CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
050823Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS
PATENT CERTIFICATION

CEFTAZIDIME FOR INJECTION USP AND DEXTROSE INJECTION USP IN THE DUXLEX® CONTAINER, 1 g and 2 g

Pursuant to 21 CFR 314.50 (i)(1)(i), in the opinion and to the best knowledge of B. Braun Medical Inc., there are no patents that claim the drug or drugs on which investigations that are relied upon in this application were conducted or that claim a use of such drug or drugs.

Rebecca A. Stolarick
Director, Regulatory Affairs

27 May 2011
Date
EXCLUSIVITY SUMMARY

NDA # 50-823     SUPPL # N/A     HFD # 520

Trade Name   Ceftazidime for Injection USP and Dextrose Injection USP in the Duplex® Container
Generic Name   N/A
Applicant Name   B. Braun Medical, Inc.
Approval Date, If Known   June 13, 2011

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.

      N/A

   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:

      N/A

   d) Did the applicant request exclusivity?

      Reference ID: 2951904
If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

N/A

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

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?

N/A

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?

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#
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#

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

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Investigation #2

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Investigation #2

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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:
Investigation #2

YES ☐ NO ☐

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:  J. Christopher Davi
Title:  Senior Regulatory Project Manager
Date:  May 18, 2009

Name of Office/Division Director signing form:  Katherine A. Laessig
Title:  Deputy Division Director

Form OGD-01347; Revised 05/10/2004; formatted 2/15/05
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JOSEPH C DAVI
05/25/2011

KATHERINE A LAESSIG
05/26/2011

Reference ID: 2951904
1.3.3 Debarment Certification

Certification of Compliance with Generic Drug Enforcement Act of 1992

Pursuant to Section 306(k) of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Drug Enforcement Act of 1992, B. Braun Medical Inc. (B. Braun) hereby certifies that it did not and will not use, in any capacity, the services of any person debarred under subsection (a) or (b) of the Generic Drug Enforcement Act of 1992 in connection with this NDA.

Kikoo Tewani
Corporate Vice President
Quality and Regulatory Compliance
# ACTION PACKAGE CHECKLIST

## APPLICATION INFORMATION

<table>
<thead>
<tr>
<th>NDA #</th>
<th>50-823</th>
<th>NDA Supplement #</th>
<th>N/A</th>
<th>If NDA, Efficacy Supplement Type</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>BLA #</td>
<td>N/A</td>
<td>BLA STN #</td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proprietary Name:</td>
<td>Cefazidine for Injection USP and Dextrose Injection USP in the Duplex Container</td>
<td>Applicant:</td>
<td>B. Braun Medical, Inc.</td>
<td>Agent for Applicant (if applicable):</td>
<td>N/A</td>
</tr>
<tr>
<td>Established/Proper Name:</td>
<td>Cefazidine for Injection USP and Dextrose Injection USP in the Duplex Container</td>
<td>Dosage Form:</td>
<td>Injection</td>
<td>Division:</td>
<td>DAIP</td>
</tr>
<tr>
<td>RPM:</td>
<td>J. Christopher Davi, MS, Sr. RPM</td>
<td>505(b)(2) Original NDAs and 505(b)(2) NDA supplements:</td>
<td>Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s)):</td>
<td>50-578 (Fortaz - GlaxoSmithKline)</td>
<td></td>
</tr>
</tbody>
</table>

(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.)

## Actions

- Proposed action
- User Fee Goal Date is **June 13, 2011**
- Previous actions (specify type and date for each action taken)

**AP** | **TA** | **CR**

**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.
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 N/A.

application characteristics

<table>
<thead>
<tr>
<th>Review priority:</th>
<th>Standard</th>
<th>Priority</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemical classification (new NDAs only):</td>
<td>Type 5</td>
<td></td>
</tr>
</tbody>
</table>

- [ ] Fast Track
- [ ] Rolling Review
- [ ] Orphan drug 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)
- [ ] Approval based on animal studies

BLAs: Subpart E
- [ ] Accelerated approval (21 CFR 601.41)
- [ ] Restricted distribution (21 CFR 601.42)
- [ ] 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

Comments: None

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 N/A

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
- Press Office notified of action (by OEP)
- Indicate what types (if any) of information dissemination are anticipated

- [ ] None
- [ ] HHS Press Release
- [ ] FDA Talk Paper
- [ ] CDER Q&As
- [ ] Other

---

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.

