(indicate date for each review)*	☒ No separate review
Statistical Review(s) *(indicate date for each review)*	☒ **1/23/13, 9/9/13**
Clinical Pharmacology ☐ None	
❖ Clinical Pharmacology Division Director Review(s) *(indicate date for each review)*	☒ No separate review
Clinical Pharmacology Team Leader Review(s) *(indicate date for each review)*	☒ No separate review
Clinical Pharmacology review(s) *(indicate date for each review)*	☒ **1/24/13, 9/9/13**
❖ OSI Clinical Pharmacology Inspection Review Summary *(include copies of OSI letters)*	☒ None requested
Nonclinical ☐ None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) *(indicate date for each review)*	☒ No separate review
• Supervisory Review(s) *(indicate date for each review)*	☒ No separate review
• Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	☒ **1/31/13, 7/11/13**
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer *(indicate date for each review)*	☒ None
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	☒ No carc
❖ ECAC/CAC report/memo of meeting	☒ None
❖ OSI Nonclinical Inspection Review Summary *(include copies of OSI letters)*	☒ None requested

Product Quality ☐ None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) *(indicate date for each review)*	☒ No separate review
• Branch Chief/Team Leader Review(s) *(indicate date for each review)*	☒ No separate review
• Product quality review(s) including ONDQA biopharmaceutics reviews *(indicate date for each review)*	☒ **12/26/12, 1/28/13, 8/21/13, 7/14/14**
❖ Microbiology Reviews ☒ NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) *(indicate date of each review)* ☐ BLAs: Sterility assurance, microbiology, facilities reviews (OMPQ/MAPCB/BMT) *(indicate date of each review)*	☒ **1/2/13, 2/15/13**
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer *(indicate date of each review)*	☒ None
❖ Environmental Assessment (check one) (original and supplemental applications)	
☒ Categorical Exclusion *(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)*	**see 8/21/13 review, page 53**
☐ Review & FONSI *(indicate date of review)*	**N/A**
☐ Review & Environmental Impact Statement *(indicate date of each review)*	**N/A**
❖ Facilities Review/Inspection	
☒ NDAs: Facilities inspections (include EER printout or EER Summary Report only; do NOT include EER Detailed Report; date completed must be within **2 years** of action date) *(only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites[5])*	Date completed: **3/19/13** ☒ Acceptable ☐ Withhold recommendation ☐ Not applicable
☐ BLAs: TB-EER (date of most recent TB-EER must be within **30 days** of action date) *(original and supplemental BLAs)*	Date completed: ☐ Acceptable ☐ Withhold recommendation
❖ NDAs: Methods Validation *(check box only, do not include documents)*	☐ Completed ☐ Requested ☐ Not yet requested ☒ Not needed (per review)

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

Day of Approval Activities	
❖ For all 505(b)(2) applications: • Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity)	☒ No changes ☐ New patent/exclusivity *(Notify CDER OND IO)*
• Finalize 505(b)(2) assessment	☒ Done
❖ Send a courtesy copy of approval letter and all attachments to applicant by fax or secure email	☒ Done
❖ If an FDA communication will issue, notify Press Office of approval action after confirming that applicant received courtesy copy of approval letter	**N/A**
❖ Ensure that proprietary name, if any, and established name are listed in the *Application Product Names* section of DARRTS, and that the proprietary name is identified as the "preferred" name	**N/A**
❖ Ensure Pediatric Record is accurate	☒ Done
❖ Send approval email within one business day to CDER-APPROVALS	☒ Done

From: Knight, Yvonne
To: "Mihir Taneja"
Cc: Fortney, Russell
Subject: RE: Information Request for NDA 205029 (Request Teleconference)
Date: Monday, June 30, 2014 8:46:00 AM

You are quite welcome and we look forward to speaking with you.

Best Regards,

Yvonne Knight

From: Mihir Taneja [mailto:mihirt@belcherpharma.com]
Sent: Friday, June 27, 2014 6:18 PM
To: Knight, Yvonne
Cc: Fortney, Russell
Subject: Re: Information Request for NDA 205029 (Request Teleconference)

Hi Yvonne,

I wanted to thank you for accommodating us with an alternate date and time for the teleconference. I have confirmed with my team and Wednesday, July 2nd at 12:00pm EST works for myself and and my team. Please use the teleconference dial in number and ID listed below. I look forward to our call. Once again, i appreciate all your help. Have a very nice weekend.

