

1 UNITED STATES DISTRICT COURT  
2 DISTRICT OF MASSACHUSETTS

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4

5 AMGEN INC., )  
 )

6 Plaintiff, )  
 )

7 vs. ) Civil Action  
 )

8 F. HOFFMANN-LA ROCHE LTD., a Swiss ) No. 05-12237 WGY  
 Company, ROCHE DIAGNOSTICS GmbH, )  
9 a German Company, and HOFFMANN-LA )  
 ROCHE, INC., a New Jersey )

10 Corporation )  
 )

11 Defendants. )  
 \_\_\_\_\_ )

12  
13  
14

15 30(b)(6) Deposition of GRAHAM MOLINEUX,  
16 at 1999 Avenue of the Stars, 17th Floor,  
17 Los Angeles, California 90067, commencing  
18 at 9:06 A.M., Wednesday, March 28, 2007,  
19 before Judith Schlüssel, CSR No. 4307.

20  
21  
22

23 - CONFIDENTIAL -

24  
25

1 Emery, representing Plaintiff Amgen, Inc.

2 MS. MORLEY: Kimberlin Morley, Amgen.

3 THE VIDEOGRAPHER: Thank you. Will the  
4 court reporter please swear in the witness.

5

6 GRAHAM MOLINEUX,

7 the witness, having been administered an oath in  
8 accordance with CCP Section 2094, testified as  
9 follows:

10

11 THE WITNESS: Yes, I do.

12

13 EXAMINATION

14 BY MR. JAGOE:

15 Q. Can you please state your full name for the  
16 record, again.

17 A. My name is Graham Molineux.

18 Q. What is your current home address?

19 A. 6394 Gabbert Road, Moorpark, California,  
20 93021.

21 Q. Where do you work, Dr. Molineux?

22 A. I work for Amgen, Inc.

23 Q. How long have you worked for Amgen, Inc.?

24 A. 13 years.

25 Q. Where did you work prior to Amgen?

1 A. The Patterson Institute for Cancer

2 Research.

3 Q. Have you worked continuously for Amgen for  
4 the past 13 years?

5 A. Yes, I have.

6 Q. What is your current position at Amgen?

7 A. I'm executive director of research.

8 Q. And as executive director of research, what  
9 are your responsibilities?

10 THE VIDEOGRAPHER: Excuse me, Counsel.

11 Blackberries, I'm sorry, are turned on.

12 THE WITNESS: My responsibilities are to  
13 manage a group of scientists involved in discovery  
14 level -- drug discovery at Amgen.

15 Q. BY MR. JAGOE: Are you responsible for all  
16 scientists at Amgen?

17 A. No. I'm responsible for a group of 12  
18 scientists.

19 Q. How many executive directors of research  
20 are there at Amgen currently?

21 A. I don't know.

22 Q. Is there more than one?

23 A. Yes.

24 Q. And the 12 scientists that you're  
25 responsible for, can you name them?

1 MR. GAEDE: Objection; incomplete

2 hypothetical. Calls for speculation.

3 THE WITNESS: I think if I were to

4 understand the MOA properly, I would need a

5 specimen, yes.

6 Q. BY MR. JAGOE: Do you know of any efforts

7 ongoing at Amgen to engage in a science-based

8 challenge to Roche's hypothesis?

9 A. No.

10 Q. I marked another document as Molineux

11 Exhibit 3 that I'm handing you. Is the document

12 that I marked as Molineux Exhibit 3 a document that

13 you authored as an Amgen employee?

14 A. Yes, it is.

15 Q. You published this in 2002?

16 A. Yes, I did.

17 Q. Did this undergo the internal review at

18 Amgen prior to publication?

19 A. Yes, it did.

20 Q. And were you trying to be accurate and

21 honest when you wrote this publication?

22 A. I was attempting to be accurate and honest,

23 yes.

24 Q. And what was the purpose of making this

25 publication?

1 A. To offer insight into the improvements  
2 which can be offered to a number of therapeutics by  
3 pegylation.

4 Q. And the potential benefits of pegylation  
5 are listed in Table 1 of this publication?

6 MR. GAEDE: Again, you may answer this  
7 generically with respect to also with PEG-EPO.  
8 Specifically, though, if there is any questions that  
9 go into the other molecules or other proteins  
10 consistent with the Court's order, that would be an  
11 improper scope. The question -- I understand this  
12 is in relation to your questions about PEG-EPO.

