

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*  
**103234Orig1s5166**

**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 manufacturing<sup>1</sup> 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.

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## APPLICATION INFORMATION

PDUFA Action Date: April 27, 2010

Applicant Name: Amgen, Incorporated

STN(s): 103234/5166

Product(s): Epogen/Procrit (epoetin alfa)

Short summary of application: Efficacy Supplement (PLR conversion)

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## FACILITY INFORMATION

Firm Name: Amgen, Inc.

Address: One Amgen Center Drive, Thousand Oaks, CA 91320

FEI: 2026154

Short summary of manufacturing activities performed: Drug Substance Bulk Manufacturing, Drug Substance and Drug Product Release Testing, Drug Substance and Drug Product Stability Testing

On March 22, 2010, Annie Dang of Amgen (via correspondence with Mona Patel)

confirmed that this site is [REDACTED] (b) (4)

This site was inspected April 7-11, 2008 by LOS-DO and classified NAI. The [REDACTED] (b) (4)

[REDACTED] CTL profiles were covered and are considered acceptable.

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<sup>1</sup>The 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."

Firm Name: Amgen, Inc.

Address: 4000 Nelson Road, Longmont, CO 80503

FEI:3002892484

Short summary of manufacturing activities performed: Drug Substance Bulk Manufacturing, Drug Substance Release Testing, Drug Substance Stability Testing

Inspected August 30 – September 3, 2010 and classified VAI. The (b) (4) profile was covered during this routine biotech cGMP inspection and is acceptable.

Firm Name: Amgen Manufacturing, Limited

Address: P.O. Box 4060, Road 31 km 24.6, Juncos, PR 00777-4060

FEI: 1000110364

Short summary of manufacturing activities performed: Drug Product Manufacturing, Drug Product Release Testing

Inspected by SJN-DO from 4/18/11-4/29/11 and initially classified OAI. This was a GMP inspection that found deficiencies (b) (4). However NGDMT does not believe the GMP deficiencies at this facility affect the nature of this supplement. NGDMT finds this site acceptable for the purposes of this supplement.

Firm Name: (b) (4)

Address: (b) (4)

FEI: (b) (4)

Short summary of manufacturing activities performed: Drug Product Manufacturing

Inspected (b) (4) and classified NAI. The (b) (4) profiles were covered and are acceptable.

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## APPLICATION INFORMATION

PDUFA Action Date: April 27, 2010

Applicant Name: Amgen, Incorporated

STN(s): 103234/5166

Product(s): Epogen/Procrit (epoetin alfa)

Short summary of application: Efficacy Supplement (PLR conversion)

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## FACILITY INFORMATION

Firm Name: Amgen, Inc.

Address: One Amgen Center Drive, Thousand Oaks, CA 91320

FEI: 2026154

Short summary of manufacturing activities performed: Drug Substance Bulk Manufacturing, Drug Substance and Drug Product Release Testing, Drug Substance and Drug Product Stability Testing

On March 22, 2010, Annie Dang of Amgen (via correspondence with Mona Patel) confirmed that this site is [REDACTED] (b) (4).

This site was inspected April 7-11, 2008 by LOS-DO and classified NAI. The [REDACTED] (b) (4) CTL profiles were covered and are considered acceptable.

Firm Name: Amgen, Inc.

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<sup>1</sup>The 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."

Address: 4000 Nelson Road, Longmont, CO 80503

FEI:3002892484

Short summary of manufacturing activities performed: Drug Substance Bulk Manufacturing, Drug Substance Release Testing, Drug Substance Stability Testing

An inspection was conducted at Amgen, Longmont, CO on January 31, 2008 for preapproval coverage of the firm's laboratory operations. The inspection was classified NAI. Although the firm's GMP inspection coverage is outdated, for purposes of this supplement, we will consider the profile acceptable and will work with the DEN-DO to expedite a surveillance inspection.

Firm Name: Amgen Manufacturing, Limited

Address: P.O. Box 4060, Road 31 km 24.6, Juncos, PR 00777-4060

FEI: 1000110364

Short summary of manufacturing activities performed: Drug Product Manufacturing, Drug Product Release Testing

Inspected June 27 – September 11, 2009 by SJN-DO and classified VAI. The (b) (4) profiles were covered and are considered acceptable.

Firm Name: (b) (4)

Address: (b) (4)

FEI: (b) (4)

Short summary of manufacturing activities performed: Drug Product Manufacturing

Inspected (b) (4) by (b) (4) and classified NAI. The (b) (4) profiles were covered and are considered acceptable.



**MEMORANDUM**

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

**SUBJECT:** Review of supplements STN 103234-5166 and 103951-5173 supporting a conversion of current labeling to the Physician's Labeling Rule (PLR) format

**FROM:** Ingrid Markovic, Ph.D., CMC Reviewer, DTP/OBP/OPS/CDER

**TO:** 103234-5166 and 103951-5173 file *10/17/08*

**THROUGH:** Barry Cherney, Ph.D., Deputy Director, DTP/OBP/OPS/CDER

**SPONSOR:** Amgen *Barry Cherney 10-17-09*

**PRODUCTS:** Epogen® (*epoetin alfa*) and Aranesp® (*darbepoetin alfa*)

**ACTION DATE:** October 24, 2008

***Recommendation***

The proposed changes supporting a conversion of the current labeling to the Physician's Labeling Rule (PLR) format are acceptable from a Chemistry Manufacturing and Controls perspective. However, the PI does not indicate that Epogen should be protected from light. The PI should be revised to reflect Epogen's sensitivity to light.

***1. Categorical exclusion from environmental assessment***

Approval of this supplement will not alter significantly the concentration or distribution of the Epogen or Aranesp substance or their degradation products in the environment according to the FDA "Guidance for Industry: Environmental Assessment of Human Drug and Biologics Applications," July 1998, CMC 6, Revision 1. The Sponsor complies with the categorical exclusion criteria listed in 21 CFR 25.31(c), and no extraordinary circumstances exist. Therefore, approval of categorical exclusion from environmental assessment is granted.

***2. Suggestions for the PLR label***

It is recommended that the wording "protect from light" is added to epogen's Package Insert. Although these two products have comparable sensitivity to light, such statement is present in the Aranesp label but it is missing from the Epogen's.

**Excerpt from the package insert:**

Epogen: (b) (4)

Aranesp: [REDACTED] (b) (4)

This point was communicated to Neal Storm from Amgen during a teleconference on October 16, 2008. He stated that he will follow up with the CMC group regarding issues with Epogen's stability in light. No commitments were made.