Kacuba, Alice

From: Kacuba, Alice
Sent: Thursday, January 29, 2009 3:53 PM
To: 'sibylle.jennings@novartis.com'
Cc: Cottrell, Christy L.
Subject: NDA 22334: Information request

Importance: High

Hi,

Then Stats reviewer has the following Information Request. Please submit an amendment ASAP.

Thank you.

Alice
Alice Kacuba, RN, MSN, RAC
Chief, Project Management Staff
Division of Drug Oncology Products
Office of Oncology Drug Products
OND/CDER/FDA
301-796-1381
(f)301-796-9845
alice.kacuba@fda.hhs.gov

Please explain the reasons for discrepancy between the following two tables. The first table is constructed based on a_anp dataset in the analysis folder and the second one from anp dataset in the listing folder. Both datasets used are from September 30, 2008 submission (SN 011).

Table 1: Antineoplastic Therapies for Cut off Date 28 Feb 2008 (Based on Analysis Data)

Therapy type	Number of patients with ANP	
	RAD001	Placebo
Missing	18	15
Chemotherapy	12	0
Hormone therapy	0	1
Immunotherapy	8	2
Anticonvulsant	11	1
Hepatic chemoembolization	14	7
Targeted therapy	54	12
Other	5	4
All	96	35

Table 2: Antineoplastic Therapies for Cut off Date 28 Feb 2008 (Based on Listing Data)

Therapy type	Number of patients with ANP	
	RAD001	Placebo
Missing	18	15
Chemotherapy	13	1

Hormone therapy	0	1
Immunotherapy	10	2
Anticonvulsant	15	8
Hepatic chemoembolization	1	0
Targeted therapy	60	15
Other	5	6
All	103	41

Tracking:	**Recipient**	**Read**
	'sibylle.jennings@novartis.com'	
	Cottrell, Christy L.	
	Chattopadhyay, Somesh	Read: 1/29/2009 3:54 PM

APPEARS THIS WAY ON ORIGINAL

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/s/

Alice Kacuba
1/29/2009 03:58:46 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Office/Division)*: OSE, Sandy Griffith

FROM *(Name, Office/Division, and Phone Number of Requestor)*: Alice Kacuba, DDOP

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
12-30-2008		22-334	labeling for NDA	12-22-08

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Afinitor	P	Oncology	March 1, 2009

NAME OF FIRM: Novartis

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE / ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE-NDA MEETING
- ☐ END-OF-PHASE 2a MEETING
- ☐ END-OF-PHASE 2 MEETING
- ☐ RESUBMISSION
- ☐ SAFETY / EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☐ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

- ☐ PRIORITY P NDA REVIEW
- ☐ END-OF-PHASE 2 MEETING
- ☐ CONTROLLED STUDIES
- ☐ PROTOCOL REVIEW
- ☐ OTHER (SPECIFY BELOW):
- ☐ CHEMISTRY REVIEW
- ☐ PHARMACOLOGY
- ☐ BIOPHARMACEUTICS
- ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE 4 STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL - BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG SAFETY

- ☐ PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ NONCLINICAL

COMMENTS / SPECIAL INSTRUCTIONS: The purpose of this consult is request review of the PPI that sponsor revised based on our letter based on your review. The revised PPI is in the edr under the Dec 22, 2008 submission.

Thank you.
Alice Kacuba

SIGNATURE OF REQUESTOR
Alice Kacuba

METHOD OF DELIVERY (Check one)
☒ DFS ☐ EMAIL ☐ MAIL ☐ HAND

PRINTED NAME AND SIGNATURE OF RECEIVER

PRINTED NAME AND SIGNATURE OF DELIVERER

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/s/

Alice Kacuba
12/30/2008 08:10:51 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Office/Division)*: OSE, Sandy Griffith

FROM *(Name, Office/Division, and Phone Number of Requestor)*: Alice Kacuba, DDOP

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
12-30-2008		22-334	Risk Mapp	12-22-08

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Afinitor	P	Oncology	March 1, 2009

NAME OF FIRM: Novartis

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE / ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE-NDA MEETING
- ☐ END-OF-PHASE 2a MEETING
- ☐ END-OF-PHASE 2 MEETING
- ☐ RESUBMISSION
- ☐ SAFETY / EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☐ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

- ☐ PRIORITY P NDA REVIEW
- ☐ END-OF-PHASE 2 MEETING
- ☐ CONTROLLED STUDIES
- ☐ PROTOCOL REVIEW
- ☐ OTHER (SPECIFY BELOW):
- ☐ CHEMISTRY REVIEW
- ☐ PHARMACOLOGY
- ☐ BIOPHARMACEUTICS
- ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE 4 STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL - BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG SAFETY

- ☐ PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ NONCLINICAL

COMMENTS / SPECIAL INSTRUCTIONS: The purpose of this consult is request review of the "no risk mapp" (Novartis says they think can be managed by labeling and routine pharmacovigilance actiivties). The submisionis totally electronic and is ithe edr. Extended user fee date=3-30-2009.

Thank you.
Alice Kacuba

SIGNATURE OF REQUESTOR
Alice Kacuba

METHOD OF DELIVERY (Check one)
☒ DFS ☐ EMAIL ☐ MAIL ☐ HAND

NTED NAME AND SIGNATURE OF RECEIVER

PRINTED NAME AND SIGNATURE OF DELIVERER

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/s/

Alice Kacuba
12/30/2008 08:38:49 PM

Kacuba, Alice

From:	Kacuba, Alice
Sent:	Thursday, December 11, 2008 4:49 PM
To:	'sibylle.jennings@novartis.com'
Subject:	FDA revised carton and container labels
Importance:	High

Hi,

The purpose of this email is to provide FDA revisions to the carton and container labels.

