

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*  
**201367Orig1s000**

**ADMINISTRATIVE and CORRESPONDENCE**  
**DOCUMENTS**

## EXCLUSIVITY SUMMARY

NDA # 201367

SUPPL #

HFD # 120

Trade Name Banzel

Generic Name rufinamide oral suspension

Applicant Name Eisai Inc.

Approval Date, If Known March 03, 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)(1)

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.

New Dosage Form indication based on bioequivalence study data.

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?

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# 021911

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:

Efficacy studies submitted under NDA 021911 and cross-referenced to this NDA.

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

Investigation #1 YES  NO

Investigation #2 YES  NO

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



Investigation #2

!

YES

! NO

Explain:

! Explain:

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

YES

NO

If yes, explain:

Name of person completing form: Su-Lin Sun, PharmD

Title: Regulatory Project Manager

Date: March 3, 2011

Name of Office/Division Director signing form: Russell G. Katz, MD

Title: Director, Division of Neurology Products

Office of Drug Evaluation I

Center for Drug Evaluation and Research

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

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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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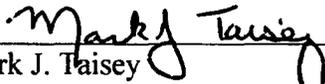
/s/  
-----

SU-LIN SUN  
03/09/2011

RUSSELL G KATZ  
03/09/2011

## DEBARMENT CERTIFICATION

Eisai, Inc., hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug and Cosmetic Act in connection with NDA 201367 for Banzel® (rufinamide) Oral Suspension.

  
\_\_\_\_\_  
Mark J. Taisey  
President, Global Regulatory Affairs CFU  
Eisai, Inc.

8 April 10  
Date

# ACTION PACKAGE CHECKLIST

## APPLICATION INFORMATION<sup>1</sup>

NDA # 201367 BLA #	NDA Supplement # BLA STN #	If NDA, Efficacy Supplement Type:
Proprietary Name: Banzel Established/Proper Name: rufinamide Dosage Form: 40mg/mL oral suspension		Applicant: Eisai Inc. Agent for Applicant (if applicable):
RPM: Su-Lin Sun, PharmD		Division: Neurology Products
<p><b>NDAs:</b>            NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1)    <input type="checkbox"/> 505(b)(2)            Efficacy Supplement:    <input type="checkbox"/> 505(b)(1)    <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the 505(b)(2) Assessment or the Appendix to this Action Package Checklist.)</p>		<p><b>505(b)(2) Original NDAs and 505(b)(2) NDA supplements:</b>            Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s)):</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p>If no listed drug, explain.</p> <p><input type="checkbox"/> This application relies on literature.  <input type="checkbox"/> This application relies on a final OTC monograph.  <input type="checkbox"/> Other (explain)</p> <p><b><u>Two months prior to each action, review the information in the 505(b)(2) Assessment and submit the draft to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.</u></b></p> <p><b><u>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</u></b></p> <p><input type="checkbox"/> No changes    <input type="checkbox"/> Updated    Date of check:</p> <p><b>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.</b></p>
❖ Actions		
<ul style="list-style-type: none"> <li>• Proposed action</li> <li>• User Fee Goal Date is waived (Orphan indication)</li> </ul>		<input type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR
<ul style="list-style-type: none"> <li>• Previous actions (specify type and date for each action taken)</li> </ul>		<input type="checkbox"/> None
❖ 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 <u>N/A</u>		<input type="checkbox"/> Received

<sup>1</sup> 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.

APPEARS THIS WAY ON ORIGINAL.

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

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

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

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

Yes       No

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

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

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

Yes       No

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

*If “No,” continue with question (3).*

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

Yes       No

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

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

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

Yes       No

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

*If “No,” continue with question (5).*

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

<p>❖ Copy of this Action Package Checklist<sup>3</sup></p>	
<p align="center"><b>Officer/Employee List</b></p>	
<p>❖ 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>)</p>	<p><input checked="" type="checkbox"/> Included</p>
<p>Documentation of consent/non-consent by officers/employees</p>	<p><input checked="" type="checkbox"/> Included</p>
<p align="center"><b>Action Letters</b></p>	
<p>❖ Copies of all action letters (<i>including approval letter with final labeling</i>)</p>	<p>Action(s) and date(s) March 3, 2011</p>
<p align="center"><b>Labeling</b></p>	
<p>❖ Package Insert (<i>write submission/communication date at upper right of first page of PI</i>)</p>	
<ul style="list-style-type: none"> <li>• Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.</li> </ul>	<p>03/02/2011</p>
<ul style="list-style-type: none"> <li>• Original applicant-proposed labeling</li> </ul>	<p>04/30/10; 06/14/10; 01/20/11</p>
<ul style="list-style-type: none"> <li>• Example of class labeling, if applicable</li> </ul>	<p>n/a</p>

<sup>3</sup> Fill in blanks with dates of reviews, letters, etc.  
Version: 8/25/10

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 checked="" type="checkbox"/> Medication Guide <input checked="" type="checkbox"/> Patient Package Insert <input checked="" type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input type="checkbox"/> None
<ul style="list-style-type: none"> <li>Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.</li> </ul>	
<ul style="list-style-type: none"> <li>Original applicant-proposed labeling</li> </ul>	MG 01/20/11; IFU 2/4/11
<ul style="list-style-type: none"> <li>Example of class labeling, if applicable</li> </ul>	n/a
❖ 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>	(see PI section)
❖ 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>	10/13/10 Proprietary name request withdrawn
❖ Labeling reviews ( <i>indicate dates of reviews and meetings</i> )	<input type="checkbox"/> RPM <input checked="" type="checkbox"/> DMEPA 11/18/2010 <input checked="" type="checkbox"/> DRISK 02/10/2011 <input checked="" type="checkbox"/> DDMAC 01/28/11 <input type="checkbox"/> CSS <input type="checkbox"/> Other reviews
<b>Administrative / Regulatory Documents</b>	
❖ Administrative Reviews ( <i>e.g., RPM Filing Review<sup>4</sup>/Memo of Filing Meeting</i> ) ( <i>indicate date of each review</i> ) ❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte ❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment ( <i>indicate date</i> )	5/19/10 NDA ACK ;6/25/10 quality Micro memo; 7/16/10 74 day filing letter; 2/18/11 RPM Filing; see individual disciplinary sections for filing related documents.  <input checked="" type="checkbox"/> Not a (b)(2) <input checked="" type="checkbox"/> Not a (b)(2)
❖ NDAs only: Exclusivity Summary ( <i>signed by Division Director</i> )	<input checked="" type="checkbox"/> Included
❖ 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>	
<ul style="list-style-type: none"> <li>Applicant is on the AIP</li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> <li>This application is on the AIP           <ul style="list-style-type: none"> <li>If yes, Center Director's Exception for Review memo (<i>indicate date</i>)</li> <li>If yes, OC clearance for approval (<i>indicate date of clearance communication</i>)</li> </ul> </li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No  <input type="checkbox"/> Not an AP action
❖ Pediatrics ( <i>approvals only</i> ) <ul style="list-style-type: none"> <li>Date reviewed by PeRC <u>n/a</u> If PeRC review not necessary, explain: <u>PREA does not apply due to orphan indication</u></li> <li>Pediatric Page/Record (<i>approvals only, must be reviewed by PERC before finalized</i>)</li> </ul>	<input checked="" type="checkbox"/> Included

<sup>4</sup> Filing reviews for scientific disciplines should be filed behind the respective discipline tab.

❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent <i>(include certification)</i>	<input checked="" type="checkbox"/> Verified, statement is acceptable
❖ Outgoing communications <i>(letters (except action letters), emails, faxes, telecons)</i>	see printed correspondences
❖ Internal memoranda, telecons, etc.	n/a
❖ Minutes of Meetings	
• Regulatory Briefing <i>(indicate date of mtg)</i>	<input checked="" type="checkbox"/> No mtg
• If not the first review cycle, any end-of-review meeting <i>(indicate date of mtg)</i>	<input checked="" type="checkbox"/> N/A or no mtg
• Pre-NDA/BLA meeting <i>(indicate date of mtg)</i>	<input checked="" type="checkbox"/> No mtg
• EOP2 meeting <i>(indicate date of mtg)</i>	<input checked="" type="checkbox"/> No mtg
• Other milestone meetings (e.g., EOP2a, CMC pilots) <i>(indicate dates of mtgs)</i>	n/a
❖ Advisory Committee Meeting(s)	<input checked="" type="checkbox"/> No AC meeting
• Date(s) of Meeting(s)	
• 48-hour alert or minutes, if available <i>(do not include transcript)</i>	
<b>Decisional and Summary Memos</b>	
❖ Office Director Decisional Memo <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
Division Director Summary Review <i>(indicate date for each review)</i>	<input type="checkbox"/> None 03/03/2011 (decisional memo)
Cross-Discipline Team Leader Review <i>(indicate date for each review)</i>	<input type="checkbox"/> None 03/02/2011
PMR/PMC Development Templates <i>(indicate total number)</i>	<input checked="" type="checkbox"/> None
<b>Clinical Information<sup>5</sup></b>	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) <i>(indicate date for each review)</i>	03/02/2011
• Clinical review(s) <i>(indicate date for each review)</i>	03/02/2011
• Social scientist review(s) (if OTC drug) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here <input type="checkbox"/> and include a review/memo explaining why not <i>(indicate date of review/memo)</i>	See Clinical Review document
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers <i>(indicate date of each review)</i>	<input checked="" type="checkbox"/> None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation <i>(indicate date of each review)</i>	<input checked="" type="checkbox"/> Not applicable
❖ Risk Management	
• REMS Documents and Supporting Statement <i>(indicate date(s) of submission(s))</i>	12/14/10 proposed REMS amend
• REMS Memo(s) and letter(s) <i>(indicate date(s))</i>	2/24/11; 2/25/11 Final REMS
• 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>	12/1/10 REMS request 2/10/11 OSE/DRISK review 1/19/11; 2/16/11 OC review
	<input type="checkbox"/> None

<sup>5</sup> Filing reviews should be filed with the discipline reviews.

❖ DSI Clinical Inspection Review Summary(ies) (include copies of DSI letters to investigators)	<input checked="" type="checkbox"/> None requested
<b>Clinical Microbiology</b> <input checked="" type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (indicate date for each review)	<input type="checkbox"/> None
Clinical Microbiology Review(s) (indicate date for each review)	<input type="checkbox"/> None
<b>Biostatistics</b> <input checked="" type="checkbox"/> None	
❖ Statistical Division Director Review(s) (indicate date for each review)	<input type="checkbox"/> None
Statistical Team Leader Review(s) (indicate date for each review)	<input type="checkbox"/> None
Statistical Review(s) (indicate date for each review)	<input type="checkbox"/> None
<b>Clinical Pharmacology</b> <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (indicate date for each review)	<input type="checkbox"/> None
Clinical Pharmacology Team Leader Review(s) (indicate date for each review)	<input type="checkbox"/> None
Clinical Pharmacology review(s) (indicate date for each review)	<input type="checkbox"/> None 6/23/10; 12/31/10
❖ DSI Clinical Pharmacology Inspection Review Summary (include copies of DSI letters)	<input type="checkbox"/> None 09/15/10; 11/19/10
<b>Nonclinical</b> <input checked="" type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (indicate date for each review)	<input type="checkbox"/> None
• Supervisory Review(s) (indicate date for each review)	<input type="checkbox"/> None
• Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	<input type="checkbox"/> None
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (indicate date for each review)	<input type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (indicate date for each review)	<input type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input type="checkbox"/> None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary (include copies of DSI letters)	<input type="checkbox"/> None requested

<b>Product Quality</b>		<input type="checkbox"/> None
<b>Product Quality Discipline Reviews</b>		
• ONDQA/OBP Division Director Review(s) <i>(indicate date for each review)</i>		<input checked="" type="checkbox"/> None
• Branch Chief/Team Leader Review(s) <i>(indicate date for each review)</i>		<input type="checkbox"/> None 6/28/10 initial assessment
• Product quality review(s) including ONDQA biopharmaceutics reviews <i>(indicate date for each review)</i>		<input type="checkbox"/> None 12/16/10; 02/23/11
❖ <b>Microbiology Reviews</b> <input checked="" type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) <i>(indicate date of each review)</i> <input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (DMPQ/MAPCB/BMT) <i>(indicate date of each review)</i>		<input type="checkbox"/> Not needed 06/18/10; 11/09/10
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer <i>(indicate date of each review)</i>		<input checked="" type="checkbox"/> None
❖ <b>Environmental Assessment (check one) (original and supplemental applications)</b>		
<input checked="" type="checkbox"/> Categorical Exclusion <i>(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)</i>		02/23/2011
<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
❖ <b>Facilities Review/Inspection</b>		
<input checked="" type="checkbox"/> NDAs: Facilities inspections (include EER printout) <i>(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<sup>6</sup>)</i>		Date completed: 12/20/2010 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable
<input type="checkbox"/> BLAs: TB-EER <i>(date of most recent TB-EER must be within 30 days of action date) (original and supplemental BLAs)</i>		Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
❖ NDAs: Methods Validation <i>(check box only, do not include documents)</i>		<input type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input checked="" type="checkbox"/> Not needed (per review)

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

## Appendix to Action Package Checklist

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

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

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

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

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

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

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

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

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

**Sun, Su-Lin**

---

**From:** Sun, Su-Lin  
**Sent:** Friday, February 25, 2011 10:51 AM  
**To:** 'Ira\_Do@eisai.com'  
**Subject:** NDA 201367 urgent information request and change request.

**Importance:** High

**Attachments:** NDA 201367--NDA 021911--FDA proposed final REMS--SS.doc

Dear Ira:

There are few requests that we would like you response as soon as possible (preferable today, but no later than COB on 2/28/11 Monday):

1. Information request from our Clinical reviewer regard to financial disclosure:

The division continues to have concern about the absence of financial disclosure for 66% of the clinical investigators (named below) for this application. This has generated several additional questions provided below.

