

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**202106Orig1s000**

**ADMINISTRATIVE and CORRESPONDENCE  
DOCUMENTS**

## EXCLUSIVITY SUMMARY

NDA # 202106

SUPPL # n/a

HFD # n/a

Trade Name: n/a

Generic Name: Meropenem for Injection USP and Sodium Chloride Injection USP in Duplex Container, for intravenous use

Applicant Name: B. Braun Medical, Inc.

Approval Date, If Known: 04/30/15

### 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?

YES  NO

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?

YES  NO

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

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

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

YES  NO

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

## **PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES**

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

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

YES  NO

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

NDA#

NDA#

NDA#

2. Combination product.

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

YES  NO

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

NDA#

NDA#

NDA#

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

**PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS**

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

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability

studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES  NO

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

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

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

YES  NO

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

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

YES  NO

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

YES  NO

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could

independently demonstrate the safety and effectiveness of this drug product?

YES  NO

If yes, explain:

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

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

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

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

Investigation #1 YES  NO

Investigation #2 YES  NO

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

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

Investigation #1 YES  NO



Investigation #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:

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Name of person completing form: **Maureen P. Dillon-Parker**  
Title: **Chief, Project Management Staff**  
Date: **04/30/15**

Name of Office/Division Director signing form: **Sumathi Nambiar, MD, MPH**  
Title: **Director, Division of Anti-Infective Products**

Form OGD-011347

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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MAUREEN P DILLON PARKER  
04/30/2015

SUMATHI NAMBIAR  
04/30/2015

# ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION <sup>1</sup>		
NDA # <b>202106</b> BLA # n/a	NDA Supplement # n/a BLA Supplement # n/a	If NDA, Efficacy Supplement Type: n/a <i>(an action package is not required for SE8 or SE9 supplements)</i>
Proprietary Name: n/a Established/Proper Name: <b>Meropenem for Injection USP and Sodium Chloride Injection USP in Duplex Container, for intravenous use</b> Dosage Form: <b>Intravenous</b>		Applicant: <b>B. Braun Medical, Inc.</b> Agent for Applicant (if applicable): n/a
RPM: <b>Maureen Dillon-Parker</b>		Division: <b>Anti-Infective Products</b>
NDA Application Type: <input type="checkbox"/> 505(b)(1) <input checked="" type="checkbox"/> <b>505(b)(2)</b> Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)  BLA Application Type: <input type="checkbox"/> 351(k) <input type="checkbox"/> 351(a) Efficacy Supplement: <input type="checkbox"/> 351(k) <input type="checkbox"/> 351(a)	<p><b><u>For ALL 505(b)(2) applications, two months prior to EVERY action:</u></b></p> <ul style="list-style-type: none"> <li><b>Review the information in the 505(b)(2) Assessment and submit the draft<sup>2</sup> to CDER OND IO for clearance.</b></li> <li><b>Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity)</b></li> </ul> <p><b>X No changes</b>  <input type="checkbox"/> New patent/exclusivity <i>(notify CDER OND IO)</i>  <b>Date of check: 4/30/15</b></p> <p><i>Note: If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</i></p>	
❖ Actions		
<ul style="list-style-type: none"> <li>Proposed action</li> <li>User Fee Goal Date is <b>04/30/15</b></li> </ul>	<b>X AP</b> <input type="checkbox"/> TA <input type="checkbox"/> CR	
<ul style="list-style-type: none"> <li>Previous actions <i>(specify type and date for each action taken)</i></li> </ul>	<b>CR 07-25-14</b>	
❖ 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 <a href="http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf">http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf</a> ). If not submitted, explain _____	<b>N/A</b> <input type="checkbox"/> Received	

<sup>1</sup> 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.

<sup>2</sup> For resubmissions, (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).

❖ Application Characteristics <sup>3</sup>	
<p>Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority            Chemical classification (new NDAs only): <b>4 – New Combination</b>  <i>(confirm chemical classification at time of approval)</i></p> <p> <input type="checkbox"/> Fast Track <input type="checkbox"/> Rx-to-OTC full switch  <input type="checkbox"/> Rolling Review <input type="checkbox"/> Rx-to-OTC partial switch  <input type="checkbox"/> Orphan drug designation <input type="checkbox"/> Direct-to-OTC  <input type="checkbox"/> Breakthrough Therapy designation         </p> <p>           NDAs: Subpart H <input type="checkbox"/> Accelerated approval (21 CFR 314.510)  <input type="checkbox"/> Restricted distribution (21 CFR 314.520)            Subpart I <input type="checkbox"/> Approval based on animal studies         </p> <p> <input type="checkbox"/> Submitted in response to a PMR  <input type="checkbox"/> Submitted in response to a PMC  <input type="checkbox"/> Submitted in response to a Pediatric Written Request         </p> <p>           BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 601.41)  <input type="checkbox"/> Restricted distribution (21 CFR 601.42)            Subpart H <input type="checkbox"/> Approval based on animal studies         </p> <p>           REMS: <input type="checkbox"/> MedGuide  <input type="checkbox"/> Communication Plan  <input type="checkbox"/> ETASU  <input type="checkbox"/> MedGuide w/o REMS  <input type="checkbox"/> REMS not required         </p> <p>Comments: n/a</p>	
❖ Public communications <i>(approvals only)</i>	
<ul style="list-style-type: none"> <li>Office of Executive Programs (OEP) liaison has been notified of action</li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> <li>Indicate what types (if any) of information were issued</li> </ul>	<input checked="" type="checkbox"/> None <input type="checkbox"/> FDA Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other
❖ Exclusivity	
<ul style="list-style-type: none"> <li>Is approval of this application blocked by any type of exclusivity (orphan, 5-year NCE, 3-year, pediatric exclusivity)?</li> <li>If so, specify the type</li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes n/a
❖ Patent Information (NDAs only)	
<ul style="list-style-type: none"> <li>Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought.</li> </ul>	<input checked="" type="checkbox"/> Verified/Not applicable <input type="checkbox"/> Not applicable because drug is an old antibiotic.