COMMENTS TO THE APPLICANT

[redacted] b(4)

Things get finalized at different times. Just got review from OSE on carton and container labels.

Thank you.

Alice
Alice Kacuba, RN, MSN, RAC
Chief, Project Management Staff
Division of Drug Oncology Products
Office of Oncology Drug Products
OND/CDER/FDA
301-796-1381
(f)301-796-9845
alice.kacuba@fda.hhs.gov

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/s/

Alice Kacuba
12/11/2008 04:52:39 PM

Kacuba, Alice

From: Kacuba, Alice
Sent: Sunday, December 07, 2008 5:59 PM
To: 'sibylle.jennings@novartis.com'
Subject: IR from Clin Pharm

Importance: High

Hi,

The purpose of this email is to request an Information Request on behalf of Clin Pharm:

It is stated in the summary of Biopharmaceutics that "All assay methods used to assess systemic exposure in human pharmacokinetic studies exhibited sufficient specificity, accuracy, precision, and sensitivity for the purposes and conclusions of the individual studies. A list of methods for each clinical pharmacology studies in Section 6, Table 6-1 and within-study validation data are provided in each clinical study report." I have not been able to locate the bioanalytical reports for multiple studies.

If they are included in the original submission please provide instructions to locate them. Specifically I need the reports for the following studies: C2106, C2104, C2108, C2118, C2222, C2235.

Please provide an estimated turn around time for this IR.

Please note that I will be off site for a mandatory 2 meeting (Mon and Tues) as will most team leaders and supervisors in OND. I will be monitoring BB. If you call me on BB, I will most likely "ignore" until I can get to a place where I can call you back.

Thank you.

Alice
Alice Kacuba, RN, MSN, RAC
Chief, Project Management Staff
Division of Drug Oncology Products
Office of Oncology Drug Products
OND/CDER/FDA
301-796-1381
(f)301-796-9845
alice.kacuba@fda.hhs.gov

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/s/

Alice Kacuba
12/7/2008 06:02:15 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

DISCIPLINE REVIEW LETTER

NDA 22-334

Novartis Pharmaceutical Corporation
Attention: Sibylle R. Jennings, Ph.D.
One Health Plaza
East Hanover, New Jersey 07936-1080

Dear Dr. Jenning:

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

Our review of the proposed tradename in your submission is complete, and we have the following comments:

1. We do not object to the proposed tradename of Afinitor

2. This proposed tradename will need to re-reviewed within 90 days of approval.

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

If you have any questions, call me at (301) 796-1381.

Sincerely,

{See appended electronic signature page}

Alice Kacuba, RN, MSN, RAC
Chief, Project Management Staff
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

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/s/

Alice Kacuba
12/7/2008 05:51:50 PM
This letter corrects a typo in the 12-4-08 letter. "..do object..." to "do not object..." The 12-4-08 letter was emailed tot he sponsor.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

DISCIPLINE REVIEW LETTER

NDA 22-334

Novartis Pharmaceutical Corporation
Attention: Sibylle R. Jennings, Ph.D.
One Health Plaza
East Hanover, New Jersey 07936-1080

Dear Dr. Jenning:

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

Our review of the proposed Patient Package Insert in your submission is complete, and we have the following comments:

1. Please revise the Patient Package Insert as attached.

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

If you have any questions, call me at (301) 796-1381.

Sincerely,

{See appended electronic signature page}

Alice Kacuba, RN, MSN, RAC
Chief, Project Management Staff
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

14 Page(s) Withheld

_____ Trade Secret / Confidential (b4)

__✓__ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Withheld Track Number: Administrative- 10

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/s/

Alice Kacuba
12/4/2008 07:20:04 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

DISCIPLINE REVIEW LETTER

NDA 22-334

Novartis Pharmaceutical Corporation
Attention: Sibylle R. Jennings, Ph.D.
One Health Plaza
East Hanover, New Jersey 07936-1080

Dear Dr. Jenning:

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

Our review of the proposed tradename in your submission is complete, and we have the following comments:

1. We do object to the proposed tradename of Afinitor

2. This proposed tradename will need to re-reviewed within 90 days of approval.

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

If you have any questions, call me at (301) 796-1381.

Sincerely,

{See appended electronic signature page}

Alice Kacuba, RN, MSN, RAC
Chief, Project Management Staff
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

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/s/

Alice Kacuba
12/4/2008 07:18:47 PM

Kacuba, Alice

From: Kacuba, Alice
Sent: Friday, November 28, 2008 10:48 AM
To: 'sibylle.jennings@novartis.com'
Cc: Bullock, Julie; Mehrotra, Nitin
Subject: RE: NDA 220334 Follow-up on TC this morning
Importance: High

Sibylle,

Please be sure that all emails are eventually sent in by Gateway. With an all electronic NDA, I can not archive incoming emails from sponsors so it is your responsibility to be sure all information sent in emails to FDA are sent in my Gateway to make a complete application.

Thank you.