(b) (4)  
[Redacted]

1. did these investigators sign a form 1572.
2. Were these investigators identified in an initial submission or protocol amendment under the rufinamide IND.
3. were these investigators directly involved in the evaluation of the research subjects?
4. Was the oral formulation administered to subjects under their immediate direction.
5. Were the bioavailability results obtained under their immediate supervision?
6. Was there more than one study site?
7. Were these investigators working at a study site with an investigator from whom financial disclosure was obtained?
8. did your attempts to follow up with these investigators involve measures such as a. >1 phone call, b. >1 registered letter, c. a web search using a public and professional databases to locate the individuals.

If the investigators cannot be located then some assurance of absence of influential interest may be provided by information on payments to the investigators, SPOOS, and proprietary interests the investigator has in Eisai.

2. Final REMS submission:



NDA 201367--NDA  
021911--FDA pr...

Per our OC reviewer---please remove the words (b) (4) on the REMS document as the division final proposal sent on 2/23/11 (see attached document). Please also provide a word document of the final REMS (after remove the (b) (4) to me, so it can be posted correctly.

Thanks,

Su Lin Sun, PharmD  
LCDR, United States Public Health Service

Reference ID: 2910663

Regulatory Project Manager  
Food and Drug Administration  
Office of Drug Evaluation I Division of Neurology Products  
Bldg. 22, Room 4209  
10903 New Hampshire Ave  
Silver Spring, MD 20903  
Office: 301 796 0036  
Fax: 301 796 9842  
Email: [Su.Lin.Sun@fda.hhs.gov](mailto:Su.Lin.Sun@fda.hhs.gov)

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/s/  
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SU-LIN SUN  
02/25/2011

## Sun, Su-Lin

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**From:** Sun, Su-Lin  
**Sent:** Wednesday, February 23, 2011 2:57 PM  
**To:** 'Ira\_Do@eisai.com'  
**Subject:** NDA 201367 minor change for IFU and comments for IFU

**Attachments:** NDA 201367 BANZEL oral suspension--FDA's comment for IFU 02232011.doc

Ira:

I just receive an email from our Team Leader--he would to change the word (b) (4) to "slowly squirt" for the IFU section and also comments for IFU. This change has also been concurred by our DRISK reviewer also.



NDA 201367  
ANZEL oral suspens

Please also change on the IFU document.

Thanks,

Su Lin Sun, PharmD  
LCDR, United States Public Health Service

Regulatory Project Manager  
Food and Drug Administration  
Office of Drug Evaluation I Division of Neurology Products  
Bldg. 22, Room 4209  
10903 New Hampshire Ave  
Silver Spring, MD 20903  
Office: 301 796 0036  
Fax: 301 796 9842  
Email: [Su.Lin.Sun@fda.hhs.gov](mailto:Su.Lin.Sun@fda.hhs.gov)

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**NDA 201367 BANZEL Oral suspension**  
**FDA's comment for IFU**  
**November 23, 2011**

1. Do not use italics and brackets in patient labeling as they are distracting to patients. We have changed that to bolded text throughout the IFU.
2. The numbered Steps and the Figures (Figure A, B etc) should be bolded for clarity, and we have done that throughout the IFU.
3. The IFU is written directly to "you", not the (b) (4). Although we recognize that in some cases the oral solution will be administered by parents to their children, the IFU is still written for "you" in patient labeling. We have changed that throughout the IFU.
4. Patients understand the verb "slowly squirt the medicine" better than they understand the verb (b) (4) so we have changed those instructions back to "slowly squirt the medicine" in the attached version.
5. The dosing table (Table 8) is much too complicated for 6th to 8th grade reading comprehension, so again we have deleted it in this version. A text box with dosing information was already added to the beginning of the IFU to help patients figure out their dose as directed by their healthcare provider or pharmacist.

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/s/  
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SU-LIN SUN  
02/24/2011

## Sun, Su-Lin

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**From:** Sun, Su-Lin  
**Sent:** Wednesday, February 23, 2011 12:24 PM  
**To:** 'Ira\_Do@eisai.com'  
**Subject:** NDA 201367 FDA final proposed PI/MG/IFU and REMS; information request for financial disclosure

**Attachments:** BANZEL Oral Suspension label FDA proposed finall -- 02 23 2011.doc; BANZEL IFU FDA marked up copy 02 23 11.doc; NDA 201367 BANZEL oral suspension--FDA's comment for IFU 02232011.doc; NDA 201367--NDA 021911--FDA proposed final REMS--022311.doc

Dear Ira:

Here are the Division's final proposed PI/MG/IFU and REMS document:

1. First document----**PI/MG only** (the IFU will be on separate document)



BANZEL Oral  
Suspension label F..

Highlight section---the addition of (b) (4) is rejected--per review team that not everything need to be in highlight section

17.1---the additional of gluten free sentence---added (to match your proposed MG changes)

\*\* there are some format changes you did, I tried to accept changes, some I am unable---please fix it for us  
Section 11---the second sentence, not sure what's wrong--the spacing between each word is bigger--try to fix, but was unable, please fix it for us.

2. Second document---**IFU only**

Lots of formate changes



BANZEL IFU FDA  
marked up copy...

3. Third document---FDA's comment for proposed IFU changes



NDA 201367  
ANZEL oral suspens

4. Fourth document---FDA proposed REMS



NDA 201367--NDA  
021911--FDA pr...

5. Information request --for financial disclosure:

[Please expand upon the last sentence of your due diligence statement \(in the financial disclosure statement of the](#)

submission) by providing further information on why the investigators [REDACTED] (b) (4)  
[REDACTED] were unreachable and documentation of the process undertaken to reach these investigators.

If you have any question, please feel free to contact me. Please resubmit the final REMS and other document as soon as possible. Please also send me an acknowledgment email if you agree with all the above proposed changed (include REMS), it will help to facilitate the process.

Thanks,

Su Lin Sun, PharmD  
LCDR, United States Public Health Service

Regulatory Project Manager  
Food and Drug Administration  
Office of Drug Evaluation I Division of Neurology Products  
Bldg. 22, Room 4209  
10903 New Hampshire Ave  
Silver Spring, MD 20903  
Office: 301 796 0036  
Fax: 301 796 9842  
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immediately following this page.

**NDA 201367 BANZEL Oral suspension**  
**FDA's comment for IFU**  
**November 23, 2011**

1. Do not use italics and brackets in patient labeling as they are distracting to patients. We have changed that to bolded text throughout the IFU.
2. The numbered Steps and the Figures (Figure A, B etc) should be bolded for clarity, and we have done that throughout the IFU.
3. The IFU is written directly to "you", not the (b) (4). Although we recognize that in some cases the oral solution will be administered by parents to their children, the IFU is still written for "you" in patient labeling. We have changed that throughout the IFU.
4. Patients understand the verb "squirt the medicine" better than they understand the verb (b) (4) so we have changed those instructions back to "squirt the medicine" in the attached version.
5. The dosing table (Table 8) is much too complicated for 6th to 8th grade reading comprehension, so again we have deleted it in this version. A text box with dosing information was already added to the beginning of the IFU to help patients figure out their dose as directed by their healthcare provider or pharmacist.