13 THE WITNESS: Table 1 lists the generic  
14 attributes that can be conferred by pegylation.

15 Q. BY MR. JAGOE: In the introduction on Page  
16 1, you said that "A number of novel drug-delivery  
17 mechanisms have been developed to increase the  
18 utility of drugs that are otherwise limited by  
19 suboptimal pharmacokinetic properties, such as poor  
20 absorption, distribution and elimination. These  
21 include continuous-release injectable and liposomal  
22 systems which alter the formation of the drug and  
23 pegylation which alters the drug molecule." Did I  
24 read that correctly?

25 A. I think you did, yes.

1 Q. And when you wrote this article in 2002,  
2 you believed that to be true?

3 A. I think it was probably written the year  
4 before.

5 Q. In 2001?

6 A. Perhaps. I don't remember the exact  
7 publication date of this article.

8 Q. But at the time you wrote that, you  
9 believed it to be true?

10 A. Yes, I did.

11 Q. That was prior to the beginning of the  
12 lawsuit against Roche?

13 A. Yes, it would have been.

14 Q. Are you aware of anything in this article  
15 that is not true or accurate?

16 A. It's a long time since I read this, but at  
17 the time I believed it to be true and accurate, yes.

18 Q. I'm going to hand you another document  
19 which I've marked as Molineux Exhibit 4.

20 A. Thank you.

21 Q. Is Molineux Exhibit 4 a publication that  
22 you made as an Amgen employee?

23 A. Yes, it is.

24 Q. And what was the purpose of this  
25 publication?



1 MR. GAEDE: Again, if you're going to be  
2 discussing this publication, the context of PEG  
3 Epoetin, that's okay, but looking at the face of  
4 this, it really goes to PEG GCSF which is clearly  
5 another compound and, therefore, as the Court's  
6 order of January 3rd, 2007 states, quote, "the case  
7 involves EPO including pegylated EPO, not other  
8 pegylated compounds." So if you're going to  
9 question him with respect to this article on what is  
10 clearly another pegylated compound, that is beyond  
11 the scope of the Court's order and I will have to  
12 instruct the witness not to answer.

13 MR. JAGOE: Can you read back the last  
14 question.

15 (Question Read)

16 MR. GAEDE: You may answer the question,  
17 Mr. Molineux, Dr. Molineux at a very high level, but  
18 as I note, again, the topic of this seems to be  
19 other pegylated compounds. So to the extent this  
20 line of questioning continues, I will instruct the  
21 witness not to answer.

22 THE WITNESS: The intention was to inform  
23 the scientific community of advances we had made in  
24 pegylation technology.

25 Q. BY MR. JAGOE: Is that pegylation

1 technology in general or pegylation technology  
2 related to a specific protein?

3 A. This particular piece refers to the general  
4 case but with a specific case of GCSF.

5 Q. I want you to look at Page 4S, which is the  
6 second page of the text. The first full paragraph  
7 in the first column, it says "pegylating a  
8 therapeutic agent may increase the hydrodynamic size  
9 above the limit of kidney filtration extending the  
10 drug's circulating half-life and increasing the  
11 patient's exposure to the drug from a single  
12 administration, thus simplifying treatment of  
13 chronic disease." Did you write that statement?

14 A. Yes, I did.

15 Q. Did you believe it to be accurate when you  
16 wrote it?

17 A. Yes, I did.

18 Q. Did this publication undergo the internal  
19 Amgen review before it was published?

20 A. Yes, it did.

21 Q. This was made prior to the onset of the  
22 current lawsuit, correct?

23 A. Yes, it was.

24 Q. The next paragraph, it says "Hydrated PEG  
25 chains are highly mobile in an aqueous medium



1 shielding antigenic determinants on the  
2 antigenic --" sorry -- "determinants on the  
3 conjugated proteins from detection by immune cells.  
4 Pegylation can also protect proteins by preventing  
5 the approach of proteolytic enzymes by processes  
6 that involve steric hindrance and/or the site  
7 specific covalent attachment of PEG to lysine which  
8 hinders trypsin cleavage." Did I read that  
9 correctly?