Alice
Alice Kacuba, RN, MSN, RAC
Chief, Project Management Staff
Division of Drug Oncology Products
Office of Oncology Drug Products
OND/CDER/FDA
301-796-1381
(f)301-796-9845
alice.kacuba@fda.hhs.gov

From: sibylle.jennings@novartis.com [mailto:sibylle.jennings@novartis.com]
Sent: Wednesday, November 26, 2008 6:37 PM
To: Bullock, Julie; Mehrotra, Nitin
Cc: Kacuba, Alice
Subject: NDA 220334 Follow-up on TC this morning

Dear Julie, dear Nitin,

Thank you very much for the helpful and constructive TC this morning.
Please find attached Table 6.2 from our response document submitted last week showing all changes and additions which we discussed this morning in track change mode. I will be in touch with you next week to update you on the actual submission date of the documentation described in the attachment.
Please let me know if you have any questions.
Thanks again and best regards,
Sibylle

Sibylle Jennings

Novartis Pharmaceuticals Corporation
PH, Dev - Oncology DRA II
USEH, Building 104 Room 3K25
Novartis Pharmaceuticals Corporation
One Health Plaza
East Hanover, NJ 07936-1080
USA
Phone: +1 862 7781196
Email : sibylle.jennings@novartis.com

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/s/

Alice Kacuba
11/28/2008 10:51:19 AM

Kacuba, Alice

From: Kacuba, Alice
Sent: Tuesday, November 04, 2008 4:21 PM
To: 'sibylle.jennings@novartis.com'
Subject: FW: Everolimus data to sponsor please.

Importance: High

Follow Up Flag: Follow up
Due By: Monday, November 03, 2008 12:30 AM
Flag Status: Flagged

Hi,

There are discrepancies with your concentration data set compared to the patient listings for the clinical pharmacology study report for c2101/02. Below are few examples of errors I found. Please resubmit a corrected data set. In addition, verify that other clinical pharmacology oncology datasets submitted are free of data errors.

Dataset c2102cnc.xpt information

study re listings

Study	Center #	Sub #	SCHTIME	CONC	treatment arm	Conc
2101	1001	10029 C2101_xxxx-10029, WK-4 6.0 hr	6	38.28	RAD001 70 mg/week	
2101	1001	10029 C2101_xxxx-10029, WK-4 8.0 hr	8	58.57	RAD001 70 mg/week	
2101	1001	10009 C2101_1001-10009-1 WK4, D1, 2h	2	-199	RAD001 30 mg/week	
2101	1001	10007 C2101_1001-10007 -1 WK4, D1 ,1	1	-199	RAD001 30 mg/week	
2101	1002	10024 C2101_1002-10024 , WK-4 24 hr	24	56.32	RAD001 10 mg/day	
2101	1002	10016 C2101_1002-10016 , WK-4 24 hr	24	43.29	RAD001 5 mg/day	

Please provide an estimated turn around time on this request.

Thank you.

Alice
Alice Kacuba, RN, MSN, RAC
Chief, Project Management Staff
Division of Drug Oncology Products
Office of Oncology Drug Products
OND/CDER/FDA
301-796-1381
(f)301-796-9845
alice.kacuba@fda.hhs.gov

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/s/
Alice Kacuba
11/4/2008 04:23:28 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-334

Novartis Pharmaceutical Corporation
Attention: Sibylle Jennings, Ph.D.
One Health Plaza
East Hanover, NJ 07936-1080

Dear Dr. Jennings:

Please refer to your June 27, 2008 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Affinitor334 (everolimus) Tablets, 5mg and 10 mg.

On October 14, 2008, we received your October 14, 2008 major amendment to this application. The receipt date is within 3 months of the user fee goal date. Therefore, we are extending the goal date by three months to provide time for a full review of the submission. The extended user fee goal date is March 30, 2009.

If you have any questions, call me at 301-796-1381.

Sincerely,

{See appended electronic signature page}

Alice Kacuba, RN, MSN, RAC
Chief, Project Management Staff
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

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/s/

Alice Kacuba
10/30/2008 06:55:43 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-334

INFORMATION REQUEST LETTER

Novartis Pharmaceuticals Corporation
Attention: Sibylle R. Jennings, Ph.D.
Associate Director, Drug Regulatory Affairs
One Health Plaza
East Hanover, New Jersey 07936-1080

Dear Dr. Jennings:

Please refer to your new drug application (NDA) received on June 30, 2008, under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Afinitor® (everolimus) Tablets.

We also refer to your submission dated September 5, 2008.

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.

b(4)

b(4)

7. Provide statistical evaluation of the updated stability data submitted in your September 5, 2008 submission. Provide analyses for all attributes (e.g., assay, water, impurities, dissolution, etc.) that have noticeable change over time.

8. Be advised that any post approval change in the drug substance CMC that has been referenced to other NDA(s) and DMF(s) must be implemented in accordance with 21 CFR 314.70.

If you have any questions, call Deborah Mesmer, Regulatory Health Project Manager, at 301-796-4023.

Sincerely,

{See appended electronic signature page}

Sarah C. Pope, Ph.D.
Branch Chief (Acting)
Division of Pre-Marketing Assessment III
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

Sarah Pope
10/17/2008 04:40:33 PM

Kacuba, Alice

From: Kacuba, Alice
Sent: Thursday, October 09, 2008 3:58 PM
To: 'sibylle.jennings@novartis.com'
Subject: Clin Pharm Information Requests (IR) X2
Importance: High

Sibylle,

Below are 2 Information Requests form Clin Pharm:

1. Please re-submit the combined data sets (individual data listings and PK parameters) for your C2101-02 PK data analysis. The data set submitted in the original submission folder rad001c2101-02 does not contain all the data. Specifically I believe it is missing the necessary data from study C2101 and this data was not found in the datasets for study C2101 (only the RAD001 + gemcitabine data was in the rad001c2101 folder).