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/s/  
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SU-LIN SUN  
02/24/2011

## Sun, Su-Lin

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**From:** Sun, Su-Lin  
**Sent:** Friday, February 11, 2011 2:42 PM  
**To:** 'Ira\_Do@eisai.com'  
**Subject:** NDA 201367

Dear Ira:

Thank you for sending me the study protocol for dosing accuracy and plunger actuation for the 20mL syringe.

Per our CMC reviewer the submitted study protocol for dosing accuracy and plunger actuation is acceptable.

[Here are comments from our CMC reviewer:](#)

Please clarify whether the 20 ml syringe is made from the same materials as the (b) (4) you originally proposed. If not, you will need to perform a drug/device compatibility study similar to the 6 hour study submitted in the original NDA.

If you have any question, please feel free to contact me.

Thanks,

Su Lin Sun, PharmD  
LCDR, United States Public Health Service

Regulatory Project Manager  
Food and Drug Administration  
Office of Drug Evaluation I Division of Neurology Products  
Bldg. 22, Room 4209  
10903 New Hampshire Ave  
Silver Spring, MD 20903  
Office: 301 796 0036  
Fax: 301 796 9842  
Email: [Su.Lin.Sun@fda.hhs.gov](mailto:Su.Lin.Sun@fda.hhs.gov)

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/s/  
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SU-LIN SUN  
02/18/2011

## Sun, Su-Lin

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**From:** Sun, Su-Lin  
**Sent:** Thursday, February 17, 2011 10:50 AM  
**To:** 'Ira\_Do@eisai.com'  
**Subject:** NDA 201367 IFU

**Attachments:** FDA proposed BANZEL revised IFU marked up copy 02 17 2011.doc

Dear Ira:

Sorry for the confusion, the FDA proposed revised IFU document that I sent you yesterday--somehow it seem like missing the [dosing text box](#) and also few instructions (within the text box).

I am sending you the revised document in which the FDA comment is on each proposed section for the IFU. Please [use this version of IFU](#) and please accept track changes if you agree with our proposal. This version may be easier to follow thru also. Please send me an email back to confirm that you receive this version.



FDA proposed  
BANZEL revised I...

Thanks,

Su Lin Sun, PharmD  
LCDR, United States Public Health Service

Regulatory Project Manager  
Food and Drug Administration  
Office of Drug Evaluation I Division of Neurology Products  
Bldg. 22, Room 4209  
10903 New Hampshire Ave  
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Email: [Su.Lin.Sun@fda.hhs.gov](mailto:Su.Lin.Sun@fda.hhs.gov)

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SU-LIN SUN  
02/18/2011

Sun, Su-Lin

---

**From:** Sun, Su-Lin  
**Sent:** Wednesday, February 16, 2011 1:28 PM  
**To:** 'Ira\_Do@eisai.com'  
**Subject:** NDA 201367

**Attachments:** BANZEL Oral Suspension label---FDA proposed text PI 02152011.doc; BANZEL MG --FDA proposed revision 02152011.doc; FDA proposed BANZEL oral suspension revised IFU 02152011.doc; Summary of FDA proposed revision for Banzel oral suspension MG & IFU--02152011.doc

Ira:

Here are our proposed PI/MG/IFU. Please accept all track changes if you agree. Please use track changes if you disagree or would like to modify.

1. **First document--PI : \*\*\* Please only review PI section (not MG portion since MG will be on another separate document); Please note 17.3 IFU is under the MG section**  
\_(minor changes--please note 17.2 MG and 17.3 IFU per our review team).



BANZEL Oral  
Suspension label--..

2. **Second document: MG only**



BANZEL MG --FDA  
proposed revis...

Once you agree this MG, please replace this version with the old one on the PI when you send us your counter proposal.

3. **Third document: IFU : there are many many revisions (some changes are easily seen on the document. I typed a summary proposed changes for MG and IFU--for additional comments and proposed changes --hope this will be easier to follow). Some of the figures may need to be relocated to different sections and adjust size and contents.**



FDA proposed  
BANZEL oral suspe..

4. **Fourth document: A summary proposed changes (that's not easily seen on the actual document) based on our review team.**



Summary of FDA  
proposed revisi...

Once again, thank you for all your help. As we discussed on the phone, please try to send your counter proposal to me at your earliest convenience, but no later than February 22, 2011 11AM.

Reference ID: 2908009

If you have any question, please feel free to contact me.

Thanks,

Su Lin Sun, PharmD  
LCDR, United States Public Health Service

Regulatory Project Manager  
Food and Drug Administration  
Office of Drug Evaluation I Division of Neurology Products  
Bldg. 22, Room 4209  
10903 New Hampshire Ave  
Silver Spring, MD 20903  
Office: 301 796 0036  
Fax: 301 796 9842  
Email: [Su.Lin.Sun@fda.hhs.gov](mailto:Su.Lin.Sun@fda.hhs.gov)

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## **Summary of FDA proposed revision for Banzel oral suspension MG**

1. add “and” on the MG title
2. Under what is Banzel section:  
added a standard language used in PI  
“It is not known if BANZEL is safe.....under 4 years of age”
3. Under Who should not take BANZEL” section  
Add “called” and “a problem” in the original sentence.
4. under How should I take BANZEL? Section  
Delete statement (b) (4)  
Rational---it’s redundant it already appears twice in the “what is the most important info I should know section”
5. Under How should I store BANZEL SECTION?  
The tablet and oral suspension sections are divided (as similar way it appear on the PI)

\*\*\* There are other minor revisions ---you can see easily from the red or blue track changes in the document.

## **Summary of FDA proposed revision for Banzel oral suspension IFU**

### **I. title section:**

1. Standard header used in PI is inserted
2. Deleted the text box concerning dosing ---because this info is redundant
3. Items that pt needs to use for procedure are listed first in standard patient labeling
4. Use single column formate for steps below to make them easier for patients to read and follow.
5. **Insert an introductory paragraph** for consistency with other patient labeling  
“Read the instructions for use.....or your treatment”----
6. **Location for figure A:**  
Figure A should be relocated to immediately below the sentence “dosing syringe. 2 dosing syringes are included in the BANZEL ORAL Suspension box.” Or right above the inserted text box

**Figure A:** should display the 2 syringes that will be included in each package

7. **Recommendations for all the figures:**

a. Label all of the figures in alphabetical order, i.e. “Figure A, Figure B” etc. and refer to each figure in the steps.

b/ All figures should be larger with larger font size for the labels within each diagram. The labels are currently very difficult to read.]

**8. Added a text box for patient to write their prescribed equally divided dose so that the information can be easily referenced**

9. **Dosing chart:**

Delete complex dosing chart located at the end of the IFU. The prescriber or pharmacist should calculate the dose in mL, not the patient.

10. Added the word “Step” before each numbered step for ease of reference for the patient.

11. under the sections for step:

a. **Figure A** should be move to the new location (as indicated on # 6 on this document). That is move below the sentence “ dosing syringe. 2 dosing syringes... in the BANZEL ORAL suspension box”

b. **Figure E:**

1. Should be move to step 4 where the instruction for using the syringes is located
2. Replace the syringe in figure E with the actual 20mL syringe to be used (with mL only, (b) (4)).
3. An arrow should point to the 20mL mark on the syringe

12. **Step 3:**

You should add a clear, detailed diagram of the bottle adaptor by itself before Figure D

13. **Step 4:**

a. This step was revised so that it is clear to the patient that the number that the patient should find on the syringe is for the morning or evening dose, not the total daily dose.

b. Move Figure E to this step as indicated on item # 11.b of this document

14. **Add a diagram (Figure H)** to show the black and white layers at the end of the plunger where the patient will look on the syringes to measure the suspension in mLs.

