

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
BLA 125276/S049

CHEMISTRY REVIEW(s)

**Therapeutic Biological Establishment Evaluation
Request (TB-EER) Form**
Version 1.0

Instructions:

The review team should email this form to the email account “CDER-TB-EER” to submit:

- 1) an initial TB-EER within 10 business days of the application filing date
- 2) a final TB-EER 15-30 days prior to the action date

Note: All manufacturing¹ locations named in the pending submission, whether contract facilities or facilities owned by the applicant, should be listed on this form. For bundled supplements, one TB-EER to include all STNs should be submitted.

APPLICATION INFORMATION

PDUFA Action Date: October 12, 2012

Applicant Name: Genentech, Inc.
U.S. License #: 1048
STN(s): 125276/49
Product(s): Actemra ® (tocilizumab)
Short summary of application: *This is an efficacy supplement that proposes a change in the indication.*

FACILITY INFORMATION

Manufacturing Location:
Firm Name: **Genentech, Inc.**
Address: **South San Francisco, CA**
FEI: **#2917293**
Short summary of manufacturing activities performed: **License Holder; Release to US market**
Inspected September 2-26, 2011 and classified VAI. Representative quality systems coverage was provided and deemed acceptable.

¹The regulations at 21 C.F.R. § 207.3(a)(8) defines “manufacturing or processing” as “the manufacture, preparation, propagation, compounding, or processing of a drug or drugs as used in section 510 of the act [21 U.S.C. § 360] and is the making by chemical, physical, biological, or other procedures of any articles that meet the definition of drugs in section 201(g) of the act. The term includes manipulation, sampling, testing, or control procedures applied to the final product or to any part of the process. The term also includes repackaging or otherwise changing the container, wrapper, or labeling of any drug package to further the distribution of the drug from the original place of manufacture to the person who makes final delivery or sale to the ultimate consumer.”

Manufacturing Location:

Firm Name: **Chugai Pharma**
 Address: **Utsunomiya-city, Tochigi, Japan**
 FEI: **# 3006942691**

Short summary of manufacturing activities performed: **Drug substance and drug product manufacturing, product testing and bulk packaging**
 Inspected January 24 – February 1, 2011 and classified VAI. Acterma manufacturing operations were covered and deemed acceptable.

Manufacturing Location:

Firm Name: **Hoffman-LaRoche**
 Address: **Kaiseraugst, Switzerland**
 FEI: **#3003973536**

Short summary of manufacturing activities performed: **Final product labeling, packaging, product warehousing and shipment for distribution**
 Inspected July 25-29, 2011 and initially classified NAI. Packaging and labeling operations for sterile products were covered and are acceptable for the purposes of this supplement.

Manufacturing

Firm Name: (b) (4)
 Address: (b) (4)
 FEI: (b) (4)

Short summary of manufacturing activities performed: **Additional warehousing**
 Inspected (b) (4) and initially classified NAI. Comprehensive cGMP coverage of sterile manufacturing operations was provided and is acceptable for the purposes of this supplement.

Manufacturing Location:

Firm Name: (b) (4)
 Address: **N/A**
 FEI: **N/A**

Short summary of manufacturing activities performed: **Receipt of shipment from Roche Kaiseraugst, warehousing and US Distribution**
 No further evaluation needed at this time.

OVERALL RECOMMENDATION

There are no pending or ongoing compliance actions to prevent approval of STN 125276s49 at this time.

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

/s/

MARISA E STOCK
09/19/2012

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APPLICATION INFORMATION

PDUFA Action Date: October 12, 2012

Applicant Name: Genentech, Inc.
U.S. License #: 1048
STN(s): 125276/49
Product(s): Actemra ® (tocilizumab)
Short summary of application: *This is an efficacy supplement that proposes a change in the indication.*

FACILITY INFORMATION

Manufacturing Location:
Firm Name: **Genentech, Inc.**
Address: **South San Francisco, CA**
FEI: **#2917293**
Short summary of manufacturing activities performed: **License Holder; Release to US market**

Manufacturing Location:
Firm Name: **Chugai Pharma**
Address: **Utsunomiya-city, Tochigi, Japan**
FEI: **# 3006942691**

¹The regulations at 21 C.F.R. § 207.3(a)(8) defines “manufacturing or processing” as “the manufacture, preparation, propagation, compounding, or processing of a drug or drugs as used in section 510 of the act [21 U.S.C. § 360] and is the making by chemical, physical, biological, or other procedures of any articles that meet the definition of drugs in section 201(g) of the act. The term includes manipulation, sampling, testing, or control procedures applied to the final product or to any part of the process. The term also includes repackaging or otherwise changing the container, wrapper, or labeling of any drug package to further the distribution of the drug from the original place of manufacture to the person who makes final delivery or sale to the ultimate consumer.”

Short summary of manufacturing activities performed: **Drug substance and drug product manufacturing, product testing and bulk packaging**

Manufacturing Location:

Firm Name: **Hoffman-LaRoche**

Address: **Kaiseraugst, Switzerland**

FEI: **#3003973536**

Short summary of manufacturing activities performed: **Final product labeling, packaging, product warehousing and shipment for distribution**

Manufacturing Location:

Firm Name:  (b) (4)

Address: 

FEI: 

Short summary of manufacturing activities performed: **Additional warehousing**

Manufacturing  (b) (4)

Firm Name: 

Address: **N/A**

FEI: **N/A**

Short summary of manufacturing activities performed: **Receipt of shipment from Roche Kaiseraugst, warehousing and US Distribution**

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

/s/

PHILANTHA M BOWEN
09/18/2012

Bowen, Philantha

From: Pohlhaus, Timothy
Sent: Friday, February 03, 2012 2:23 PM
To: Bowen, Philantha
Cc: Pohlhaus, Timothy; CDER-TB-EER
Subject: Initial TB-EER Response - sBLA 125276/49 (Actemra)

Attachments: Initial TB-EER Response - STN 125276-49.doc; sBLA 125276 (actemra) form-356h.pdf; BLA 125276(49) - TB-EER (Initial Request).doc

The Division of Good Manufacturing Practice Assessment has completed its review and evaluation of the TB-EER for STN 125276/49. Please see the attached form for individual site compliance statuses. There are no pending or ongoing compliance actions that prevent approval of this supplement.



Initial TB-EER
Response - STN ...

Timothy J. Pohlhaus, Ph.D.
Interdisciplinary Scientist, Chemist
Food and Drug Administration
CDER/OC/OMPQ
10903 New Hampshire Avenue
Building 51, Room 1333
Silver Spring, MD 20993
Phone - (301) 796-5224

From: Bowen, Philantha
Sent: Monday, January 30, 2012 6:28 PM
To: CDER-TB-EER
Subject: sBLA 125276/49 (Actemra) - Initial TB-EER

Hi,

Attached is an initial TB-EER for BLA 125276/49 (Actemra). This efficacy supplement proposes a change in indication. The PDUFA date is October 12, 2012.

I have attached the 356h with the sites outlined for review.



sBLA 125276 actemra) form-356..



BLA 125276(49) - TB-EER (Initi...

Sincerely,

Philantha

Philantha M. Bowen, MPH, BSN, RN
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Sr. Regulatory Management Officer
Food and Drug Administration

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