

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**103792Orig1s5311**

**ADMINISTRATIVE and CORRESPONDENCE  
DOCUMENTS**

**From:** Tilley, Amy  
**Sent:** Thursday, February 20, 2014 4:25 PM  
**To:** 'Thambipillai, Dhushy'  
**Subject:** sBLA 103792 5311 Herceptin Eff Suppl – FDA Revised label sent 2–20–14

**Importance:** High

**Attachments:** FDA revised label 2–20–14.doc  
[Dhushy,](#)

Please see the attached FDA revised label with minor changes to Tables 1 and 7.

We request your response to these minor changes as soon as possible. If you agree with our minor changes please officially submit the agreed upon label to the BLA and send me a courtesy copy via email.

Thanks.  
*Amy*

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**From:** Thambipillai, Dhushy [mailto:dhushy.thambipillai@roche.com]  
**Sent:** Thursday, February 20, 2014 12:59 PM  
**To:** Tilley, Amy  
**Subject:** Re: sBLA 103792 5311 Herceptin Eff Suppl - FDA Revised label

Dear Amy

Genentech has reviewed the FDA revised label for Herceptin (BL103792/S–5311) and is in agreement with all of the Agency’s proposed revisions. As such, all changes have been accepted. Additional editorial type changes have been made to the label as follows and are captured as track changes in the attached Genentech revised Herceptin PI.

- Recent Major Changes – Dosage and Administration (2)  
– as there are now changes to two subsections (2.1 and 2.3) under Dosage and Administration
- Table 1, Table 6 and Table 7 footnotes  
– based on Agency recommendations to change the sequence of footnotes in Table 1, the sequence of footnotes in Table 6 and Table were also re–ordered for better readability

- 7 Drug Interactions
  - The word 'carboplatin' was added to align with the currently approved Herceptin label – this update was made per FDA request (BL103792/S-5305 approved Nov 20, 2013) but was not captured in the USPI submitted with S-5311.
- Other minor editorial changes on pg. 25 and 35

Please note that the revised label will be formally submitted to BLA103792 next week.

Kind regards,  
Dhushy

**Dhushy Thambipillai**  
Program Manager, PDRP

Hoffmann-La Roche Limited  
7070 Mississauga Road  
Mississauga, ON L5N 5M8 Canada

Tel: + 1 905 542 5882  
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e-mail: [dhushy.thambipillai@roche.com](mailto:dhushy.thambipillai@roche.com)

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On Tue, Feb 18, 2014 at 5:49 PM, Tilley, Amy <[Amy.Tilley@fda.hhs.gov](mailto:Amy.Tilley@fda.hhs.gov)> wrote:  
Dhushy,

Below is the FDA Revised label for Herceptin sBLA 103792/5311 for Genentech's review.

We respectfully request your response **no later than 4 pm on Thursday, February 20, 2014.**

Kindly confirm receipt of this email.

Regards.

*Amy Tilley*

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Amy Tilley | Regulatory Project Manager | Division of Oncology Products  
1,  
CDER, FDA 10903 New Hampshire Avenue, Room 2177 | Silver Spring,  
MD 20993  
☎ 301.796.3994 (phone) • 301.796.9845 (fax) | ✉ [amy.tilley@fda.hhs.gov](mailto:amy.tilley@fda.hhs.gov)

36 Page(s) 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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AMY R TILLEY  
02/20/2014

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

## REQUEST FOR OPDP (previously DDMAC) LABELING REVIEW CONSULTATION

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

TO: <b>CDER-OPDP-RPM</b>		FROM: (Name/Title, Office/Division/Phone number of requestor) Amy Tilley/RPM/OHOP/DOP1/301-796-3994	
REQUEST DATE December 17, 2013	IND NO.	NDA/BLA NO sBLA 103792/5311 S-5150 PMC 1 & 3	TYPE OF DOCUMENTS (PLEASE CHECK OFF BELOW)
NAME OF DRUG Herceptin (trastuzumab)	PRIORITY CONSIDERATION Priority	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE (Generally 1 week before the wrap-up meeting)  If Priority = April 21, 2014 If Std = August 1, 2014
NAME OF FIRM: Genentech, Inc		PDUFA Date: If Priority = May 28, 2014 If Standard = September 26, 2014	

### TYPE OF LABEL TO REVIEW

<b>TYPE OF LABELING:</b> (Check all that apply) <input checked="" type="checkbox"/> PACKAGE INSERT (PI) <input type="checkbox"/> PATIENT PACKAGE INSERT (PPI) <input type="checkbox"/> CARTON/CONTAINER LABELING <input type="checkbox"/> MEDICATION GUIDE <input type="checkbox"/> INSTRUCTIONS FOR USE (IFU)	<b>TYPE OF APPLICATION/SUBMISSION</b> <input type="checkbox"/> ORIGINAL NDA/BLA <input type="checkbox"/> IND <input checked="" 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 checked="" type="checkbox"/> LABELING REVISION  <b>For OSE USE ONLY</b> <input type="checkbox"/> REMS
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### EDR link to submission:

<<http://cberedrweb.fda.gov:8080/esp/cberedr.jsp?folderObjId=0bbcaea6813678dc>>

**Please Note:** There is no need to send labeling at this time. OPDP reviews substantially complete labeling, which has already been marked up by the CDER Review Team. After the disciplines have completed their sections of the labeling, a full review team labeling meeting can be held to go over all of the revisions. Within a week after this meeting, "substantially complete" labeling should be sent to OPDP. Once the substantially complete labeling is received, OPDP will complete its review within 14 calendar days.

