Exhibit 4 to Declaration of Dr. Sven-Michael Cords in Support of Roche's Opposition to Amgen's Motion for Summary Judgment of Infringement of '422 Claim 1, '933 Claim 4, and '698 Claim 6 (DN 600)

UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

AMGEN INC., Plaintiff, vs. F. HOFFMANN-LA ROCHE LTD, ROCHE DIAGNOSTICS GMBH, AND HOFFMANN-LA ROCHE INC., Defendants	CIVIL ACTION No.: 05-CV-12237WGY

DECLARATION OF DR. MARKUS DEMBOWSKI

I, Markus Dembowski, Ph.D., hereby declare under penalty of perjury that:

1. I am currently a manager in development analytics for Roche Diagnostics GmbH office in Penzberg, Germany, one of three German offices for F. Hoffmann-La Roche Ltd., the parent company for defendant Hoffmann-La Roche Inc. laboratories, a wholly-owned subsidiary of Roche Holding Ltd, located in Basel, Switzerland, all of which are hereinafter collectively termed "Roche". I have been an employee of Roche Diagnostics GmbH since 2001, and have been in my current position of being a manager in development analytics since 2003. I am knowledgeable in the areas of biological analytics using a variety of analytical methods including mass spectrometric analysis and I am responsible for the development of analytical methods, analysis of samples generated during development and routine production of pharmaceutical agents as well as the preparation of GMP and regulatory documents at Roche Diagnostics GmbH. Within the Mircera project, my main tasks have been to develop, validate and use a method for quantification of positional isomers, to do other testing for extended

characterization of the molecule as well as to create documents relevant for GMP and regulatory purposes. My responsibility for the current declaration was planning and coordination of the experiments needed to prepare and analyze the samples used in Dr. Cords experiments.

2. My C.V. is attached as Exhibit A.

3. The samples which I prepared to include in the Bioassay study performed by Dr. Sven-Michael Cords in April of 2007 were the deglycosylated and "mock-treated" Epoetin beta samples (which I may refer to herein as "EPO" and "EPO K", respectively) and deglycosylated and "mock-treated" Mircera samples (which I may refer to herein as "CERA" and "CERA K", respectively). All reagents used were pharmaceutical grade.

A. Preparation of EPO and Mircera Samples

4. The EPO and Mircera drug substance samples used in the Cords experiments were prepared at Roche Diagnostics GmbH in Penzberg, Germany. In Roche documents, Mircera is referred to as compound number RO0503821.

5. The EPO sample is the material used for pegylation of RO0503821 drug substance batch G011.00 and contains EPO from batches G080.02P1, lot PZ0606E101; G080.03P1, lot PZ0606E102; G080.04P1, lot PZ0606E103; G080.06P1, lot PZ0607E103; G080.08P1, lot PZ0606E107; G080.09P1, lot PZ0606E108; and G080.10P1, lot PZ0606E109. All EPO batches included into the starting material for pegylation of Mircera drug substance batch G011.00 were released according to the specification for EPO and Mircera, respectively.

6. The bioactivity of EPO is standardized against the in-house reference preparation valid at the time of release of a drug substance batch. Currently, the reference preparation EAS-0612, (950 IU/mL) is used which is derived from EPO RS G067.09 used for physico-chemical

analysis. The bioactivity of the in house reference preparation is calibrated against the European standard BRP2 (32500 IU).

7. The Mircera sample used in the Cords experiments is an aliquot from drug substance batch G011.00 prepared in 2006 and compared to Roche's reference preparation CAS04-10 used for the bioassay. RS CAS04-10 is derived from RS Mircera RS 782 386 00 used for biochemical analysis derived from drug substance batch G002.04E prepared in 2003. The activity of the bioassay RS CAS04-10 was calibrated against the previous reference preparation PAS02-08.

B. Preparation of Deglycosylated EPO and Deglycosylated Mircera Samples

8. The deglycosylated samples of EPO and Mircera were prepared by diluting the original EPO and Mircera samples in 10 mM sodium/potassium phosphate containing 100 mM NaCl and 0.01 % Polysorbate 20, pH 7.5 to establish a concentration of 0.20 mg/mL. The N-glycosidase F was resuspended to a solution of 1U/μL and the neuraminidase solution was adjusted to 0.04 U/μL.