2. Please resubmit the data set and provide the nominal sampling times (0, 1, 1.5 etc) for your concentration data for study C2119. In addition, please ensure that all of the other PK studies include the nominal time as a column for the concentration data sets and resubmit if necessary.

3. Please provide an estimated turn around time as the clin pharm reviewer has identified these IRs as Urgent.

Thnak you.

Alice

Alice Kacuba, RN, MSN, RAC
Chief, Project Management Staff
Division of Drug Oncology Products
Office of Oncology Drug Products
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(f)301-796-9845
alice.kacuba@fda.hhs.gov

From: sibylle.jennings@novartis.com [mailto:sibylle.jennings@novartis.com]
Sent: Thursday, October 09, 2008 2:36 PM
To: Kacuba, Alice
Subject: Fw: Request for data for Everolimus.... follow-up on upcoming dataset submissions

Dear Alice,

This is to briefly update you on the upcoming dataset submissions in response to the

information requests dated Oct 2 and Oct 8, 2008.
We experienced major problems with our IT systems today, which will unfortunately cause a one day delay for the planned submission of the datasets for study C2107 (biomarkers) and C2239 (full efficacy and safety datasets), so submission date will be Monday, Oct 13.
The submission of the adverse event datasets for study C2107 requested yesterday is targeted for next Wednesday, Oct 15.
The by patient listings that are under preparation following the TC with Dr Ryan on September 24 are targeted to be submitted early next week as well.
Please let me know if you have any questions.
Best regards,
Sibylle

Sibylle Jennings, PhD
Novartis Pharmaceuticals Corporation
Sr. Assoc. Director, Drug Regulatory Affairs - Oncology
USEH, Building 104 / Room 2E27
Novartis Pharmaceuticals Corporation
One Health Plaza
East Hanover, NJ 07936-1080
USA
Phone: +1 8627781196
Fax: +1 9737815217
Cell: +1 8625964679
Email : sibylle.jennings@novartis.com

----- Forwarded by Sibylle Jennings/PH/Novartis on 10/09/2008 02:27 PM -----

Sibylle Jennings/PH/Novartis
10/08/2008 03:12 PM

To
alice.kacuba@fda.hhs.gov
cc

Subject
Re: FW: Request for data for Everolimus....

Hi Alice,
At the moment everything is prepared to submit the previously requested datasets this Friday (Oct 10). We probably need slightly more time for adding the AE datasets for study 2107. I will follow-up with you tomorrow on when you can expect our response(s) to the last submission requests.

Kind regards,
Sibylle

Sibylle Jennings, PhD
Novartis Pharmaceuticals Corporation
Sr. Assoc. Director, Drug Regulatory Affairs - Oncology
USEH, Building 104 / Room 2E27
Novartis Pharmaceuticals Corporation

One Health Plaza
East Hanover, NJ 07936-1080
USA
Phone: +1 8627781196
Fax: +1 9737815217
Cell: +1 8625964679
Email : sibylle.jennings@novartis.com

"Kacuba, Alice" <alice.kacuba@fda.hhs.gov>
10/08/2008 02:46 PM

Please respond to
alice.kacuba@fda.hhs.gov

To
sibylle.jennings@novartis.com
cc

Subject
FW: Request for data for Everolimus....

Hi,
Regarding last Information Request:
Please submit adverse event data also for C2107 study.

Study C2107:
10 mg/day was identified as the optimum dose by PK-PD modeling. However, the submission only contains the PK data. Kindly provide the other relevant data including biomarkers and adverse events.

Thank you.
Alice
Alice Kacuba, RN, MSN, RAC
Chief, Project Management Staff
Division of Drug Oncology Products
Office of Oncology Drug Products
OND/CDER/FDA
301-796-1381
(f)301-796-9845
alice.kacuba@fda.hhs.gov

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/s/

Alice Kacuba
10/9/2008 04:01:06 PM

Kacuba, Alice

From: Kacuba, Alice
Sent: Wednesday, October 08, 2008 2:46 PM
To: sibylle.jennings@novartis.com
Subject: FW: Request for data for Everolimus....

Importance: High

Hi,

Regarding last Information Request:

Please submit adverse event data also for C2107 study.

Study C2107:

10 mg/day was identified as the optimum dose by PK-PD modeling. However, the submission only contains the PK data. Kindly provide the other relevant data including biomarkers and adverse events.

Thank you.

Alice
Alice Kacuba, RN, MSN, RAC
Chief, Project Management Staff
Division of Drug Oncology Products
Office of Oncology Drug Products
OND/CDER/FDA
301-796-1381
(f)301-796-9845
alice.kacuba@fda.hhs.gov

Tracking:	**Recipient**	**Read**
	sibylle.jennings@novartis.com	
	Mehrotra, Nitin	Read: 10/8/2008 2:48 PM

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/s/

Alice Kacuba
10/8/2008 02:51:55 PM
Sent by email 10-8-08.

MEMORANDUM OF TELECON

DATE: September 24, 2008

APPLICATION NUMBER: NDA 22-334

BETWEEN:

Andrea Kay (clinical)
Peter Berry (medical writing)
Tomas Haas (statistics)
Lilla di Scala (Statistics)
Sibylle Jennings (DRA US).
Representing: Novartis Pharmaceutical Corporation

AND

Division of Drug Oncology Products, HFD-150
Name: Qin Ryan, M.D., Medical reviewer
Somesh Cahattopadhyay, Ph.D., Statistical Reviewer

SUBJECT: Discussion of data sets that FDA requested.