Phone Number: (b) (4)
Access Code: (b) (4)

Regards,

Mihir Taneja
Belcher Pharmaceuticals, LLC
6911 Bryan Dairy Road
Largo, FL 33777
Ph: 727-471-0850 ext 250
Email: mihirt@belcherpharma.com

> **From:** "Knight, Yvonne" <Yvonne.Knight@fda.hhs.gov>
> **Date:** June 27, 2014 at 11:11:09 AM EDT
> **To:** Mihir Taneja <mihirt@belcherpharma.com>
> **Cc:** "Fortney, Russell" <Russell.Fortney@fda.hhs.gov>
> **Subject: RE: Information Request for NDA 205029 (Request Teleconference)**
>
> Hi Mihir,

Is your team available for Wednesday July 2,2014 at 12:00 PM (EST)?

Yvonne Knight

From: Mihir Taneja [mailto:mihirt@belcherpharma.com]
Sent: Friday, June 27, 2014 12:03 AM
To: Knight, Yvonne
Cc: Fortney, Russell
Subject: Re: Information Request for NDA 205029 (Request Teleconference)

Hi Yvonne,

I wanted to get back with you as promptly as possible. Some of my key team members are traveling and will not be available on Monday. Is it possible we can have the call on Tuesday or any other day next week. Aside from Monday, my team is fairly flexible for the balance of the week. If this is acceptable, please provide me a day and times that best works for you and your team and we will be sure to accommodate. I look forward to hearing from you.

Regards,

Mihir Taneja | Vice President

Belcher Pharmaceuticals, LLC
6911 Bryan Dairy Road | Largo, FL 33777 | USA
Office (727) 471-0850 Ext 250 | Fax (727) 471-0858 | Mobile (b) (6) (b) (6)
mihirt@belcherpharma.com | www.belcherpharma.com

advance.

On Jun 26, 2014, at 4:21 PM, "Knight, Yvonne" <Yvonne.Knight@fda.hhs.gov> wrote:

> Hi Mr. Taneja,
>
> My apologizes, it is actually for **Monday June 30, 2014 at 9 AM (EST).**
>
> Kind Regards,
>
> Yvonne Knight
>
> ---
>
> **From:** Knight, Yvonne
> **Sent:** Thursday, June 26, 2014 4:19 PM
> **To:** 'mihirt@belcherpharma.com'
> **Cc:** Knight, Yvonne; Fortney, Russell
> **Subject:** Information Request for NDA 205029 (Request Teleconference)
> **Importance:** High
>
> Good afternoon Mr. Taneja,
>
> Per our conversation, we have the following information request concerning Belcher's New Drug Application (NDA) NDA 205029. We request a teleconference to this IR request for **Tuesday July 1, 2014 9 AM (EST)**.
>
> The information we would like to discuss is as follows:
>
> 1. The specification for (b) (4) revised drug product specification, and stability data/shelf-life.
>
> **Please confirm receipt of this Information Request and we ask you to provide a call-in# for the teleconference. Feel free to contact me if you have any questions.**
>
> Best Regards,

Yvonne Knight, MS
Regulatory Health Project Manager
Division of New Drug Quality Assessment
FDA/CDER/OPS/ONDQA
10903 New Hampshire Avenue
Bldg. 21, Room 2667
Silver Spring, MD 20993-0002
Phone: 301.796.2133
Email: yvonne.knight@fda.hhs.gov

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/s/

YVONNE L KNIGHT
06/30/2014

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 205029

ACKNOWLEDGE –
CLASS 2 RESUBMISSION

Belcher Pharmaceuticals, LLC
Attention: Mihir Taneja
Vice President
6911 Bryan Dairy Road
Suite 210
Largo, FL 33777

Dear Mr. Taneja:

We acknowledge receipt on January 29, 2014, of your resubmission to your new drug application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for epinephrine injection 1 mg/mL.

We consider this a complete, class 2 response to our October 4, 2013, action letter. Therefore, the user fee goal date is July 29, 2014.

If you have any questions, call Russell Fortney, Regulatory Project Manager, at (301) 796-1068.