<sup>3</sup> 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.

<b>CONTENTS OF ACTION PACKAGE</b>	
<b>Officer/Employee List</b>	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list ( <i>approvals only</i> )	<b>X Included</b>
Documentation of consent/non-consent by officers/employees	<b>X Included</b>
<b>Action Letters</b>	
❖ Copies of all action letters ( <i>including approval letter with final labeling</i> )	Action(s) and date(s) <b>Complete Response 07/25/14</b> <b>Approval 04/30/15</b>
<b>Labeling</b>	
❖ Package Insert ( <i>write submission/communication date at upper right of first page of PI</i> )	
<ul style="list-style-type: none"> <li>• Most recent draft labeling (<i>if it is division-proposed labeling, it should be in track-changes format</i>)</li> </ul>	<b>X Included</b>
<ul style="list-style-type: none"> <li>• Original applicant-proposed labeling</li> </ul>	<b>X Included</b>
❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling ( <i>write submission/communication date at upper right of first page of each piece</i> )	<input type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <b>X None</b>
<ul style="list-style-type: none"> <li>• Most-recent draft labeling (<i>if it is division-proposed labeling, it should be in track-changes format</i>)</li> </ul>	<input type="checkbox"/> Included
<ul style="list-style-type: none"> <li>• Original applicant-proposed labeling</li> </ul>	<input type="checkbox"/> Included
❖ Labels ( <b>full color</b> carton and immediate-container labels) ( <i>write submission/communication date on upper right of first page of each submission</i> )	
<ul style="list-style-type: none"> <li>• Most-recent draft labeling</li> </ul>	<b>X Included</b>
❖ Proprietary Name <ul style="list-style-type: none"> <li>• Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>)</li> <li>• Review(s) (<i>indicate date(s)</i>)</li> </ul>	<b>N/A; name not requested.</b> n/a
❖ Labeling reviews ( <i>indicate dates of reviews</i> )	RPM: <b>X None</b> DMEPA: (2) <b>06/10/14; 01/26/15</b> DMPP/PLT (DRISK): <b>X None</b> OPDP: (2) <b>07/02/14; 03/03/15</b> SEALD: <b>X None</b> CSS: <b>X None</b> Product Quality <b>X None</b> Other: <b>X None</b>

Administrative / Regulatory Documents	
❖ RPM Filing Review <sup>4</sup> /Memo of Filing Meeting (indicate date of each review) ❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Committee	Enclosed; 02/11/14 <input type="checkbox"/> Not a (b)(2) 6/10/14; 03/23/15
❖ NDAs only: Exclusivity Summary ( <i>signed by Division Director</i> )	X Included 4/30/15
❖ Application Integrity Policy (AIP) Status and Related Documents <a href="http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm">http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm</a>	
• Applicant is on the AIP	<input type="checkbox"/> Yes X No
• This application is on the AIP ○ If yes, Center Director's Exception for Review memo ( <i>indicate date</i> ) ○ If yes, OC clearance for approval ( <i>indicate date of clearance communication</i> )	<input type="checkbox"/> Yes X No  <input type="checkbox"/> Not an AP action
❖ Pediatrics ( <i>approvals only</i> ) • Date reviewed by PeRC <u>N/A</u> If PeRC review not necessary, explain: <b>PeRC not triggered/not required</b>	
❖ Outgoing communications: letters, emails, and faxes considered important to include in the action package by the reviewing office/division (e.g., clinical SPA letters) ( <i>do not include previous action letters, as these are located elsewhere in package</i> )	Enclosed
❖ 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 ( <i>indicate date of mtg</i> )	X N/A or no mtg
• Pre-NDA/BLA meeting ( <i>indicate date of mtg</i> )	11/04/2010
• EOP2 meeting ( <i>indicate date of mtg</i> )	X No mtg
• Mid-cycle Communication ( <i>indicate date of mtg</i> )	X N/A
• Late-cycle Meeting ( <i>indicate date of mtg</i> )	X N/A
• Other milestone meetings (e.g., EOP2a, CMC pilots) ( <i>indicate dates of mtgs</i> )	N/A
❖ Advisory Committee Meeting(s)	X No AC meeting
• Date(s) of Meeting(s)	N/A
Decisional and Summary Memos	
❖ Office Director Decisional Memo ( <i>indicate date for each review</i> )	X None
Division Director Summary Review ( <i>indicate date for each review</i> )	07/25/14; 04/30/15
Cross-Discipline Team Leader Review ( <i>indicate date for each review</i> )	07/05/14; 04/30/15
PMR/PMC Development Templates ( <i>indicate total number</i> )	X None

<sup>4</sup> Filing reviews for scientific disciplines are **NOT** required to be included in the action package.