The patient should measure from the white layer at the end of the plunger, not the black layer, as up to 1ML of suspension could be lost.

15. **Step 9:**

We recommend stating in Step 9 that BNAZEL should be squirted into the corner of the patient's mouth. This is the usual method used to avoid choking when administering oral liquid formulations, especially in children.

16. **Step 10:**

Please add a diagram of a person rinsing the syringe by drawing up tap water from a cup. (Figure J).

17. **Dosing chart:**

We deleted the complex dosing chart below and added a text box at the beginning of the IFU for the patient to write their prescribed equally divided doses in mL. The prescriber or pharmacist should calculate the dose in mL, not the patient. Additionally, to avoid patient confusion only one unit of measure should be referred to in the IFU, so references to (b) (4) should be deleted.]

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/s/  
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SU-LIN SUN  
02/18/2011

## Sun, Su-Lin

---

**From:** Sun, Su-Lin  
**Sent:** Thursday, February 03, 2011 2:01 PM  
**To:** 'Ira\_Do@eisai.com'  
**Subject:** NDA 201367

**Sensitivity:** Confidential

**Attachments:** BANZEL Oral Suspension\_approved + Oral Susp FDA draft 020311.doc

Dear Ira:

Here is the Division's proposed draft PI.



BANZEL Oral  
uspension approve.

We are going to wait until we received the IFU (instruction for Use) and review & modify the MG during our next labeling meeting (2/10/11).

Below are the request from our review team, which was communicated to you by Dr. Katz during our Tcon today at 1:00PM.

1. Please send sample of oral syringes, measuring devices and bottle for Banzel oral suspension to Sulin as soon as possible
2. Please submit any data show persistent marking on the oral syringes over time of use.
3. Recommend provide multiple syringes (2 or 3 oral syringes) with each bottle package.
4. Please provide rational on how to matching amount dispensed at certain time frame (1 month or 3 month supply)? Recommend considering smaller bottle size for future.

If you have any question, please free to contact me.

Thanks,

Su Lin Sun, PharmD  
LCDR, United States Public Health Service

Regulatory Project Manager  
Food and Drug Administration  
Office of Drug Evaluation I Division of Neurology Products  
Bldg. 22, Room 4209  
10903 New Hampshire Ave  
Silver Spring, MD 20903  
Office: 301 796 0036  
Fax: 301 796 9842  
Email: [Su.Lin.Sun@fda.hhs.gov](mailto:Su.Lin.Sun@fda.hhs.gov)

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23 Pages of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page.

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/s/  
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SU-LIN SUN  
02/04/2011

## Sun, Su-Lin

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**From:** Sun, Su-Lin  
**Sent:** Monday, January 31, 2011 10:19 PM  
**To:** 'Ira\_Do@eisai.com'  
**Subject:** NDA 201367

**Importance:** High  
**Sensitivity:** Confidential

Dear Ira:

Our review team would like me to inform you that if you agree in writing , to submit a revised dosing device within three months of the NDA 201367 Banzel oral suspension approval which displays the unit of measure in milliliters (mL) only and displays the drug name " Banzel" (rufinamide). Then the Division is willing to consider the temporary use of [REDACTED] (b) (4)

Thanks,

Su Lin Sun, PharmD  
LCDR, United States Public Health Service

Regulatory Project Manager  
Food and Drug Administration  
Office of Drug Evaluation I Division of Neurology Products  
Bldg. 22, Room 4209  
10903 New Hampshire Ave  
Silver Spring, MD 20903  
Office: 301 796 0036  
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Email: [Su.Lin.Sun@fda.hhs.gov](mailto:Su.Lin.Sun@fda.hhs.gov)

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/s/  
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SU-LIN SUN  
01/31/2011

## Sun, Su-Lin

---

**From:** Sun, Su-Lin  
**Sent:** Wednesday, December 15, 2010 1:36 PM  
**To:** 'Ira\_Do@eisai.com'  
**Cc:** Kelley, Laurie  
**Subject:** NDA 201367

**Importance:** High  
**Sensitivity:** Confidential

**Attachments:** NDA 201367 Banzel ---FDA label and labeling comments to the sponsor 12152010.pdf

Dear Dr. Do:

Attached to this message is a request from Division of Neurology and Division of Medication Error Prevention and Analysis (DMEPA) Label and Labeling review team related to their ongoing review of NDA 201367 Banzel (rufinamide) oral suspension 40mg/mL. Please submit your response to this request in electronic archival format as an amendment to the NDA 201367.



NDA 201367 Banzel  
---FDA label...

Responses should be sent as an official amendment (1 original & 2 copies) to your NDA at the below address. It is acceptable for you to email your response to me in advance of a formal, archival submission as long as both communications (email & archive) contain identical information.

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

We ask that you please respond to this request as soon as possible, no later than January 3, 2011.

If you have any question, please let me know.

Thank you,

Su Lin Sun, PharmD  
LCDR, United States Public Health Service

Regulatory Project Manager  
Food and Drug Administration  
Office of Drug Evaluation I Division of Neurology Products  
Bldg. 22, Room 4209  
10903 New Hampshire Ave  
Silver Spring, MD 20903  
Office: 301 796 0036  
Fax: 301 796 9842  
Email: [Su.Lin.Sun@fda.hhs.gov](mailto:Su.Lin.Sun@fda.hhs.gov)

**NDA 201367 Banzel (rufinamide) oral suspension 40mg/mL  
FDA Label and Labeling comments to the sponsor  
12/15/2010**

**A. Container Labels and Carton Labeling**

- 1) Relocate the strength (40 mg/mL) to a location in close proximity to the proprietary and established name (adjacent to or directly underneath) on the container labels and carton labeling. The presentation of the strength (40 mg/mL) is currently located at the bottom right corner of the principal display panel below the total volume (460 mL) on the container label and carton labeling. The presentation for the strength for oral suspension products is typically presented in a prominent manner directly underneath the proprietary and established name to assure that the strength is clearly visible for proper dosing and administration.
- 2) There is no reference to the inclusion of measuring devices on the container label or carton labeling. Add a statement on the carton labeling that clearly indicates there are measuring devices included and they are for oral use. For example: “This product is packaged with a calibrated (milliliters) oral syringe [REDACTED] (b) (4) for accurate dosing.”
- 3) Add a statement to the principal display panel of the container label and the carton labeling stating that this product is “For Oral Administration Only.” Postmarketing experience has demonstrated that wrong route of administration errors have occurred in the clinical setting when oral liquid products have been inadvertently been administered as injections. Because this product is an oral suspension (liquid), and the product is supplied with a syringe, DMEPA believes that there is a risk of wrong route of administration and the risk can be minimized by adding the “For Oral Administration Only” warning statement to the container label and carton labeling.
- 4) Assure that bar coding is included on the container labels and carton labeling. The images of the container label and carton labeling are not presented with a bar code. Pursuant to 21 CFR 201.25, “Manufacturers, repackers, relabelers, and private label distributors of a human prescription drug product or an over-the-counter (OTC) drug product that is regulated under the Federal Food, Drug, and Cosmetic Act or the Public Health Service Act are subject to these bar code requirements unless they are exempt from the registration and drug listing requirements in section 510 of the Federal Food, Drug, and Cosmetic Act..”
- 5) Add the instructions “Shake the bottle vigorously before administration” should be added to the container label and the carton labeling. These instructions are included in the package insert labeling Dosage and Administration section and therefore, should also be included on the container label and carton labeling to assure that the patient is given the appropriate instructions prior to administration.
- 6) Revise the font color presentation used the present the proprietary and established name on the carton labeling to increase the prominence. The color contrast used with the white font against the green background makes it difficult to visualize the proprietary and established name.