9. Then 1 μL of the N-glycosidase F solution and 1 μL of the neuraminidase solution was added to 100 μL of the 0.20 mg/mL solutions of EPO and Mircera, which were then incubated over night at 37°C. The next day, 5 μL of 10 % TFA (Trifluoroacetic acid) was added per 100 μL of sample volume.

10. Separation of EPO and Mircera from the neuraminidase and N-glycosidase F was performed by means of reverse phase chromatography using a C8 reversed phase column (Brownlee Columns, Aquapore RP-300, 7 μ, 220 x 4.6 mm). The chromatography conditions were as follows:

Injection volume: 2.5 mL

Solvent A: 0.1 % TFA in water

Solvent B: 84 % Acetonitrile, 0.1 % TFA in water

Column Temperature: ambient

Gradient Conditions:

Time [min]	% B	Time [min]	% B
0	10	45	100
5	10	48	100
10	45	49	10
40	65	64	10

11. After chromatographic separation, the samples were dried in a speed vac and resuspended in dilution buffer to obtain sample concentrations amounting to approximately 0.20 mg/mL. Samples were then split into different portions and stored/shipped frozen at -70°

C. Analytics of the Samples

12. To verify deglycosylation, several analytical protocols were employed. After the samples were thawed, SDS PAGE, RP-HPLC, SE-HPLC and LysC peptide mapping were performed in order to analyze the samples.

SDS Page Analysis

13. SDS PAGE (Sodium dodecyl Sulfate PolyAcrylamide Gel Electrophoresis) of reduced samples followed by Coomassie staining was used to check the integrity of the molecules as well as the success of the deglycosylation reactions. SDS PAGE analysis of EPO and Mircera samples was done using a 4-20% gradient Tris-Glycine Gel (Invitrogen). Samples were diluted in 2x Tris-Glycine SDS sample buffer (Invitrogen) and 10x NuPAGE Sample Reducing Agent (Invitrogen) was added to the samples. After denaturation and reduction for 5 min at 70 °C, volumes of samples corresponding to 1.75 µg of sample were loaded on the gel, electrophoresis

was performed at 125 V for about 100 min, followed by staining with Novex Simply Blue SafeStain (Invitrogen).

Reverse Phase HPLC (RP-HPLC) Analysis

14. RP-HPLC was used in order to check for aggregates and to verify the success of the deglycosylation. In addition, the method was also applied for determination of the sample concentrations of the samples. Determination of the sample concentrations was performed by integration of EPO- or Mircera peak areas of the samples and comparison of the peak areas to the respective calibration curves of EPO or Mircera obtained in the same series. To verify the success of deglycosylation, the retention times of the EPO and Mircera peaks of samples before and after deglycosylation were compared to each other.

15. For RP-HPLC of Mircera samples, the samples (100 µL) were loaded onto a RP-Poroshell 300SB C8 column (2,1 x 75mm, 300A, Agilent # 660750-906) and eluted using the following chromatography conditions:

Flowrate: 1.0 mL/min

Solvent A: 0.3 % TFA in water

Solvent B: 84 % Acetonitrile, 0.2 % TFA in water

Column Temperature: 60°C

Gradient Conditions:

Time [min]	% B	Time [min]	% B
0	40	20	100
4	52	21	0
7	52	22	0
9	58	23	100
13	58	24	100
14	62	25	40
18	62	28	40
19	100		

16. Eluted products were monitored by UV absorption at 215 nm.

17. For RP-HPLC of EPO samples, the samples (100 µL) were loaded onto an Aquapore RP-300 Octyl, 7 column, (220mm x 2,1mm) and eluted using the following chromatography conditions:

Flowrate: 0.5 mL/min

Solvent A: 10 % acetonitrile, 0.1 % TFA, in water

Solvent B: 70 % Acetonitrile, 0.1 % TFA in water

Column Temperature: ambient

Gradient Conditions:

Time [min]	% B	Time [min]	% B
0	0	36	0
30	100	50	0
35	100		

18. Eluted products were monitored by UV absorption at 215 nm.

Size Exclusion HPLC (SE-HPLC) Analysis

19. SE-HPLC was used to check for aggregates. The samples (150 µL) were loaded onto a size-exclusion chromatography column (TSK G3000SWxl Tosoh Bio, No. 08541, Int. No. 115) and eluted at ambient temperature with running buffer (200 mM potassium dihydrogen phosphate, 250 potassium chloride, pH 7.0) at 0.5 mL/min, detection was performed at 280 nm.