<b>Clinical</b>	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) ( <i>indicate date for each review</i> )	<b>X No separate review</b>
• Clinical review(s) ( <i>indicate date for each review</i> )	<b>11/20/13; 4/27/15</b>
• Social scientist review(s) (if OTC drug) ( <i>indicate date for each review</i> )	<b>X None</b>
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here <b>X</b> and include a review/memo explaining why not ( <i>indicate date of review/memo</i> )	<b>04/29/15</b>
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers ( <i>indicate date of each review</i> )	<b>X None</b>
❖ Controlled Substance Staff review(s) and Scheduling Recommendation ( <i>indicate date of each review</i> )	<b>X N/A</b>
❖ Risk Management <ul style="list-style-type: none"> <li>• REMS Documents and REMS Supporting Document (<i>indicate date(s) of submission(s)</i>)</li> <li>• REMS Memo(s) and letter(s) (<i>indicate date(s)</i>)</li> <li>• Risk management review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>)</li> </ul>	<b>N/A</b> <b>N/A</b> <b>X None</b>
❖ OSI Clinical Inspection Review Summary(ies) ( <i>include copies of OSI letters to investigators</i> )	<b>X None requested</b>
<b>Clinical Microbiology</b> <input type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) ( <i>indicate date for each review</i> )	<b>X No separate review</b>
Clinical Microbiology Review(s) ( <i>indicate date for each review</i> )	<b>05/14/14; 6/27/14</b>
<b>Biostatistics</b> <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) ( <i>indicate date for each review</i> )	<b>N/A</b>
Statistical Team Leader Review(s) ( <i>indicate date for each review</i> )	<b>X No separate review</b>
Statistical Review(s) ( <i>indicate date for each review</i> )	<b>11/20/13</b>
<b>Clinical Pharmacology</b> <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) ( <i>indicate date for each review</i> )	<b>N/A</b>
Clinical Pharmacology Team Leader Review(s) ( <i>indicate date for each review</i> )	<b>X No separate review</b>
Clinical Pharmacology review(s) ( <i>indicate date for each review</i> )	<b>06/20/14; 03/13/15</b>
❖ OSI Clinical Pharmacology Inspection Review Summary ( <i>include copies of OSI letters</i> )	<b>X None requested</b>

<b>Nonclinical</b> <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) ( <i>indicate date for each review</i> )	N/A
• Supervisory Review(s) ( <i>indicate date for each review</i> )	X No separate review
• Pharm/tox review(s), including referenced IND reviews ( <i>indicate date for each review</i> )	05/22/14; 04/23/15 (memo)
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer ( <i>indicate date for each review</i> )	X None
❖ Statistical review(s) of carcinogenicity studies ( <i>indicate date for each review</i> )	X No carc
❖ ECAC/CAC report/memo of meeting	X None Included in P/T review, page n/a
❖ OSI Nonclinical Inspection Review Summary ( <i>include copies of OSI letters</i> )	X None requested
<b>Product Quality</b> <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews	
• Tertiary review ( <i>indicate date for each review</i> )	N/A
• Secondary review (e.g., Branch Chief) ( <i>indicate date for each review</i> )	X No separate review
• Integrated Quality Assessment (contains the Executive Summary and the primary reviews from each product quality review discipline)( <i>indicate date for each review</i> )	ONDQA 06/20/14; 07/24/14; 04/29/15 ; Biowaiver Request review 06/02/14; Micro Ster 06/30/14
❖ Reviews by other disciplines/divisions/Centers requested by product quality review team ( <i>indicate date of each review</i> )	X None
❖ Environmental Assessment (check one) (original and supplemental applications)	
<input checked="" type="checkbox"/> Categorical Exclusion ( <i>indicate review date</i> )( <i>all original applications and all efficacy supplements that could increase the patient population</i> )	Page 57-58/CMC Review dated 06/20/14
<input type="checkbox"/> Review & FONSI ( <i>indicate date of review</i> )	N/A
<input type="checkbox"/> Review & Environmental Impact Statement ( <i>indicate date of each review</i> )	N/A
❖ Facilities Review/Inspection	
<input checked="" type="checkbox"/> NDAs: Facilities inspections ( <i>action must be taken prior to the re-evaluation date</i> ) ( <i>only original applications and efficacy supplements that require a manufacturing facility inspection(e.g., new strength, manufacturing process, or manufacturing site change)</i> )	Date completed: 04/29/15 X Acceptable Re-evaluation date: <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable
❖ NDAs: Methods Validation ( <i>check box only, do not include documents</i> )	X Completed P.55 CMC Review <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input type="checkbox"/> Not needed (per review)

Day of Approval Activities	
❖ For all 505(b)(2) applications: <ul style="list-style-type: none"> <li>• Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity)</li> </ul>	<b>X No changes</b> <input type="checkbox"/> New patent/exclusivity ( <i>Notify CDER OND IO</i> )
<ul style="list-style-type: none"> <li>• Finalize 505(b)(2) assessment</li> </ul>	<b>X Done</b>
❖ For Breakthrough Therapy (BT) Designated drugs: <ul style="list-style-type: none"> <li>• Notify the CDER BT Program Manager</li> </ul>	<input type="checkbox"/> Done <b>N/A</b> ( <i>Send email to CDER OND IO</i> )
❖ For products that need to be added to the flush list (generally opioids): <a href="#">Flush List</a> <ul style="list-style-type: none"> <li>• Notify the Division of Online Communications, Office of Communications</li> </ul>	<input type="checkbox"/> Done <b>N/A</b>
❖ Send a courtesy copy of approval letter and all attachments to applicant by fax or secure email	<b>X Done</b>
❖ If an FDA communication will issue, notify Press Office of approval action after confirming that applicant received courtesy copy of approval letter	<input type="checkbox"/> Done <b>N/A</b>
❖ Ensure that proprietary name, if any, and established name are listed in the <i>Application Product Names</i> section of DARRTS, and that the proprietary name is identified as the “preferred” name	<input type="checkbox"/> Done <b>N/A</b>
❖ Ensure Pediatric Record is accurate	<input type="checkbox"/> Done <b>N/A</b>
❖ Send approval email within one business day to CDER-APPROVALS	<b>X Done</b>