Sincerely,

{See appended electronic signature page}

Edward Fromm, R.Ph., RAC
Chief, Project Management Staff
Division of Cardiovascular and Renal Products
Office of Drug Evaluation 1
Center for Drug Evaluation and Research

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/s/

EDWARD J FROMM
02/07/2014

PeRC PREA Subcommittee Meeting Minutes
September 4, 2013

PeRC Members Attending:
Lynne Yao
Robert "Skip" Nelson
Karen Davis-Bruno
Rosemary Addy
Patricia Dinndorf
Tom Smith
Julia Pinto
Ethan Hausman
Peter Starke
Wiley Chambers
Andrew Mulberg
Andrew Mosholder
Colleen LoCicero
Dianne Murphy
Gregory Reaman
Dionna Green
Daiva Shetty
Lisa Kammerman
George Greeley
Jane Inglese

Guests Attending:
Robert Guidos
Richard Moscicki
Renan Bonnel (OPT)
Nichella Simms (PMHS)
Gilbert Burckart (OCP)
Courtney Suggs (OCP)
Richard Whitehead (DMEP)
Bradley McEvoy (OB)
Jaya Vaidyanathan (OCP)
Lokesh Jain (OCP)
David Carlson (DMEP)
Margaret Lin (DNP)
Hao Zhu (OCP)
Ellis Unger (ODE4)
Jing Zhang (DPP)
George Kordzakhia (DBI)
Linda Fossom (DPP)
Jenn Sellers (DPP)
Hiren Patel (DPP)
Joshua Lloyd (DAAAP)
Swati Patwardhan (DAAAP)
Juli Tomaino (DGIEP)
Anil Rajpal (DGIEP)
Nitin Mehrotra (OCP)
Karen Mahoney (DMEP)
Andre Jackson (OCP)
Sue-Chih Lee (PMTL)
Jian Wang (OCP)
Russel Fortney (DCRP)
Gail Moreschi (DCRP)
Shari Targum (DCRP)
Vicki Moyer (PMHS)
Amy Taylor (PMHS)
Melissa Tassinari (PMHS)

Agenda

(b) (4)

NDA 205029 Epinephrine Injection Full Waiver

(b) (4)

2 Pages have been Withheld in Full as b4 (CCI/TS) immediately following this page.

Epinephrine Injection Full Waiver

- NDA 205029 seeks marketing approval for Epinephrine injection for increasing systemic arterial blood pressure in acute hypotensive states associated with septic shock.
- The application was submitted on December 4, 2012, and has a PDUFA foal date of October 4, 2013.
- The application triggers PREA as directed to a new indication.
- A full waiver is being requested because studies are impossible or highly impractical.
- *Division justification for waiver:* The number of pediatric patients that have septic shock in a given year is below 6,500. Only a portion of these patients will require a vasopressor infusion for hypotension associated with septic shock. The yearly actual use of all vasopressors, for all conditions, in all pediatric patients is below 3,500 procedures. The number of pediatric patients that would benefit from this drug is below a substantial number of pediatric patients according to past FDA guidance and these patients are geographically dispersed. In addition, septic shock is an acute condition with rapid onset. Such factors make clinical studies in pediatric patients for this drug's indication highly impractical or impossible.

PeRC Recommendations:

- The PeRC did not agree with the Division to grant a full waiver in pediatric patients because studies are impossible or highly impractical.
- The PeRC recommended that the Division advise the sponsor that its pediatric plan is deficient and ask the sponsor to submit information from all available sources, including literature, to appropriately label the product for the pediatric population.
- Additional items and comments:
    - The PeRC will provide a reference to the Division on the incidence of septic shock in children in the United States.

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/s/

JANE E INGLESE
09/22/2013

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 205029

PROPRIETARY NAME REQUEST
UNACCEPTABLE

Belcher Pharmaceuticals, LLC
6911 Bryan Dairy Road Suite 210
Largo, Florida 33777

ATTENTION: Mihir Taneja
Vice President

Dear Mr. Taneja:

Please refer to your New Drug Application (NDA) dated and received December 4, 2012, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Epinephrine Injection, USP 1:1000 (1 mg/mL).

We also refer to your January 3, 2013, correspondence, received January 3, 2013, requesting review of your proposed proprietary name, (b) (4) We have completed our review of this proposed proprietary name and have concluded that this name is unacceptable for the following reasons:

(b) (4)

(b) (4)

(b) (4)

We note that your submission dated January 3, 2013 included an alternate proprietary name, (b) (4) Although we have not completed a safety review of your alternate name at this time, we want to advise you that this alternate name is (b) (4)

(b) (4)

(b) (4)

For this reason we do not recommend that you submit (b) (4) for evaluation.

If you wish to submit an alternative name, we refer you to the Guidance for Industry, *Contents of a Complete Submission for the Evaluation of Proprietary Names,* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM075068.pdf and "PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2008 through 2012".

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Cherye Milburn, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-2084. For any other information regarding this application contact Russell Fortney, Regulatory Project Manager in the Office of New Drugs (OND) at 301-796-1068.