Version: 3/15/11

Reference ID: 2959797
### Exclusivity

- **Is approval of this application blocked by any type of exclusivity?**
  - No □ Yes □

- **NDAs and BLAs:** Is there existing orphan drug exclusivity for the “same” drug or biologic for the proposed indication(s)? 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.
  - No □ Yes □
  - If yes, NDA/BLA # and date exclusivity expires:

- **(b)(2) NDAs only:** Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*
  - No □ Yes □
  - If yes, NDA # and date exclusivity expires:

- **(b)(2) NDAs only:** Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*
  - No □ Yes □
  - If yes, NDA # and date exclusivity expires:

- **(b)(2) NDAs only:** Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*
  - No □ Yes □
  - If yes, NDA # and date exclusivity expires:

- **NDAs only:** Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? *(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.)*
  - No □ Yes □
  - If yes, NDA # and date 10-year limitation expires:

### Patent Information (NDAs only)

- **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.
  - Verified □ Not applicable because drug is an old antibiotic.

- **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(j)(1)(i)(A) □ Verified
  - 21 CFR 314.50(j)(1)
    - (ii) □ (iii) □

- **[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).
  - No paragraph III certification Date patent will expire

- **[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). *(If the application does not include any paragraph IV certifications, mark “N/A” and skip to the next section below (Summary Reviews)).*
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:

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Have 45 days passed since the patent owner’s receipt of the applicant’s notice of certification?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(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))).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If “Yes,” skip to question (4) below. If “No,” continue with question (2).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(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)?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>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.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If “No,” continue with question (3).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(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))).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>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.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(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)?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>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).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If “No,” continue with question (5).</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
(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?

(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).

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).

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.

---

**CONTENTS OF ACTION PACKAGE**

- Copy of this Action Package Checklist³
  - Yes

**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)
  - Action(s) and date(s) June 13, 2011

**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.
    - May 18, 2011
  - Original applicant-proposed labeling
    - September 10, 2010
  - Example of class labeling, if applicable
    - N/A

---

³ Fill in blanks with dates of reviews, letters, etc.
<table>
<thead>
<tr>
<th>Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling (write submission/communication date at upper right of first page of each piece)</th>
<th>Medication Guide</th>
<th>Patient Package Insert</th>
<th>Instructions for Use</th>
<th>Device Labeling</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.</td>
<td>N/A</td>
<td></td>
<td></td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>• Original applicant-proposed labeling</td>
<td>N/A</td>
<td></td>
<td></td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>• Example of class labeling, if applicable</td>
<td>N/A</td>
<td></td>
<td></td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Labels (full color carton and immediate-container labels) (write submission/communication date on upper right of first page of each submission)</td>
<td>N/A</td>
<td></td>
<td></td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>• Most-recent draft labeling</td>
<td>September 10, 2010</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proprietary Name</td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Acceptability/non-acceptability letter(s) (indicate date(s))</td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Review(s) (indicate date(s))</td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Labeling reviews (indicate dates of reviews and meetings)</td>
<td>RPM October 1, 2010</td>
<td>DMEPA May 4, 2011</td>
<td>DRISK</td>
<td>DDMAC April 13, 2011</td>
<td>CSS</td>
</tr>
</tbody>
</table>

**Administrative / Regulatory Documents**

| Administrative Reviews (e.g., RPM Filing Review\^4/Memo of Filing Meeting) (indicate date of each review) | October 1, 2010 | Not a (b)(2) 505(b)(2) clearance on May 24, 2011 | Not a (b)(2) |
| All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte |                         |                                               |
| NDA (b)(2) Approvals Only: 505(b)(2) Assessment (indicate date) |
| 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](http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm) | N/A             | Yes | No |
| • Applicant is on the AIP |
| • This application is on the AIP |
| • If yes, Center Director’s Exception for Review memo (indicate date) |
| • If yes, OC clearance for approval (indicate date of clearance communication) |
| Pediatrics (approvals only) |
| • Date reviewed by PeRC March 9, 2011 |
| If PeRC review not necessary, explain: Already appropriately labeled for pediatric patients (can not give partial doses with Duplex package configuration) |
| Pediatric Page/Record (approvals only, must be reviewed by PERC before finalized) |
| 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 (include certification) | Included |