10 A. Yes, I think you did.

11 Q. Did you believe that to be accurate at the  
12 time you published this paper?

13 MR. GAEDE: I'm going to lodge an objection  
14 here that if one goes to the two footnotes that are  
15 referred to in that sentence, they refer  
16 specifically to pegylated interferons as well as  
17 apparently pegylated proteins which is by Delgado,  
18 Francis and Fisher from 1992, and I'm unaware of  
19 that source making reference specifically to PEG  
20 erythropoietin, so therefore your question is  
21 outside the scope of the Court's order in that you  
22 are asking about other pegylated compounds and  
23 instruct the witness not to answer.

24 Q. In the next sentence, it says "Compared  
25 with their non-pegylated counterparts, other

1 potential benefits of pegylated biomolecules are  
2 greater biological activity, greater passive tumor  
3 targeting of liposomes, longer circulating  
4 half-life, lower peak plasma concentrations, smaller  
5 fluctuations in plasma concentrations, less  
6 enzymatic degradation, less immunogenicity and  
7 antigenicity, less toxicity, greater solubility,  
8 less frequent administration, greater patient  
9 adherence and improved quality of life." Did you  
10 write that statement?

11 MR. GAEDE: Again, if you look at footnotes  
12 6 through 10 that are right there on that statement,  
13 all of those references do not reference PEG  
14 erythropoietin and therefore the question is --

15 MR. JAGOE: Just instruct him not to answer  
16 and we'll save time. We don't need your testimony  
17 about what the references say.

18 MR. GAEDE: No. You're outside of a court  
19 order.

20 MR. JAGOE: Tell him not to answer. Don't  
21 read what you think those references say.

22 MR. GAEDE: I'm just looking to the  
23 references. You're reading a sentence, you're  
24 omitting the references, and the references on their  
25 face refer to other pegylated compounds which the

1 court order clearly says are not an issue in this  
2 case.

3 MR. JAGOE: All you have to do is instruct  
4 him not to answer and he won't answer.

5 MR. GAEDE: I'm trying to see if we can  
6 work with you here but you insist on violating the  
7 court order. I'm trying to see if there is a way I  
8 can do this to allow you to ask questions that you  
9 cannot properly frame because you insist on  
10 violating the order. If you let me look at the  
11 question, I'll make my objection and then he will  
12 answer.

13 You may answer the question, did you write  
14 that statement.

15 THE WITNESS: I wrote that statement.

16 Q. BY MR. JAGOE: Did you believe it to be  
17 accurate at the time you wrote it?

18 A. Is that a second question I can answer?

19 MR. GAEDE: You may answer the question,  
20 although we should recognize that he is omitting his  
21 references to the footnotes which make reference to  
22 other pegylated compounds and he is omitting that  
23 fact from the record intentionally.

24 THE WITNESS: I believe it to be accurate  
25 when I wrote it.

1 Q. BY MR. JAGOE: On the next page, there is a  
2 bottom first column, last paragraph, "The  
3 pharmacokinetic profile of proteins can be improved  
4 by attaching one linear or branched PEG at a single  
5 site or several small PEG chains at several sites."

6 A. I'm sorry. Where are you?

7 Q. Page 5S, column one, last paragraph. Did  
8 you write that statement?

9 A. Yes, I did.

10 Q. Since your counsel wants to put the  
11 footnote into the record, you reference, Reference  
12 15. Whose paper is reference 15?

13 A. That would appear to be the paper by Bailon  
14 and Berthold.

15 Q. Are you familiar with that paper?

16 A. I was at the time but I don't recall its  
17 contents now.

18 Q. Did you believe it to be a reputable paper  
19 at the time you cited it?

20 A. Yes, I did.

21 Q. Now, on the Page 7S, top of the page, in  
22 the middle of the paragraph, there is a sentence,  
23 "Conjugation methods must be optimized for each  
24 protein." Did you write that statement?

25 MR. GAEDE: I'm sorry. Where are you?

1 MR. JAGOE: 7S, column one, first paragraph

2 in the middle.

3 MR. GAEDE: Thank you. You didn't identify

4 where it was on all that text.