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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MAUREEN P DILLON PARKER  
05/04/2015

~~✓~~ CARTON/Container

**Dillon Parker, Maureen P**

**From:** Kristina.Hahn-Major@bbraun.com  
**Sent:** Monday, April 27, 2015 8:58 AM  
**To:** Dillon Parker, Maureen P  
**Subject:** RE: Meropenem NDA202106; FDA revised labeling  
**Attachments:** LD-440-2 Y37-002-488 FPL actual.pdf; LD-439-2 Y37-002-489 FPL actual.pdf

Good morning Maureen,

I received the below email (in italic) from our Labeling group regarding the container files I sent you on Friday. I apologize for any inconvenience.

*I realized this morning that the files I provided on Friday were not at actual size. I have reattached new files for the 2 labels that are at 100%.*

Kind regards,  
Kristina

Kristina Hahn-Major, M.S.  
Senior Specialist, Regulatory Affairs  
Supervisor of RA Operations

B. Braun Medical Inc.  
PL-RA-US-01  
901 Marcon Boulevard  
Allentown, PA 18109  
Phone: 610-596-2768  
Work Cell: (b) (6)  
Fax: 610-266-4962  
Email: kristina.hahn-major@bbraun.com

From: "Dillon Parker, Maureen P" <Maureen.DillonParker@fda.hhs.gov>  
To: "Kristina.Hahn-Major@bbraun.com" <Kristina.Hahn-Major@bbraun.com>,  
Cc: "Pamela.Skoutelas@bbraun.com" <Pamela.Skoutelas@bbraun.com>  
Date: 04/24/2015 10:12 AM  
Subject: RE: Meropenem NDA202106; FDA revised labeling

Thank you Kristina.  
I will give your directions a try.  
Maureen

## Dillon Parker, Maureen P

---

**From:** Dillon Parker, Maureen P  
**Sent:** Tuesday, July 01, 2014 5:12 PM  
**To:** 'kristina.hahn-major@bbraun.com'  
**Cc:** Dillon Parker, Maureen P  
**Subject:** Draft Meropenem in Duplex Labeling



FINAL DRAFT  
LABELING 07.01....

Hello Kristina,

Attached please find the Division's revised 'DRAFT' labeling for Meropenem for Injection USP and Sodium Chloride Injection USP [NDA 202106] and comments on the Carton/Container labeling. Please review and let me know of any questions. Additionally, please see requested revisions to the container labels and the rationale for the use of 'Duplex Container' below.

### Revisions to All Container Labels (500 mg and 1 g)

1. The Principal Display Panel (PDP) contains the (b)(4) abbreviation. Replace the (b)(4) abbreviation with the word "Intravenous" as per FDA Guidance for Industry titled *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* which states that "The route of administration should be described without abbreviation." Additionally, the correct administration technique for the product is via intravenous infusion; therefore, revise the statement (b)(4) to "For Intravenous Infusion Only". This change will also be consistent with the information provided in the dosage and administration sections of the prescribing information labeling.
2. Ensure that the established name and strength are the most prominent information on the PDP by increasing their font size. Ensure that the units of measure are next to the numbers (e.g. 500 mg) in the strength statement for clarity. To accommodate the revision above and improve readability, consider relocate the strength to below the product name or adjust the size of the fonts accordingly. Also, the statement (b)(4) [please revise to read "DUPLEX Container"] competes for prominence with the product name and strength. Decrease the size of the statement and consider relocating it further away from the name and strength.
3. The following statements are important use information and lack appropriate prominence on the label: "For Intravenous Infusion Only (as per A1 above)", "Use only after mixing contents of both chambers", and "Single dose". Increase the prominence of these important statements by increasing their font size, placing each statement on a separate line, and by adding white/empty space between these statements and the rest of the text on the label below, to decrease clutter.
4. The mock-up labels do not indicate where the lot number and expiration date will appear, as per 21CFR 201.17 and 21CFR 201.18, please indicate where the required lot number and expiration date will appear on the labels (or if the lot and expiration will be embossed on the bag).

5. The reference number (REF 3183-11) is not standard information listed on container labels in the United States and may lead to confusion. Also the number competes for prominence with important prescribing information and creates clutter; therefore, consider deleting this number or relocate it away from the name and strength, such as to the bottom left corner of the label.
6. To decrease clutter and improve readability, decrease the font size of the NDC number and relocate it such as to the upper right corner of the label.
7. The following sections appear to be out of order: Reconstitution, Prior to Reconstitution, and After Reconstitution. Consider revising the order of these sections for flow and clarity (e.g., by listing the "Prior to Reconstitution" section first, followed by "Reconstitution" section and "After Reconstitution" section).

Rationale for use of 'Duplex Container' vs (b) (4)

The draft product title guidance states that the term

(b) (4)  
(b) (4)  
(b) (4) Both CDER and USP recommend use of this term as defined. The duplex is a dual compartment IV container that stores the diluent and drug powder in two separate compartments until administration. It does not (b) (4)  
Therefore the use of the term (b) (4) for this product does not really meet the CDER and USP definition; the term "container" is appropriate.

Please let me know that you receive this communication and that the attached file opens correctly.