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

Reference ID: 2959797
<table>
<thead>
<tr>
<th>Category</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outgoing communications (letters (except action letters), emails, faxes, telecons)</td>
<td>Included</td>
</tr>
<tr>
<td>Internal memoranda, telecons, etc.</td>
<td>N/A</td>
</tr>
<tr>
<td>Minutes of Meetings</td>
<td></td>
</tr>
<tr>
<td>- Regulatory Briefing (indicate date of mtg)</td>
<td>No mtg</td>
</tr>
<tr>
<td>- If not the first review cycle, any end-of-review meeting (indicate date of mtg)</td>
<td>N/A or no mtg</td>
</tr>
<tr>
<td>- Pre-ND/A/BLA meeting (indicate date of mtg)</td>
<td>No mtg</td>
</tr>
<tr>
<td>- EOP2 meeting (indicate date of mtg)</td>
<td>No mtg</td>
</tr>
<tr>
<td>- Other milestone meetings (e.g., EOP2a, CMC pilots) (indicate dates of mtgs)</td>
<td>None</td>
</tr>
<tr>
<td>Advisory Committee Meeting(s)</td>
<td>No AC meeting</td>
</tr>
<tr>
<td>- Date(s) of Meeting(s)</td>
<td>N/A</td>
</tr>
<tr>
<td>- 48-hour alert or minutes, if available (do not include transcript)</td>
<td>N/A</td>
</tr>
</tbody>
</table>

### Decisional and Summary Memos

- Office Director Decisional Memo (indicate date for each review) | None
- Division Director Summary Review (indicate date for each review) | None June 13, 2011
- Cross-Discipline Team Leader Review (indicate date for each review) | None June 2, 2011
- PMR/PMC Development Templates (indicate total number) | None

### Clinical Information

- Clinical Reviews
  - Clinical Team Leader Review(s) (indicate date for each review) | June 8, 2011
  - Clinical review(s) (indicate date for each review) | April 19, 2011
  - 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) | No studies were performed
- 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) | Not applicable
- Risk Management
  - REMS Documents and Supporting Statement (indicate date(s) of submission(s)) | None
  - REMS Memo(s) and letter(s) (indicate date(s)) | OSE Consult - March 29, 2011
  - 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) | None requested
- DSI Clinical Inspection Review Summary(ies) (include copies of DSI letters to investigators) | None requested