**OSE/DRISK ONLY:** For REMS consults to OPDP, send a word copy of all REMS materials and the most recent labeling to CDER DDMAC RPM. List out all materials included in the consult, broken down by audience (consumer vs provider), in the comments section below.

### COMMENTS/SPECIAL INSTRUCTIONS:

Mid-Cycle Meeting: TBS  
Labeling Meetings: TBS  
Wrap-Up Meeting: TBS

### SIGNATURE OF REQUESTER

Amy Tilley *(See appended electronic signature page)*

### SIGNATURE OF RECEIVER

### METHOD OF DELIVERY (Check one)

eMAIL

HAND

12/05/2013

Reference ID: 3424044

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/s/  
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AMY R TILLEY  
12/17/2013

**REQUEST FOR CONSULTATION**

TO (Division/Office):

**Mail: OSE CDER OSE Consults**

FROM:

Amy Tilley/OHOP/DOP1 301-796-3994

DATE

December 17, 2013

IND NO.

BLA NO.

103792/5311  
Supp 5150 PMC 1 & 3

TYPE OF DOCUMENT

Efficacy Supplement

DATE OF DOCUMENT

November 26, 2013

NAME OF DRUG

Herceptin (trastuzumab)

PRIORITY CONSIDERATION

Priority

CLASSIFICATION OF DRUG

DESIRED COMPLETION DATE

If Priority = April 21, 2014  
If Std = August 1, 2014

NAME OF FIRM: Genentech, Inc.

**REASON FOR REQUEST**

**I. GENERAL**

- |  |   |  |
|--|---|--|
| <input type="checkbox"/> NEW PROTOCOL                  | <input type="checkbox"/> PRE-NDA MEETING            | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT               | <input type="checkbox"/> END OF PHASE II MEETING    | <input type="checkbox"/> FINAL PRINTED LABELING        |
| <input type="checkbox"/> NEW CORRESPONDENCE            | <input type="checkbox"/> RESUBMISSION               | <input checked="" type="checkbox"/> LABELING REVISION  |
| <input type="checkbox"/> DRUG ADVERTISING              | <input checked="" type="checkbox"/> SAFETY/EFFICACY | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE   |
| <input type="checkbox"/> ADVERSE REACTION REPORT       | <input type="checkbox"/> CONTROL SUPPLEMENT         | <input type="checkbox"/> FORMULATIVE REVIEW            |
| <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION |   | <input type="checkbox"/> OTHER (SPECIFY BELOW):        |
| <input type="checkbox"/> MEETING PLANNED BY            |   |  |

**II. BIOMETRICS**

STATISTICAL EVALUATION BRANCH

STATISTICAL APPLICATION BRANCH

- TYPE A OR B NDA REVIEW  
 END OF PHASE II MEETING  
 CONTROLLED STUDIES  
 PROTOCOL REVIEW  
 OTHER (SPECIFY BELOW):

- CHEMISTRY REVIEW  
 PHARMACOLOGY  
 BIOPHARMACEUTICS  
 OTHER (SPECIFY BELOW):

**III. BIOPHARMACEUTICS**

- DISSOLUTION  
 BIOAVAILABILITY STUDIES  
 PHASE IV STUDIES

- DEFICIENCY LETTER RESPONSE  
 PROTOCOL-BIOPHARMACEUTICS  
 IN-VIVO WAIVER REQUEST

**IV. DRUG EXPERIENCE**

- PHASE IV 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

PRECLINICAL

**COMMENTS/SPECIAL INSTRUCTIONS:** The proposed labeling changes provided in this sBLA are based on safety and efficacy results for Herceptin in combination with doxorubicin, cyclophosphamide, and paclitaxel for the adjuvant treatment of HER2-overexpressing early breast cancer from the Joint Analysis of Studies NSABP B-31 and NCCTG N9831 (Final Study Report No. 1055656), after a median follow-up of approximately 8 years.

An update to the Herceptin (trastuzumab) labeling is also proposed based on the potential for medication error with ado-trastuzumab emtansine (Kadcyla).

Table 1 provides a tabular listing of annotations that support the proposed label language. Sub sections of Sections 2 Dosage & Administration, 5 Warnings and precautions, 6 Adverse Reactions, and 14 Clinical Studies of the Herceptin label is being updated to include new clinical and safety data from the above mentioned studies and the medication error statement.

EDR link to submission: <<http://cberedrweb.fda.gov:8080/esp/cberedr.jsp?folderObjId=0bbcaea6813678dc>>

SIGNATURE OF REQUESTER

Amy Tilley ;See appended electronic signature page;

METHOD OF DELIVERY (Check all that apply)

- EMAIL  DARRTS  HAND

SIGNATURE OF RECEIVER

SIGNATURE OF DELIVERER

06/18/2013

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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AMY R TILLEY  
12/17/2013