Best Regards,

Maureen

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Maureen P. Dillon-Parker | Chief, Project Management Staff |  
Division of Anti-Infective Products | Office of Antimicrobial Products |  
Center for Drug Evaluation and Research |  
ph: 301.796.0706 | fax: 301.796.9882 |  
Email: [maureen.dillonparker@fda.hhs.gov](mailto:maureen.dillonparker@fda.hhs.gov)

*Please consider the environment before printing this e-mail*

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/s/  
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MAUREEN P DILLON PARKER  
07/02/2014



NDA 202106

**INFORMATION REQUEST**

B. Braun Medical Inc.  
Attention: Rebecca Stolarick  
Corporate Vice President, Regulatory Affairs  
901 Marcon Blvd.  
Allentown, PA 18109

Dear Ms. Stolarick:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Meropenem for Injection USP and Sodium Chloride Injection USP in the Duplex Container.

We are reviewing the Chemistry, Manufacturing, and Controls section of your submission and have the following comments and information requests. We request a prompt written response by June 13, 2014, in order to continue our evaluation of your NDA.

According to the draft labeling, the proposed drug product shelf life after activation is “1 hour at room temperature (b) (4) or 15 hours under refrigeration (b) (4)”. However, in the stability section of application, the proposed product shelf life after activation is (b) (4) which is not supported by the stability data. Please revise the proposed shelf life after activation to “1 hour at room temperature (b) (4) or 15 hours under refrigeration (b) (4)” in the stability section of the NDA (Module 3, Section P.8).

If you have any questions, call Navdeep Bhandari, Regulatory Health Project Manager, at (240) 402 -3815.

Sincerely,

*{See appended electronic signature page}*

Rapti D. Madurawe, Ph.D.  
Branch Chief, Branch V  
Division of New Drug Quality Assessment II  
Office of New Drug Quality Assessment  
Center for Drug Evaluation and Research

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/s/  
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DOROTA M MATECKA  
06/05/2014



NDA 202106

**INFORMATION REQUEST**

B. Braun Medical Inc.  
Attention: Rebecca Stolarick  
Corporate Vice President, Regulatory Affairs  
901 Marcon Blvd.  
Allentown, PA 18109

Dear Ms. Stolarick:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Meropenem for Injection USP and Sodium Chloride Injection USP in the Duplex Container.

We are reviewing the Chemistry, Manufacturing, and Controls section of your submission and have the following comments and information requests. We request a prompt written response by May 27, 2014, in order to continue our evaluation of your NDA.

1. We acknowledge that the acceptance criteria of assay for Meropenem for Injection have been revised to (b) (4)% and the target fill weight has been revised to (b) (4)% of the label claim of meropenem. However, the acceptance criterion for filling weight ((b) (4) % of label claim of meropenem) has not been updated. Please provide drug product specification with updated fill weight acceptance criteria ((b) (4)% of label claim of meropenem).
2. Revise relevant sections of the application (batch formula, manufacture, etc.) with filling overage updated from (b) (4)% to (b) (4)%.
3. Table 3 on pg. 10-12/96 in section 3.2.P.2 of your NDA is missing item 5. Please submit an updated version of Table 3 with complete items (1 to 10).

If you have any questions, call Navdeep Bhandari, Regulatory Health Project Manager, at (240) 402 -3815.

Sincerely,

*{See appended electronic signature page}*

Rapti D. Madurawe, Ph.D.  
Branch Chief, Branch V  
Division of New Drug Quality Assessment II  
Office of New Drug Quality Assessment  
Center for Drug Evaluation and Research

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/s/  
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BALAJEE SHANMUGAM  
05/22/2014



Pre-NDA 202106

**MEETING MINUTES**

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

Dear Dr. Olinger:

Please refer to your pre-assigned number (NDA) for Meropenem for Injection USP and Sodium Chloride Injection USP in the Duplex Container, 0.5g and 1g.

We also refer to the pre-NDA meeting between representatives of your firm and the Division of Anti-Infective and Ophthalmology Products on November 4, 2010. The purpose of the meeting was to discuss a 505(b)(2) application proposed for a meropenem finished product in the Duplex Container.

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

If you have any questions, call Kyong Hyon, Regulatory Project Manager, at (301) 796-0734.

Sincerely yours,

*{See appended electronic signature page}*

Katherine Laessig, M.D.  
Deputy Director  
Division of Anti-Infective and Ophthalmology Products  
Office of Antimicrobial Products  
Center for Drug Evaluation and Research

Enclosure – Meeting Minutes



FOOD AND DRUG ADMINISTRATION  
CENTER FOR DRUG EVALUATION AND RESEARCH

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**MEMORANDUM OF MEETING MINUTES**

**Meeting Type:** Pre-NDA  
**Meeting Category:** Guidance

**Meeting Date and Time:** November 4, 2010, 10:00 AM – 11:00 NOON (EST)  
**Meeting Location:** 10903 New Hampshire Avenue, Silver Spring, MD 20993, Building 22, Room 1315

**Application Number:** Pre-NDA 202106  
**Product Name:** Meropenem for Injection USP and Sodium Chloride Injection USP in the Duplex<sup>®</sup> Container, 0.5g and 1g  
**Indication:** Treatment Complicated skin and skin structure infections and intra-abdominal infections  
**Sponsor/Applicant Name:** B. Braun Medical Inc.  
**Meeting Recorder:** Kyong Hyon