HISTORY: The Division had sent Information Requests to the Sponsor. The Sponsor requested a tcon to clarify the requests prior to submitting the datasets.

TODAY'S PHONE CALL: **IR Discussion with the applicant**

FDA Requests:

1. Please identify which dataset contains reasons for PFS events and reason, censor date, censor information.

Discussion: The applicant will submit these datasets from the Feb 28, 2008 cut-off date with the safety update submission.

2. Please provide an exploratory analysis on the difference of PFS between the central review and investigator assessment.

Discussion: Applicant will submit all listings and tables from the Feb 28 2008 cut off date. FDA recommends the applicant provide a listing with all PFS disagreements between the IRC and investigator assessments. As requested by the applicant, the FDA would suggest

the following headings for the PFS disagreements:

Subject ID	Randomized treatment	PFS Status by IRC (event or censor	PFS Status by INV	Date of PFS by IRC	Date of PFS by INV	Difference (days)	Reason of IRC assessment	Reason of INV assessment	Comments
Example	1	Censor	PD	5/1/10	7/20/10	80	CT with 6 lesions	CT with 3 lesion	Inadequate assessment by IND

3. Please provide analysis of missing tumor assessments for both central and local assessments.

Discussion: The applicant would submit missing tumor assessment exploratory analyses from the Feb 28, 2008 cut-off date.

FDA additional requests:

1. Please explain the difference between AND (number of subjects = 69) dataset in *listings* folder and A_AND (number of subjects = 59) dataset in *analysis* folder and why the numbers of subjects in those two datasets are different. Please submit these datasets also from the Feb 28, 2008 cut-off date.

2. According to Table 14.2-1.20, 6 subjects with SD received post-study antineoplastic treatments. Please explain how to verify each subject who received post-study antineoplastic therapy before or after PD in AND and A_AND datasets.

3. The applicant clarified that ORR of both cut-off dates in the efficacy report and update (Aug 26, 2008) were based on the IRC assessment. FDA asked the applicant to submit the investigators' ORR analysis from both cut-off dates.

4. There were 50 unknown status subjects from the Feb 28, 2008 cut-off ORR analysis. Please provide a summary of all reasons for their unknown status.

Final Discussion:

- The applicant will review and respond to the FDA additional requests.
- The applicant will submit the complete datasets from the Feb 28, 2008 cut-off date and study C2240 post-text output tables and listings for PFS, OS and ORR update with the safety update submission. Other items discussed today will be submitted as separate submissions.

Qin Ryan, M.D., Medical Reviewer & Meeting Chair

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/s/

Qin Ryan
10/7/2008 07:11:00 PM
Thanks!

Kacuba, Alice

From: Kacuba, Alice
Sent: Tuesday, September 23, 2008 1:23 PM
To: 'sibylle.jennings@novartis.com'
Subject: 22-334 Information Requests-Stats

Importance: High

Hi,

The purpose of this email is to send Stats Information Requests.

1. Please identify which data set contains reasons for PFS events and reason, censor date, censor information.

2. Please provide an exploratory analysis on the difference of PFS between the central review and investigator assessment.

3. Please provide analysis of missing tumor assessments for both central and local.

Thank you.

Alice
Alice Kacuba, RN, MSN, RAC
(Acting) Chief, Project Management Staff
Division of Drug Oncology Products
Office of Oncology Drug Products
OND/CDER/FDA
301-796-1381
(f)301-796-9845
alice.kacuba@fda.hhs.gov

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/s/

Alice Kacuba
9/23/2008 01:28:38 PM

Kacuba, Alice

From: Kacuba, Alice
Sent: Monday, September 22, 2008 8:02 AM
To: sibylle.jennings@novartis.com
Subject: Information Requests from Clinical Reviewer

Importance: High

Hi,

The purpose of this email is to communicate Information Requests from Clinical Reviewer.

1. Please provide a detailed efficacy update, which should have similar but up dated contents as the original C2240 study report (fits M5).

2. Please provide raw and derived data sets for the efficacy update.

3. When will be your anticipated date for safety up date (including data sets) submission?

Please provide an estimated response time.

Thank you.

Alice
Alice Kacuba, RN, MSN, RAC
Chief, Project Management Staff
Division of Drug Oncology Products
Office of Oncology Drug Products
OND/CDER/FDA
301-796-1381
(f)301-796-9845
alice.kacuba@fda.hhs.gov

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/s/

Alice Kacuba
9/22/2008 08:07:06 AM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 22-334

PRIORITY REVIEW DESIGNATION

Novartis Pharmaceuticals Corporation
Attention: Dr. Sibylle Jennings
Assistant Director of Drug Regulatory Affairs
One Health Plaza
East Hanover, New Jersey 07936-1080

Dear Dr. Jennings:

Please refer to your new drug application (NDA) dated June 27, 2008, received June 30, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for Afinitor Tablets 5mg and 10 mg.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application is considered filed 60 days after the date we received your application in accordance with 21 CFR 314.101(a). The review classification for this application is **Priority**. Therefore, the user fee goal date is December 30, 2008.

While conducting our filing review, we identified potential review issues and will communicate them to you on or before September 12, 2008.

If you have any questions, call Dillard Woody, Regulatory Project Manager, at (301) 796-4097.