**B. Dispenser Set (Oral Dosing Syringe)** (b) (4)

1) Remove the (b) (4) from the oral dosing syringe (b) (4).  
(b) (4) the graduated syringe (b) (4) are presented in milliliters (b) (4).  
Banzel Oral Suspension is dosed in milliliters and therefore, milliliters (mL) should be the only unit of measure displayed on the syringe (b) (4). Postmarketing experience has demonstrated that dosing errors have occurred when there is discordance between the units of measurement on the measuring device and product labeling.<sup>1</sup> DMEPA believes that in order to reduce the risk of wrong dose medication errors, only the intended unit of measurement (milliliters) should be displayed on the measuring syringe (b) (4).

(b) (4)

3) Add the product name (Banzel) to the oral dosing syringe (b) (4).  
Since the Applicant is supplying this product with measuring devices specific to use with Banzel, we recommend that the product name is included on the measuring devices so that patients can readily identify the correct measuring device for this product and minimize confusion with other measuring devices they may have.

**REFERENCE**

(b) (4)

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/s/  
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SU-LIN SUN  
12/15/2010



NDA 201-367

**INFORMATION REQUEST**

Eisai Inc.  
Attention: Robert Clark  
Associate Director, Regulatory Affairs CMC  
300 Tice Boulevard  
Woodcliff Lake, NJ 07677

Dear Mr. Clark:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Rufinamide Oral Suspension.

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 in order to continue our evaluation of your NDA.

1. Provide physicochemical test USP <661> results for the (b) (4) closure cap (DMF- (b) (4)) or provide exact reference (volume, section, pages numbers) to the DMF where these information can be found.
2. Provide information on the composition of bottle (e.g. resin, colorant, additives, mold release agent etc.), including their manufacturing process, specification and results of compendial testing (e.g. USP <661>) for the bottle (DMF (b) (4)) or provide exact reference (volume, section, pages numbers) to the DMF where these information can be found.
3. Provide justification why (b) (4)  
(b) (4)  
(b) (4)  
. Provide your justification along with relevant data (b) (4)  
(b) (4)  
(b) (4)
4. Clarify the rational for in process particle size limit of (b) (4) (b) (4) (b) (4)
5. A paddle method of 50 rpm for a suspension preparation might be too high speed to distinguish any differences if exists. It is therefore recommended to evaluate the effect of paddle speed (particularly at a lower speed than 50 rpm) on dissolution.
6. Provide in process particle size data for the batches C1275A005, C1275A007, C1275A008 & C1275A006 that was measured by (b) (4) analyzer.
7. The accuracy and precision of the related substances (b) (4) was found to be variable from the given analytical method validation study. For example,

- (b) (4)
- provide clarification why the accuracy and precision of the method should be considered as acceptable.
8. Provide detailed analytical method with validation results for the (b) (4) used for the in process particle size determination.
  9. Provide the detailed statistical analysis report on the assay of (b) (4) potassium sorbate that was used to support the extrapolation of the expiration dating period for the drug product.
  10. (b) (4)
  11. It is recommended that you add appropriate instruction for shaking the product prior to use by patient or dispensing pharmacist to the label.
  12. On the product label, it is recommended that you put the strength, 40 mg/ml next to the “(rufinamide) ORAL SUSPENSION” instead of the right hand bottom corner.

If you have any questions, contact Teshara G. Bouie, Regulatory Project Manager, at (301) 796-1649.

Sincerely,

*{See appended electronic signature page}*

Ramesh Sood, Ph.D.  
Branch Chief  
Division of New Drug Quality Assessment I  
Office of New Drug Quality Assessment  
Center for Drug Evaluation and Research

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/s/  
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RAMESH K SOOD  
12/03/2010

**REQUEST FOR DDMAC LABELING REVIEW CONSULTATION**

**\*\*Please send immediately following the Filing/Planning meeting\*\***

TO:  <b>CDER-DDMAC-RPM</b> Michael Wade	FROM: (Name/Title, Office/Division/Phone number of requestor)  Division of Neurology products Su-Lin Sun (301) 796-0036
--	--

REQUEST DATE 12/03/2010	IND NO.	NDA/BLA NO.  NDA 201367	TYPE OF DOCUMENTS (PLEASE CHECK OFF BELOW)  New NDA (new dosage form)
----------------------------	---------	-------------------------------	--

NAME OF DRUG  Banzel (rufinamide oral suspension)	PRIORITY CONSIDERATION  Standard	CLASSIFICATION OF DRUG  anticonvulsants	DESIRED COMPLETION DATE (Generally 1 week before the wrap up meeting)  January 11, 2011
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NAME OF FIRM: EISAI Inc	PDUFA Date: 03/03/2011
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**TYPE OF LABEL TO REVIEW**

<b>TYPE OF LABELING:</b> (Check all that apply) <input checked="" type="checkbox"/> PACKAGE INSERT (PI) <input checked="" type="checkbox"/> PATIENT PACKAGE INSERT (PPI) <input checked="" type="checkbox"/> CARTON/CONTAINER LABELING <input checked="" type="checkbox"/> MEDICATION GUIDE <input checked="" type="checkbox"/> INSTRUCTIONS FOR USE(IFU)	<b>TYPE OF APPLICATION/SUBMISSION</b> <input checked="" type="checkbox"/> ORIGINAL NDA/BLA <input type="checkbox"/> IND <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> SAFETY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> PLR CONVERSION	<b>REASON FOR LABELING CONSULT</b> <input type="checkbox"/> INITIAL PROPOSED LABELING <input type="checkbox"/> LABELING REVISION
---	--	--

**EDR link to submission:**  
 The network location is : <\\CDSESUB1\EVSPROD\NDA201367\201367.ENX>  
 FYI—DMEPA has complete 1 labeling review—document in DARRTs---comments will be sent to sponsor  
 The PI/MG will be the same as NDA 21911 Banzel (rufinamide tablets)---with addition of this new formulation added. The last final REMS approval for label and labeling for NDA 21911 was in  
 DMEPA recommend sponsor to submit IFU--this will be communicate to sponsor by DNP.  
 The action goal date is 03/03/2011. Rusty would like to have it finished early.