**FDA ATTENDEES**

**Division of Anti-Infective and Ophthalmology Products (DAIOP)**

Wiley Chambers, MD, Acting Director  
Katherine Laessig, MD, Deputy Director  
Sumathi Nambiar, MD, MPH, Deputy Director for Safety  
Thomas Smith, MD, Clinical Team Leader  
Benjamin Lorenz, MD, Clinical Reviewer  
Mark Gamalo, PhD, Statistical Reviewer  
Amy Ellis, PhD, Pharmacology/Toxicology Reviewer  
Ryan Owen, PhD, Clinical Pharmacology Reviewer  
Frederic Marsik, PhD, Clinical Microbiology Team Leader  
Kerian Grande, PhD, Clinical Microbiology Reviewer  
Rapti Madurawe, PhD, Pharmaceutical Assessment Team Leader, Branch IV, ONDQA  
Zi-Qiang Gu, PhD, Office of Compliance Reviewer  
Steven Fong, PhD, Microbiology Quality Reviewer  
Kyong Hyon, Regulatory Project Manager

**EXTERNAL CONSTITUENT ATTENDEES: (Sponsor)**

**B. Braun Medical Inc.**

Susan Olinger, JD, Corporate Vice President, Regulatory Affairs  
Kimberly Ernst, Director, Regulatory Affairs  
Patricia Smith, BS, Senior Specialist, Regulatory Affairs  
Nicholas Wu, MS, Manager, R&D Engineering



**BACKGROUND**

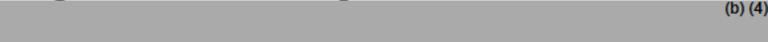
The Sponsor submitted a Pre-NDA Type B meeting request on August 9, 2010 to discuss their 505(b)(2) application proposed for a meropenem finished product in the Duplex container. The face-to-face meeting was granted on August 20, 2010 and scheduled to occur on November 4, 2010. The meeting package (MP) was submitted on September 30, 2010. The Division sent preliminary written responses to the Sponsor's questions from the MP on October 26, 2009 via e-mail.

**SUMMARY OF DISCUSSION**

The following is a summary of the minutes of the face-to-face meeting held on November 4, 2010, including prior communication. The Sponsor's initial questions from the MP are in bold followed by responses from the Division, and the points discussed during the face-to-face meeting.

The meeting started with the introduction of the attendees and a brief description of the purpose of the meeting. The Sponsor stated that they would like to discuss only the Regulatory portion of questions from their MP during this meeting.

**COMPLIANCE**

**Question 1: Does the Division agree with the overall plan to manufacture this carbapenem product using**  (b) (4)

**Division Response (per October 26, 2010 e-mail):** We do not have any objection for using  (b) (4) to manufacture of this product, as long as any  (b) (4)

- No further discussion was needed.

**Question 2: Does the Division agree with the overall plan to use a [REDACTED] (b) (4) [REDACTED] (b) (4) to produce the exhibit batches on the [REDACTED] (b) (4) while the proposed commercial scale batches will be manufactured on a [REDACTED] (b) (4)**

**Division Response (per October 26, 2010 e-mail):** We do not have any objection for the proposed approach. However, the [REDACTED] (b) (4) has to be properly qualified before its use in commercial manufacturing. It is also important to ensure that the quality of the product produced from the [REDACTED] (b) (4) is consistent with that of the exhibit batches. Furthermore, the final acceptability will be evaluated during the PAI/cGMP inspection.

- No further discussion was needed.

**Question 3:B. Braun/FACTA proposes to have the commercial machine installed for the pre-approval inspection by FDA for this application. The proposed commercial machine, [REDACTED] (b) (4)**

**Does the Division agree with this strategy?**

**Division Response (per October 26, 2010 e-mail):** We do not have any objection with your strategy. However, the final acceptability will be evaluated during the PAI/cGMP inspection.

**Discussion at the November 4, 2010 face-to-face meeting:** The Agency quality microbiologist noted that validations conducted for the [REDACTED] (b) (4) and emphasized that separate validations should be conducted for each line prior to product manufacture.

**Question 4: The proposed plan is to upgrade the [REDACTED] (b) (4) [REDACTED] (b) (4) once the exhibit batches are manufactured. Does the Division agree? Because this machine, [REDACTED] (b) (4) is the proposed commercial line for future manufacturing, it most likely will not be operating when the pre-approval inspection occurs. Is this acceptable?**

**Division Response (per October 26, 2010 e-mail):** Again, we do not have any objection to your strategy. However, the final acceptability will be evaluated during the PAI/cGMP inspection.

- No further discussion was needed.

## **REGULATORY**

**Question 1: B. Braun is proposing to** [REDACTED] (b) (4)

**Does the Division agree with this proposal?**

**Division Response (per October 26, 2010 e-mail):** No. The Division recommends stability data from three primary batches of drug product at each of the two strengths, as given in ICH Q1A.

[REDACTED] (b) (4)  
[REDACTED] ICH  
Q1A recommends two of the three stability batches be at least at pilot scale.

### **Discussion at the November 4, 2010 face-to-face meeting:**

- The Sponsor stated that they will provide stability data for three lots of the 500 mg strength and three lots of the 1 g strength as recommended by the Division.
- The Division had concerns about how [REDACTED] (b) (4)

[REDACTED] (b) (4)  
The Division reiterated that [REDACTED] (b) (4)

[REDACTED] separate validations must be conducted for each line prior to product manufacture.

**Question 2: Is it acceptable to submit the 505(b)(2) application with** [REDACTED] (b) (4)

**Division Response (per October 26, 2010 e-mail):** No. The Division recommends 12-months of long-term, 6-months accelerated data, and intermediate data if appropriate, as recommended in ICH Q1A. The shelf life granted will be based on the amount of stability data presented. Diluent stability should be evaluated under the ICH Q1A conditions for aqueous products packaged in semi-permeable containers.