Sincerely,

{See appended electronic signature page}

Kellie Taylor, PharmD, MPH
Deputy Director
Division of Medication Error Prevention and Analysis
Office of Medication Error Prevention and Risk Management
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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/s/

KELLIE A TAYLOR
04/03/2013

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 205029

INFORMATION REQUEST

Belcher Pharmaceuticals, LLC
Attention: Mihir Taneja
Vice President
6911 Bryan Dairy Road
Suite 210
Largo, FL 33777

Dear Mr. Taneja:

Please refer to your New Drug Application (NDA) dated November 30, 2012, received December 4, 2012, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for (b) (4) (epinephrine injection) 1 mg/mL.

We have reviewed the patent certifications included in your submission and have the following comments. We request a prompt written response in order to continue our evaluation of your NDA.

Under 21 CFR 314.54(a)(1)(vi), a 505(b)(2) application must contain a patent certification or statement (stating that a method of use patent does not claim a use for which the applicant is seeking approval) with respect to any relevant patents that claim the listed drug or that claim any other drugs on which investigations relied on by the applicant for approval of the application were conducted, or that claim a use for the listed or other drug. Your 505(b)(2) application relies upon the Agency's finding of safety and effectiveness for Twinject (NDA 20800), but does not contain an appropriate patent certification with respect to each patent listed in FDA's "Approved Drug Products with Therapeutic Equivalence Evaluation" (the Orange Book) for the listed drug. For Twinject (NDA 20800), the Orange Book currently lists two unexpired patents, 7297136 and 7621891. You must provide an appropriate patent certification for each of the unexpired patents and indicate to which patent the certification pertains by including the relevant patent number in the certification statement.

If you wish to dispute the accuracy or relevance of the patent information currently listed in the Orange Book for Twinject (NDA 20800), please notify the Agency as described under 21 CFR 314.53(f).

If you have any questions, please call Russell Fortney, Regulatory Project Manager, at (301) 796-1068.

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Director
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

NORMAN L STOCKBRIDGE
02/20/2013

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 205029

FILING COMMUNICATION

Belcher Pharmaceuticals, LLC
Attention: Mihir Taneja
Vice President
6911 Bryan Dairy Road
Suite 210
Largo, FL 33777

Dear Mr. Taneja:

Please refer to your New Drug Application (NDA) dated November 30, 2012, received December 4, 2012, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for (b) (4) (epinephrine injection) 1 mg/mL.

We also refer to your amendments dated January 3, 4, and 8, 2013.

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 October 4, 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 September 4, 2013. We are not currently planning to hold an advisory committee meeting to discuss this application.

At this time we have the following requests for additional information:

1. Please provide patient level data from the following publication,

   Abboud I, Lerolle N, Urien S, *et al*. Pharmacokinetics of epinephrine in patients with septic shock: modelization and interaction with endogenous neurohormonal status. Crit Care. 2009 Jul 21;13(4):R120.

   Data requested:

   - PK: Epinephrine and norepinephrine plasma concentrations at C_0 and C_1. Include data [if any] for any measurements made between C_0 and C_1.

- PD: Systolic BP, diastolic BP, mean BP and heart rate at C_0, C_1 and at time points when infusion rate was adjusted.
- Dose: Epinephrine infusion rates at C_0, C_1 and at time points when infusion rate was adjusted.
- Patient characteristics: Age, gender, body weight, SAPS II score and disease etiology.

The data from this publication is useful that it is derived from septic shock patients and reflects the most recent available information including the bioanalytical method used. A concentration-blood pressure relationship constructed using this data can help evaluate effectiveness and provide dosing instructions in the product label. Further, the literature available on dose-blood pressure relationship from healthy subjects (n=3) and septic shock patients (n=1) are not recent and the doses studied fall on the lower end of your proposed dosing regimen. Therefore, we recommend you to request the authors of the publication and acquire the patient level PK/PD data as described.

2. Provide copies of the epinephrine drug substance Certificates of Analysis (from vendor) for lots used in manufacturing the drug product stability batches and any subsequent drug product batches.

3. Epinephrine drug substance employed in manufacturing the drug product is (b) (4) . However, information provided in the application does not include an evaluation of epinephrine for chiral purity in the finished product. Provide data that support evaluation of drug product for potential (b) (4) from manufacturing process conditions and over the shelf life. If there is evidence of any (b) (4) in the drug product, we recommend that you include the limits of acceptance for epinephrine chiral impurity in the drug product and monitor for changes in the drug product over shelf-life.