---

5 Filing reviews should be filed with the discipline reviews.
<table>
<thead>
<tr>
<th>Clinical Microbiology</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Microbiology Team Leader Review(s) (indicate date for each review)</td>
<td>None March 17, 2011</td>
</tr>
<tr>
<td>Clinical Microbiology Review(s) (indicate date for each review)</td>
<td>None March 17, 2011</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Biostatistics</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statistical Division Director Review(s) (indicate date for each review)</td>
<td>None</td>
</tr>
<tr>
<td>Statistical Team Leader Review(s) (indicate date for each review)</td>
<td>None January 11, 2011</td>
</tr>
<tr>
<td>Statistical Review(s) (indicate date for each review)</td>
<td>None January 10, 2011</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical Pharmacology</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Pharmacology Division Director Review(s) (indicate date for each review)</td>
<td>None</td>
</tr>
<tr>
<td>Clinical Pharmacology Team Leader Review(s) (indicate date for each review)</td>
<td>None March 10, 2011</td>
</tr>
<tr>
<td>Clinical Pharmacology review(s) (indicate date for each review)</td>
<td>None March 10, 2011</td>
</tr>
<tr>
<td>DSI Clinical Pharmacology Inspection Review Summary (include copies of DSI letters)</td>
<td>None</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nonclinical</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacology/Toxicology Discipline Reviews</td>
<td>None</td>
</tr>
<tr>
<td>ADP/T Review(s) (indicate date for each review)</td>
<td>None</td>
</tr>
<tr>
<td>Supervisory Review(s) (indicate date for each review)</td>
<td>None September 30, 2010</td>
</tr>
<tr>
<td>Pharm/tox review(s), including referenced IND reviews (indicate date for each review)</td>
<td>None September 30, 2010</td>
</tr>
<tr>
<td>Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (indicate date for each review)</td>
<td>None</td>
</tr>
<tr>
<td>Statistical review(s) of carcinogenicity studies (indicate date for each review)</td>
<td>No carc</td>
</tr>
<tr>
<td>ECAC/CAC report/memo of meeting</td>
<td>None Included in P/T review, page</td>
</tr>
<tr>
<td>DSI Nonclinical Inspection Review Summary (include copies of DSI letters)</td>
<td>None requested</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Product Quality</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product Quality Discipline Reviews</td>
<td>None</td>
</tr>
<tr>
<td>ONDQA/OBP Division Director Review(s) (indicate date for each review)</td>
<td>None</td>
</tr>
<tr>
<td>Branch Chief/Team Leader Review(s) (indicate date for each review)</td>
<td>None</td>
</tr>
<tr>
<td>Product quality review(s) including ONDQA biopharmaceutics reviews (indicate date for each review)</td>
<td>None April 28, 2011 and May 19, 2011</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Microbiology Reviews</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>NDAs: Microbiology reviews (sterility &amp; pyrogenicity) (OPS/NDMS) (indicate date of each review)</td>
<td>Not needed April 28, 2011</td>
</tr>
<tr>
<td>BLAs: Sterility assurance, microbiology, facilities reviews (DMPQ/MAPCB/BMT) (indicate date of each review)</td>
<td></td>
</tr>
<tr>
<td>Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer (indicate date of each review)</td>
<td>None</td>
</tr>
<tr>
<td>Environmental Assessment (check one) (original and supplemental applications)</td>
<td></td>
</tr>
<tr>
<td>--------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>☑ Categorical Exclusion (indicate review date) (all original applications and all efficacy supplements that could increase the patient population)</td>
<td></td>
</tr>
<tr>
<td>CMC Review, pg. 88</td>
<td></td>
</tr>
<tr>
<td>April 18, 2011</td>
<td></td>
</tr>
<tr>
<td>☐ Review &amp; FONSI (indicate date of review)</td>
<td></td>
</tr>
<tr>
<td>☐ Review &amp; Environmental Impact Statement (indicate date of each review)</td>
<td></td>
</tr>
<tr>
<td>Facilities Review/Inspection</td>
<td></td>
</tr>
<tr>
<td>☑ NDAs: Facilities inspections (include EER printout) (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)</td>
<td></td>
</tr>
<tr>
<td>Date completed: Facilities acceptable through 9/22/2012</td>
<td></td>
</tr>
<tr>
<td>☑ Acceptable</td>
<td></td>
</tr>
<tr>
<td>☐ Withhold recommendation</td>
<td></td>
</tr>
<tr>
<td>☐ Not applicable</td>
<td></td>
</tr>
<tr>
<td>☐ BLAs: TB-EER (date of most recent TB-EER must be within 30 days of action date) (original and supplemental BLAs)</td>
<td></td>
</tr>
<tr>
<td>Date completed: N/A</td>
<td></td>
</tr>
<tr>
<td>☑ Acceptable</td>
<td></td>
</tr>
<tr>
<td>☐ Withhold recommendation</td>
<td></td>
</tr>
<tr>
<td>☐ NDAs: Methods Validation (check box only, do not include documents)</td>
<td></td>
</tr>
<tr>
<td>☐ Completed</td>
<td></td>
</tr>
<tr>
<td>☐ Requested</td>
<td></td>
</tr>
<tr>
<td>☐ Not yet requested</td>
<td></td>
</tr>
<tr>
<td>☑ Not needed (per review)</td>
<td></td>
</tr>
</tbody>
</table>

---

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

/s/

----------------------------------------------------
JOSEPH C DAVI
06/13/2011
Dear Pattie,

The following Information Request is from our CMC reviewer in reference to NDA 50-823.

We concur with the proposed 9-month expiration dating period.

Regarding the Comparability Protocol to support the process change and extension of expiry, we cannot accept this protocol in its current form. At this point in the NDA review cycle it will not be possible to accept the data that are necessary to support the changes without an extension of the review clock. Additionally, we do not feel that it would be appropriate to submit this information as a CBE supplement for the following reasons:

- Need for data to assure that the modified process and equipment provide suitable sterility assurance
- There does not seem to be knowledge at present regarding how the [REDACTED]

In addition to the information described in Part V of your comparability protocol, we recommend that the following information be submitted as a Prior-Approval supplement to support the changes:

- A suitably detailed description of equipment and process parameters, and sterility validation information, [REDACTED]
- A summary of available knowledge on how the [REDACTED]

If you wish to retain the comparability protocol in the NDA, please also modify bullet 2 (Part V) to specify statistical analysis, and clarify that the proposed expiry in bullet 3 will not exceed 12 months based on 6 months of long-term data per the ICH Q1E approach.