### **Discussion at the November 4, 2010 face-to-face meeting:**

- The Sponsor inquired if they could submit [REDACTED] (b) (4)

[REDACTED] The Division stated that a complete submission is expected at the time of NDA submission and the Division would only grant

expiration date based on the amount of stability data submitted. The Division would not guarantee review of data submitted during the review cycle.

**Question 3: Does the Division agree that additional diluent(s) listed in the RLD package insert be added to this 505(b)(2) application as a Prior Approval Supplement with 3 month data for 1 lot of each strength with both room temperature and accelerated stability studies?**

**Division Response (per October 26, 2010 e-mail):** Additional diluents as listed in the RLD may be added as Prior Approval supplements. The Division requests at least 6 months long-term, and accelerated data (and intermediate data, if appropriate) for at least two batches tested under the ICH Q1A stability conditions for aqueous products packaged in semi-permeable containers.

**Discussion at the November 4, 2010 face-to-face meeting:**

- The Sponsor inquired if 3 month of room temperature and accelerated stability data for 1 lot would be sufficient for each new diluent added. The Division responded that if the Sponsor were requesting only 3 month of expiration date, then the 3 months data would be acceptable. However, if the Sponsor was to seek a longer expiration date, then they should submit stability data to cover the proposed expiry period.
- The Sponsor inquired if the diluent(s) listed in the RLD package insert could be added to the same 505(b)(2) NDA application as Prior Approval Supplements. The Division stated that they may need to revise their response given in the October 26, 2010 email as the addition of a new diluent changes the drug product and may require a separate NDA. The Division state that they will consult the Office of Regulatory Affairs at FDA and will inform the Sponsor at a later time.

**Post-meeting Comment:** The Division informed the Sponsor after the meeting that the same product in a different diluent should be submitted under a new 505(b)(2) NDA; each diluent warrants a new separate 505(b)(2) NDA.

**Additional Comments:**

- The application should contain comparative impurity profiles of Merrem and Meropenem Injection USP in the Duplex<sup>®</sup> Container.
- As long as there are no impurities or degradation products in Meropenem Injection USP in Duplex<sup>®</sup> Container that exceed ICH qualification threshold levels or the levels in comparable marketed products such as Merrem<sup>®</sup>, we do not anticipate that nonclinical testing will be necessary for this product. Approval via the 505(b)(2) pathway would be appropriate, with you requesting that the Division rely on its prior findings for safety for Merrem<sup>®</sup>, which you have listed in the briefing document as the appropriate reference listed drug.

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/s/  
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KATHERINE A LAESSIG  
11/24/2010

**From:** Gu, Zi Qiang  
**Sent:** Tuesday, October 26, 2010 1:52 PM  
**To:** Hyon, Kyong  
**Subject:** RE: RE: Pre-NDA 202106, Meropenem for Injection USP and Sodium Chloride Injection USP in the Duplex Container

**Attachments:** Memo\_Response\_2010\_Oct25.doc

Hi, Kyong:

I did some minor edit in my response (Highlighted in red color).

Thanks,

Zi-Qiang



Memo\_Response\_2  
010\_Oct25.doc (...)

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**From:** Hyon, Kyong  
**Sent:** Monday, October 25, 2010 2:00 PM  
**To:** Miller, Stephen; Sloan, Milton J; Pohlhaus, Timothy; Gu, Zi Qiang  
**Cc:** Smith, Thomas; Lorenz, Benjamin; Laessig, Katherine A  
**Subject:** RE: Pre-NDA 202106, Meropenem for Injection USP and Sodium Chloride Injection USP in the Duplex Container

Hello all,

Please review/edit the comments to the Sponsor's MP questions.

Thanks! ----- Kyong

<< File: E-mail MPCom 04Nov10F2F.doc >>

**MEMORANDUM** DEPARTMENT OF HEALTH AND HUMAN SERVICES  
PUBLIC HEALTH SERVICE  
FOOD AND DRUG ADMINISTRATION  
CENTER FOR DRUG EVALUATION AND RESEARCH

**DATE:** October 25, 2010

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

Phone (610) 596-2517  
Fax (610) 596-2686

**THROUGH:** Review Team for Pre-NDA 202106

**FROM:** Kyong Hyon  
Regulatory Project Manager  
Division of Anti-Infective and Ophthalmology Products  
(301) 796-0734  
(301) 796-9881 (Fax)  
[kyong.hyon@fda.hhs.gov](mailto:kyong.hyon@fda.hhs.gov)

**SUBJECT:** Pre-NDA 202106, Meropenem for Injection USP and Sodium Chloride Injection USP in the Duplex<sup>®</sup> Container, 0.5g and 1g

The following are the Division's preliminary responses to the questions posted in your meeting package dated September 28, 2010. The original questions are reproduced in bold below, followed by Division's response.

**COMPLIANCE**

**1. Does the Division agree with the overall plan to manufacture this carbapenem product using [REDACTED] (b) (4)**

**Division Response:** We do not have any objection for using [REDACTED] (b) (4) to manufacture of this product, as long as any [REDACTED] (b) (4)

2. Does the Division agree with the overall plan to use a (b) (4) (b) (4) to produce the exhibit batches on the (b) (4) while the proposed commercial scale batches will be manufactured on a (b) (4) (b) (4)

**Division Response:** We do not have any objection for the proposed approach. However, the (b) (4) has to be properly qualified before its use in commercial manufacturing. It is also important to ensure that the quality of the product produced from the (b) (4) is consistent with that of the exhibit batches. Furthermore, the final acceptability will be evaluated during the PAI/cGMP inspection.