4. Provide justification for (b) (4) epinephrine in the manufacturing process as the batch analysis and stability data consistently show epinephrine assay values range from (b) (4) and (b) (4) respectively.

5. You have submitted stability data in the application from batches manufactured in 2003 and 2004. Clarify whether or not these batches were manufactured employing identical formulation free of preservatives, manufacturing and (b) (4) as proposed for marketing. If not, provide stability data generated from drug product batches that conform to proposed manufacturing process for commercialization as the data presented in the application cannot be considered as primary stability data for assignment of shelf-life.

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.

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.

We acknowledge receipt of your request for a full waiver of pediatric studies for this application. Once we have reviewed your request, we will notify you if the full waiver request is denied and a pediatric drug development plan is required.

If you have any questions, please call Russell Fortney, Regulatory Project Manager, at (301) 796-1068.

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Director
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

NORMAN L STOCKBRIDGE
02/07/2013

From: Mesmer, Deborah
To: "Mihir Taneja"
Subject: NDA 205029 Information Request
Date: Thursday, January 03, 2013 12:19:58 PM

Dear Mr. Taneja,

Please refer to NDA 205029 for Epinephrine Injection. We have the following requests:

Provide a complete list of all the Drug Substance and Drug Product manufacturing, testing, processing, packaging and labeling facilities. Submit this information either on, or as an attachment to, the Form 356h.

- Include the full corporate name of the facility and address where the manufacturing function is performed, including the FEI number, and specific manufacturing responsibilities for each facility. Include any DMF numbers, if applicable.
- Provide the name and title of an onsite contact person for each facility, including their phone number, fax number, and email address.
- Provide a statement indicating readiness for inspection for each facility.

Please provide this information by COB **on January 4, 2013**, and include a courtesy copy to me by email.

Please acknowledge receipt of this message, and let me know if you have any questions.

Sincerely,

Deborah Mesmer

Deborah Mesmer
Regulatory Project Manager for Quality

Office of New Drug Quality Assessment (ONDQA)
Division of New Drug Quality Assessment (DNDQA1)
Food and Drug Administration
White Oak Building 21, Rm 1627
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

(301) 796-4023
deborah.mesmer@fda.hhs.gov

From: Mihir Taneja [mailto:mihirt@belcherpharma.com]
Sent: Thursday, January 03, 2013 10:55 AM
To: Mesmer, Deborah
Subject: RE: NDA 205029

He Deborah,

Please let this email act as authorization for you to convey information regarding NDA 205029 via email. Please don't hesitate to contact me if you have any questions.

Best Wishes,

Mihir Taneja

Mihir Taneja | Vice President
Belcher Pharmaceuticals, LLC
6911 Bryan Dairy Road | Largo, FL 33777 | USA
Office (727) 471-0850 Ext 250 | Fax (813) 438-2040 | Mobile (b) (6)
mihirt@belcherpharma.com | www.belcherpharma.com

From: Mesmer, Deborah [mailto:Deborah.Mesmer@fda.hhs.gov]
Sent: Wednesday, January 02, 2013 11:25 PM
To: 'mihirt@belcherpharma.com'
Subject: NDA 205029
Importance: High

Dear. Mr. Taneja,

Please authorize me to convey information requests for NDA 205029 via email.

Sincerely,

Deborah Mesmer

Deborah Mesmer
Regulatory Project Manager for Quality
Office of New Drug Quality Assessment (ONDQA)
Division of New Drug Quality Assessment (DNDQA1)
Food and Drug Administration
White Oak Building 21, Rm 1627
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
(301) 796-4023
deborah.mesmer@fda.hhs.gov

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/s/

DEBORAH M MESMER
01/03/2013

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 205029

NDA ACKNOWLEDGMENT

Belcher Pharmaceuticals, LLC
Attention: Ms. Mihir Taneja
Vice President
6911 Bryan Dairy Road, Suite 210
Largo, FL 33777

Dear Ms. Taneja:

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

Name of Drug Product: Epinephrine Injection, USP 1:1000 (mg/mL)

Date of Application: December 4, 2012

Date of Receipt: December 4, 2012

Our Reference Number: NDA 205029

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 February 2, 2013, in accordance with 21 CFR 314.101(a).

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 Cardiovascular and Renal Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

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If you have any questions, please contact:

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Regulatory Health Project Manager
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Sincerely,

{See appended electronic signature page}

Edward Fromm, R.Ph., RAC
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