**Please Note: There is no need to send labeling at this time. DDMAC reviews substantially complete labeling, which has already been marked up by the CDER Review Team. The DDMAC reviewer will contact you at a later date to obtain the substantially complete labeling for review.**

**COMMENTS/SPECIAL INSTRUCTIONS:**  
  
 Mid-Cycle Meeting: [09/04/2010]  
  
 Labeling Meetings: [02/01/11, 02/08/11, 02/15/11; 02/22/11]  
  
 Wrap-Up Meeting: [1/20/11]

SIGNATURE OF REQUESTER Su Lin Sun

SIGNATURE OF RECEIVER <b>Reference ID: 2872107</b>	METHOD OF DELIVERY (Check one) <input type="checkbox"/> eMAIL <input type="checkbox"/> HAND
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APPEARS THIS WAY ON ORIGINAL.

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/s/  
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SU-LIN SUN  
12/03/2010

Sun, Su-Lin

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**From:** Sun, Su-Lin  
**Sent:** Tuesday, November 30, 2010 6:29 PM  
**To:** 'Ira\_Do@eisai.com'  
**Subject:** REMS request for Banzel (NDAs 21911 and 201367)

**Importance:** High  
**Sensitivity:** Confidential

**Attachments:** REMS MedGuide ONLY Attachments A and B For Industry.doc

Dear Dr. Do:

The Risk Evaluation and Mitigation Strategy (REMS) for Banzel (rufinamide) oral tablets (NDA 21911) was originally approved on November 14, 2008 and modified on November 8, 2010. Your REMS consists of a comprehensive Medication Guide and a timetable for submission of assessments of the REMS. Your submitted NDA 201367, which is still under review, provides for a new oral formulation for Banzel (rufinamide). You have proposed modifications to the Medication Guide to include the new formulation, but you have not yet submitted a REMS document or assessment of the REMS. In accordance with section 505-1(g)(2)(A) of the of the Federal Food, Drug, and Cosmetic Act (FDCA), you are required to submit an assessment and propose a modification of the existing REMS.

We request that you submit a proposed REMS as an amendment to NDA 201367 and a REMS modification with assessment (Prior Approval Supplement) to NDA 21911. Your proposed REMS and REMS modification submissions should both include a revised comprehensive Medication Guide that is consistent with the Medication Guide approved on November 8, 2010 and that includes the new formulation for which you are seeking approval. The proposed REMS and REMS modification submissions should also both include a revised REMS and a revised REMS supporting document (see attached REMS Appendices A and B).

The timeline for submission of assessments of your REMS will remain the same as was approved in your original REMS on November 14, 2008. Therefore, in your revised REMS documents, please specifically state the following in the section entitled **Timetable for Submission of Assessments**:

"Eisai, Inc. will submit REMS assessments to FDA 18 months, 3 years and 7 years from the date of initial approval of the REMS (November 14, 2008) according to the schedule below:

1<sup>st</sup> FDAAA assessment: March 14, 2010 (18 months from approval)

2<sup>nd</sup> FDAAA assessment: November 14, 2011 (3 years from approval)

3<sup>rd</sup> FDAAA assessment: November 14, 2015 (7 years from approval)

Eisai, Inc. will submit each assessment so it will be received by the FDA on or before the due date."

Your proposed REMS modification should include an assessment of your approved REMS, to determine if the REMS is meeting its goals. If it is too early to assess your REMS, please declare this in the cover letter for your REMS modification submission by including the following statement in your cover letter: "It is too early to assess the REMS. The Medication Guide would be adequate with the proposed modifications to achieve its purpose."

We request that you submit your proposed REMS and REMS modification with assessment as described above by the close of business on December 7, 2010. Please let me know if you have any questions regarding this request.

Reference ID: 2871017



REMS MedGuide  
ONLY Attachments..

Thanks,

Su Lin Sun, PharmD  
LCDR, United States Public Health Service

Regulatory Project Manager  
Food and Drug Administration  
Office of Drug Evaluation I Division of Neurology Products  
Bldg. 22, Room 4209  
10903 New Hampshire Ave  
Silver Spring, MD 20903  
Office: 301 796 0036  
Fax: 301 796 9842  
Email: [Su.Lin.Sun@fda.hhs.gov](mailto:Su.Lin.Sun@fda.hhs.gov)

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immediately following this page.

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/s/  
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SU-LIN SUN  
12/01/2010



NDA 201367

**PROPRIETARY NAME REQUEST  
WITHDRAWN**

Eisai, Inc.  
300 Tice Boulevard  
Woodcliff Lake, New Jersey, 07667

ATTENTION: Ira Pham Do, PharmD  
Senior Manager, Regulatory Affairs

Dear Dr. Do:

Please refer to your New Drug Application (NDA) dated April 30, 2010, received May 3, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Rufinamide Oral Suspension, 40 mg/ml.

We acknowledge receipt of your September 8, 2010 correspondence, on September 9, 2010, notifying us that you are withdrawing your request for a review of the proposed proprietary name Banzel Oral Suspension. This proposed proprietary name request is considered withdrawn as of September 8, 2010.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, call Laurie Kelley, Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-5068. For any other information regarding this application, contact the Office of New Drugs (OND) Regulatory Project Manager Su-Lin Sun at (301) 796-0036.

Sincerely,

*{See appended electronic signature page}*

Carol Holquist, RPh  
Director  
Division of Medication Error Prevention and Analysis  
Office of Surveillance and Epidemiology  
Center for Drug Evaluation and Research

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/s/

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DENISE P TOYER on behalf of CAROL A HOLQUIST  
10/13/2010



NDA 201367

## FILING COMMUNICATION

Eisai Inc.  
Attention: Ira Pham Do, PharmD  
Senior Manager, Regulatory Affairs  
300 Tice Boulevard  
Woodcliff Lake, NJ 07677

Dear Dr. Do:

Please refer to your new drug application (NDA) dated April 30, 2010, received May 03, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for Banzel (rufinamide) oral suspension 40mg/mL.

We also refer to your additional submissions dated June 14, 2010 and June 15, 2010.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Standard**. Therefore, the user fee goal date is March 3, 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, mid-cycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by February 3, 2011.

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

1. You have not provided any assessment of the stability of the drug substance to potential polymorphism once formulated in the product. As rufinamide is a poorly soluble drug substance, changes to the solid state characteristics (e.g., hydrate formation) could adversely impact bioavailability.

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.

We also request that you submit the following information:

1. In Module 3.2.R Regional Information, the Methods Validation section is included under the "Comparability Protocol" heading. Please correct this in a future submission by placing the Methods Validation section under its own heading within Module 3.2.R.
2. We note that, in Module 1 Section 1.4.4 and Module 2 Section 2.7.4 of this NDA, there is reference to a controlled study of rufinamide (Study Report E202080-A001-301) originally submitted to IND 35,534 on April 29, 2010. Please submit the full study report and any associated datasets to this application to facilitate full review of this NDA.
3. We refer to our June 28, 2010 Information Request letter, which contains several requests related to Product Quality Microbiology. Please respond to these requests as soon as possible.
4. 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.