5 MR. JAGOE: Sorry.

6 THE WITNESS: The question? I'm sorry.

7 Q. BY MR. JAGOE: Did you write that?

8 A. Yes, I did.

9 Q. What did you mean by that?

10 A. I meant that for each protein, since this  
11 technology can be applied to many proteins, the  
12 specific protein PEG conjugation be considered in  
13 how to make it on a case-by-case basis.

14 Q. Why would you have to consider it on a  
15 case-by-case basis?

16 MR. GAEDE: Again, objection; calls for  
17 speculation. Calls for expert witness testimony. I  
18 assume your question is with respect to PEG-EPO?

19 MR. JAGOE: With respect to this sentence  
20 you wrote in your article.

21 THE WITNESS: Different proteins may be  
22 sensitive to pegylation at different sites.

23 Q. BY MR. JAGOE: So if you pegylated one  
24 site, you may get a good compound and if you  
25 pegylated another site, you may not get a good



1 compound?

2 MR. GAEDE: Objection; mischaracterizes the  
3 witness' testimony. Now we're clearly into other  
4 compounds which is beyond the scope of the Court's  
5 order. Instruct the witness not to answer.

6 Q. BY MR. JAGOE: I marked another document as  
7 Molineux Exhibit 5. Is Molineux Exhibit 5 a paper  
8 that you wrote as an Amgen employee?

9 A. Yes, it is.

10 Q. You published this in 2003?

11 A. It would appear so, yes.

12 Q. And you published it prior to the onset of  
13 the current lawsuit?

14 A. Yes.

15 Q. And you believed the contents of this  
16 article to be accurate when you wrote them?

17 A. Yes, I did.

18 Q. They are an honest reflection of your view  
19 of the art?

20 MR. GAEDE: Objection; vague and ambiguous.  
21 Calls for speculation. Mischaracterizes the  
22 document, and this document specifically relates to  
23 Pegfilgrastim which is another compound. You may  
24 answer that question if you can. Other than that,  
25 we're into a question about Pegfilgrastim and we're

1 not going there.

2 THE WITNESS: This paper represents my

3 views at that time, yes.

4 Q. BY MR. JAGOE: And on the first page in the

5 second column, there is a heading Pegylation

6 Technology. What did you mean to discuss under that

7 heading?

8 A. I intended to discuss the different ways in

9 which PEG can be attached to protein molecules.

10 Q. What are the different ways PEG can be

11 attached to protein molecules?

12 MR. GAEDE: Again, I understand this line

13 of questioning to be in the context of your staying

14 within the Court's order with respect to PEG

15 Epoetin. If that understanding is incorrect and you

16 intend this question to be with respect to other

17 compounds, you are outside the Court's order. Could

18 you please clarify.

19 MR. JAGOE: I think it relates to PEG

20 Epoetin as well.

21 MR. GAEDE: Then that's fine.

22 THE WITNESS: In this part of the paper, I

23 made no reference to PEG Epoetin. I'm not clear

24 what it is you want me to say.

25 Q. BY MR. JAGOE: I want to know if the PEG

1 technology that you're talking about -- I want to  
2 know what are the specific PEG technologies you're  
3 referring to in this section of your paper?

4 A. I see. So the technologies I was referring  
5 to are different types of PEG, different sizes,  
6 complexities, different sites of attachment and  
7 different chemistries used for attachment.

8 Q. Depending on which of those variables one  
9 chooses, you would affect whether or not you're  
10 going to get a safe and efficacious drug at the end,  
11 right?

12 MR. GAEDE: Objection. Instruct the  
13 witness not to answer. That's clearly outside of  
14 the scope of the Court's order. It's also vague and  
15 ambiguous, improper expert witness testimony.  
16 Incomplete hypothetical. Instruct not to answer.

17 Q. BY MR. JAGOE: In the next section, it says  
18 "molecular properties of pegylated proteins." Are  
19 you with me?

20 A. Yeah.

21 Q. It says "The physiochemical properties of  
22 pegylated proteins generally differ from those of  
23 the parent molecule. Pegylation may induce changes  
24 in conformation, electrostatic binding properties  
25 and hydrophobicity resulting in steric interference