LysC Peptide Mapping with UV and Mass Spectrometric Detection

20. LysC Peptide Mapping with UV (220 nm) and online mass detection (LC-TOF mass spectrometer equipped with a z-spray ion source was used) was performed in order to verify the identity of the samples as well as to confirm the deglycosylation. LysC peptide mapping is suitable to confirm the deglycosylation of the samples because of the slowed retention of the deglycosylated LysC-peptides as compared to the glycosylated LysC peptides.

21. Samples (10 µL) were loaded onto a Phenomenex Jupiter C18 column (2.0 x 150 mm, Phenomenex 00F-4053-B0) and then eluted using the following chromatography conditions:

Flowrate: 0.2 mL/min

Solvent A: 0.1 % TFA in water

Solvent B: 70 % Acetonitrile, 0.1 % TFA in water

Column Temperature: 56°C

Gradient Conditions:

Time [min]	% B	Time [min]	% B
0	0	47	100
40	80	49	0
42	100	64	0

22. Analysis of the chromatograms obtained by UV detection (220 nm) confirms the absence of glycosylated peptides, the analysis of the peaks by mass spectrometric detection confirms the identity of the molecule.

C. Preparation of EPO K and Mircera K Samples

23. EPO K and Mircera K were prepared as described for deglycosylated EPO and deglycosylated Mircera in section B above, except they were not treated with N-glycosidase F and neuraminidase, the enzymes used to facilitate deglycosylation.

24. Thus, these samples were created by diluting the original EPO and Mircera samples in 10 mM sodium/potassium phosphate containing 100 mM NaCl and 0.01 % Polysorbate 20, pH 7.5 to establish a concentration of 0.20 mg/mL. N-glycosidase F and neuraminidase were not added to the samples, however. The EPO and Mircera samples were then incubated over night at 37°C and the next day, 5 µL 10 % TFA was added per 100 µL of sample volume.

25. Separation by reverse phase chromatography, drying of the samples and resuspension in dilution buffer as well as the analysis of the samples were performed as described above.

Signed under the pains and penalties of perjury this 11th day of May, 2007.

/s/
Dr. Markus Dembowski

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EXHIBIT A

Dr. Markus Dembowski

BUSINESS:
Roche Diagnostics GmbH
Nonnenwald 2
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PERMANENT:
Schaffhauser Str. 18
81476 Munich/Germany

EDUCATION:

1990 to 1995 **Studies of Biochemistry, finished with degree Master of Science in Biology**
Moscow State University "Lomonossow"/Russia, Faculty of Biology, Department of Biochemistry
Title of Diploma Thesis: "Investigations on the mechanism of interaction between pyruvate analogues and pyruvate dehydrogenase"

1995 to 2001 **PhD student, finished with degree "Dr.rer.nat"**
Ludwig Maximilian University Munich/Germany, Institute for Physiological Chemistry
Title of the PhD Thesis: „Characterization, biogenesis and mechanism of the protein translocase of the outer mitochondrial membrane from *Neurospora crassa*"

EXPERIENCE:

2001 to 2003 **Postdoc at Roche Diagnostics GmbH, Penzberg/Germany**
Development of methods for extended characterization of pharmaceutical proteins, application for comparability studies and testing of samples from development and routine production, preparation of GMP- and regulatory documents

Since 2003 **Manager Development Analytics at Roche Diagnostics GmbH, Penzberg/Germany**
Development and validation of methods for extended characterization of pharmaceutical proteins, application for testing of samples from development and routine production, project management, preparation of GMP- and regulatory documents

PUBLICATIONS:

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- Dembowski M (2006) ”Use of Mass Spectrometric Methods in Quality Control”, Talk given at the 3rd symposium of the practical applications of mass spectrometry in the biotechnology and pharmaceutical industries, 2006 in La Jolla, USA
- Dembowski M (2007) ”How to Define IEC Specifications – as Parameter for Consistency or Purity?”, talk given at the CMC Strategy Forum Europe 2007 in Brussels, Belgium