3. B. Braun/FACTA proposes to have the commercial machine installed for the pre-approval inspection by FDA for this application. The proposed commercial machine, (b) (4)

Does the Division agree with this strategy?

**Division Response:** We do not have any objection with your strategy. However, the final acceptability will be evaluated during the PAI/cGMP inspection.

4. The proposed plan is to upgrade the (b) (4) once the exhibit batches are manufactured. Does the Division agree? Because this machine, (b) (4) is the proposed commercial line for future manufacturing, it most likely will not be operating when the pre-approval inspection occurs. Is this acceptable?

**Division Response:** Again, we do not have any objection with your strategy. However, the final acceptability will be evaluated during the PAI/cGMP inspection.

## REGULATORY

1. B. Braun is proposing to (b) (4)

Does the Division agree with this proposal?

**Division Response:** No. The division recommends stability data from three primary batches of drug product at each of the two strengths, as given in ICH Q1A.

(b) (4)

(b) (4)  
ICH Q1A  
recommends two of the three stability batches be at least at pilot scale.

**2. Is it acceptable to submit the 505(b)(2) application with** (b) (4)

**Division Response:** No. The division recommends 12-months of long-term, 6-months accelerated data, and intermediate data if appropriate, as recommended in ICH Q1A. The shelf life granted will be based on the amount of stability data presented. Diluent stability should be evaluated under the ICH Q1A conditions for aqueous products packaged in semi-permeable containers.

**3. Does the Division agree that additional diluent(s) listed in the RLD package insert be added to this 505(b)(2) application as a Prior Approval Supplement with 3 month data for 1 lot of each strength with both room temperature and accelerated stability studies?**

**Division Response:** Additional diluents as listed in the RLD may be added as Prior Approval supplements. The division requests at least 6 months long-term, and accelerated data (and intermediate data, if appropriate) for at least two batches tested under the ICH Q1A stability conditions for aqueous products packaged in semi-permeable containers.

**Additional Comments:**

- The application should contain comparative impurity profiles of Merrem and Meropenem Injection USP in the Duplex® Container.
- As long as there are no impurities or degradation products in Meropenem Injection USP in Duplex® Container that exceed ICH qualification threshold levels or the levels in comparable marketed products such as Merrem®, we do not anticipate that nonclinical testing will be necessary for this product. Approval via the 505(b)(2) pathway would be appropriate, with the sponsor requesting that the Division rely on its prior findings for safety for Merrem®, which the sponsor has listed in the briefing document as the appropriate reference listed drug. (from AE)

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/s/  
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KYONG M HYON  
11/12/2010

**From:** Gu, Zi Qiang

**Sent:** Friday, October 15, 2010 9:09 AM

**To:** Hyon, Kyong

**Cc:** Cruz, Concepcion; Hong, Jaewon

**Subject:** RE: Meeting Forward Notification: FW: FILING MEETING - (b)(4)

**Attachments:** Pre-NDA 202106\_ MP Questions\_B Braun.doc

Hi, Kyong:

I am not able to attend the meeting this morning since I have a pre-scheduled doctor's appointment. I am sending you my draft response to the MP questions. Please let me know if you have any questions.

Thanks,

Zi-Qiang

1. A list of proposed questions, grouped by discipline.

COMPLIANCE

1. Does the Division agree with the overall plan to manufacture this carbapenem product using [REDACTED] (b) (4)

We do not have any objection for using [REDACTED] (b) (4) to manufacture of this product, as long as any [REDACTED] (b) (4)

2. Does the Division agree with the overall plan to use a [REDACTED] (b) (4) [REDACTED] to produce the exhibit batches on the [REDACTED] (b) (4) while the proposed commercial scale batches will be manufactured on a [REDACTED] (b) (4)

We do not have any objection for the proposed approach. However, firm have to properly qualify the [REDACTED] (b) (4) before its commercial manufacturing. The firm also has to compare the quality of the product produced from the [REDACTED] (b) (4) to that of the exhibit batches to ensure the quality is consistent. Furthermore, the final acceptability will be evaluated during the PAI/cGMP inspection.

3. B. Braun/FACTA proposes to have the commercial machine installed for the pre-approval inspection by FDA for this application. The proposed commercial machine, [REDACTED] (b) (4)

Does the Division agree with this strategy?

We do not have any objection with your strategy. However, the final acceptability will be evaluated during the PAI/cGMP inspection.

4. The proposed plan is to upgrade the [REDACTED] (b) (4) once the exhibit batches are manufactured. Does the Division agree? Because this machine, [REDACTED] (b) (4) is the proposed commercial line for future manufacturing, it most likely will not be operating when the pre-approval inspection occurs. Is this acceptable?

**Pre -NDA 202106 Meropenem for Injection USP and Sodium Chloride Injection USP in the Duplex<sup>®</sup> Container**

1.6.1 Meeting Packet



Again, we do not have any objection with your strategy. However, the final acceptability will be evaluated during the PAI/cGMP inspection.

**REGULATORY**

1. B. Braun is proposing to [REDACTED] (b) (4)  
[REDACTED] Does the Division agree with this proposal?
2. Is it acceptable to submit the 505(b)(2) application with [REDACTED] (b) (4)  
[REDACTED]
3. Does the Division agree that additional diluent(s) listed in the RLD package insert be added to this 505(b)(2) application as a Prior Approval Supplement with 3 month data for 1 lot of each strength with both room temperature and accelerated stability studies?

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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KYONG M HYON  
11/12/2010