Sincerely,

{See appended electronic signature page}

Robert Justice, MD
Director
Division of Drug Oncology Products
Office of Oncology Drug Products
Office of New Drugs
Center for Drug Evaluation and Research

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/s/

Dillard H Woody
9/2/2008 02:00:37 PM

DSI CONSULT: Request for Clinical Inspections

Date: August 5, 2008

To: Constance Lewin, M.D., M.P.H, Branch Chief, GCP1
Tejashri Purohit-Sheth, M.D., Branch Chief (Acting), GCP2
Name of DSI Primary Reviewer (if known)
Division of Scientific Investigations, HFD-45
Office of Compliance/CDER

Through: Qin Ryan, M.D., Medical Officer, DDOP
Ramzi Dagher M.D., Medical Team Leader and Deputy Director, DDOP
Robert Justice MD, Division Director, DDOP

From: Dillard Woody, Regulatory Health Project Manager, DDOP

Subject: **Request for Clinical Site Inspections**

I. General Information

Application#: NDA-22-334
Applicant/ Applicant contact information (to include phone/email): Dr. Sibylle Jennings, 862-778-1196, sibylle.jennings@novartis.com
Drug Proprietary Name: Afinitor (everolimus)
NME: Yes
Review Priority: Priority

Study Population includes < 17 years of age: No
Is this for Pediatric Exclusivity: No

Proposed New Indication(s): advanced Renal Cell Carcinoma (RCC)

PDUFA: December 30, 2008
Action Goal Date: December 20, 2008
Inspection Summary Goal Date: November 20, 2008

II. Protocol/Site Identification

A single randomized study, RAD001C2240 titled "A randomized, double-blind, placebo-controlled, multicenter phase III study to compare the safety and efficacy of RAD001 plus Best Supportive Care (BSC) versus BSC plus Placebo in patients with metastatic carcinoma of the kidney which has progressed on VEGF receptor tyrosine kinase inhibitor therapy", was submitted to support approval of everolimus for treatment of advanced renal cell carcinoma. The following sites were identified as essential to evaluate the study quality and integrity (Table below). The basis of the site selection was the number of enrolled patients and PFS events. As discussed with DSI medical officer, Dr. SK Young, site 604 was inspected a few years ago and was generally in order. Therefore, we only request that site 513, 606 and 756 be inspected.

Site Number / PI	Enrollment	Events	Address	Email / Phone number
513 / Robert Motzer	21 (E= 12, P = 9)	13 (E= 5, P = 8)	Memorial Sloan-Kettering Cancer Center 1275 York Avenue New York, NY 10021	motzerr@mskcc.org +1 646 422 4312
604 / Bernard Escudier	42 (E =26, P = 16)	21 (E=8, P = 13)	Institut Gustave Roussy 39 rue Camille Desmoulins Villejuif 94805 France	escudier@igr.fr +33 56 142 4119
606 / Stephane Oudard	30 (E=24, P=6)	12 (E=7, P=5)	Hôpital Georges Pompidou 20, rue Leblanc Paris 75015 France	stephane.oudard@hop.egp.ap-hop-paris.fr +33 38 811 6344
756 / Camillo Porta	24 (E=21, P=3)	12 (E=10, P=2)	Center IRCCS San Matteo University Hospital Piazzale Golgi, 19 Pavia 1-27100 Italy	c.porta@smatteo.pv.it +39 0382 502544

III. Site Selection/Rationale

See section II.

Rationale for DSI Audits

The review team is interested to know whether the AEs, disease evaluations and progression events documented in medical records are consistent with CRFs. In addition, it is important to identify any violation of enrollment criteria in the medical records that is not noted on CRFs.

Domestic Inspections:

Reasons for inspections (please check all that apply):

__x__ Enrollment of large numbers of study subjects
____ High treatment responders (specify):
__x__ Significant primary efficacy results pertinent to decision-making
____ There is a serious issue to resolve, e.g., suspicion of fraud, scientific misconduct, significant human subject protection violations or adverse event profiles.
____ Other (specify):

International Inspections:

Reasons for inspections (please check all that apply):

__X__ There are insufficient domestic data
____ Only foreign data are submitted to support an application
____ Domestic and foreign data show conflicting results pertinent to decision-making
____ There is a serious issue to resolve, e.g., suspicion of fraud, scientific misconduct, or significant human subject protection violations.
____ Other (specify) (Examples include: Enrollment of large numbers of study subjects and site specific protocol violations. This would be the first approval of this new drug and most of the limited experience with this drug has been at foreign sites, it would be desirable to include one foreign site in the DSI inspections to verify the quality of conduct of the study).

Should you require any additional information, please contact Dillard Woody at 301-796-4097 or Dr. Qin Ryan at 301-796-1449.

Concurrence: (as needed)

_____ Medical Team Leader
_____ Medical Reviewer
_____ Division Director (for foreign inspection requests or requests for 5 or more sites only)

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/s/

Alice Kacuba
8/26/2008 05:59:06 PM

Ramzi Dagher
8/27/2008 10:14:50 AM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-334

NDA ACKNOWLEDGMENT

Novartis Pharmaceuticals Corporation
Attention: Dr. Sibylle Jennings
Assistant Director of Drug Regulatory Affairs
One Health Plaza, East Hanover, New Jersey 07936-1080

Dear Dr. Jennings:

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

Name of Drug Product: Afinitor (everolimus) Tablets 5mg and 10 mg

Date of Application: July 29, 2008

Date of Receipt: July 30, 2008

Our Reference Number: NDA 22-334

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 September 28, 2008 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/oc/datacouncil/spl.html. 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 Drug Oncology 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/cder/ddms/binders.htm.