Thanks,

Althea Cuff
Regulatory Health Project Manager
Office of New Drugs Quality Assessment
301-796-4061
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

STEPHEN P MILLER
04/08/2011
I concur with these IR comments
NDA 50-823

FILING COMMUNICATION

B. Braun Medical, Inc.
Attention: Susan Olinger, J.D.
Corporate Vice President, Regulatory Affairs
901 Marcon Boulevard
Allentown, PA  18109

Dear Dr. Olinger:

Please refer to your new drug application (NDA) dated August 12, 2010, received August 13, 2010, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Ceftazidime for Injection USP and Dextrose Injection, USP in the Duplex® Container, 1g and 2g.

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 was 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 June 13, 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 April 25, 2011.

During our filing review of your application, we identified the following potential review issues pertaining to the methods to be used in and the controls used for the manufacture, processing and holding of the drug substance or drug product.

1. The application lacks information for ceftazidime including:
   i. A certificate of analysis
   ii. Specifications
   iii. Storage conditions and expiration period
   iv. Characteristics (such as solubility, pH, )
v. Lot numbers of the ceftazidime used in the registration batches (i.e., DP Lots #13121, 131122 and 13127)

2. The application lacks information for the diluent stability testing. If this information is contained in another application, authorization to reference that application is needed.

3. A comprehensive impurity comparison of your drug product in the Duplex container with the reference listed drug (RLD) was not included. This comparison should have included the chromatograms (scaled suitably to view the impurity peaks) and a quantitative comparison of the impurity peaks in a tabular format. If any new impurities were identified, toxicology qualification information should have been provided.

4. The overage of ceftazidime is not supported. The overage for the diluent is not supported.

5. Information is lacking on the accuracy/variance of your powder and liquid filling lines.

We do not expect a response to this letter. 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, and we may not review all responses during the current review cycle.

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

If you have not already done so, you must 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. The content of labeling must be in the Prescribing Information (physician labeling rule) format.

**REQUIRED PEDIATRIC ASSESSMENTS**

This drug product may be fully labeled for use in all appropriate pediatric populations. We will notify you if we determine that the current pediatric labeling is not adequate. If we determine that the current pediatric labeling is not adequate, you will need to submit a pediatric plan for the relevant pediatric age group(s).

We also 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 of our decision.
If you have any questions, call J. Christopher Davi, MS, Senior Regulatory Project Manager, at (301) 796-0702.

Sincerely,

{See appended electronic signature page}

Katherine A. Laessig, MD
Deputy Division Director
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

KATHERINE A LAESSIG
10/13/2010
DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 50-823

NDA ACKNOWLEDGMENT

B. Braun Medical, Inc.
Attention: Susan J. Olinger, J.D.
Corporate Vice President, Regulatory Affairs
901 Marcon Boulevard
Allentown, PA  18109

Dear Dr. Olinger:

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

Name of Drug Product: Ceftazidime for Injection USP and Dextrose Injection USP in the Duplex® Container

Date of Application: August 12, 2010

Date of Receipt: August 13, 2010

Our Reference Number: NDA 50-823

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 October 12, 2010, 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 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 Anti-Infective and Ophthalmology 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 J. Christopher Davi, MS, Senior Regulatory Project Manager, at (301) 796-0702.

Sincerely,

{See appended electronic signature page}

Frances LeSane
Chief, Project Management Staff
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
<table>
<thead>
<tr>
<th>Application Type/Number</th>
<th>Submission Type/Number</th>
<th>Submitter Name</th>
<th>Product Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>NDA-50823</td>
<td>ORIG-1</td>
<td>B BRAUN MEDICAL INC</td>
<td>CEFTAZIDIME INJ/DEXTROSE INJ 1G/2G DUPLE</td>
</tr>
</tbody>
</table>

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

/s/

Frances V LESANE
09/02/2010