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

### **REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because this drug product for this indication has orphan drug designation, you are exempt from this requirement.

If you have any questions, call Sulin Sun, PharmD, Regulatory Project Manager, at (301) 796-0036.

Sincerely,

*{See appended electronic signature page}*

Russell Katz, M.D.  
Division Director  
Division of Neurology Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

Application  
Type/Number

Submission  
Type/Number

Submitter Name

Product Name

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NDA-201367

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ORIG-1

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EISAI INC

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RUFINAMIDE ORAL  
SUSPENSION

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/s/  
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RUSSELL G KATZ  
07/16/2010



NDA 201367

**INFORMATION REQUEST**

Eisai Inc.  
Attention: Ira Pham Do, PharmD  
Senior Manager, Regulatory Affairs  
300 Tice Boulevard  
Woodcliff Lake, NJ 07677

Dear Dr. Do:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Banzel (rufinamide) Oral Suspension (40mg/mL).

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 in order to continue our evaluation of your NDA.

1. Provide test methods and acceptance criteria to demonstrate the product is free of the objectionable microorganism *Burkholderia cepacia*. We recommend that potential sources are examined and sampled as process controls, and these may include raw materials and the manufacturing environment. A risk assessment for this species in the product and raw materials is recommended to develop sampling procedures and acceptance criteria. Your test method should be validated and a discussion of those methods should be provided. Test methods validation should address multiple strains of the species and cells that are acclimated to the environments (e.g., warm or cold water) that may be tested.

If you have any questions, contact Teshara G. Bouie, Regulatory Project Manager, at (301) 796-1649.

Sincerely,

*{See appended electronic signature page}*

Ramesh Sood, Ph.D.  
Branch Chief  
Branch I, Division of New Drug Quality Assessment I  
Office of New Drug Quality Assessment  
Center for Drug Evaluation and Research

Application  
Type/Number

Submission  
Type/Number

Submitter Name

Product Name

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NDA-201367

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ORIG-1

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EISAI INC

-----  
RUFINAMIDE ORAL  
SUSPENSION

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/s/  
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RAMESH K SOOD

06/28/2010

## MEMORANDUM



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

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**DATE:** June 23, 2010

**TO:** Eisai Inc., 300 Tice Blvd., Woodcliff Lake, NJ 07677

**FROM:** Vinayak B Pawar, Ph.D., Senior Reviewer, OPS NDMS

**THROUGH:** Tu-Van Lambert, Project manager, ONDQA

**SUBJECT:** Objectionable opportunistic pathogen *Burkholderia cepacia*

---

**In order to complete the product quality microbiology review of NDA 201367, the following issue needs to be addressed by Eisai Inc.**

### **FDA Question**

1. Provide test methods and acceptance criteria to demonstrate the product is free of the objectionable microorganism *Burkholderia cepacia*. We recommend that potential sources are examined and sampled as process controls, and these may include raw materials and the manufacturing environment. A risk assessment for this species in the product and raw materials is recommended to develop sampling procedures and acceptance criteria. Your test method should be validated and a discussion of those methods should be provided. Test methods validation should address multiple strains of the species and cells that are acclimated to the environments (e.g., warm or cold water) that may be tested.

### ***Justification:***

*Burkholderia cepacia* is an opportunistic pathogen that is commonly found in water and soil. It is often present in commercial water systems as well as natural environments. It is capable of growing in distilled water. Strains of this species can grow in the presence of disinfectants and antimicrobial preservatives, and are used commercially in bioremediation to degrade toxic chemicals. Recent recalls due to this species in non-sterile drug and cosmetic products have been reported and it has been implicated in deaths among compromised patients. *B. cepacia* may be difficult to recover with bacteriological media when present in water that is cold (<7°C) or is very warm (>46°C).

### ***Comments:***

Finished products that do not purport to be sterile are expected to meet the requirements of 21CFR211.113(a) Control of microbiological contamination. USP <1111> provides recommended microbial limits for certain classes of non-sterile products. In addition, there should be a risk

## MEMORANDUM

assessment that addresses other objectionable microorganisms, including *B. cepacia*. Generally, aqueous products should be tested for *B. cepacia* and process controls should include tests of potential sources of this species. Potential sources may include raw materials and the manufacturing environment.

Since there is no test method in the compendia that applicants can reference, the application should provide a narrative or procedure describing the test. A validation study is recommended and should include recovery studies that use a variety of strains of *B. cepacia*. Factors such as steps to acclimate the cells to the original product or the environmental source may be helpful (e.g., warm or cold distilled water) rather than just challenging the system with cells from growth medium.

**END**

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201367	ORIG-1	EISAI INC	RUFINAMIDE ORAL SUSPENSION

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/s/

VINAYAK B PAWAR  
06/25/2010

STEPHEN E LANGILLE  
06/28/2010

12 pm 6/14/10

Good Morning,

As mentioned by phone a few minutes ago we have the following clinical pharmacology questions. Please respond asap and reply to all above.

Thank you,  
Cathy

1. We understand that the analytical method validation is the same as the original NDA. However, each study should have its own bioanalytical validation data. You have only submitted a mean analytical validation data for the pivotal bioequivalence Study E2080-E044-003 as given in Table 2.7.1-2 in Module 2. Please provide the complete validation report with individual data for the standard curves and the quality control samples.
2. Study center name for the Pivotal BE Study E2080-E044-003 is provided as given below, but is not clear whether that is the analytical site as well since the complete study bioanalytical validation report is not submitted. Please clarify.

**Investigator(s):**

Darren Wilbraham, MBBS, DCPSA

**Study Center(s):**

Quintiles Ltd. Guys Drug Research Unit (GDRU)  
6 Newcomen Street  
London SE1 1YR  
United Kingdom

Cathleen Michaloski, BSN / MPH  
Senior Regulatory Project Manager  
Division of Neurology Products  
Center for Drug Evaluation and Research  
Food and Drug Administration  
ph 301-796-1123  
email: [cathleen.michaloski@fda.hhs.gov](mailto:cathleen.michaloski@fda.hhs.gov)

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/s/  
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CATHLEEN B MICHALOSKI  
06/14/2010



NDA 201367

**NDA ACKNOWLEDGMENT**

Eisai Inc.  
Attention: Ira Pham Do, PharmD  
Senior Manager, Regulatory Affairs  
300 Tice Boulevard  
Woodcliff Lake, NJ 07677

Dear Dr. Do:

We have received your New Drug Application (NDA) submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: Banzel (rufinamide)  
Oral Suspension (40mg/mL)

Date of Application: April 30, 2010

Date of Receipt: May 03, 2010

Our Reference Number: NDA 201367

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 July 02, 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 content of labeling must conform to the content and format requirements of revised 21 CFR 201.56-57.

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 Neurology 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 me at (301) 796-0036.

Sincerely,

*{See appended electronic signature page}*

Sulin Sun, PharmD  
Regulatory Project Manager  
Division of Neurology Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

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Banzel (rufinamide) Oral  
Suspension

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/s/  
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SU-LIN SUN  
05/19/2010



APPEARS THIS WAY ON ORIGINAL.

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/s/  
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TU-VAN L LAMBERT

05/18/2010