If you have any questions, call Dillard Woody, Regulatory Project Manager, at (301) 796-4097.

Sincerely,

{See appended electronic signature page}

Dillard H. Woody Jr.
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

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/s/

Dillard H Woody
8/6/2008 10:21:57 AM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Office/Division)*: CDER OSE Consults

FROM *(Name, Office/Division, and Phone Number of Requestor)*:
Dillard H.Woody Jr., Regulatory Health Project Manager
Division of Drug Oncology Products
Office of Oncology Drug Products, 301-796-4097

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
August 1, 2008		22-334	New NDA	June 30, 2008

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Afinitor (everolimus) Tablets	Priority	Oncology	October 30, 2008 pdufa date=12/30/2008

NAME OF FIRM: Novartis Oncology

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE / ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE-NDA MEETING
- ☐ END-OF-PHASE 2a MEETING
- ☐ END-OF-PHASE 2 MEETING
- ☐ RESUBMISSION
- ☐ SAFETY / EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☐ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

- ☐ PRIORITY P NDA REVIEW
  END-OF-PHASE 2 MEETING
  CONTROLLED STUDIES
  PROTOCOL REVIEW
- ☐ OTHER (SPECIFY BELOW):

- ☐ CHEMISTRY REVIEW
- ☐ PHARMACOLOGY
- ☐ BIOPHARMACEUTICS
- ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE 4 STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL - BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG SAFETY

- ☐ PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ NONCLINICAL

COMMENTS / SPECIAL INSTRUCTIONS: The purpose of this consult is to request review of the proposed tradename for the NDA 22-33-Afinitor. The proposed labeling and labels are in the edr under June 30, 2008 submission.
PDUFA DATE: December 30, 2008
The new NDA is in the edr.

SIGNATURE OF REQUESTOR	METHOD OF DELIVERY (Check one)
Dillard Woody	☒ DFS ☐ EMAIL ☐ MAIL ☒ HAND
NTED NAME AND SIGNATURE OF RECEIVER	PRINTED NAME AND SIGNATURE OF DELIVERER

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/s/

Dillard H Woody
8/1/2008 08:00:40 AM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Office/Division)*: OSE Consults

FROM *(Name, Office/Division, and Phone Number of Requestor)*:
Dillard H. Woody Jr., Regulatory Health Project Manager
Division of Drug Oncology Products
Office of Oncology Drug Products, 301-796-4097

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
July 22, 2008		22-334	New NDA	June 30, 2008

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Afinitor (everolimus) Tablets	Priority	Oncology	October 30, 2008 pdufa date=12/30/2008

NAME OF FIRM: Novartis Oncology

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE / ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE-NDA MEETING
- ☐ END-OF-PHASE 2a MEETING
- ☐ END-OF-PHASE 2 MEETING
- ☐ RESUBMISSION
- ☐ SAFETY / EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☒ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

- ☐ PRIORITY P NDA REVIEW
  END-OF-PHASE 2 MEETING
  CONTROLLED STUDIES
  PROTOCOL REVIEW
- ☐ OTHER (SPECIFY BELOW):

- ☐ CHEMISTRY REVIEW
- ☐ PHARMACOLOGY
- ☐ BIOPHARMACEUTICS
- ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
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- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ NONCLINICAL

COMMENTS / SPECIAL INSTRUCTIONS: The purpose of this consult is to request evaluation of the proposed Patient Information Leaflet. The proposed labeling is in the edr.

SIGNATURE OF REQUESTOR
Dillard Woody

METHOD OF DELIVERY (Check one)
☒ DFS ☐ EMAIL ☐ MAIL ☐ HAND

PRINTED NAME AND SIGNATURE OF RECEIVER

PRINTED NAME AND SIGNATURE OF DELIVERER

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/s/

Dillard H Woody
7/31/2008 01:57:51 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Office/Division)*: JuWon Lee, DDMAC
Keith Olin, DDMAC

FROM *(Name, Office/Division, and Phone Number of Requestor)*:
Dillard H.Woody Jr., Regulatory Health Project Manager
Division of Drug Oncology Products
Office of Oncology Drug Products, 301-796-4097

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
July 24, 2008		22-334	New NDA	June 30, 2008

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Afinitor (everolimus) Tablets	Priority	Oncology	October 30, 2008 pdufa date=12/30/2008

NAME OF FIRM: Novartis Oncology

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
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- ☐ FINAL PRINTED LABELING
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- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☒ OTHER *(SPECIFY BELOW)*:

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- ☐ BIOPHARMACEUTICS
- ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE 4 STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL - BIOPHARMACEUTICS
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IV. DRUG SAFETY

- ☐ PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
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- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ NONCLINICAL

COMMENTS / SPECIAL INSTRUCTIONS: The purpose of this consult is to request evaluation of the proposed labeling. I will invite you to the labeling meetings. The proposed labeling is in the edr under the June 30, 2008 submission.

SIGNATURE OF REQUESTOR	METHOD OF DELIVERY (Check one)
Dillard Woody	☒ DFS ☐ EMAIL ☐ MAIL ☐ HAND
PRINTED NAME AND SIGNATURE OF RECEIVER	PRINTED NAME AND SIGNATURE OF DELIVERER

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/s/

Dillard H Woody
7/24/2008 02:23:16 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Office/Division)*: Devi Kozeli, IRT
CDER DCRP QT

FROM *(Name, Office/Division, and Phone Number of Requestor)*:
Dillard H.Woody Jr., Regulatory Health Project Manager
Division of Drug Oncology Products
Office of Oncology Drug Products, 301-796-4097

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
July 23, 2008		22-334	New NDA	June 30, 2008

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Afinitor (everolimus) Tablets	Priority	Oncology	October 30, 2008 pdufa date=12/30/2008

NAME OF FIRM: Novartis Oncology

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
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- ☐ PRE-NDA MEETING
- ☐ END-OF-PHASE 2a MEETING
- ☐ END-OF-PHASE 2 MEETING
- ☐ RESUBMISSION
- ☐ SAFETY / EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☒ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

- ☐ PRIORITY P NDA REVIEW
  END-OF-PHASE 2 MEETING
  CONTROLLED STUDIES
- ☐ PROTOCOL REVIEW
- ☐ OTHER (SPECIFY BELOW):

- ☐ CHEMISTRY REVIEW
- ☐ PHARMACOLOGY
- ☐ BIOPHARMACEUTICS
- ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE 4 STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL - BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG SAFETY

- ☐ PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ NONCLINICAL

COMMENTS / SPECIAL INSTRUCTIONS: The purpose of this consult is to request a review of the results of a Healthy Volunteer thorough QT study (C2118)

This submission is in the edr under NDA 22-334. The MO = Dr. Ryan

SIGNATURE OF REQUESTOR	METHOD OF DELIVERY (Check one)
Dillard Woody	☒ DFS ☐ EMAIL ☐ MAIL ☐ HAND
NTED NAME AND SIGNATURE OF RECEIVER	PRINTED NAME AND SIGNATURE OF DELIVERER

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/s/

Dillard H Woody
7/24/2008 01:28:09 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Division/Office)*: OPS, Microbiology Staff (HFD-805)
Attn: James McVey (301-769-1572
WO-51 Room 4162

FROM: Dillard Woody, Project Manager, OND/DDOP
WO-22 Room 2341, 301-796-4097

DATE:	IND NO.:	NDA NO.:	TYPE OF DOCUMENT:	DATE OF DOCUMENT:
July 24, 2008		22-334	New NDA	June 30, 2008

NAME OF DRUG:	PRIORITY CONSIDERATION:	CLASSIFICATION OF DRUG:	DESIRED COMPLETION DATE:
Afinitor (everolimus) Tablets	Priority	Oncology	October 30, 2008 pdufa date=12/30/2008

NAME OF FIRM:

REASON FOR REQUEST

I. GENERAL

NEW PROTOCOL	PRE–NDA MEETING	RESPONSE TO DEFICIENCY LETTER
PROGRESS REPORT	END OF PHASE II MEETING	FINAL PRINTED LABELING
NEW CORRESPONDENCE	RESUBMISSION	LABELING REVISION
DRUG ADVERTISING	SAFETY/EFFICACY	ORIGINAL NEW CORRESPONDENCE
ADVERSE REACTION REPORT	PAPER NDA	FORMULATIVE REVIEW
MANUFACTURING CHANGE/ADDITION	CONTROL SUPPLEMENT	OTHER (*SPECIFY BELOW*):
MEETING PLANNED BY		

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
TYPE A OR B NDA REVIEW ND OF PHASE II MEETING ONTROLLED STUDIES ROTOCOL REVIEW OTHER:	CHEMISTRY REVIEW PHARMACOLOGY BIOPHARMACEUTICS OTHER:

III. BIOPHARMACEUTICS

DISSOLUTION	DEFICIENCY LETTER RESPONSE
BIOAVAILABILTY/PK STUDIES	PROTOCOL-BIOPHARMACEUTICS
PHASE IV STUDIES	IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL	REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES	SUMMARY OF ADVERSE EXPERIENCE
CASE REPORTS OF SPECIFIC REACTIONS (List below)	POISON RISK ANALYSIS
COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP	

V. SCIENTIFIC INVESTIGATIONS

CLINICAL	PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS: This consult is to request a review of the micro portion of the new NDA.
This new NDA is indicated for treatment of advanced renal cell carcinoma (RCC).
This submission is in the EDR.
PDUFA Goal date (6 months): 12/30/2008
☑

SIGNATURE OF REQUESTER:	METHOD OF DELIVERY (Check one):
Dillard Woody *{See appended electronic signature page}*	☑ DFS/DARRTS EMAIL MAIL HAND
SIGNATURE OF RECEIVER:	SIGNATURE OF DELIVERER:

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/s/

Dillard H Woody
7/24/2008 02:18:36 PM

Woody, Dillard

From: Woody, Dillard
Sent: Thursday, July 24, 2008 11:45 AM
'sibylle.jennings@novartis.com'
Kacuba, Alice
Subject: IR for NDA 22334

Hello,

The Medical Officer for NDA 22334 has the following requests:

1. Please submit a good clinical practice statement or where it is located in you NDA submission.

2. Please indicate where the address, PI name and contact phone number of the study sites (2240) located in your submission. If they are not included in the submission, please submit these information for the following 4 sites: 513, 604, 606, and 756.

Thank you,
Woody

Tell us where it is
in each study report

Woody, Dillard

From: Woody, Dillard
Sent: Wednesday, July 23, 2008 12:55 PM
: 'sibylle.jennings@novartis.com'
: Kacuba, Alice
Subject: CMC question with dataset

The file d_fmtdat.xpt in m5\datasets\rad001c2240\analysis folder has not been created correctly. When we try to extract the formats from that dataset, it gives the following error:

```
ERROR: This range is repeated, or values overlap: 3-3.
```

Please submit the corrected file.

Appears This Way
On Original